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Title: No effects of statins on improvement of alopecia areata: a four year retrospective cohort study in a metropolitan area

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Abstract

Background: Statin use is widespread. Statins+/-ezetimibe is thought to promote improvement in alopecia areata, an autoimmune disease characterized by round patches of non-scarring hair loss.

Objective: To elucidate the relationship between statins and alopecia areata improvement.

Methods: Retrospective cohort study of 6617 patients with hair disorders who visited a large metropolitan healthcare system between June 2013 to May 2017. The primary outcome was an improvement in alopecia areata after exposure to statins using statistical analyses (relative risk, logistic regression).

Results: Best predictors of AA include age and whether patients received intralesional triamcinolone acetonide injections. Statins are not an independent predictor of AA improvement. Age is a confounding factor for evaluating the use of statins on improvement of AA.

Limitations: Since this study involves retrospective chart review, the design has limited ability to determine causality, though this was mitigated by statistical methods.

Conclusions: Our data do not support statins as an effective therapy for alopecia areata.

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Disclaimer: The views expressed in the submitted article are author's own and not an official position of the institution.

Introduction

Alopecia areata (AA) affects 2 million people in the United States. AA is characterized by loss of hair in round, patchy areas commonly on the scalp and face, but can also affect any hair-bearing area of the body. There are various types of AA, including acute, which occurs within a month and usually spontaneously resolves, and chronic, which often has an unpredictable disease course. Factors for worse prognosis include earlier disease onset, longer duration of disease, higher severity of involvement (SALT score >70%), and comorbid autoimmune conditions such as atopic dermatitis, allergic rhinitis, and thyroid disease (Lepe et al. 2024). For treatment of mild to moderate patchy AA in adults, intralesional corticosteroids such as triamcinolone acetonide (Kenalog) injections are often used as first line in the clinic, while topical steroids, contact sensitizers such as DNCB (Dinitrochlorobenzene), minoxidil, or anthracyclin have also demonstrated effectiveness. While PRP (platelet rich plasma) injections are also used for treatment of AA, their results have been variable (Malhotra et al. 2023).

Several studies have demonstrated that statins have a therapeutic effect on hair regrowth in AA. As an autoimmune disease, AA involves inflammatory attacks on hair follicle cells. Although generally used for lowering LDL cholesterol, statins have been shown to exert anti-inflammatory effects via the JAK/STAT pathway in cellular studies, inhibiting secretions of cytokines while upregulating Treg cells (Zeiser et al. 2018). Lattouf et al. conducted a prospective pilot study in 29 AA patients. Patients were on simvastatin 40 mg/ezetimibe 10 mg combination. 14/19 patients responded positively to the treatment. 5 who continued the statin treatment remained stable, while 5 who discontinued the treatment relapsed (Lattouf et al. 2015). Two case studies demonstrated statins efficacy in hair regrowth of alopecia areata patients (Ali and Mark 2010, Robins et al. 2007). Another case series yielded positive results for statins' effects on AA with a statin/ezetimibe and dexamethasone combination (Camacho et al. 2017).

Several studies yielded negative results. Choi et al. conducted an open prospective study of 14 patients with severe recalcitrant alopecia areata. Patients were placed on combination simvastatin 40 mg/ezetimibe 10 mg and followed over 3 months. The results were unsatisfactory: improved alopecia in 4 patients only (Choi et al. 2017). Loi et al. conducted a case series following 17 AA patients on simvastatin/ezetimibe 40 mg/10 mg daily for 6 months. 14 did not have hair regrowth, 2 had transient regrowth, and 1 had patchy regrowth that was not cosmetically acceptable (Loi et al. 2016). Freitas et al. followed 12 AA patients in the study. 67% had no hair regrowth, 24% transient diffuse or patchy hair regrowth, and 24% patchy regrowth of pigmented hair which was not cosmetically satisfactory (Freitas et al. 2017).

Several mice studies have demonstrated that statins improve hair regrowth in AA. In one mouse study, simvastatin/ezetimibe was shown to result in a greater improvement in hair regrowth than simvastatin alone. There was an increase in the number of FOXP3+ Treg cells in the mice treated with simvastatin (Jimenez et al. 2014, 2015). In another mouse study, mice treated with topical simvastatin had lower phosphorylated levels of STAT1, which suggests involvement of the JAK/STAT pathway (DeCanto et al. 2015).

