

Inflammatory comorbidity and quality-of-life burden in psoriasis with multiple biologic failure: a retrospective cohort study

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Abstract

Background

Multiple biologic failure (MBF) was defined by a standardised institutional rule: receipt of ≥ 3 biologics from ≥ 2 mechanistic classes, each administered for ≥ 3 months. We assessed factors associated with this treatment-pathway phenotype and compared early skin and quality-of-life outcomes.

Methods

This retrospective single-centre cohort included 545 adults with psoriasis, of whom 50 (9.2%) had clinician-recorded MBF. Multivariable logistic regression assessed associations with inflammatory comorbidities, cardiometabolic factors and overall comorbidity burden. Outcomes at weeks 12–16 included 90% improvement in Psoriasis Area and Severity Index (PASI90) and Dermatology Life Quality Index (DLQI) 0/1.

Results

MBF was independently associated with psoriatic arthritis (adjusted odds ratio [aOR] 4.25, 95% confidence interval [CI] 2.24–8.05), inflammatory bowel disease (aOR 6.94, 95% CI 1.85–26.02) and each additional comorbidity (aOR 1.34, 95% CI 1.12–1.61). The IBD estimate was based on 12 patients and was considered hypothesis-generating. PASI90 achievement was similar between groups (75.0% vs. 74.8%; aOR 0.85, 95% CI 0.37–1.94), whereas DLQI 0/1 was less frequent with MBF (64.4% vs. 80.9%; aOR 0.29, 95% CI 0.13–0.62).

Conclusion

Clinician-recorded MBF was associated with inflammatory comorbidity, multimorbidity and persistent quality-of-life burden despite comparable early skin responses. These findings may reflect biological refractoriness, treatment-pathway complexity, or a combination of both, which cannot be fully disentangled within the present study design.

1 Introduction

Psoriasis is a chronic immune-mediated inflammatory disease whose burden extends well beyond the skin. In addition to cutaneous manifestations, patients frequently develop psoriatic arthritis (PsA), inflammatory bowel disease (IBD), cardiometabolic disorders and substantial impairment in health-related quality of life, all of which contribute to increased disease complexity and healthcare utilisation [1–4]. The advent of biologic therapies has transformed the management of moderate-to-severe

psoriasis, making sustained skin clearance and minimal residual disease achievable treatment goals for many patients [2–4].

Despite these therapeutic advances, a small but clinically challenging subgroup repeatedly switches between biologic therapies because of inadequate efficacy, secondary loss of response, intolerance or other treatment-limiting factors. This phenotype has been described using heterogeneous terms, including *multi-biologic use*, *multi-failure* and multiple biologic failure (MBF), with no universally accepted operational definition [5–9]. Consequently, reported prevalence and associated clinical characteristics vary considerably across studies.

The clinical significance of MBF extends beyond repeated therapeutic changes. Patients requiring multiple biologic switches consume disproportionate healthcare resources, have fewer remaining therapeutic options and frequently require individualised treatment strategies. However, it remains uncertain whether MBF simply reflects cumulative therapeutic exposure or identifies a distinct subgroup of patients with a broader inflammatory disease burden [5–10].

Emerging evidence suggests that systemic inflammatory comorbidities may play an important role in this phenotype. PsA increases treatment complexity, is associated with more frequent biologic switching and often requires multidomain therapeutic decision-making [10, 11]. Likewise, coexisting IBD shares pathogenic inflammatory pathways with psoriasis while simultaneously restricting therapeutic choices because some biologic mechanisms may improve, worsen or be contraindicated in intestinal disease [12]. Beyond inflammatory comorbidities, accumulated multimorbidity may further complicate long-term disease control. Nevertheless, conventional treatment outcomes, particularly skin clearance alone, may underestimate the persistent burden experienced by these patients.

We hypothesised that clinician-recorded multiple biologic failure is associated with multidomain inflammatory burden. Therefore, we aimed to identify the clinical factors independently associated with clinician-recorded MBF in a hospital-based psoriasis cohort and to determine whether patients with MBF differ from other biologic-treated patients in both early skin response and patient-reported quality-of-life outcomes. Because line-level treatment chronology and adjudicated reasons for discontinuation were unavailable, the study addresses correlates of a clinician-recorded treatment-pathway phenotype rather than confirmed pharmacological refractoriness.

2 Materials and methods

2.1 Study design and participants

We conducted a retrospective observational study using a structured hospital psoriasis database. The dates from 31 January 2024 to 1 April 2026 denote the period of retrospective record review and data extraction, not patient inclusion. The study included 545 unique patients. Reporting follows the STROBE statement [13].

