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ORIGINAL ARTICLE

Low utilization of statins in patients with dermatomyositis/polymyositis and hyperlipidemia: a multicenter USA-based study (2013–2023)

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Abstract

Objective While the cardioprotective benefits of statins for rheumatoid arthritis (RA) patients are well-established, there might be a hesitation in recommending them for dermatomyositis/polymyositis (DM/PM) patients with hyperlipidemia (HLD), particularly with myopathy. We sought to contrast statin prescription patterns between DM/PM-HLD and RA-HLD patients and delve into the mortality variations among DM/PM-HLD statin users and non-users.

Methods We examined a decade's worth of anonymized US health data from the TriNetX database. Inclusion criteria were a subsequent HLD diagnosis after an initial DM/PM or RA diagnosis. We compared statin initiation rates and mortality outcomes, adjusting for demographics and cardiovascular risks through propensity score matching.

Results The analysis comprised 33,000 RA-HLD and 1079 DM/PM-HLD patients. RA-HLD patients exhibited higher statin initiation (27.4%) than DM/PM-HLD patients (17.91%, $p < 0.0001$). Notably, DM/PM-HLD statin users ($n = 311$) presented a reduced mortality rate (75 deaths/1000/year) compared to non-users ($n = 661$) with 147 deaths/1000/year ($p = 0.0273$, HR = 0.515, CI 0.28–0.93).

Conclusion There is a marked disparity in statin initiation between DM/PM-HLD and RA-HLD patients, accompanied by elevated mortality in DM/PM-HLD non-users. It is imperative for further research to elucidate this discrepancy and formulate patient-centric cardiovascular guidelines for DM/PM-HLD patients.

Key Points
- *Statin initiation among patients with DM/PM-HLD is significantly lower than that with RA-HLD.*
- *Mortality rates within the statin initiator DM/PM-HLD were significantly lower compared to non-statin DM/PM-HLD initiators, spanning multiple time intervals.*

Keywords Dermatomyositis · HMG Co-A reductase · Hyperlipidemia · Mortality · Rheumatoid arthritis · Statin

Introduction

Despite the availability of multiple medications for the treatment of hyperlipidemia, HMG-CoA reductase inhibitors, more informally known as statins, remain a first-line therapy [1]. Statins are highly effective agents that have demonstrated remarkable efficacy in reducing cardiovascular complications, including coronary and cerebrovascular events. Their effectiveness is demonstrated by data from large, randomized, placebo-controlled trials containing diverse patient populations and retrospective investigations focusing on subgroups, such as patients with rheumatoid arthritis (RA).

Statin use has been associated with markedly reduced all-cause mortality in patients with Systemic Autoimmune Rheumatic Diseases (SARD) [2] with studies assessing its effectiveness in reducing mortality in RA [3, 4]. Moreover, the benefits of statins extend beyond just lowering lipids, as their pleiotropic anti-inflammatory properties modify local and

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systemic immune responses. However, despite their benefits, a recent international audit of 14,503 RA patients uncovered a striking gap in treating hyperlipidemia. For instance, less than half of the patients in this study received any form of lipid-lowering therapy (LLT), and a paltry 24% was treated with statin monotherapy [5]. These findings suggest a significant lack of recognition of cardiovascular risk in patients with RA [5]

Dermatomyositis (DM) and polymyositis (PM) are autoimmune conditions that cause inflammation of muscles. Although research on these conditions is limited compared to RA, recent data suggest that DM/PM patients are at increased risk of developing atherosclerotic cardiovascular diseases (ASCVD) [6–10] and that ASCVD are the leading cause of death in patients with DM/PM [11]. However, no large-scale studies have examined if statins are routinely prescribed and how they affect the mortality rate in this population.

In addition to under-recognition, one possible reason for hesitancy in prescribing statins to DM/PM patients may relate to concern for statin-associated muscle complications, such as pain, weakness, and cramps, which affect nearly 5% to 20% of patients [12]. Moreover, statins are also associated with other, albeit rare, severe complications like rhabdomyolysis, occurring in approximately 0.4 per 10,000 patient-years. Further, the risk of severe complications may be higher in patients with pre-existing comorbidities or polypharmacy [12, 13]. Another serious concern is the development of statin-induced immune-mediated necrotizing myopathy (IMNM), a rare condition characterized by autoantibodies targeting the HMG-CoA reductase protein [14].

Given these concerns, clinicians managing patients with underlying inflammatory myopathies may hesitate to initiate statin therapy, even though reports suggest statins are well-tolerated in PM/DM patients [15]. However, there is a conspicuous absence of large-scale studies evaluating statin use in DM or PM patients. To address this knowledge gap, we compared the statin initiation rate among patients with DM/PM and HLD to those with RA and HLD. Our decision to incorporate a comparative RA-HLD cohort is grounded in studies demonstrating that RA patients are also at an elevated risk for ASCVD [16]. Our objective was two-fold: first, to assess whether a diagnosis of DM/PM leads to underutilization of statins in the management of HLD and, second, to explore the impact of statin usage on mortality in individuals with DM/PM-HLD.

Methods

Data collection methodology

We leveraged the expansive TriNetX Research Network, a repository of de-identified electronic health records from over 120 global healthcare organizations. This dataset, largely composed of US data, also includes EHRs from patients in Canada and South America, Europe, and Asia. The refresh rate for health records varies between daily and bi-monthly updates depending on the institution. The network complies with ISO 27001:2013 and HIPAA Security Rule, ensuring data security. Our analysis specifically engaged U.S. data from 2013 to 2023, collected as of 25th of August 2023. Since this study used only de-identified patient records as determined by TriNetX experts, it was exempt from Institutional Review Board approval.

Analyses and cohort formation

We created the cohorts through ICD-10, RxNorm, TNX-curated, and LOINC codes on TriNetX to identify diagnoses, medications, comorbidities, and laboratory results with the list of codes in Supplemental Table 1.

Analysis A: statin initiation rates the general population with HLD and RA-HLD vs DM/PM-HLD without immunosuppression filtering

In the first segment of Analysis A (A1), we compared Cohort 1, representing the general population with an HLD diagnosis within the past one to ten years, with Cohort 2, which encompassed patients initially diagnosed with DM/PM followed by an HLD diagnosis within one day to ten years. In the second analysis (A2), we compared Cohort 2 and Cohort 3. Cohort 3 comprised patients initially diagnosed with RA followed by HLD within the same timeframe as Cohort 2 (Figure 1). We conducted both A1 and A2 without applying any immunosuppression filtering. This comprehensive assessment involved the comparison of demographic profiles, cardiovascular risk factors (Supplemental Tables 2 and 3), and the overall rate of statin initiation for both Analysis 1 and 2 (Table 1).

Analysis B: statin initiation rates RA-HLD vs DM/PM-HLD with immunosuppression filtering

Following the implementation of immunosuppressive filtration, we conducted a comparison of statin initiation rates review of RA-HLD (Cohort 2) and DM/PM-HLD (Cohort 3) requiring that patients were on immunosuppression at the study inclusion (Figure 1). Baseline characteristics including demographic information, cardiovascular comorbidities (Table 2), immunosuppression, labs (Table 3), and available antibodies profiles (Supplemental Table 4), the overall of statin initiation rates and the specific statin utilization were investigated (Table 4).

