Cardiometabolic multimorbidity is common among patients with psoriasis and is associated with poorer outcomes compared to those without comorbidity

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INTRODUCTION

Chronic inflammatory disease is often accompanied by concurrent comorbid conditions. When two or more comorbid conditions coexist with an index disease, it is referred to as multimorbidity (1). The concept of multimorbidity has become an important topic of research as it is associated with poorer health outcomes, reduced quality of life, and increased risk of mortality (2–6). A recent meta-analysis that assessed community-based studies from high- and low-income countries provided global pooled prevalence estimates of multimorbidity at 33% (7). There is a positive correlation between aging and the prevalence of multimorbidity could rise due to the increasing life expectancy of the population. It is therefore critical that health outcomes, reduced quality of life, and increased risk of mortality (2–6). A recent meta-analysis that assessed community-based studies from high- and low-income countries provided global pooled prevalence estimates of multimorbidity at 33% (7). There is a positive correlation between aging and the prevalence of multimorbidity. While this study provides insight into the general concept that increased comorbid disease burden associates with poorer therapeutic response, the study did not stratify by therapeutic class. Understanding how multimorbidity may impact specific therapies in achieving treatment outcomes among patients with inflammatory disease could be useful in personalizing care.

Psoriasis, a chronic immune-mediated inflammatory disease, is associated with multiple comorbid conditions and has many approved targeted treatments (12,13). Until recently, outcomes research in psoriasis has primarily focused on the presence of a single comorbidity, specifically obesity, and reduced rates of achieving treatment goals (14–18). We have recently shown that both obesity and diabetes (DM) were associated with reduced odds of achieving PASI75 among real-world psoriasis patients initiating a biologic. Interestingly, while obesity and DM appeared to have an impact across all patients initiating biologic therapy, results stratified by biologic class suggested that these comorbidities may be more impactful for patients initiating tumor necrosis factor inhibitors (TNFi) or interleukin-17 inhibitors (IL-17i) rather than those using interleukin-12/23 inhibitors or interleukin-23 inhibitors (IL-23i or IL-12/23i) (19). Of note, nearly 25% of patients in this study had 2+ metabolic...
comorbidities (obesity, DM, HTN, hyperlipidemia [HLD]). Whether metabolic multimorbidity impacts treatment response in patients with psoriasis is unknown. Psoriasis may be a prototypical disease to explore the impact of multimorbidity among patients treated with targeted biologic therapy.

This study aimed to investigate the association of metabolic multimorbidity status with biologic response among patients with psoriasis. Using a North American-based psoriasis registry, we described metabolic comorbid disease (DM, HTN, HLD) burden among patients initiating a biologic and determined the odds of achieving treatment outcomes at six months following drug initiation in the presence of 0, 1, or 2+ metabolic comorbidities. Given the suggested differences among biologic classes observed in our prior study in this cohort, we stratified patients by drug class (TNFi, IL-17i, IL-23i and IL-12/23i) to determine if this was further impacted by multimorbidity. We hypothesized that patients with metabolic multimorbidity (2+ metabolic comorbidities) would have worse response to biologic therapy at six months compared to patients with one or no comorbidities in the overall population, and that the association between multimorbidity and response may differ for patients initiating different biologic classes.

### Methods

#### Data source and study cohort

The CorEvitas Psoriasis Registry is a prospective, observational, disease-based registry of patients with PsO under the care of a dermatologist in the US and Canada, the design of which was previously described (20). Briefly, since the Registry launch in April 2015, patients initiating a systemic therapy for the treatment of psoriasis have been enrolled and data are collected from both patients and their treating dermatologists during routine clinical encounters at approximately 6-month intervals. Data from the registry as of June 10, 2020, was used for this study.