2.2 Outcome definition

The primary outcome was clinician-recorded multiple biologic failure (MBF), identified in the institutional psoriasis database as the binary variable *superfailure*. The standardised institutional operational definition required receipt of ≥ 3 biologics from ≥ 2 mechanistic classes, each administered for ≥ 3 months. This objective rule was applied uniformly from the clinical treatment history and did not depend on physician-specific judgement; therefore, no interobserver adjudication was required. Throughout the manuscript, this variable is referred to as clinician-recorded MBF because the available data did not permit differentiation of primary non-response, secondary loss of efficacy, intolerance, adverse events or non-medical switching.

2.3 Clinical variables

Demographic variables included age, sex and approximate psoriasis duration. The year of psoriasis onset was obtained during clinical history taking from the patient-reported first manifestation of the disease; approximate duration was calculated as the database cut-off year (2026) minus that onset year. Clinical characteristics comprised body mass index (BMI), baseline Psoriasis Area and Severity Index (PASI), baseline Dermatology Life Quality Index (DLQI), nail involvement, special-site psoriasis and previous exposure to ciclosporin or phototherapy. Treatment-pathway variables included the number of documented distinct biologics, previous exposure to tumour necrosis factor (TNF), interleukin (IL)-12/23, IL-17 and IL-23 inhibitor classes, individual biologic-agent exposure, the current or last recorded agent and mechanism, and duration of the current treatment.

Based on biological plausibility and previous evidence linking systemic inflammation with therapeutic complexity, the prespecified primary explanatory variables were psoriatic arthritis (PsA) and inflammatory bowel disease (IBD) [10–12]. Dyslipidaemia and metabolic syndrome were additionally evaluated as markers of cardiometabolic burden because these conditions have previously been associated with poorer psoriasis outcomes and biologic treatment patterns [5].

Overall multimorbidity was assessed using a simple comorbidity count, obtained by summing the presence of 12 predefined conditions: obesity, diabetes mellitus, hypertension, dyslipidaemia, metabolic-associated fatty liver disease, PsA, IBD, cardiovascular disease, malignancy, psychiatric disorders, hypothyroidism and other relevant comorbidities. The latter category comprised additional diagnoses recorded in free text, most commonly hyperuricaemia, asthma, chronic obstructive pulmonary disease, fibromyalgia, chronic kidney disease or renal insufficiency, endometriosis and coeliac disease; individually rarer autoimmune, neurological, musculoskeletal, respiratory and transplant-related disorders were also included. This category contributed a maximum of one point per patient. Because PsA and IBD were included within the composite variable, analyses evaluating the individual inflammatory comorbidities and the overall comorbidity burden were performed using separate multivariable models to avoid collinearity.

An exploratory inflammatory burden score ranging from 0 to 3 was also constructed by assigning one point each for PsA, IBD and baseline PASI ≥ 10 . PASI ≥ 10 was used as a pragmatic threshold for substantial baseline cutaneous disease severity. Because PASI is a skin-severity measure rather than a systemic comorbidity, this investigator-developed score combines heterogeneous domains. As baseline PASI may also have been influenced by previous treatments, the score was considered descriptive and hypothesis-generating rather than a validated prognostic instrument and was not intended for clinical decision-making.

2.4 Treatment-pathway variables and early response

Previous ciclosporin and phototherapy and nail involvement were evaluated as exploratory care-pathway or phenotype signals. These variables can be influenced by disease severity, contraindications, calendar era and access and were not interpreted causally. Early response was assessed at weeks 12–16 using absolute PASI, 90% improvement in PASI (PASI90), DLQI and DLQI 0/1. Change was follow-up minus baseline; therefore, a more negative value indicates greater improvement. DLQI is a validated 10-item dermatology-specific quality-of-life instrument [3].

2.5 Statistical analysis

Continuous variables were summarised using mean (standard deviation) or median (interquartile range) and compared with Welch's t test or the Mann–Whitney test, as appropriate. Categorical variables were summarised as n/N (%) and compared using χ^2 or Fisher's exact tests. The prespecified primary comparison for metabolic syndrome used Pearson's χ^2 test. Table 1 P values were unadjusted descriptive comparisons. The Benjamini–Hochberg false-discovery-rate family comprised the three exploratory adjusted treatment-pathway associations: nail involvement, previous ciclosporin and previous phototherapy. Prespecified component-model variables, early response outcomes and the single exploratory inflammatory score were not included in this family. Given the small number of IBD observations, an additional univariable Firth penalised logistic sensitivity analysis was performed using Jeffreys' correction, with a profile penalised-likelihood confidence interval and penalised-likelihood-ratio P value. The expanded logistic model included age per 10 years, sex, psoriasis duration per 10 years, PsA, IBD, dyslipidaemia and metabolic syndrome. A separate burden model included age, sex, duration and the simple comorbidity count. Variance inflation factors assessed collinearity. Model discrimination and Brier score were internally assessed using 500 bootstrap samples with optimism correction.