The objective of this study is to determine the effect of statins and statins+/-ezetimibe on AA and elucidate whether statins+/-ezetimibe will improve hair regrowth for AA patients. The hypothesis is that statins will improve alopecia areata hair regrowth.

Methods

Study design and size

The study is an observational retrospective cohort study and includes all the patients with hair disorders (n=6617) over an observation period of four years (June 28, 2013 to May 2, 2017) in a health system based in Los Angeles, California. Patients receiving inpatient statins only were excluded (n=17) since we are looking at long term statin use (Supplemental Figure 1). Patients who only had one SALT score, patch size, or number of patches were considered lost to follow up over this time period and were excluded from the AA improvement part of the study (Supplemental Figure 2). The population of patients who participated in the study were those identified with hair disorders by dermatologists whether they were on statins or not at the beginning of the study. The cohort study was an appropriate first study because of its relatively low cost compared to randomized clinical trials and can help guide the direction of future studies.

Data collection, setting, and participants

The health information of 6617 patients with hair disorders was obtained through a large university health system. All procedures were performed in compliance with relevant laws and institutional guidelines. The time period for this cohort is June 28, 2013 to May 2, 2017. The information obtained includes the patient's diagnosis (alopecia areata [ICD-9 704.01 and ICD-10 L63.9], alopecia totalis [L63.0], alopecia universalis [L63.1], ophiasis [L63.2], and other alopecia areata [L63.8], and other nonalopecia disorders), whether they were receiving intralesional triamcinolone acetonide injections (px_code 11900 and 11901), and whether they were taking statins+/-ezetimibe (epic_medication_id 6465, 8893, 10469, 10470, 10471, 11110, 11111, 11112, 11364, 11365, 11366, 11367, 19176, 19177, 19178, 23449, 28645, 32128, 34153, 35134, 35135, 35136, 36606, 36607, 36608, 36609, 36612, 39220, 39221, 39222, 39223, 89698, 89700, 89701, 89703, 104572, 104573, 104574, 124248, 124250). Demographics information was also obtained, including patient age, sex, race, and ethnicity (Tan et al. 2024). In addition, the electronic medical records of all patients diagnosed with AA were manually reviewed for changes in SALT score, patch size, number of patches, or qualitative improvement for characterization of AA improvement.

Statistical methods

Data from various sources were compiled into a composite spreadsheet. Categorical data were encoded into dummy variables (e.g. 0=no AA, 1=AA). Quantitative variables were encoded into 0, 1, 2... with a legend corresponding to each number.

Contingency tables

To describe the relative risk of diagnosis of AA, two by two contingency tables were constructed from observed frequencies of patients with AA and those with no AA, stratified by demographic factors and/or statin use and steroid injections. Similar contingency tables were made for AA improvement. For analysis, Fisher's exact test was chosen. Relative risk and 95% confidence interval were calculated using Koopman asymptotic score. GraphPad Prism 8 was used to perform calculations and make graphs.

Logistic regressions/curve fitting

Regressions were chosen to analyze the relationship between AA and multiple variables because of their high statistical power. Logistic regression was chosen because of a binomial distribution (0=no AA, 1=AA). Simple logistic regressions were first performed for two variables at a time. Multiple logistic regressions were then performed for AA and several independent variables. Measures of correlation strength were calculated, including the Tjur's R squared and McFadden's R squared. The goodness of fit was calculated by the ROC curve, with a greater area suggesting a better fit. GraphPad Prism 8 and RStudio were used for calculations.

Missing data, confounding, loss to follow up, bias

Missing data (follow up visits)/loss to follow up was accounted for by exclusion from multiple logistic regression analysis in the improvement part of the study. Possible bias was accounted for in the following ways: confounding - multivariate regression analyses were performed with controlling for confounding as described above, selection -

study design includes not just dermatology clinic patients but all patients with hair disorders at a metropolitan health care system over a certain time period, and loss to follow up - patients with less than 2 SALT scores, patch sizes, or number of patches were excluded from the improvement part of the analysis.