### Table 1. Baseline patient characteristics by number of comorbidities (diabetes, hypertension, hyperlipidemia): overall.

| Demographics | 0 | 1 | 2+ | p |
|--------------|---|---|----|---|
| **Demographics** | | | | |
| Age (years), mean(sd) | 43.9 (13.8) | 54.6 (12.1) | 58.9 (11.4) | <.001 |
| Female, n(%) | 708 (48.9) | 312 (43.2) | 358 (47.5) | .042 |
| Race, n(%) | | | | .028 |
| White | 1,100 (76.0) | 569 (78.8) | 556 (73.7) | | |
| African-American | 33 (2.3) | 21 (2.9) | 28 (3.7) | | |
| Asian | 137 (9.5) | 51 (7.1) | 88 (11.7) | | |
| Other | 177 (12.2) | 81 (11.2) | 82 (10.9) | | |
| Hispanic ethnicity, n(%) | 131 (9.1) | 60 (8.5) | 51 (6.8) | .181 |
| Insurance, n(%) | | | | |
| None | 60 (4.3) | 18 (2.6) | 18 (2.5) | .032 |
| Private | 1,137 (81.4) | 530 (75.8) | 487 (66.4) | <.001 |
| Medicare | 110 (7.9) | 133 (19.0) | 228 (31.1) | <.001 |
| Medicaid | 131 (9.4) | 76 (10.9) | 107 (14.6) | .001 |
| **Education level, n(%)** | | | | <.001 |
| High school graduate or less | 402 (27.8) | 237 (32.8) | 304 (40.4) | | |
| Some college | 403 (27.9) | 205 (28.4) | 226 (30.1) | | |
| College graduate or higher | 640 (44.3) | 280 (38.8) | 222 (29.5) | | |
| **Work status, n(%)** | | | | <.001 |
| Full time | 985 (68.2) | 426 (59.1) | 326 (43.4) | | |
| Part time | 128 (8.9) | 44 (6.1) | 39 (5.2) | | |
| Not working for pay | 87 (6.0) | 44 (6.1) | 49 (6.5) | | |
| Student | 61 (4.2) | 6 (0.8) | 6 (0.8) | | |
| Disabled | 67 (4.6) | 57 (7.9) | 101 (13.4) | | |
| Retired | 117 (8.1) | 144 (20.0) | 233 (31.0) | | |
| **Lifestyle** | | | | <.001 |
| Smoking status, n(%) | | | | <.001 |
| Never | 759 (52.9) | 317 (44.4) | 313 (42.1) | | |
| Former smoker | 386 (26.9) | 280 (39.2) | 315 (42.3) | | |
| Current smoker | 291 (20.3) | 117 (16.4) | 116 (15.6) | | |
| Alcohol status, n(%) | | | | <.001 |
| No alcohol use | 430 (31.3) | 245 (37.0) | 338 (48.6) | | |
| Casual | 715 (52.1) | 307 (46.4) | 275 (39.6) | | |
| Daily | 227 (16.5) | 110 (16.6) | 82 (11.8) | | |
| BMI, mean (sd) | 30.1 (6.8) | 33.0 (7.8) | 33.7 (7.1) | <.001 |
| BMI, n(%) | | | | <.001 |
| Normal (18.5–24.9) | 358 (25.0) | 94 (13.1) | 63 (8.5) | | |
| Overweight (25.0–29.9) | 441 (30.8) | 194 (27.0) | 194 (26.1) | | |
| Obese (≥30.0) | 633 (44.2) | 430 (59.9) | 487 (65.5) | | |
| **History of comorbidities, n (%)** | | | | <.001 |
| Cancer | 103 (7.1) | 72 (10.0) | 93 (12.3) | | |
| Infection | 499 (34.5) | 287 (39.8) | 353 (46.8) | | |
| CVD | 53 (3.7) | 86 (11.9) | 184 (24.4) | | |
| Hypertension | 0 (0.0) | 436 (60.4) | 696 (92.3) | | |
| Hyperlipidemia | 0 (0.0) | 191 (26.5) | 641 (85.0) | | |
| Diabetes | 0 (0.0) | 95 (13.2) | 412 (54.6) | | |
| Depression | 225 (15.5) | 155 (21.5) | 215 (28.5) | | |
| Anxiety | 277 (19.1) | 186 (25.8) | 188 (24.9) | |
which included 11,332 enrolled patients with visits occurring from April 15, 2015, to June 6, 2020.