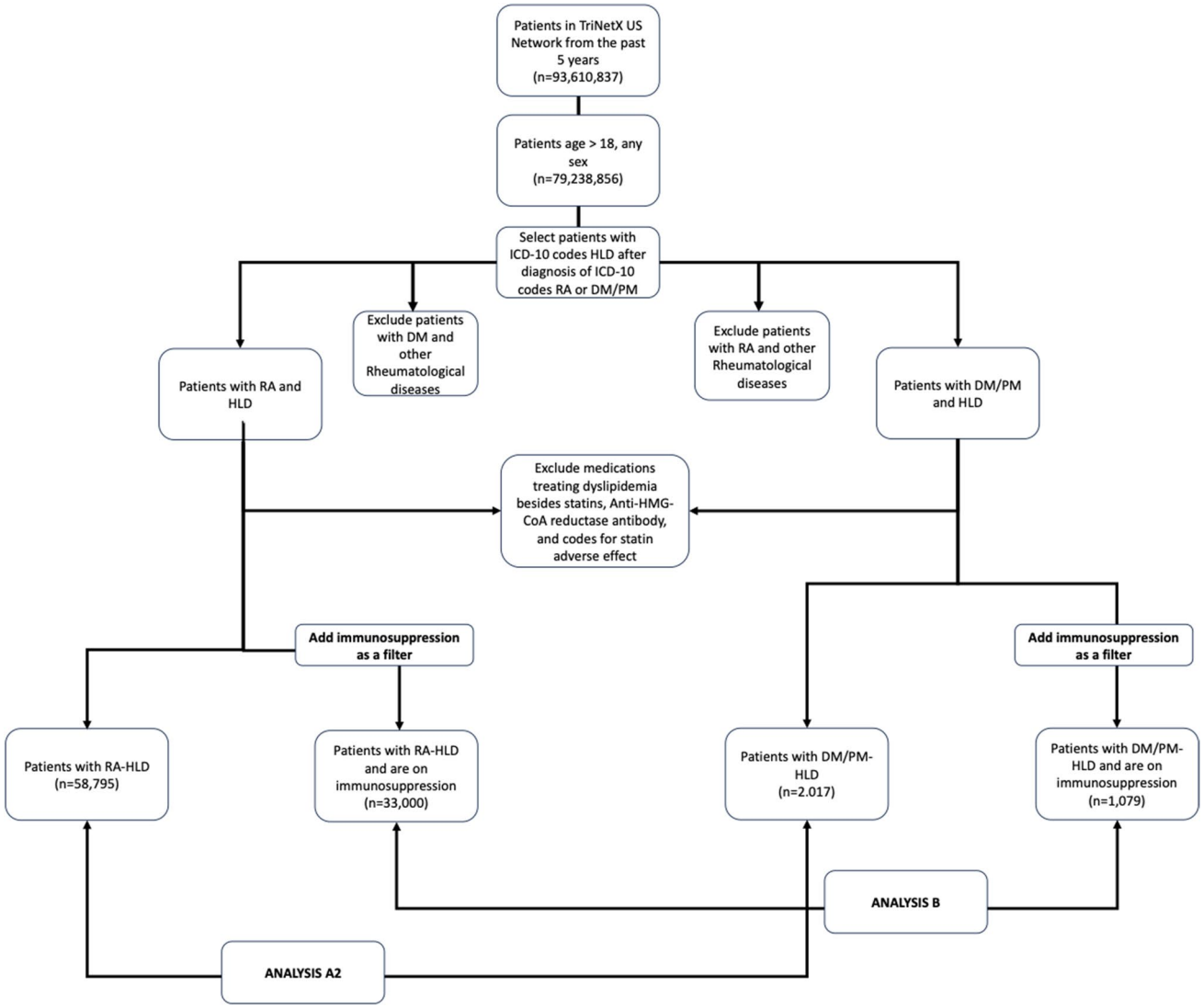

Fig. 1 Flowchart of cohort formation and analysis framework

Immunosuppressive filtering To improve the accuracy and reliability of our study's cohorts, we used immunosuppressive filtering, which included only patients taking immunosuppressive drugs at the time of study entry (index event) (Table 3). This stringent criterion increased the likelihood of these patients obtaining specialized rheumatological care [17]. Within our study, the RA and DM/PM cohorts were consistently managed with either conventional disease-modifying antirheumatic drugs (DMARDs) or biologic DMARDs (bDMARDs). We excluded patients from the RA cohort (Cohort 3) undergoing Intravenous Immunoglobulin (IVIG) therapy. In contrast, the DM/PM cohort (Cohort 2) excluded individuals treated with agents targeting anti-tumor necrosis factor (TNF), interleukin-6 (IL-6), or interleukin-1 (IL-1).

Analysis C: mortality rate comparison in statin initiators vs statin non-initiators DM/PM-HLD

Subsequently, we compared the mortality rates in Cohort 4, consisting of DM/PM-HLD patients on statins after their DM/PM diagnosis, with Cohort 5, comprising DM/PM-HLD patients without statins. This comparison included an examination of the demographics of these two cohorts and their prevalence of cardiovascular comorbidities. Analysis C included an evaluation for differences in mean CPK derived from aggregated data across three time points (3 months prior to statin initiation, 3 months after, and 6 months after statin initiation).

Table 1 Statin initiation following HLD diagnosis among General Population-HLD and DM/DM-HLD for Analysis A1 and between RA-HLD and DM/PM-HLD for Analysis A2

Analysis A1							
Unadjusted risk ratio *3,213,649 patients in General Population-HLD and 523 patients in DM/PM-HLD were excluded from results because they had the outcome prior to the time window*				**Adjusted risk ratio** *658 patients in General Population-HLD and 523 patients in DM/PM-HLD were excluded from results because they had the outcome prior to the time window*			
General Population-HLD ($n=7,995,967$)	DM/DM-HLD ($n=1,494$)	p value*	Confidence interval (CI)	General Population-HLD ($n=2107$)	DM/DM-HLD ($n=1494$)	p value*	CI
2,256,093 (28.21%)	302 (20.21%)	<0.0001	1.18, 1.42%	1359 (31.94%)	302 (20.21%)	<0.0001	1.29, 1.66%
Analysis A2							
Unadjusted risk ratio *17,827 patients in RA-HLD and 523 patients in DM/PM-HLD were excluded from results because they had the outcome prior to the time window*				**Adjusted risk ratio** *586 patients in RA-HLD and 523 patients in DM/PM-HLD were excluded from results because they had the outcome prior to the time window*			
RA-HLD ($n=40,968$)	DM/DM-HLD ($n=1494$)	p value*	Confidence interval (CI)	RA-HLD ($n=1431$)	DM/DM-HLD ($n=1494$)	p value*	CI
40,968 (25.01%)	302 (20.21%)	<0.0001	2.72%, 6.88%	354 (24.74%)	302 (20.21%)	0.0034	1.50, 7.55%

*p is significant if <0.05

Exclusion criteria

We aimed to achieve cohort purity by excluding, from all the cohorts, patients with autoimmune diseases presenting RA and DM/PM-like symptoms. These include psoriatic arthritis, systemic lupus erythematosus (SLE), scleroderma, Sjogren's syndrome, anti-neutrophil cytoplasmic antibody (ANCA) associated vasculitis, polyarteritis nodosa (PAN), inclusion body myositis, and Takayasu arteritis. As we sought to explore the potential for statin monotherapy in HLD patients, we excluded patients on non-statin lipid-lowering treatments such as fibrates, niacin, bile acids sequestrants, PCSK-9 inhibitors, and bempedoic acid. Lastly, to exclude patients with documented SAMS, those with statin-related muscle adverse effects, a history of rhabdomyolysis, and those with HMGCR autoantibody presence.