2.6 Adjusted response analyses and missing data

Binary response models adjusted for baseline outcome value, psoriasis duration, PsA, comorbidity count excluding PsA and IBD, any special-site involvement and current treatment mechanism. Linear DLQI-change models used heteroscedasticity-consistent (HC3) standard errors and the same adjustment set; a further model added PASI change. Analyses used complete cases for the variables in each model; no outcome or covariate values were imputed. Tests were two-sided and 95% confidence intervals (CIs) are reported. Statistical analyses were performed using IBM SPSS Statistics for Windows, version 29.0 (IBM Corp., Armonk, NY, USA).

3 Results

3.1 Patient characteristics

The study included 545 adults with psoriasis, of whom 50 (9.2%) fulfilled the clinician-recorded definition of multiple biologic failure (MBF) and 495 (90.8%) did not. Patients with MBF had a longer disease duration than those without MBF (27.6 vs. 22.5 years; mean difference 5.10 years, 95% CI 1.40–8.81; $P = 0.008$), whereas age, sex distribution, body mass index and baseline PASI were comparable between groups (Table 1). Baseline DLQI was numerically lower in the MBF group but did not differ significantly (12.0 vs. 13.6; $P = 0.076$).

At weeks 12–16, PASI was available for 475/495 patients without MBF (96.0%) and 45/50 with MBF (90.0%); PASI90 was derivable for 473/495 (95.6%) and 44/50 (88.0%), respectively. DLQI was available for 476/495 patients without MBF (96.2%) and 45/50 with MBF (90.0%).

Table 1
Selected cohort characteristics by clinician-recorded multiple biologic failure phenotype

Characteristic	No MBF (n = 495)	MBF (n = 50)	P value
Age, years	52.31 ± 15.40	55.16 ± 13.25	0.158
Male sex	294/495 (59.4%)	28/50 (56.0%)	0.642
Psoriasis duration, years	22.54 ± 13.34	27.64 ± 12.39	0.008
BMI, kg/m ²	27.57 [24.22–31.95]	28.56 [25.25–33.12]	0.249
Baseline PASI	12.14 ± 5.94	11.32 ± 6.83	0.418
Baseline DLQI	13.60 ± 5.55	12.02 ± 5.92	0.076
Psoriatic arthritis	91/495 (18.4%)	25/50 (50.0%)	< 0.001
Inflammatory bowel disease	7/495 (1.4%)	5/50 (10.0%)	0.003
Dyslipidaemia	177/495 (35.8%)	26/50 (52.0%)	0.031
Metabolic syndrome	125/495 (25.3%)	19/50 (38.0%)	0.05
Simple comorbidity count	1.90 ± 1.75	2.78 ± 1.76	0.001
Nail involvement	250/495 (50.5%)	34/50 (68.0%)	0.025
Previous ciclosporin	170/495 (34.3%)	10/50 (20.0%)	0.041
Previous phototherapy	82/495 (16.6%)	15/50 (30.0%)	0.031

Values are mean ± standard deviation, median [interquartile range], or n/N (%). Welch's t test was used for age, psoriasis duration, baseline PASI, baseline DLQI and simple comorbidity count; the Mann–

Whitney test was used for BMI. P values are unadjusted and descriptive. BMI, body mass index; DLQI, Dermatology Life Quality Index; MBF, multiple biologic failure; PASI, Psoriasis Area and Severity Index.

3.2 Systemic inflammatory comorbidity was more frequent in clinician-recorded MBF

Patients with MBF exhibited a markedly greater burden of inflammatory comorbidity than those without MBF. Psoriatic arthritis (PsA) was present in half of patients with MBF compared with fewer than one in five patients without MBF (50.0% vs. 18.4%; unadjusted OR 4.44, 95% CI 2.44–8.08; $P < 0.001$). Although inflammatory bowel disease (IBD) was present in only 12 patients overall, it was more frequent among patients with MBF (10.0% vs. 1.4%; unadjusted OR 7.75, 95% CI 2.36–25.40; Fisher's $P = 0.003$). In the additional univariable Firth penalised sensitivity analysis, the association was similar in direction and magnitude (OR 7.87, 95% profile penalised-likelihood CI 2.38–24.57; $P = 0.001$). Because this sensitivity analysis was univariable and based on only 12 IBD observations, it does not remove the imprecision of the multivariable estimate.