This study included the 2,952 patients with a history of plaque psoriasis who initiated a biologic therapy for the treatment of psoriasis at or after their enrollment visit (baseline) and had a subsequent 6-month (defined as 5–9-month window) follow-up visit available. Patients who were underweight (BMI < 18.5) at baseline were excluded (n = 28) and patients without metabolic comorbidity information at baseline were excluded (n = 1), resulting in a total of 2,923 patients available for analysis.

**Metabolic comorbidities**

Metabolic comorbidities included physician-reported history of HTN, HLD, and DM at baseline. A single multimorbidity variable was created to define a patient as having a history of 0 (no history of physician-reported HTN, HLD, or DM), 1 (history of only 1 of HTN, HLD, or DM), or 2+ (history of 2 or more of HTN, HLD, or DM) comorbidities at baseline. Obesity was defined at baseline as BMI ≥ 30 kg/m².

**Treatment response outcomes**

Disease severity measures are collected at all CorEvitas visits and include physician-assessed Psoriasis Area and Severity Index (PASI), percentage of affected body surface area (BSA), and Investigator’s Global Assessment (IGA). The following outcomes were calculated based on measures collected at baseline and the 6-month follow-up visit: achievement of 75% (PASI75), 90% (PASI90) improvement in PASI, BSA of 1% or lower (BSA ≤ 1), and clear-to-minimal status for IGA (score of 0 or 1, IGA 0/1).

**Other variables**

Information on patient demographics (patient-reported: age, sex, race [White, Black, Asian, Other/unknown], ethnicity [Hispanic or not], insurance coverage [none, private, Medicare, Medicaid], highest education level [high school graduate or less, some college, college graduate or higher], employment status, lifestyle [patient-reported smoking status [never smoked, former smoker, current smoker], alcohol use [no alcohol use, casual use: 1–6 drinks per week, daily use: 1+ drinks per day]), history of other comorbidities [cancer, infections, cardiovascular disease, depression, anxiety, dermatologist-identified psoriatic arthritis], psoriasis duration, and psoriasis treatment characteristics (number of prior biologics and number of prior nonbiologic systemic therapies; class of initiated biologic therapy [TNFi, IL-17i, IL-12/23i or IL-23i]) were ascertained at baseline.

**Statistical analysis**

Summary statistics for patient characteristics at baseline (mean and standard deviation (SD) for continuous variables, and frequency counts and percentage for categorical variables) were reported stratified by number of comorbidities (0, 1, or 2+). Differences in characteristics among the comorbidity groups were tested using analysis of variance for continuous variables, and chi-squared independence tests for categorical/dichotomous variables; Fisher’s exact tests were used for categorical/dichotomous variables with category size smaller than 5.

The associations between number of metabolic comorbidities and achievement of each treatment response outcome at 6-months post-biologic initiation were evaluated by using logistic regression models calculating the odds ratios and 95% CIs for achieving the outcome for patients in the 1 and 2+ comorbidity groups relative to those in the 0 comorbidity group (reference group). Three models utilizing a priori selected covariates were performed (1) unadjusted (no covariates), (2) adjusted for