Results

Patient characteristics

There are in total 6617 patients in this cohort. Average age is 48 years (SD=18). Females consist of 73%. Patients are predominantly white (54%). AA patients (n=1127) have an average age of 41 years (SD=18). Females consist of 61%. White patients represent 41.3%, followed by Asian (14.1%), Hispanic or Latino (10.9%), and African American (6.2%). Non-AA patients (n= 5490) have an average age of 49 (SD=18). Females consist of 74%. White patients represent 57%, followed by Asian (8.2%), Hispanic or Latino (8.1%), and African American (6.6%) (Table 1).

	Alopecia areata	Not alopecia areata
Total (%)	1127 (17%)	5490 (83%)
Average age (yr)	41	49
Statins (%)	129 (1.9%)	1019 (15%)
Not taking statins (%)	998 (15%)	4471 (68%)
Sex		
Female (%)	692 (11%)	4087 (62%)
Male (%)	435 (6.6%)	1403 (21%)
Race		
American Indian (%)	4 (0.06%)	17 (0.26%)
Asian (%)	159 (2.4%)	448 (6.8%)
African American (%)	70 (1.1%)	363 (5.5%)
Pacific Islander (%)	3 (0.05%)	5 (0.08%)
White (%)	466 (7.0%)	3128 (47%)
Multiple races (%)	12 (0.18%)	30 (0.45%)
Other (%)	205 (3.1%)	774 (12%)
Unknown (%)	208 (3.1%)	725 (11%)
Ethnicity		
Cuban (%)	0 (0%)	3 (0.05%)
Hispanic or Latino (%)	123 (1.9%)	447 (6.8%)
Spanish (%)	12 (0.18%)	38 (0.57%)
Mexican (%)	14 (0.21%)	41 (0.62%)
Puerto Rican (%)	1 (0.02%)	1 (0.02%)
Not Hispanic or Latino (%)	776 (12%)	4220 (64%)
Unknown (%)	201 (3.0%)	740 (11%)

Table 1. Alopecia areata. Patient characteristics. Patients are counted by category and their percentage of the total are represented in parentheses. Total patients = 6617. Average age = 48 (SD=18). Females 73%. White 54%, African American 6.6%, Hispanic 8.7%, Asian 9.2%.

Analytical Results

Predictors of AA

The factor contributing most to a diagnosis of AA is age, as younger patients <20 yr old are more likely to be diagnosed with AA (<12 yr: RR=7.0, 95%CI=[4.74,10.36]), while older patients greater than 40 yr are less likely to be diagnosed with AA (41-50 yr: RR=0.26, 95%CI=[0.23,0.30]; >50yr RR=0.69, 95%CI=[0.62, 0.75]) (Figure 1). Sex and race are slightly worse predictors of AA, as males (RR=1.51, 95%CI=[1.38,1.65]) and all races except for white are slightly more likely to be diagnosed with AA (Figure 1). Taking statins of any intensity (Table 2) was associated with less AA (all statins: RR=0.6167, 95%CI=[0.5188, 0.738], low intensity: RR=0.44, 95%CI=[0.21, 0.88], moderate intensity: RR=0.57, 95%CI=[0.45, 0.72], high intensity: RR=0.63, 95%CI=[0.45, 0.88], statin + ezetimibe: RR=1.04, 95%CI=[0.24, 4.51]), while receiving intralesional triamcinolone injections was associated with more AA (RR=6.41, 95%CI=[5.76,7.13]) (Figure 1). Of note, older patients were more likely to be taking statins than younger patients (Figure 2).