Patients with MBF also had a higher overall comorbidity burden (mean count 2.78 vs. 1.90; $P = 0.001$). Dyslipidaemia (52.0% vs. 35.8%; $P = 0.031$) and metabolic syndrome (38.0% vs. 25.3%; $P = 0.05$) were more frequent in MBF, although these associations appeared weaker than those observed for inflammatory comorbidities (Table 1).

3.3 Multivariable associations with clinician-recorded MBF

After adjustment for age, sex, disease duration, dyslipidaemia and metabolic syndrome, PsA remained the strongest independent correlate of MBF (adjusted OR [aOR] 4.25, 95% CI 2.24–8.05; $P < 0.001$). IBD also showed an association after adjustment, although the estimate was imprecise and was interpreted as hypothesis-generating (aOR 6.94, 95% CI 1.85–26.02; $P = 0.004$) (Table 2, Fig. 1).

Disease duration showed a weaker association with MBF (aOR per 10 years 1.25, 95% CI 0.97–1.59; $P = 0.079$), whereas neither dyslipidaemia nor metabolic syndrome remained independently associated after adjustment.

The model demonstrated acceptable discrimination (optimism-corrected area under the receiver operating characteristic curve (AUROC) 0.725) and good calibration (optimism-corrected Brier score 0.081), with no evidence of problematic collinearity (variance inflation factors 1.01–1.91).

Table 2
Multivariable associations with clinician-recorded multiple biologic failure

Model	Variable	Adjusted OR (95% CI)	P value
Expanded component model	Age, per 10 years	0.86 (0.65–1.14)	0.307
	Male sex	0.99 (0.53–1.85)	0.974
	Duration, per 10 years	1.25 (0.97–1.59)	0.079
	Psoriatic arthritis	4.25 (2.24–8.05)	< 0.001
	Inflammatory bowel disease	6.94 (1.85–26.02)	0.004
	Dyslipidaemia	1.64 (0.72–3.74)	0.238
	Metabolic syndrome	1.19 (0.49–2.85)	0.703
Comorbidity-burden model	Duration, per 10 years	1.29 (1.03–1.62)	0.027
	Per additional comorbidity	1.34 (1.12–1.61)	0.002
Exploratory inflammatory score	Per 1-point increase	2.40 (1.50–3.83)	< 0.001

The component and comorbidity-count models were estimated separately because the count contains psoriatic arthritis and inflammatory bowel disease. The inflammatory score was adjusted for age, sex and duration. CI, confidence interval; OR, odds ratio.

3.4 Multimorbidity burden was associated with clinician-recorded MBF

To avoid collinearity between inflammatory comorbidities and overall disease burden, a separate multivariable model evaluated the effect of cumulative comorbidity. Each additional comorbidity increased the odds of MBF by 34% (aOR 1.34, 95% CI 1.12–1.61; $P = 0.002$), while disease duration remained independently associated (aOR per 10 years 1.29, 95% CI 1.03–1.62; $P = 0.027$).

Similarly, the exploratory inflammatory burden score showed a progressive shift toward higher values in patients with MBF and remained associated with the phenotype after adjustment for age, sex and disease duration (aOR per point 2.40, 95% CI 1.50–3.83; $P < 0.001$). Because the score is investigator-developed, combines a cutaneous severity measure with comorbidities and may be influenced by previous treatment, it should be interpreted only as descriptive and hypothesis-generating, not as a validated predictive or clinical decision tool (Online Resource 1).

3.5 Early skin and quality-of-life outcomes

Despite their greater systemic inflammatory burden, patients with MBF achieved skin responses comparable to those without MBF. Mean PASI improvement from baseline to weeks 12–16 was almost identical between groups (-10.93 vs. -11.25 ; mean difference 0.32 , 95% CI -1.75 to 2.38 ; $P = 0.760$),

and PASI90 responses were similarly frequent (75.0% vs. 74.8%; adjusted OR 0.85, 95% CI 0.37–1.94; P = 0.694) (Table 3, Fig. 2).

In contrast, patient-reported outcomes showed a different pattern. Although the unadjusted difference in DLQI improvement was attenuated after multivariable adjustment, patients with MBF remained significantly less likely to achieve complete or near-complete quality-of-life normalisation. DLQI 0/1 was achieved by 64.4% of patients with MBF compared with 80.9% of those without MBF (adjusted OR 0.29, 95% CI 0.13–0.62; P = 0.001).