| Disease characteristics | 0 (N = 1447) | 1 (N = 722) | 2+ (N = 754) | p |
|-------------------------|-------------|-------------|-------------|---|
| Psoriasis duration (years); mean (sd) | 13.7 (11.9) | 16.4 (14.3) | 17.6 (14.7) | <.001 |
| Comorbid psoriatic arthritis (PsA), n (%) | 526 (36.9) | 311 (43.9) | 366 (49.0) | <.001 |
| Psoriatic arthritis duration (years), mean (sd) | 6.3 (7.6) | 7.9 (8.4) | 9.4 (11.1) | <.001 |
| IGA | Clear | 36 (2.5) | 27 (3.7) | 18 (2.4) | .087 |
| | Almost clear | 75 (5.2) | 31 (4.3) | 25 (3.3) | |
| | Mild | 238 (16.5) | 123 (17.0) | 109 (14.5) | |
| | Moderate | 834 (57.7) | 406 (56.2) | 434 (57.8) | |
| | Severe | 262 (18.1) | 135 (18.7) | 168 (22.3) | |
| | BSA, mean (sd) | 14.2 (15.5) | 13.4 (14.9) | 14.6 (14.9) | .284 |
| | PASI, mean (sd) | 8.5 (7.8) | 8.1 (7.4) | 8.8 (7.0) | .241 |
| | Current phototherapy use | 43 (3.0) | 25 (3.5) | 28 (3.7) | .618 |
| | Current topical use | 695 (48.0) | 324 (44.9) | 365 (48.4) | .304 |
| | Biologic class | TNFi | 283 (19.6) | 121 (16.8) | 147 (19.5) | .505 |
| | | IL-17i | 573 (39.6) | 321 (44.5) | 336 (44.6) | |
| | | IL-23i or IL-12/23i | 591 (40.8) | 280 (38.8) | 271 (35.9) | |
| | Number of prior non-biologics, categorical | 0 | 660 (45.6) | 279 (38.6) | 297 (39.4) | <.001 |
| | | 1 | 581 (40.2) | 283 (39.2) | 298 (39.5) | |
| | | 2+ | 206 (14.2) | 160 (22.2) | 159 (21.1) | |
| | Number of prior biologics, categorical | 0 | 597 (41.3) | 215 (29.8) | 237 (31.4) | <.001 |
| | | 1 | 374 (25.8) | 182 (25.2) | 183 (24.3) | |
| | | 2 | 212 (14.7) | 134 (18.6) | 133 (17.6) | |
| | | 3+ | 264 (18.2) | 191 (26.5) | 201 (26.7) | |
Table 3. Association of metabolic comorbidity with PASI75 response at 6-months among patients in CorEvitas Psoriasis Registry who initiated biologic therapy.

| Metabolic comorbidity | N total patients | N respond at 6-mos (%) | Model 1 | Model 2 | Model 3 |
|-----------------------|------------------|------------------------|--------|--------|--------|
| Overall               |                  |                        |        |        |        |
| 0                     | 1447             | 897 (62)               | REF    | REF    | REF    |
| 1                     | 722              | 394 (55)               | 0.74   | 0.61   | 0.82   |
| 2+                    | 754              | 402 (53)               | 0.70   | 0.59   | 0.77   |
| Obesity               |                  |                        |        |        |        |
| No                    | 1345             | 842 (63)               | –      | REF    | REF    |
| Yes                   | 1550             | 839 (54)               | 0.74   | 0.64   | 0.78   |
| TNF                   |                  |                        |        |        |        |
| 0                     | 283              | 162 (57)               | REF    | REF    | REF    |
| 1                     | 121              | 46 (38)                | 0.46   | 0.30   | 0.50   |
| 2+                    | 147              | 75 (51)                | 0.78   | 0.52   | 0.90   |
| Obesity               |                  |                        |        |        |        |
| No                    | 268              | 156 (58)               | –      | REF    | REF    |
| Yes                   | 281              | 127 (45)               | 0.61   | 0.43   | 0.68   |
| IL-17                 |                  |                        |        |        |        |
| 0                     | 573              | 359 (63)               | REF    | REF    | REF    |
| 1                     | 321              | 183 (57)               | 0.79   | 0.60   | 0.79   |
| 2+                    | 336              | 175 (52)               | 0.65   | 0.49   | 0.66   |
| Obesity               |                  |                        |        |        |        |
| No                    | 546              | 351 (64)               | –      | REF    | REF    |
| Yes                   | 673              | 362 (54)               | 0.68   | 0.53   | 0.70   |
| IL-23 + IL-12/23      |                  |                        |        |        |        |
| 0                     | 591              | 376 (64)               | REF    | REF    | REF    |
| 1                     | 280              | 165 (59)               | 0.82   | 0.61   | 1.06   |
| 2+                    | 271              | 152 (56)               | 0.73   | 0.55   | 0.95   |
| Obesity               |                  |                        |        |        |        |
| No                    | 531              | 335 (63)               | –      | REF    | REF    |
| Yes                   | 596              | 330 (59)               | 0.87   | 0.68   | 0.93   |