Ultimately, we excluded patients with RA from Cohorts 2, 4, and 5 (the cohorts with DM/PM diagnosis) and patients with DM/PM from Cohort 3, the cohort with the RA diagnosis.

Primary outcome

For Analysis A and B, statin initiation, determined by RxNorm codes for HMG CoA reductase inhibitors, served as our primary outcome. RxNorm codes for HMG CoA reductase inhibitors included atorvastatin, pitavastatin, rosuvastatin, pravastatin, fluvastatin, simvastatin, and lovastatin. As for Analysis C, the primary outcome was mortality determined by TriNetX software.

Analytical framework

Defining the index event and time window

Our analysis begins with defining an index event, which is the basis for outcome measurement, and a time window, which is the duration following the index event during which the outcome is evaluated.

In our study, the index event is the HLD diagnosis following either an RA or DM/PM diagnosis for Analyses A and B; for Analysis C, we added statin initiation after their HLD diagnosis in the DM/PM. The time window for statin initiation starts one month, and that of mortality starts one day after the index event, and both last up to ten years.

Covariate and propensity scoring

In Analyses A, B, and C, we applied PSM while accounting for several relevant covariates. These covariates included age, race, sex, ethnicity, and specific ASCVD risk factors, such as hypertension, diabetes mellitus, and nicotine dependence (smoking). Furthermore, PSM encompassed a range of cardiovascular diseases, including atherosclerotic heart disease, heart failure, acute myocardial infarction, peripheral vascular disease, and cerebral infarction. In addition to these, fatty liver disease, liver cirrhosis, and chronic kidney disease (CKD) were integrated into the PSM model due to their associations with heightened cardiovascular risk.

In Analysis C, we took a thorough approach by including a wider range of covariates to ensure balanced comparison of mortality rates. This comprehensive set encompassed HbA1C levels, total cholesterol, LDL, and HLD. We also

Table 2 Baseline characteristics of RA-HLD and DM/PM-HLD with immunosuppression before and propensity score matching (Analysis B)

	Unadjusted baseline characteristics				Adjusted baseline characteristics			
	RA-HLD ($n=33{,}000$)	DM/PM-HLD ($n=1079$)	p value*	Std diff.**	RA-HLD ($n=1081$)	DM/PM-HLD ($n=1079$)	p value*	Std diff.**
Age at index Mean ± SD	62.4 ± 12.8	58.6 ± 13.7	< 0.0001	0.2884	58.7 ± 14	58.6 ± 13.7	0.9024	0.0053
Sex								
Female	24,741 (74.97%)	750 (69.38%)	< 0.0001	0.1250	763 (70.71%)	750 (69.38%)	0.5410	0.0263
Male	8237 (24.96%)	331 (30.62%)	< 0.0001	0.1266	172 (15.94%)	329 (30.49%)	0.5410	0..0263
Race								
White	24,272 (73.55%)	732 (67.72%)	< 0.0001	0.1284	737 (68.30%)	732 (67.72%)	0.5410	0.0263
Black	4228 (12.81%)	177 (16.37%)	0.0006	0.1010	172	175 (16.22%)	0.8604	0.0076
Asian	796 (2.42%)	44 (4.07%)	0.0005	0.0937	41 (3.80%)	44 (4.07%)	0.7399	0.0143
American Indian	141 (0.43%)	10 (0.93%)	0.0153	0.0608	0 (0%)	10 (0.93%)	0.0015	0.1368
Native Hawaiian	68 (0.21%)	0 (0%)	0.1352	0.0643	10 (0.93%)	0 (0%)	0.0015	0.1368
Unknown	3495 (10.59%)	127 (11.75%)	0.2243	0.0368	128 (11.86%)	126 (11.75%)	0.9468	0.0029
Cardiovascular risk factors and cardiovascular disease								
	Unadjusted risk ratio				**Adjusted risk ratio**			
Hypertension	12,453 (37.74%)	353 (32.66%)	0.0007	0.1066	334 (30.96%)	353 (32.72%)	0.3799	0.0378
Diabetes mellitus	4868 (14.75%)	203 (18.78%)	0.0003	0.1080	198 (18.35%)	202 (18.72%)	0.8246	0.0095
Smoking	2478 (7.51%)	44 (4.07%)	< 0.0001	0.1476	33 (3.06%)	44 (4.07%)	0.2018	0.0550
CAD	2509 (7.60%)	78 (7.22%)	0.6360	0.0148	70 (6.49%)	78 (7.22%)	0.4956	0.0293
Heart failure	1840 (5.58%)	64 (5.92%)	0.6273	0.0148	52 (4.82%)	64 (5.92%)	0.2521	0.0493
Myocardial infarction	582 (1.76%)	23 (2.13%)	0.3725	0.0264	21 (1.95%)	23 (2.13%)	0.7606	0.0131
Stroke	671 (2.03%)	18 (1.67%)	0.3973	0.0273	23 (1.11%)	18 (1.67%)	0.2700	0.0575
PVD	768 (2.33%)	16 (1.48%)	0.0675	0.0062	11 (1.02%)	26 (1.48%)	0.3329	0.0417
CKD	2141 (4.49%)	67 (6.20%)	0.7032	0.0119	58 (5.38%)	67 (6.20%)	0.4069	0.0357
Fatty liver	673 (2.04%)	39 (3.52%)	0.0008	0.0899	31 (2.87%)	37 (3.43%)	0.4597	0.0318
Liver cirrhosis	286 (0.87%)	10 (0.93%)	0.8386	0.0062	10 (0.93%)	10 (0.93%)	1.0000	< 0.0001

*p is significant if < 0.05

**If the standard mean difference was less than 0.1, it means the groups were well matched

took into account treatment-related covariates like CCB (calcium channel blockers), ACEi (angiotensin-converting enzyme inhibitors), ARBs (angiotensin II receptor blockers), BBs (beta blockers), nitroglycerin, aspirin, hydrochlorothiazide, anticoagulants, and K+-sparing agents. Additionally, other factors such as pulmonary embolism, pneumonia, COPD (chronic obstructive pulmonary disease), depression, and NSAIDs were included. Finally, we factored in all immunosuppressive medications, including methotrexate, azathioprine, mycophenolate, IVIG, tacrolimus, cyclosporine, tofacitinib, prednisone, cyclophosphamide, and baseline CPK.

Association measurement analysis

We utilized The TriNetX Research Network to match the cohorts according to patient numbers, thereby providing a sound basis for comparison. All statistical analyses were conducted using the TriNetX Advanced Analytics Platform. The precise methodologies for these computations are proprietary and are safeguarded under trade secret laws. This platform enabled us to calculate measures of association, including risk difference, risk ratio, and odds ratio. These were computed with a 95% confidence interval and a significance threshold of p <0.05 (2-sided).

The risk ratio for statin initiation post the index event was evaluated. This metric assesses the strength of the association between the exposure to either RA or DM/PM and the outcome, which in this case is statin initiation identified using the RxNorm code. Patients who had a statin use record before the study period were excluded from analyses A and B of association measures. This ensured that the calculated risk ratio accurately represented the rate of statin initiation rather than ongoing use.