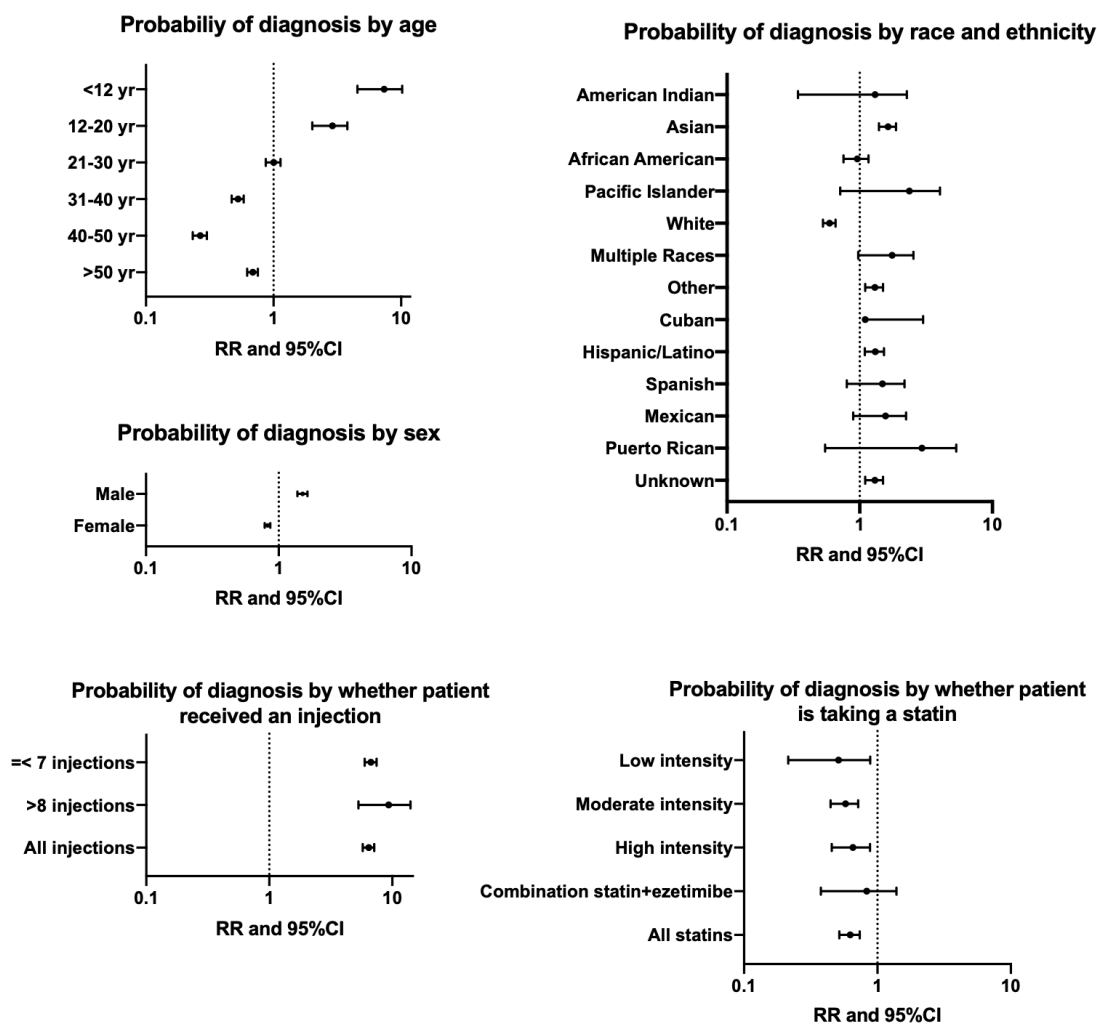


Figure 1. Alopecia areata. Probability of diagnosis. Patients are split into categories and the observed frequencies are counted for those diagnosed with AA and those not diagnosed with AA in each category. Relative risk (RR) and 95% confidence interval (95%CI) are calculated from contingency tables and plotted on the x axis in forest plots.

The dotted line at “1” represents a RR of 1 or no difference between the observed frequency of those with AA and those without AA. Results are interpreted as statistically significant when the 95%CI line does not cross the marker at 1 ($p<0.05$). Overall, younger or male patients, all races except whites, and patients who received injections are more likely to have AA. Patients taking statins are less likely to have AA.