Model 1: number of metabolic comorbidities; Model 2: model 1 plus obesity; Model 3: model 2 plus age, sex, race, smoking, education, duration of psoriasis, dermatologist-identified psoriatic arthritis, and number of prior biologics.

Results

There were 2923 patients available for the study (Table 1). The proportions of women in the 0, 1 and 2+ metabolic comorbidity groups were 49%, 43% and 48%, respectively. Those who had 1 or 2+ comorbidities were older (mean (SD) age 55 (12) years; overall p < .001).

The proportions of patients in the 0, 1 and 2+ comorbidity groups utilizing Medicaid (9%, 11%, 15%, respectively, p = .001) and Medicare (8%, 19%, 31%, respectively, p < .001) differed with the highest frequencies in the 2+ group. The distribution of educational attainment differed among the 0, 1 and 2+ groups (p < .001) with the proportions reporting ‘college graduate or higher’ of 44%, 39% and 30%, respectively. Work status also differed among the 0, 1 and 2+ groups (p < .001) with 5%, 8% and 13%, respectively, reporting ‘disabled’, and 8%, 20% and 31%, respectively, reporting ‘retired’ (Table 1).

The proportions of patients reporting obesity differed among the 0, 1, and 2+ comorbidity groups (p < .001): 44% in the 0 group compared to roughly 60% in the 1 comorbidity group and nearly 66% in the 2+ group. Likewise, proportions reporting history of other comorbidities, including cancer, infection, cardiovascular disease, depression, and anxiety, differed among the groups (all p < .001), with the 1 and 2+ groups generally having higher frequencies compared to the 0 group (Table 1).

Disease characteristics

At time of biologic initiation, duration of psoriatic disease was 13.7 years for those with 0 comorbidities, 16.4 years for patients reporting 1 comorbidity, and 17.6 years in the 2+ group (p < .001). The proportions of patients with dermatologist-identified psoriatic arthritis varied across groups (p < .001), with 44% and 49% in the 1 and 2+ comorbidity groups, respectively, compared to 37% in the 0 group. Means for cutaneous measures of disease severity (IGA, BSA, PASI) were similar at baseline among the groups (all p > .05) (Table 2).

Treatment history

The number of prior biologics used differed among the comorbidity groups (p < .001, Table 2). In the 0, 1 and 2+ groups, proportions who were biologic-naïve were 41%, 30% and 31% respectively, and proportions who used 3 or more biologics were 18%, 27% and 27%, respectively. Prior non-biologic use also differed (p < .001), with 14%, 22% and 21% reporting 2+ prior therapies in the 0, 1 and 2+ groups, respectively.

Association of response to biologic therapy with number of metabolic comorbidities

Among all patients, in unadjusted analyses the 1 and 2+ comorbidity groups had 26% lower (OR = 0.74, 95% CI: 0.61–0.8) and 30% lower (OR = 0.70, 95% CI: 0.59–0.84) odds of achieving PASI75 at six months, respectively, compared to patients in the 0 group (Table 3). Following adjustment for obesity and other covariates, the 1 comorbidity group had 18% lower (OR = 0.82, 95% CI: 0.67–1.00) and the 2+ group 23% lower (OR = 0.77, 95% CI: 0.63–0.96) odds of PASI75 achievement. In the same
regression model, obesity was associated with 22% decreased odds of achieving PASI75 (OR = 0.78, 95% CI: 0.67–0.92). Results for PASI90 were similar: in the fully adjusted model, both the 1 comorbidity group (OR = 0.82, 95% CI: 0.67–1.01) and the 2+ group (OR = 0.82, 95% CI: 0.66–1.02) had 18% lower odds of achieving PASI90 relative to the 0 group, though CIs included 1.0, while obesity was associated with 28% lower odds (OR = 0.72, 95% CI: 0.61–0.84) (Table 4).