Table 3 Baseline laboratory indices and immunosuppression at index event

Lab results (mean)				
	RA-HLD ($n=33,000$)	DM/PM-HLD ($n=1076$)	p value*	Std diff.**
HDL	46.7 ± 20.9 *Data from 4616 (13.99%) patients*	46.2 ± 18.1 *Data from 118 (10.92%) patients*	0.0041	0.0931
LDL	88.3 ± 31.2 *Data from 4498 (13.63%) patients*	92.8 ± 28.3 *Data from 117 (10.82%) patients*	0.0079	0.0859
Total cholesterol	160 ± 35 *Data from 4345 (13.17%) patients*	168 ± 45.7 *Data from 110 (10.18%) patients*	0.0041	0.0933
Total triglycerides	122 ± 72.7 *Data from 4669 (14.15%) patients*	165 ± 12.4 *Data from 131 (12.12%) patients*	0.0590	0.0601
Creatine kinase (CK)	140 ± 293 *Data from 1605 (4.86%) patients*	450 ± 1283 *Data from 493 (45.61%) patients*	< 0.0001	1.0620
Erythrocyte sedimentation rate (ESR)	25.1 ± 23.5 *Data from 10,711 (32.46%) patients*	24.1 ± 22.5 *Data from 321 (29.70%) patients*	0.0561	0.0597
C-reactive protein (CRP)	13.7 ± 30.9 *Data from 9370 (28.39%) patients*	13 ± 27.6 *Data from 275 (25.44%) patients*	0.0331	0.0669
Immunosuppressive medications				
	RA-HLD ($n=33,000$)	DM/PM-HLD ($n=1081$)	p value	Std diff.**
Prednisone	9864 (29.89%)	460 (42.55%)	< 0.0001	0.2658
Methotrexate	9214 (27.92%)	205 (18.94%)	< 0.0001	0.2126
Azathioprine	405 (1.23%)	143 (13.23%)	< 0.0001	0.4764
Mycophenolate mofetil	295 (0.89%)	217 (20.07%)	< 0.0001	0.4764
Mycophenolic acid	114 (0.35%)	42 (3.88%)	< 0.0001	0.2479
Leflunomide	2268 (8.06%)	10 (0.92%)	< 0.0001	0.34955
Sulfasalazine	1932 (5.86%)	10 (0.92%)	< 0.0001	0.2750
Tacrolimus	316 (0.96%)	79 (7.31%)	< 0.0001	0.3232
Cyclosporine	355 (1.08%)	19 (1.76%)	0.0342	0.0577
Hydroxychloroquine	6027 (18.26%)	160 (14.80%)	0.0037	0.0933
Infliximab	715 (2.17%)	0 (0%)	< 0.0001	0.2105
Adalimumab	2345 (7.11%)	10 (0.93%)	< 0.0001	0.3188
Etanercept	1930 (5.85%)	0 (0%)	< 0.0001	0.3525
Certolizumab pegol	283 (0.86%)	0 (0%)	0.0022	0.1315
Golimumab	312 (0.35%)	0 (0%)	0.0013	0.1382
Abatacept	1016 (3.08%)	0 (0%)	< 0.0001	0.2521
Tocilizumab	699 (2.19%)	0 (0%)	< 0.0001	0.2080
Rituximab	568 (1.72%)	43 (3.98%)	< 0.0001	0.1359
Tofacitinib	1379 (4.18%)	10 (0.93%)	< 0.0001	0.2074
Baricitinib	50 (0.15%)	0 (0%)	0.2003	0.0551
Upadacitinib	324 (0.98%)	10 (0.93%)	0.8521	0.0058
IVIG	95 (0.29%)	97 (8.97%)	< 0.0001	0.4224

*p is significant if < 0.05

For Analysis C, we used the Kaplan-Meier analysis sourced from TriNetX. This includes the hazard ratio, a measure indicating the rate at which individuals in our study group first experience a specific outcome, in our context, mortality.

Analysis C: CPK comparison in statin initiators vs statin non-initiators DM/PM-HLD

To assess the differences in mean CPK values across three time points (3 months prior to statin initiation, 3 months

Table 4 Statin initiation following HLD diagnosis among RA-HLD and DM/DM-HLD with immunosuppression for Analysis B

Unadjusted risk ratio *12,545 patients in RA-HLD and 305 patients in DM/PM-HLD were excluded from results because they had the outcome prior to the time window*				**Adjusted risk ratio** *382 patients in RA-HLD and 305 patients in DM/PM-HLD were excluded from results because they had the outcome prior to the time window*			
RA-HLD ($n=20,455$)	DM/DM-HLD ($n=776$)	p value*	Confidence interval (CI)	RA-HLD ($n=697$)	DM/DM-HLD ($n=776$)	p value*	CI
5529 (27.03%)	139 (17.91%)	<0.0001	6.35, 11.88%	191 (27.40%)	139 (17.91%)	<0.0001	5.33, 13.86%

Individual statin distribution codes among RA-HLD and DM/PM-HLD with immunosuppression cohorts 2018–2023

Statin	RA-HLD	DM/PM-HLD	p value*	CI
Atorvastatin	4658/25,213 (18.46%) *7787 patients in RA-HLD were excluded from results because they were on a statin prior to the time window*	110/907 (12.14%) *174 patients in RA-HLD were excluded from results because they were on a statin prior to the time window*	<0.0001	4.17, 8.53%
Pravastatin	763/31,355 (2.43%) *1645 patients in RA-HLD were excluded from results because they were on a statin prior to the time window*	19/1044 (1.82%) *37 patients in RA-HLD were excluded from results because they were on a statin prior to the time window*	0.2039	−0.22, 1.44%
Rosuvastatin	1959/31,064 (6.31%) *1937 patients in RA-HLD were excluded from results because they were on a statin prior to the time window*	53/1009 (5.25%) *72 patients in RA-HLD were excluded from results because they were on a statin prior to the time window*	0.1743	−0.35, 2.46%
Lovastatin	84/32,626 (0.26%) *374 patients in RA-HLD were excluded from results because they were on a statin prior to the time window*	0/1,076 (0%) *5 patients in RA-HLD were excluded from results because they were on a statin prior to the time window*	0.0956	0.22, 0.31%
Simvastatin	523/30,651 (1.71%) *374 patients in RA-HLD were excluded from results because they were on a statin prior to the time window*	10/1031 (0.97%) *50 patients in RA-HLD were excluded from results because they were on a statin prior to the time window*	0.0711	0.12, 1.35%
Fluvastatin	10/32,986 (0.07%) *14 patients in RA-HLD were excluded from results because they were on a statin prior to the time window*	0/1081 (0%) *0 patients in RA-HLD were excluded from results because they were on a statin prior to the time window*	0.5670	0.01, 0.05%
Pitavastatin	22/32,951 (0.07%) *49 patients in RA-HLD were excluded from results because they were on a statin prior to the time window*	0/1080 (0%) *1 patient in RA-HLD was excluded from results because he/she was on a statin prior to the time window*	0.3956	0.04, 0.10%

*p is significant if <0.05

after, and 6 months), we employed a bootstrapping approach due to the aggregated nature of the data. For each group, we simulated a sample distribution based on the provided mean, minimum, and maximum CPK values. Using these simulated distributions, we generated 1000 bootstrapped samples and computed the mean CPK for each sample. Python programming language was utilized, making extensive use of the pandas library for data processing and manipulation. Statistical analyses, including bootstrapping, were conducted using the SciPy and NumPy libraries.

Results

Analysis A: statin initiation rates between General Population-HLD patients vs DM/PM-HLD and RA-HLD vs DM/PM-HLD

In a preliminary analysis of larger cohorts without immunosuppression filtering, we compared the baseline characteristics of General Population-HLD patients (n=11,212,300) and DM/PM-HLD patients (n=2017) in Analysis A1 (Supplemental Table 2). We compared RA-HLD patients (n=58,795) with the same DM/PM-HLD cohort in Analysis A2 (Supplemental Table 3).