Table 3
Early Psoriasis Area and Severity Index and Dermatology Life Quality Index outcomes

Outcome	No MBF	MBF	Effect estimate (95% CI)	P value
PASI change	−11.25 ± 6.08 (n = 475)	−10.93 ± 6.65 (n = 45)	Difference 0.32 (− 1.75 to 2.38)	0.760
PASI90	354/473 (74.8%)	33/44 (75.0%)	Adjusted OR 0.85 (0.37–1.94)	0.694
DLQI change	−12.37 ± 5.62 (n = 476)	−10.44 ± 5.16 (n = 45)	Difference 1.92 (0.30–3.55)	0.021
Adjusted DLQI change	—	—	Adjusted difference 0.47 (− 0.12 to 1.05)	0.116
DLQI 0/1	385/476 (80.9%)	29/45 (64.4%)	Adjusted OR 0.29 (0.13–0.62)	0.001

Change is follow-up minus baseline; positive group differences indicate less improvement with MBF. Adjusted models included baseline value, duration, psoriatic arthritis, other comorbidity burden, special-site involvement and current mechanism. CI, confidence interval; DLQI, Dermatology Life Quality Index; MBF, multiple biologic failure; OR, odds ratio; PASI, Psoriasis Area and Severity Index.

3.6 Treatment-pathway characteristics and exploratory associations

The MBF group had more documented distinct biologic exposures than the non-MBF group (median 3 [IQR 3–4] vs. 1 [IQR 1–2]) and had received agents from more mechanistic classes (mean 2.76 ± 0.59 vs. 1.27 ± 0.52). Among patients with MBF, documented previous or current exposure comprised adalimumab (70%), etanercept (40%), infliximab (20%) and certolizumab (8%); ustekinumab (54%); secukinumab (32%), ixekizumab (24%), brodalumab (16%) and bimekizumab (4%); and guselkumab (28%), risankizumab (34%) and tildrakizumab (14%). Their current or last recorded mechanisms were IL-23 inhibitors in 29/50 (58%), IL-17 inhibitors in 18/50 (36%), TNF inhibitors in 2/50 (4%) and a non-biologic agent in 1/50 (2%). Median duration of the current treatment was 4.19 years [IQR 2.33–5.09] in

the MBF group and 4.28 years [IQR 2.08–6.99] in the non-MBF group. The extract did not contain the ordered sequence and duration of every historical line or line-specific reasons for discontinuation.

Exploratory analyses identified nail involvement (aOR 2.11, 95% CI 1.11–4.03; $P = 0.024$; $q = 0.031$) and previous phototherapy (aOR 2.10, 95% CI 1.07–4.13; $P = 0.031$; $q = 0.031$) as being associated with MBF, whereas previous ciclosporin exposure showed an inverse association (aOR 0.45, 95% CI 0.21–0.93; $P = 0.031$; $q = 0.031$). These q values were calculated across the prespecified three-variable exploratory treatment-pathway family. Given the retrospective design, the findings should be interpreted as markers of treatment pathway rather than evidence of causal treatment effects. Full estimates are presented in Online Resource 1.

4 Discussion

This study identified psoriatic arthritis (PsA), inflammatory bowel disease (IBD) and overall multimorbidity as correlates of clinician-recorded multiple biologic failure (MBF) in psoriasis. Patients with MBF achieved early skin responses similar to those without MBF but were less likely to reach complete or near-complete quality-of-life normalisation. The classification reflects a treatment-pathway phenotype and cannot be assumed to represent confirmed pharmacological refractoriness.

The most consistent finding was the strong association between MBF and PsA. This association persisted after multivariable adjustment and across alternative sensitivity analyses, although residual confounding and outcome misclassification remain possible. The finding is biologically plausible. Psoriasis and PsA represent different manifestations of the same immune-mediated disease spectrum, and patients with musculoskeletal involvement frequently require more complex therapeutic decision-making, multidomain disease control and repeated treatment adaptations [10, 11]. Consequently, repeated biologic switching in these patients may reflect the challenge of simultaneously controlling skin, joint and patient-reported outcomes rather than resistance of cutaneous disease alone.

IBD also showed an adjusted association with MBF. However, only 12 patients had IBD, and the wide confidence interval makes the magnitude uncertain and the finding hypothesis-generating rather than evidence of a robust independent predictor. The univariable Firth sensitivity analysis supported the direction of the association but could not overcome the sparse data or address multivariable small-sample bias. Psoriasis and IBD share overlapping inflammatory pathways involving the IL-23/Th17 axis, while coexistence of both diseases narrows therapeutic options because biologic mechanisms differ in their efficacy across skin and intestinal disease [12]. In routine practice, treatment decisions may therefore reflect the complexity of multisystem inflammatory disease rather than greater skin severity alone.

Beyond individual inflammatory comorbidities, patients with MBF also exhibited a greater cumulative comorbidity burden. This observation reinforces the concept that MBF develops within a broader context of systemic disease rather than representing an isolated dermatological problem. Chronic inflammation, metabolic dysfunction and long-standing disease may interact to increase therapeutic complexity over

time, although the present study cannot establish causal relationships. The independent association between overall multimorbidity and MBF supports a more comprehensive assessment of these patients beyond conventional measures of skin severity.