Among patients who initiated an IL-17i, in the fully adjusted model those in the 2+ comorbidity group had 34% lower odds of achieving PASI75 at six months compared to the 0 group (OR 0.66, 95% CI: 0.48–0.91), while there was no association for the 1 comorbidity group (OR = 0.79, 95% CI: 0.58–1.08) (Table 3). Obesity was associated with 30% lower odds of achieving PASI75 in IL-17i initiators (OR = 0.70, 95% CI: 0.54–0.90). For the TNFi initiators, the 1 comorbidity group had 50% decreased odds of achieving PASI75 (OR = 0.50, 95% CI: 0.30–0.82), while there was no association in the 2+ group in the fully adjusted model (OR = 0.90, 95% CI: 0.54–1.48). For the TNFi initiators, obesity was associated with 45% lower odds of achieving PASI75 at 6-months (OR = 0.55, 95% CI: 0.37–0.82). There were no associations between number of comorbidities or obesity with PASI75 response among IL-23 or IL-12/23 initiators. Results were consistent for PASI90 response (Table 4).

For the response outcome of BSA ≤ 1 at six months, the number of comorbidities was not associated with response in the full cohort (Supplemental Table 1). Further, there were no associations for number of comorbidities within each biologic class, with the exception of the 2+ group having 29% lower odds compared to the 0 group among IL-17i initiators (OR = 0.71, 95% CI: 0.52–0.98). Obesity was associated with lower odds of BSA ≤ 1 response in the overall cohort, and for IL-17i and TNFi initiators. Patterns of association for the IGA 0/1 outcome across drug classes were similar to those observed for the BSA ≤ 1 outcome, though in TNFi initiators the 1 comorbidity group had 47% reduced odds of achievement of IGA 0/1 (OR = 0.53, 95% CI: 0.32–0.87) and number of comorbidities was not associated with IGA 0/1 response among IL-17i initiators (Supplemental Table 2).

Table 4. Association of metabolic comorbidity with PASI90 response at 6-months among patients in CorEvitas Psoriasis Registry who initiated biologic therapy.

| Metabolic comorbidity | N total patients | N respond at 6-mos (%) | Model 1 | Model 2 | Model 3 |
|-----------------------|------------------|------------------------|---------|---------|---------|
| **Overall**            |                  |                        |         |         |         |
| No                    | 1447             | 666 (46)               | REF     | REF     | REF     |
| 1                     | 722              | 274 (38)               | 0.72 (0.60, 0.86) | 0.75 (0.63, 0.91) | 0.82 (0.67, 1.01) |
| 2+                    | 754              | 285 (38)               | 0.71 (0.60, 0.85) | 0.77 (0.64, 0.92) | 0.82 (0.66, 1.02) |
| **Obesity**            |                  |                        |         |         |         |
| No                    | 1345             | 631 (47)               | –       | REF     | REF     |
| Yes                   | 1559             | 586 (38)               | –       | 0.72 (0.62, 0.84) | 0.72 (0.61, 0.84) |
| **TNF**                |                  |                        |         |         |         |
| No                    | 283              | 112 (40)               | REF     | REF     | REF     |
| 1                     | 121              | 28 (23)                | 0.46 (0.28, 0.75) | 0.48 (0.29, 0.78) | 0.56 (0.33, 0.97) |
| 2+                    | 147              | 54 (37)                | 0.89 (0.59, 1.34) | 1.01 (0.66, 1.55) | 1.25 (0.74, 2.10) |
| **IL-17**              |                  |                        |         |         |         |
| No                    | 268              | 112 (42)               | –       | REF     | REF     |
| Yes                   | 281              | 82 (29)                | –       | 0.57 (0.40, 0.83) | 0.55 (0.37, 0.82) |
| **IL-23 + IL-12/23**   |                  |                        |         |         |         |
| No                    | 546              | 263 (48)               | –       | REF     | REF     |
| Yes                   | 673              | 258 (38)               | –       | 0.70 (0.55, 0.88) | 0.67 (0.52, 0.86) |