Both sets of data revealed noticeable differences in the rate at which statins were started between the groups, even after adjusting using PSM (Table 1). Before any adjustments, the general population with the HLD group began statins at a rate of 21.82%. In comparison, the RA-HLD group had a slightly higher initiation rate of 25.01%, while the DM/PM-HLD group mirrored the general population with a rate of 21.82%. The differences were statistically significant: For Analysis 1 (A1), the values were $p<0.0001$ with a confidence interval (CI) ranging from 1.18% to 1.42%, and for Analysis 2 (A2), the values were $p<0.0001$ with a CI between 2.72 and 6.88%.

After adjusting the data using PSM, the discrepancies remained evident. The General Population-HLD group's initiation rate increased to 31.94%, the RA-HLD group's rate dropped slightly to 24.74%, and the DM/PM-HLD group's rate remained the most modest at 20.21%. The adjusted differences continued to be statistically significant. For A1, the values were $p<0.0001$ with a CI between 1.29 and 1.66%. Meanwhile, A2 showed values of $p=0.0034$ and a CI ranging from 1.50 to 7.55%.

Analysis B: comprehensive assessment with immunosuppression filtering: DM/PM-HLD and RA-HLD vs DM/PM-HLD

Considering these findings, we proceeded to Analysis B, which incorporated immunosuppression filters.

Baseline characteristics

Demographics The demographic analysis revealed that the average age was slightly higher in the RA-HLD group (n=33,000) (62.4 years) compared to the DM/PM-HLD group (n=1079) (58.6 years). In both cohorts, females were predominant, comprising 74.97% of RA-HLD patients and 69.38% of DM/PM-HLD patients (Table 2).

When it came to racial composition, the RA-HLD patients were primarily White (73.55%), followed by Black (12.81%) and Asian (2.42%), with 10.59% of patients having an unknown racial background. Similarly, in the DM/PM-HLD cohort, Whites made up the majority (67.72%), followed by Black (16.37%) and Asian (4.07%), and 11.75% were of an unknown race.

Cardiovascular comorbidities Hypertension was present in 37.74% of RA-HLD patients, contrasting with 32.66% in the DM/PM-HLD group ($p=0.007$). Smoking was reported in 7.51% of RA-HLD patients and 4.07% of DM/PM-HLD patients ($p<0.0001$). Conversely, diabetes mellitus and fatty liver were more common in DM/PM-HLD patients, with prevalence rates of 18.78% and 3.52%, respectively, against 14.75% and 2.04% in RA-HLD patients ($p=0.0003$ for diabetes and $p=0.008$ for fatty liver). There were no significant differences in CAD, heart failure, MI, stroke, PVD, CKD, and liver cirrhosis between the groups ($p>0.05$) (Table 2).

Baseline laboratory indices Patients in both cohorts showed varying availability of Laboratory results at the Index Event, ranging from 10.18 to 32.46% depending on the test. DM/PM-HLD patients displayed higher baseline lipid values, LDL ($p=0.0079$), total cholesterol (0.0041), and lower HDL levels ($p=0.0041$) compared to RA-HLD patients. However, no significant difference was seen in total triglyceride levels ($p=0.0590$). DM/PM-HLD patients had a higher average creatine kinase level of 450, compared to 140 in RA-HLD patients ($p<0.0001$). The differences in erythrocyte sedimentation rate were not statistically significant ($p=0.0561$) and showed higher rates for C-reactive protein for the RA-HLD group ($p=0.0331$) (Table 3).

Baseline immunosuppressive medication Prednisone was commonly used in both study cohorts. However, it was more frequently observed in the DM/PM-HLD group (42.55%) compared to the RA-HLD group (29.89%) ($p<0.0001$). Methotrexate was more commonly prescribed among RA-HLD patients, with 27.92% of patients receiving this medication, as opposed to 18.94% in the DM/PM-HLD group ($p<0.0001$). On the other hand, azathioprine and mycophenolate were less common in the RA-HLD cohort, with a mere 1% of patients on each of these drugs. These medications were more prevalent in the DM/PM-HLD group, with

azathioprine and mycophenolate being used by 13.23% and 20.07% of patients, respectively ($p<0.0001$). About 16.34% of RA-HLD patients were treated with anti-TNF agents, and 6% received abatacept. The use of intravenous immunoglobulin (IVIG) was markedly higher in the DM/PM-HLD group at 8.97% vs. 0.29% in RA-HLD patients ($p<0.0001$). Concerning Janus kinase (JAK) inhibitors, patients with RA-HLD were three times as likely to be on therapy vs. DM/PM-HLD patients (5.31 vs. 1.86%, $p<0.0001$). Finally, Rituximab was three times more prevalent in the DM/PM-HLD group (3.98%) compared to the RA-HLD group (1.72%, $p<0.0001$) (Table 3).

Autoantibody results For the Analysis B RA-HLD cohort, comprising 33,000 subjects, we delved into various autoantibody tests available. For the ANA test, out of 1914 conducted, 500 or 26.11% were positive, and 1371 or 71.67% turned out negative, with the rest unspecified. Moving on to the rheumatoid factor (RF) tests from a sample of 9307, we found 5369 (57.68%) positive results, 2048 (22.01%) negative, and 1890 (20.31%) indeterminate. Further, of the 7444 CCP tests done, 2711 (36.42%) were positive, 2584 (34.71%) were negative, and the remaining 2149 (28.87%) were undetermined. These findings are elaborated in Supplemental Table 4.

For the myositis cohort, consisting of 1081 subjects, we examined 1182 available autoantibody tests. From this, 641 (54.23%) were specific to myositis. Of these specific tests, 79 (12.32%) returned positive, predominantly for Jo-1, while 478 (74.57%) were negative and 84 (13.11%) unspecified. The residual 541 tests (45.77%) pertained to myositis-associated antibodies: 178 (32.90%) were positive, mainly for SSA; 220 (40.67%) negative; and 143 (25.43%) remained undetermined. Additionally, from this cohort, ANA tests (with a 1:80 titer) were conducted 78 times resulting in 27 positives. RF tests, conducted 102 times, produced 20 positives, and CCP tests, conducted 101 times with a threshold of >20, reported 10 positives. The details of these findings are also presented in Supplemental Table 4.

Initiation rates for statin treatment (composite outcome) In this analysis, the model measured the first instance of statin use as a composite outcome within the defined study period. The RA-HLD and DM/PM-HLD groups demonstrated relatively low initiation rates for statin therapy (Table 4). The RA-HLD group had a noticeably higher rate of statin initiation at 27.03% compared to 17.91% in the DM/PM-HLD group ($p<0.0001$, CI 6.35–11.88%). Even after adjusting for cardiovascular risk factors, the DM/PM-HLD group consistently had significantly lower statin initiation rates (RR 17.91% vs 27.40%; CI 5.33–13.86%, $p=0.003$).

Individual statin usage distribution In this analysis aspect, each specific statin medication was assessed independently (Table 4). Thus, some patients may have been counted multiple times if they used more than one type of statin. For instance, if a patient were prescribed both atorvastatin and pravastatin, they would be included in the counts for each of these individual statins but only once for the composite outcome.