Our findings both agree with and extend previous studies. Jin et al. identified hyperlipidaemia, previous systemic treatment and several sociodemographic characteristics as predictors of multiple biologic failure in the CorEvitas registry [5], whereas PsA was not the dominant determinant. Likewise, multicentre European cohorts have consistently shown that repeated biologic switching is uncommon but clinically heterogeneous [6–9]. Differences in healthcare systems, treatment availability, referral patterns, outcome definitions and calendar periods probably account for much of this variability. Rather than contradicting previous reports, our study complements them by suggesting that inflammatory comorbidities may be the prominent correlates of MBF in tertiary-care practice.

Perhaps the most clinically relevant observation was the discordance between physician-assessed and patient-reported outcomes. Patients with MBF achieved early skin clearance comparable to that of the remainder of the cohort, yet were significantly less likely to reach complete or near-complete quality-of-life normalisation. This finding is consistent with residual disease burden despite control of cutaneous inflammation, but it does not establish its cause. Persistent musculoskeletal symptoms, cumulative treatment burden, difficult-to-treat anatomical sites, psychological distress or other unmeasured dimensions of disease may all contribute to this discrepancy. These results reinforce the growing recognition that psoriasis should be managed as a multidomain disease in which patient-reported outcomes complement traditional physician-assessed measures of disease activity [3, 4].

The exploratory associations observed for previous phototherapy, nail involvement and previous ciclosporin should be interpreted cautiously. These variables are likely to reflect historical treatment pathways, disease phenotype and prescribing practices rather than direct causal determinants of MBF. Likewise, the exploratory inflammatory burden score was intended only to describe the observed phenotype and should not be considered a validated prognostic instrument or used for clinical decision-making. Future studies should determine whether composite multidomain scores better identify patients at risk of repeated biologic failure.

The present study has several limitations. First, although MBF was defined by a standardised institutional rule, the analysis used the clinician-recorded binary outcome. Second, the database contained cumulative agent and mechanism exposure, the current or last treatment and current-treatment duration, but not the complete ordered chronology or duration of every historical line, reasons for discontinuation, adherence or drug survival. Primary failure, secondary loss of response, adverse-event discontinuation and non-medical switching could not therefore be distinguished. Third, the 12–16-week endpoints characterise early response only; drug survival, time to subsequent switching, secondary loss of response and long-term PASI and DLQI outcomes were unavailable. Fourth, the retrospective single-centre tertiary-referral design introduces referral, information and residual confounding biases. Patients with complex psoriasis, PsA or multimorbidity may be over-represented, potentially inflating

observed associations and limiting generalisability to broader outpatient populations. Fifth, the 50 MBF events yielded approximately seven events per predictor in the seven-variable expanded model; despite prespecification and bootstrap assessment, multivariable estimates require cautious interpretation. Sixth, the small number of patients with IBD resulted in wide confidence intervals; the univariable Firth analysis supports the direction of association but does not eliminate sparse-data uncertainty in the adjusted model. Seventh, PASI and DLQI follow-up completeness was modestly lower in the MBF group, so complete-case response analyses remain vulnerable to differential missingness. Finally, multiple exploratory analyses increase the possibility of chance findings despite false-discovery-rate adjustment.

These limitations also identify priorities for future research. Prospective multicentre studies should adopt a standardised definition of MBF based on documented therapeutic failure rather than treatment exposure alone, incorporating line-level treatment chronology, reasons for discontinuation, adherence, drug persistence and multidomain disease activity [14]. Such datasets would allow distinction between true biological refractoriness and treatment pathway complexity while facilitating development of clinically applicable prediction models.

5 Conclusion

In this single-centre tertiary-care cohort, clinician-recorded MBF was associated with PsA, IBD, multimorbidity and a lower likelihood of DLQI 0/1 despite similar early PASI responses; the sparse IBD finding remains hypothesis-generating. These results support multidimensional assessment but do not distinguish biological refractoriness from treatment-pathway complexity, may not generalise to broader outpatient populations and require multicentre prospective validation.

Declarations

Article type

Original Research Article

Supplementary information

Online Resource 1 contains Supplementary Tables S1–S4 and Supplementary Figs. S1–S2: exposure-based sensitivity analyses (Table S1), exploratory adjusted treatment-pathway associations with Benjamini–Hochberg q values (Table S2 and Fig. S2), early-outcome completeness by group (Table S3), documented treatment-pathway characteristics (Table S4), and the distribution of the exploratory inflammatory burden score (Fig. S1).