Model 1: number of metabolic comorbidities; Model 2: model 1 plus obesity; Model 3: model 2 plus age, sex, race, smoking, education, duration of psoriasis, dermatologist-identified psoriatic arthritis, and number of prior biologics.

Discussion

In our real-world cohort of psoriasis patients initiating biologic therapy, comorbid metabolic diseases were associated with decreased likelihoods of achieving treatment response at six months. Among all patients, the presence of one or more metabolic comorbidity was associated with lower odds of PASI75 response, even after accounting for concomitant obesity. Results suggested that among IL-17i initiators, patients with 2+ comorbidities (multimorbidity), had the lowest odds of response, independent of obesity. Furthermore, obesity was independently associated with lower odds of response consistently, with the exception of patients who initiated IL-23—IL-12/23.

In the study cohort, 25% reported history of either HTN, HLD, or DM, and 26% reported at least 2 of these conditions. Prior research has suggested a linear relationship between severity of psoriasis and risk of comorbidities, such as obesity, HTN, HLD, or DM (21–26); yet in the present cohort, there were not significant differences in measures of disease severity at baseline between the 0, 1, and 2+ comorbidity groups. Those with multiple metabolic comorbidities were older, and more often reported characteristics of socioeconomic disadvantage, such as lower levels of education attainment, non-active work status, and use of state and federal medical insurance programs.
While some of these characteristics may be associated with age, socioeconomic disadvantage and metabolic multimorbidity have been shown to be correlated (2,3). Interestingly, lower socioeconomic status has also been associated with decreased odds of biologic response in psoriasis patients (27). Patients with multimorbidity in our study also reported increased frequencies of other comorbidities such as history or cancer, infection, cardiovascular disease, depression, and anxiety. The medical complexity of these patients was further highlighted by their reported higher prior use of 2+ nonbiologic and/or 3+ biologic therapies at time of therapy initiation. Despite these patterns of patient demographics, disease characteristics, and prior treatments, we found that multimorbidity was independently associated with poorer treatment outcomes.

Previous studies have established a link between obesity and decreased frequencies of biologic efficacy (14–19). Our study supports the current literature and provides further, clinically useful data indicating that obesity decreases likelihoods of PASI75 and PASI90 at six months by 22% and 28%, respectively, independent of concomitant metabolic comorbid disease. For those on TNFi or IL-17i, likelihoods of achieving PASI75 and PASI90 by six months were decreased by roughly a third in the presence of obesity, whereas in patients who initiated IL-12/23i or IL-23i, obesity was not associated with achieving PASI75 or PASI90.

In the fully adjusted model, history of 1 or 2+ metabolic comorbid conditions resulted in decreased likelihoods of PASI75. Overall, treatment responses were similar in the 1 and 2+ comorbidity groups. This suggests that the presence of even one metabolic comorbidity is a significant factor to consider when initiating a biologic for the treatment of psoriasis. However, it is important to note that this association was only observed for the PASI75 outcome. While the presence of 1 or 2+ metabolic comorbid conditions decreased likelihoods of all outcomes (PASI75, PASI90, BSA ≤ 1, IGA 0/1) when controlling for obesity alone (model 2), the attenuation of the relationship between metabolic comorbidity and treatment outcomes from model 2 to model 3 suggests that other covariates are possibly at play, for example the presence of psoriatic arthritis or the number of prior biologic exposures.