The RA-HLD group had a higher proportion of patients using Atorvastatin when compared to the DM/DM-HLD group (18.46% vs. 12.14%, $p<0.0001$). Usage rates for pravastatin, rosuvastatin, and simvastatin showed no significant differences between the groups. Lastly, no recorded instances of lovastatin, fluvastatin, and pitavastatin use in the DM/PM-HLD cohort were recorded.

Analysis C: mortality rate comparison between statin and non-statin initiators in the DM/HLD group

Through this analysis, we aimed to assess how statin utilization can affect the mortality rate in the DM/PM population.

Demographics

The analysis of the demographics revealed a significant difference in average age. The mean age was noticeably higher in the group of DM/PM-HLD patients using statins ($n=311$) at 61 years compared to the group of patients not taking statins ($n=661$) at 56.6 years ($p<0.0001$). In the DM/PM-HLD with statins, Females made up 65.70% of patients, whereas in the other cohort, they made up 70.80%. As for the racial composition, these two groups followed the same trends as the DM/PM-HLD cohort of Analysis B: Whites, followed by Blacks, then Asians, and the remaining were of unknown race (Table 5).

Cardiovascular comorbidities

The rates of cardiovascular comorbidities were higher in the DM/PM-HLD with statin cohort than in the without statin cohort. The statin cohort had significantly higher rates of hypertension (59.49% vs. 31.32%, $p<0.0001$), diabetes (39.23% vs. 16.34%, $p<0.0001$), chronic heart disease (17.69% vs. 6.35%, $p<0.0001$), heart failure (14.15% vs. 4.99%, $p<0.0001$), CKD (14.79% vs. 3.33%, $p<0.0001$), congenital heart malformation (3.26% vs. 0%, $p<0.0001$), atrial fibrillation (7.17% vs. 3.33%, $p=0.0026$), myocardial infarction (4.20% vs. 1.66%, $p=0.0184$), and stroke (4.50% vs. 1.51%, $p=0.005$). Likewise, within the group of DM/PM-HLD patients taking statins, there was a higher occurrence of fatty liver, COPD, and pneumonia, with prevalence

rates of 8.68%, 7.07%, and 3.26%, respectively. In contrast, among DM/PM-HLD patients not using statins, these conditions were less common, with prevalence rates of 4.39%, 3.63%, and 6.20%, respectively. These differences were statistically significant, with p-values of 0.0074 for fatty liver, 0.008 for COPD, and 0.0099 for pneumonia. The groups had no significant differences for the remaining comorbidities (p>0.05) (Table 5).

Baseline laboratory indices

Significant differences between the two cohorts of DM/PM-HLD patients appeared from our laboratory analysis (Table 5). Notably, the cohort on statins had higher LDL values, 118 ± 40.9, than their non-statin counterparts (107 ± 30.7) (p=0.0125). Similarly, total cholesterol levels, the statin-treated group had substantially higher levels (203 ± 55.7) compared to the non-statin group (184 44.7) (p=0.0022). In contrast, the DM/PM-HLD group that was not taking statins had considerably higher Creatine Kinase levels (512 ± 1610) than the cohort that was (219,449), with a p value of 0.0143. There was no significant difference observed in HDL, ESR, CRP, and HbA1C.

Baseline medications

Our findings reveal significant differences in medication usage patterns between these two groups (Table 5). Notably, mycophenolate mofetil and insulin were more commonly prescribed to patients in the DM/PM with statin group, with usage rates of 29.58% and 23.79%, respectively, compared to 23.30% and 8.02% in the DM/PM without statin group ($p < 0.0001$ for both). Furthermore, anticoagulants, aspirin, calcium channel blockers, beta blockers, ACE inhibitors, and angiotensin II inhibitors showed significantly higher utilization rates in the DM/PM with statin group ($p < 0.0001$ for all). Nitroglycerin also exhibited a higher usage rate among DM/PM with statin individuals (9.00%) compared to the DM/PM without statin group (3.48%) ($p = 0.0003$).

Mortality rates in DM/PM-HLD patients: statin initiators vs. non-initiators

In a propensity score-matched cohort, which consisted of 218 subjects each for both statin initiators and non-initiators, there was a well-balanced distribution in terms of age, sex, BMI, alcohol and tobacco use, comorbidities, medication usage, HbA1C, and baseline cholesterol levels.

Notably, among patients with DM/PM, there was a significant reduction in mortality rates for those initiating statin therapy compared to their counterparts who did not initiate statins. Over a 10-year follow-up period, statin initiators had 16 deaths, equating to an overall mortality rate of 75 deaths per 1000 person-years. Conversely, non-initiators experienced 32 deaths, translating in an overall mortality rate of 147 deaths per 1000 person-years. Statin initiation was associated with a hazard ratio (HR) for overall mortality of 0.515 (p=0.0273, 95% CI, 0.28–0.93) throughout the entire follow-up period.

When observing truncated follow-up intervals of one, three, five, and seven years, the benefit of statin initiation persisted. The HR for mortality with statin use was 0.194 (p=0.0039, 95% CI, 0.03–0.5) at 1 year, 0.0028 (p=0.0028, 95% CI, 0.14–0.70) at 3 years, 0.463 (p=0.0148, 95% CI, 0.25–0.87) at 5 years, and 0.524 (p=0.0327, 95% CI, 0.29–0.95) at 7 years (as detailed in Table 6).

CPK comparison before and after statin use in statin DM/HLD users

To evaluate the impact of statin usage on CPK levels in DM/HLD patients, we compared mean CPK values at three intervals: 3 months before statin initiation, 3 months post-initiation, and 6 months post-initiation, between statin and non-statin users. The confidence intervals (CIs) for these periods were (166.00, 462.94), (157.27, 544.57), and (150.07, 541.01) respectively. The overlapping CIs indicate that the variations in CPK levels between the two groups might not hold statistical significance.

Discussion

In this retrospective, population-based study, we observed a pronounced underutilization of statins in DM/PM-HLD patients compared to RA-HLD patients. Specifically, a decade post-HLD diagnosis, after adjusting for cardiovascular determinants, only 17.91% of DM/PM-HLD patients had begun statin monotherapy, compared to 27.40% of RA-HLD patients. Notably, DM/PM-HLD patients not on statins witnessed an almost doubled mortality rate (147 deaths/1000/year) over ten years than their DM/PM-HLD counterparts on statins (75 deaths/1000/year; p=0.0273, HR=0.515, CI 0.28–0.93).

Our results align with a smaller US study in which merely 15% (33 out of 214) of IIM patients received statins, primarily due to elevated CVD risks from hypertension, diabetes, or dyslipidemia [15]. Additionally, our findings support previous reports of RA undertreatment [18]; an audit from 2014 to 2019 identified 28.8% of RA cohorts in North America on statins. Unlike ours, the study also evaluated the concomitant use of other lipid-lowering agents with statins in RA-HLD (2.3%) and combination therapy (1%) [5]. However, we purposely narrowed our focus to statin monotherapy, excluding patients on alternate lipid-lowering treatments, because we hypothesized that healthcare teams would have specific concerns about this treatment in myopathic DM/PM patients.