Competing interests:

The authors have no relevant financial or non-financial interests to disclose.

Ethics approval:

This study was performed in line with the principles of the Declaration of Helsinki. The study protocol was approved by the Provincial Research Ethics Committee of Granada, Spain (approval no. DERM_HUSC_2025_010).

Consent to participate:

The requirement for individual informed consent was waived because of the retrospective design and the use of pseudonymised registry data, in accordance with national regulations.

Consent for publication:

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Author Contribution

José Molina-Espinosa: Conceptualization, Methodology, Investigation, Data curation, Formal analysis, Validation, Visualization, Project administration, and Writing – original draft. Pedro José Ezomo-Gervilla: Data curation, Methodology, Validation, and Writing – review & editing. Diego Gallego-García: Data curation, Validation, and Writing – review & editing. Daniel Robles-Murcia: Writing – review & editing. José Carlos Ruiz-Carrascosa: Supervision, Interpretation of the results. Ricardo Ruiz-Villaverde: Project administration, Interpretation of the results. All authors reviewed and approved the final version of the manuscript and agree to be accountable for all aspects of the work.

Data Availability

The data that support the findings of this study are available from the corresponding author upon reasonable request, subject to institutional and ethics restrictions.

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Figures

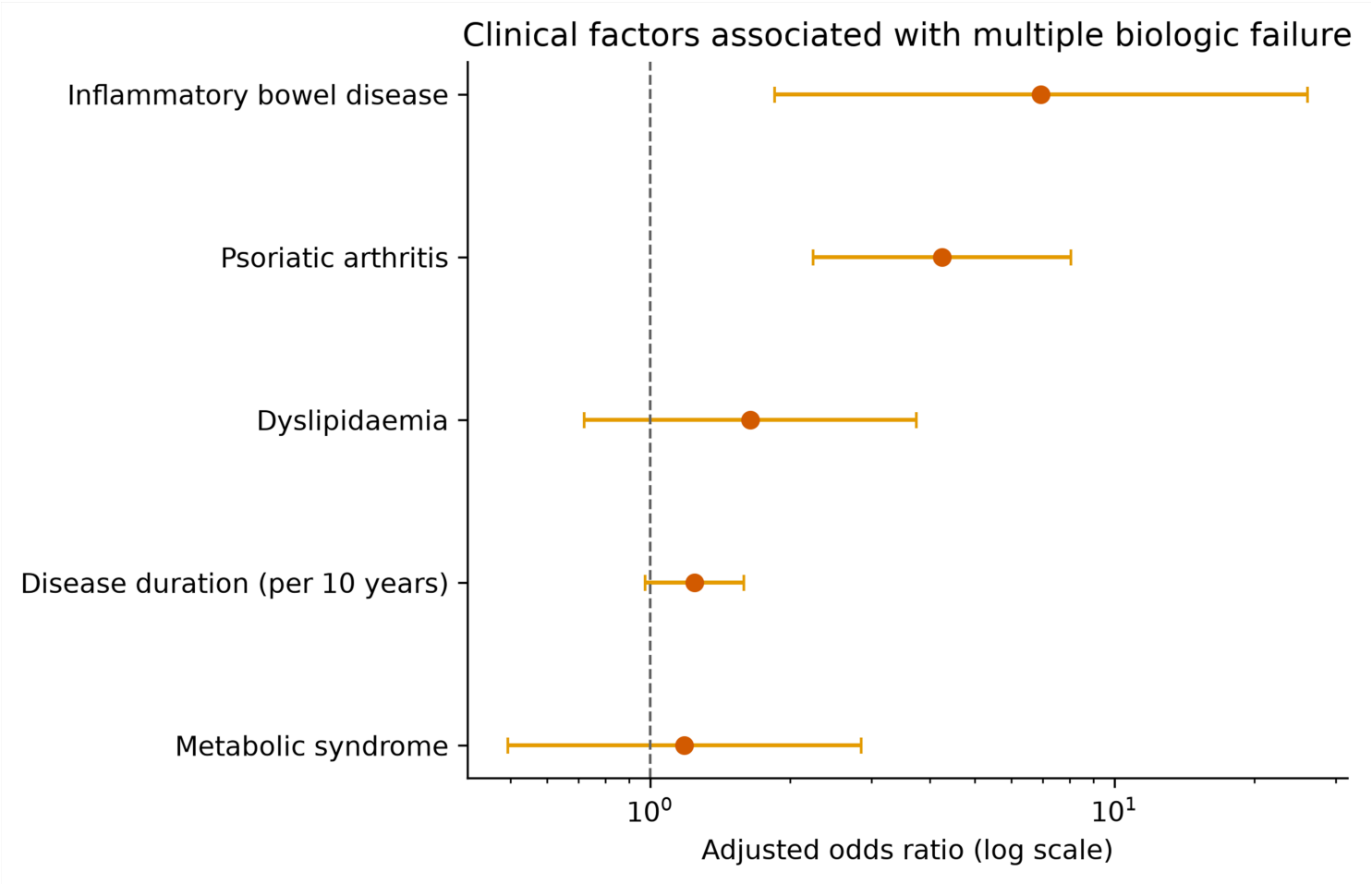


Figure 1

Adjusted associations in the expanded component model. Points are adjusted odds ratios and bars are 95% confidence intervals on a logarithmic scale. The full model additionally included age and sex

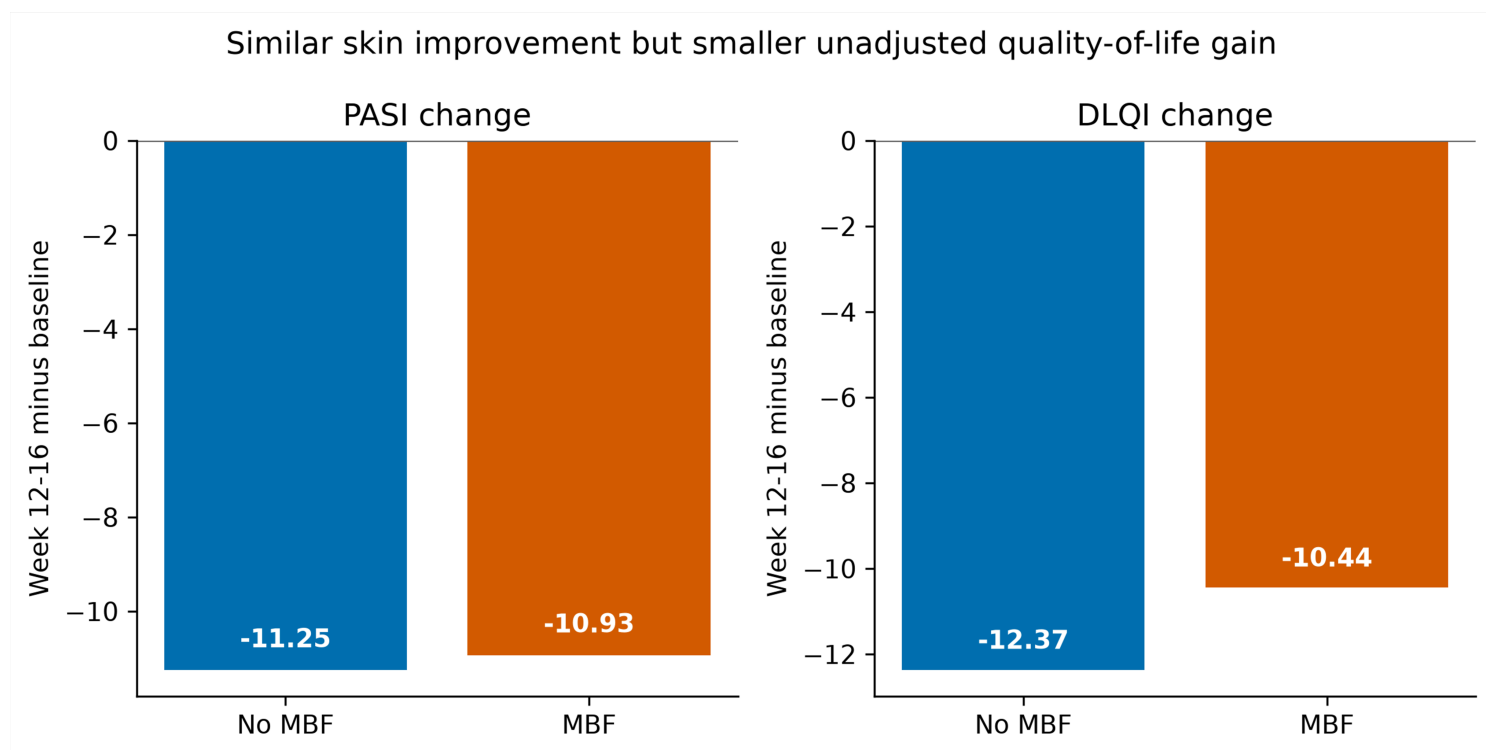


Figure 2

Mean change in Psoriasis Area and Severity Index and Dermatology Life Quality Index from baseline to weeks 12-16. More negative values indicate greater improvement. Comparisons shown are unadjusted; adjusted estimates are reported in Table 3

Supplementary Files

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