High-Intensity Statin	Moderate-Intensity Statin	Low-Intensity Statin
Atorvastatin 40–80 mg	Atorvastatin 10–20 mg	Simvastatin 10 mg
Rosuvastatin 20–40 mg	Rosuvastatin 5–10 mg	Pravastatin 10–20 mg
	Simvastatin 20–40 mg	Lovastatin 20 mg
	Pravastatin 40–80 mg	Fluvastatin 20–40 mg
	Lovastatin 40 mg	Pitavastatin 1 mg
	Fluvastatin XL 80 mg	
	Fluvastatin 40 mg bid	
	Pitavastatin 2–4 mg	

^aFrom: Stone NJ, Robinson JG, Lichtenstein AH et al. 2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Journal of the American College of Cardiology 2014;63:2889–934.

doi:10.1371/journal.pone.0154952.t001

Table 2. Alopecia areata. Statin intensity. High intensity, moderate intensity, and low intensity statins are categorized according to their median LDL-C reduction.

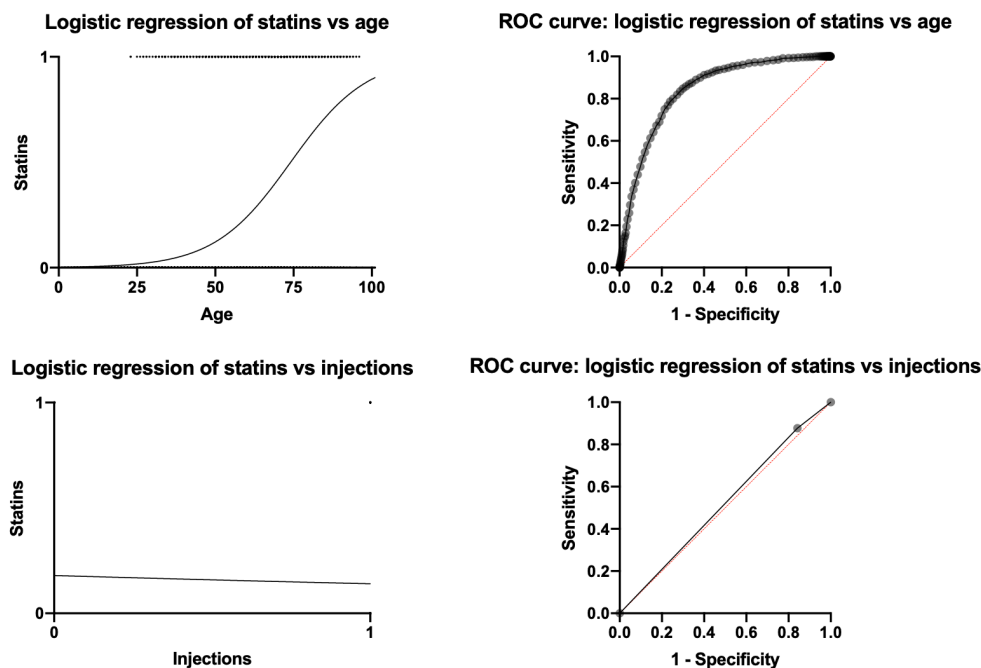


Figure 2. Alopecia areata. Statins and age are positively correlated. Scatterplots are created from patient data with statins (0=no, 1=yes) on the y axis and age (yr) and injections (0=no, 1=yes) on the x axes, respectively, and their

respective logistic regression curves are overlaid. ROC curves are next to their respective graphs. There is a high correlation between statins and age (AUC=0.84). In contrast, there is very low correlation between statins and injections (AUC=0.52).

Effect of statins

Statins have no independent effect on AA

While statins seem to be associated with less AA, logistic regressions demonstrate that the association is not much better than random (simple logistic regression: AA vs statins: AUC=0.54) (Figure 3). Removing statins from the variables has no effect on goodness of fit (multiple logistic regression: AA vs age, sex, statin, injection: AUC=0.78; AA vs age, sex, injection: AUC=0.78; AA vs age, sex, statins: AUC=0.64; AA vs sex, statins, AUC=0.63) (Figure 4, Figure 5).