Table 5 Baseline characteristics of DM/PM with statin and DM/PM without statin before and propensity score matching (Analysis C)

	Unadjusted baseline characteristics				**Adjusted baseline characteristics**			
	DM/PM with statin ($n=311$)	DM/PM without statin ($n=661$)	p value*	Std diff.**	DM/PM with statin ($n=217$)	DM/PM without statin ($n=217$)	p value*	Std diff.**
Age at index Mean ± SD	61 ± 12.7	56.6 ± 14.1	< 0.0001	0.3231	59.8 ± 12.6	59.2 ± 13.6	0.6317	0.0461
Sex								
Female	203 (65.70%)	468 (70.80%)	0.1086	0.1099	144 (66.36%)	140 (64.52%)	0.6864	0.0388
Male	108 (34.3%)	193 (29.20%)	0.0821	0.1188	74 (34.10%)	68 (31.34%)	0.5393	0.0590
Race								
White	194 (62.38%)	451 (68.23%)	0.0717	0.1231	149 (68.66%)	139 (64.06%)	0.3097	0.0977
Black	62 (19.94%)	99 (14.98%)	0.0524	0.1309	35 (16.13%)	40 (18.43%)	0.5256	0.0610
Asian	19 (6.11%)	29 (4.39%)	0.2477	0.0773	10 (4.61%)	15 (6.91%)	0.3030	0.0990
Unknown	36 (11.58%)	81 (12.25%)	0.7617	0.0209	24 (11.06%)	23 (10.60%)	0.8772	0.0148
Lifestyle factors								
BMI	29.4 ± 7.53	28.7 ± 6.82	0.3747	0.0966	29.1 ± 7.35	29.4 ± 7.19	0.7879	0.045415
Smoking	20 (6.43%)	25 (3.78%)	0.0668	0.1205	12 (5.53%)	10 (4.61%)	0.6616	0.0420
Alcohol use	10 (3.26%)	10 (1.51%)	0.0811	0.1122	10 (4.61%)	0 (0%)	0.0014	0.3108
Measures of comorbidities								
	Unadjusted risk ratio				Adjusted risk ratio			
Hypertension	185 (59.49%)	207 (31.32%)	< 0.0001	0.5899	112 (51.61%)	117 (53.92%)	0/6307	0.0462
Diabetes mellitus	122 (39.23%)	108 (16.34%)	< 0.0001	0.5285	64 (29.49%)	70 (32.59%)	0.5330	0.0599
Chronic heart disease	55 (17.69%)	42 (6.35%)	< 0.0001	0.3539	26 (11.98%)	29 (13.36%)	0.6651	0.0416
Heart failure	44 (14.15%)	33 (4.99%)	< 0.0001	0.3151	18 (8.30%)	21 (9.68%)	0.6146	0.0484
Atrial fibrillation	24 (7.17%)	22 (3.33%)	0.0026	0.1930	13 (5.99%)	16 (7.37%)	0.5642	0.0554
Myocardial infarction	13 (4.20%)	11 (1.66%)	0.0184	0.1498	10 (4.61%)	10 (4.61%)	1.000	< 0.0001
Stroke	14 (4.50%)	10 (1.51%)	0.0051	0.1757	10 (4.61%)	10 (4.61%)	1.000	< 0.0001
CKD	46 (14.79%)	25 (3.78%)	< 0.0001	0.3863	13 (5.99%)	18 (8.30%)	0.3514	0.0896
Congenital heart malformations	10 (3.26%)	0 (0%)	< 0.0001	0.2578	0 (0%)	0 (0%)	-	-
End-stage renal disease	10 (3.26%)	10 (1.51%)	0.0811	0.1122	10 (4.61%)	10 (4.61%)	1.000	< 0.0001
Malignancy	10 (3.26%)	10 (1.51%)	0.0811	0.1122	10 (4.61%)	10 (4.61%)	1.000	< 0.0001
Fatty liver	27 (8.68%)	29 (4.39%)	0.0074	0.1744	16 (7.37%)	11 (5.07%)	0.3204	0.0955
Liver cirrhosis	10 (3.26%)	10 (1.51%)	0.0811	0.1122	10 (4.61%)	10 (4.61%)	1.000	< 0.0001
Varicose veins	10 (3.26%)	10 (1.51%)	0.0811	0.1122	10 (4.61%)	10 (4.61%)	1.000	< 0.0001
Chronic obstructive pulmonary disease (COPD)	22 (7.07%)	24 (3.63%)	0.0184	0.1534	17 (7.83%)	14 (6.45%)	0.5761	0.0537
Pulmonary embolism	10 (3.26%)	15 (2.27%)	0.3847	0.0580	10 (4.61%)	10 (4.61%)	1.000	< 0.0001
Pulmonary fibrosis	37 (11.90%)	60 (9.10%)	0.1712	0.0921	25 (11.52%)	22 (10.14%)	0.6431	0.0445
Pneumonia	34 (10.93%)	41 (6.20%)	0.0099	0.1696	20 (9.22%)	17 (7.83%)	0.6061	0.0495
Depression	40 912.86%)	79 (11.95%)	0.6864	0.0276	27 (12.44%)	22 (10.14%)	0.4482	0.0729
Dementia	10 (3.26%)	10 (1.51%)	0.0811	0.1122	10 (4.61%)	10 (4.61%)	1.000	< 0.0001
Medications								
Prednisone	181 (58.20%)	377 (57.04%)	0.7320	0.0236	122 (56.22%)	118 (54.38%)	0.6994	0.0371
Methylprednisolone	88 (28.30%)	150 (22.69%)	0.0581	0.1288	54 (24.89%)	50 (23.04%)	0.6528	0.0432
Methotrexate	70 (22.51%)	154 (23.30%)	0.2374	0.0820	54 (24.89%)	50 (23.04%)	07191	0.0345

Table 5 (continued)