When stratifying the biologics by class, the adjusted results here suggest that those initiating IL-17i with history of metabolic multimorbidity are less likely to respond by 6-months compared to those without comorbidity. Why the IL-17i class may be less effective in the presence versus absence of multiple comorbidities is not fully understood. However, we have recently shown that psoriasis patients with DM treated with IL-17i are less likely to achieve treatment targets at six months (19). Considering this, we found that more than half of patients in our study with 2+ metabolic comorbidities had a history of DM. It is possible that the effect we observed in the multimorbidity group, then, was due to the presence of DM. Of note, the T-helper 17 (Th17) cell pathway that drives psoriasis has also been found to be elevated in patients with diabetes (28).

Associations between comorbidity burden and outcomes for TNFi initiators varied. Having 1 comorbidity was associated with poorer response, while there was no association for the 2+ group, which was inconsistent with our hypothesis. Further assessment of the TNFi initiators in our study found that those with 1 comorbidity were more frequently biologic-experienced (data not shown) compared to those in the 2+ group. While we did adjust for number of prior biologics in our multivariable analyses, previous biologic therapy use is a major negative predictor of treatment response (29), which may have contributed to the unexpected observation among the TNFi group. Metabolic multimorbidity was not associated with treatment response for the IL-23i or 12/23i class. It is possible this may be due to their mechanism of action targeting a cytokine upstream of IL-17 signaling and Th17 cell maintenance. The heterogeneity of results among the biologic classes may suggest that the presence of comorbid disease impacts the effectiveness of each biologic class differently (19).

A major strength of this study was the use of real-world data from the CorEvitas Psoriasis Registry. This allowed us to report on the prevalence of multimorbidity and prospectively assess treatment outcomes for multiple biologic classes among psoriasis patients seen in clinical practices. However, there were limitations. The CorEvitas Psoriasis Registry is based in the United States and Canada, thus findings may not be generalizable to other settings. Further, recruitment of both dermatologists and their participating patients is voluntary, therefore the CorEvitas Registry may not be representative of all psoriasis patients initiating biologic therapy. Additionally, obesity and histories of DM, HTN, and HLD were obtained at baseline at the time of biologic initiation. While unlikely over a 6-month follow-up period, changes in these comorbidities throughout treatment were not evaluated. It should also be noted that due to potential channeling bias, patients who initiated different biologic classes may differ on key characteristics that could influence response to therapy (e.g. prior biologic-experience), thus based on the findings of this analysis we cannot conclude that variations in the association between metabolic comorbidities and response among drug classes are due solely to the different mechanisms of action.

**Conclusion**

In this real-world study using a North American-based registry of individuals with psoriasis initiating biologic therapy, we provide odds ratios for achieving specific treatment outcomes among psoriasis patients with metabolic comorbidity, multimorbidity, and obesity. The presence of one or multiple metabolic comorbidities was associated with a reduced likelihood of achieving PASI75, independent of obesity and other covariates such as psoriatic arthritis. Further, multimorbidity may be particularly impactful for those treated with IL-17i. Our findings highlight the importance of assessing for comorbid disease burden as this may impact response. Psoriasis patients with comorbid conditions may need to be monitored more closely to ensure adequate response to therapy.

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**IRB approval status**

Exempt.
Disclosure statement

Dr. Enos has served as a consultant on an advisory board for UCB and Amgen. Dr. Van Voorhees has received grants and research support from Lilly and AbbVie. She has also served as a consultant for Amgen, Boehringer Ingelheim, BMS, UCB, and Novartis. Vanessa Ramos has no conflicts of interest. Blessing Dube, Robert McClean, and Nicole Foster are employees of CorEvitas, LLC. Tin-Chi Lin was an employee of CorEvitas, LLC, at the time of this analysis.

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Data availability statement

Data are available from CorEvitas, LLC through a commercial subscription agreement and are not publicly available. No additional data are available from the authors.

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