Mycophenolate mofetil	92 (29.58%)	154 (23.30%)	0.0356	0.1429	61 (28.11%)	55 (25.35%)	0.5152	0.0625
Azathioprine	56 (18.01%)	120 (18.15%)	0.9555	0.0038	39 (17.97%)	35 (16.13%)	0.6097	0.0490
Hydroxychloroquine	53 (17.04%)	138 (20.88%)	0.1604	0.0980	38 (17.52%)	38 (17.52%)	1.0000	< 0.0001
IVIG	39 (12.54%)	76 (11.50%)	0.6388	0.0321	28 (12.90%)	19 (8.76%)	0.7051	0.0363
Tofacitinib	10 (3.22%)	10 (1.51%)	0.0811	0.1122	10 (4.61%)	10 (4.61%)	1.0000	< 0.0001
Rituximab	18 (5.79%)	43 (6.51%)	0.6670	0.0299	12 (5.53%)	13 (5.99%)	0.8368	0.0198
Cyclophosphamide	10 (3.22%)	10 (1.51%)	0.0811	0.1122	10 (4.61%)	10 (4.61%)	1.0000	< 0.0001
Insulin	74 (23.79%)	53 (8.02%)	< 0.0001	0.4418	38 (17.52%)	36 (16.59%)	0.7985	0.0245
Anticoagulants	130 (41.80%)	142 (21.48%)	< 0.0001	0.4477	74 (34.01%)	68 (31.34%)	0.5393	0.0590
Aspirin	85 (27.33%)	79 (11.95%)	< 0.0001	0.3946	45 (20.74%)	42 (19.36%)	0.7191	0.0345
Nitroglycerin	28 (9.00%)	23 (3.48%)	0.0003	0.2298	14 (6.45%)	16 (7.37%)	0.7051	0.0363
Calcium channel blockers	97 (31.19%)	86 (13.01%)	< 0.0001	0.4490	52 (23.96%)	50 (23.04%)	0.8209	0.0217
Beta blockers	126 (40.51%)	133 (2.12%)	< 0.0001	0.4550	74 (34.10%)	71 (32.72%)	0.7601	0.0293
ACE inhibitors	73 (23.47%)	65 (9.83%)	< 0.0001	0.3724	43 (19.82%)	37 (17.05%)	0.4576	0.0714
Angiotensin II inhibitors	57 (18.33%)	65 (9.83%)	0.0002	0.2461	35 (16.30%)	34 (15.67%)	0.8956	0.0126
Aldosterone antagonists and other K + sparing agents	16 (5.15%)	23 (3.48%)	0.2172	0.0820	11 (5.07%)	10 (4.61%)	0.8230	0.0215
Naproxen	16 (5.15%)	19 (2.87%)	0.0764	0.1159	11 (5.07%)	11 (5.07%)	1.0000	< 0.0001
Ibuprofen	58 (18.65%)	79 (11.95%)	0.0051	0.1869	35 (16.30%)	32 (14.75%)	0.6902	0.0383
Celecoxib	10 (3.22%)	15 (2.27%)	0.3847	0.0580	10 (4.61%)	10 (4.61%)	1.0000	< 0.0001
Laboratory measurements								
HDL	50.1 ± 21 *Data from 163 (52.41%) patients*	50.2 ± 22.8 *Data from 139 (21.03%) patients*	0.9736	0.0038	50.8 ± 21.7 *Data from 95 (43.78%) patients*	47.6 ± 21.4 *Data from 91 (41.94%) patients*	0.3102	0.1493
LDL	118 ± 40.9 *Data from 157 (50.481%) patients*	107 ± 30.7 *Data from 131 (19.82%) patients*	0.0125	0.3010	120 ± 42.8 *Data from 89 (41.01%) patients*	107 ± 33.1 *Data from 84 (38.71%) patients*	0.0224	0.3518
Total cholesterol	203 ± 55.7 *Data from 158 (50.80%) patients*	184 ± 44.7 *Data from 136 (20.58%) patients*	0.0022	0.3645	207 ± 60.5 *Data from 93 (42.86%) patients*	184 ± 45.8 *Data from 89 (41.01%) patients*	0.0052	0.4205
Creatine kinase (CK)	219 ± 449 *Data from 189 (60.77%) patients*	512 ± 1,610 *Data from 398 (60.21%) patients*	0.0143	0.2479	210 ± 384 *Data from 128 (58.99%) patients*	767 ± 2,183 *Data from 123 (56.68%) patients*	0.0048	0.3560
Erythrocyte sedimentation rate (ESR)	26.4 ± 22.6 *Data from 128 (41.16%) patients*	22.3 ± 21.5 *Data from 287 (43.42%) patients*	0.0769	0.1866	24.5 ± 21.9 *Data from 86 (39.63%) patients*	23.5 ± 23.9 *Data from 102 (47.01%) patients*	0.7837	0.0404
C-reactive protein (CRP)	12.5 ± 28.3 *Data from 127 (40.84%) patients*	12.7 ± 27.2 *Data from 256 (38.73%) patients*	0.9411	0.0080	8.88 ± 18.1 *Data from 82 (37.79%) patients*	17.5 ± 26.7 *Data from 83 (38.25%) patients*	0.0162	0.3786
HbA1C	6.55 ± 1.71 *Data from 146 (46.95%) patients*	6.31 ± 1.84 *Data from 143 (21.63%) patients*	0.2526	0.1348	6.29 ± 1.77 *Data from 78 (35.94%) patients*	6.32 ± 1.84 *Data from 77 (35.48%) patients*	0.9147	0.0172

*p is significant if < 0.05

**If the standard mean difference was less than 0.1, it means the groups were well matched

Table 6 Mortality rates in DM/PM patients with and without statin use over multiple time intervals

Follow-up period	DM/PM with statin		DM/PM without statin				
	Number of deaths (*N*)	Mortality (number of deaths/1000) per year	Number of deaths (*N*)	Mortality (number of deaths/1000) per year	*p* value*	Hazard ratio	CI
1 year	10/218	46	15/218	68	0.0039	0.194	0.03, 0.5
3 years	10/215	45	25/218	114	0.0028	0.316	0.14, 0.70
5 years	14/212	66	30/216	138	0.0148	0.463	0.25, 0.87
7 years	16/214	75	31/218	142	0.0327	0.524	0.29, 0.95
10 years	16/214	75	32/218	147	0.0273	0.515	0.28, 0.93

This study investigated the mortality implications of statin undertreatment in the DM/PM-HLD demographic. DM/PM-HLD patients under statin therapy exhibited a 50% reduction in mortality compared to their counterparts without statin intervention. While no specific studies have explored the direct impact of statin usage on mortality in the DM/PM population, our findings align with existing research focused on mortality among patients with RA and SARD, which included approximately 8% of DM/PM patients where statin use correlated with a 28% decrease in mortality [19]. A separate investigation into SARD patients on statin therapy corroborated these observations, demonstrating a decline in mortality rates [2], with another study identifying an uptick in mortality among RA patients upon cessation of statin therapy [20].

Interestingly, pitavastatin and fluvastatin were notably absent from DM/PM-HLD treatments. This absence is significant since these statins have been reported to be associated with a reduced risk of myopathy, and their use could be particularly beneficial for DM/PM-HLD patients [21, 22].

The observed clear undertreatment and its mortality implications in DM/PM-HLD underline the urgent need for heightened awareness regarding the cardiovascular risks of chronic inflammatory diseases like DM/PM. Despite the frequent prescription of statins to DM/PM patients, comprehensive guidelines detailing risk assessment, the optimal choice of statin, monitoring of side effects, and therapeutic strategies remain absent. Future research should prioritize establishing the safety of various statins in DM/PM, and potential barriers to statin initiation should be investigated, covering aspects like physician awareness, patient preferences, and medication risks.

Factors potentially contributing to DM/PM undertreatment include a lack of systematic screening, ambiguous clinical guidelines for DM/PM, and unclear physician responsibility for CVD risk management. Misinterpretation of symptoms, such as mistaking dyspnea on exertion indicative of CVD for pulmonary involvement, could be another contributor. Additionally, statins' potential muscle-related side effects might discourage their prescription, especially considering DM/PM patients' elevated CPK levels. However, our findings on CPK before and after statin initiation in the DM/PM-HLD group did not show significant differences, indicating the need for more in-depth studies.

Our study is confined by its retrospective nature, potentially impacting data quality, particularly regarding medication compliance. In previous studies, ICD-10 codes for DM/PM showed an 89% positive predictive value (PPV) and 84% sensitivity for DM/PM identification [23], while RA displayed 82% PPV and 76% sensitivity [24]. We enhanced the reliability of ICD-10 codes by mandating the presence of immunosuppressive medication in our analysis and excluding other autoimmune disease diagnosis codes. Exclusively focusing on statin initiation and sidelining other HLD therapies restricted our insights into alternate treatment pathways but sharpened our observation of statin underuse. Furthermore, our findings might not translate globally due to differing lipid-lowering therapy practices, and our ten-year observational period might overlook current trends in statin prescription potentially influenced by the remission of inflammatory myopathy.

Conclusion

This analysis demonstrates a marked disparity in HLD management in DM/PM patients compared to RA and the general population with HLD. The increased mortality risk for DM/PM-HLD patients not on statins highlights the importance of collaborative management among primary care professionals, rheumatologists, and cardiologists to improve preventive care delivery for these patients.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s10067-023-06801-7.

Data Availability The deidentifiable data supporting the findings of this study are available on the TriNetX platform and can be accessed upon reasonable request.

Compliance with ethical standards

Disclosures None.

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