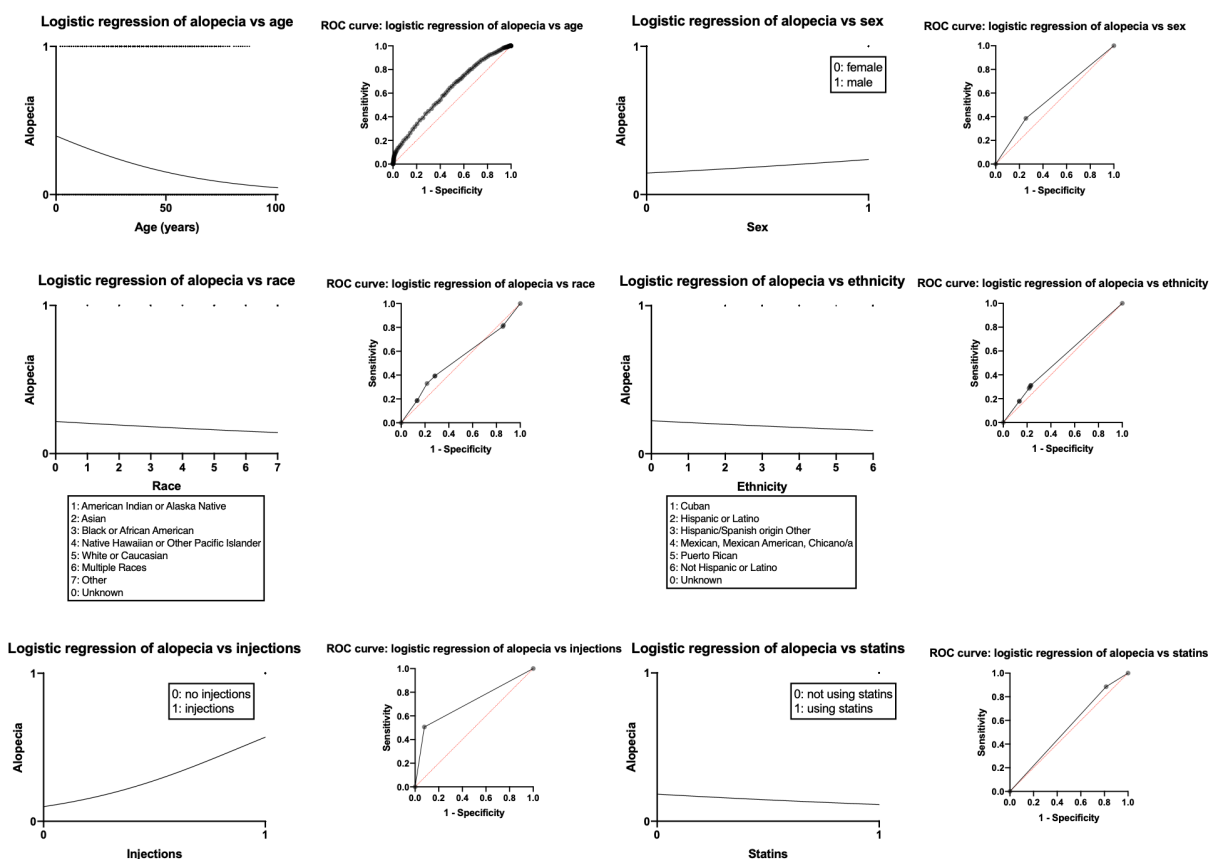
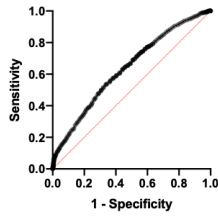
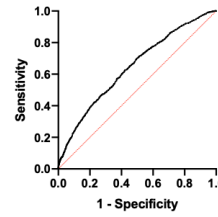


Figure 3. Alopecia areata. Simple logistic regressions and their ROC curves. Patient data are plotted on scatterplots with the y axis representing diagnosis of alopecia areata (0=no, 1=yes) and the x axis representing various categories (age, sex, age, race, ethnicity, injections, statins). The logistic regression curve or best fit curve is overlaid on the scatterplot. The ROC (receiver operating characteristic) curve is plotted next to its respective logistic regression plot. The ROC curve measures the diagnostic ability of the logistic regression curve (goodness of fit). The higher the area under the ROC curve (AUC), the better the fit. The red line represents a random fit (AUC=0.5). Overall, the injections logistic regression curve is best fit (AUC=0.71), demonstrating that patients are more likely to have AA if they had an injection. The age regression curve is the second best fit (AUC=0.62), demonstrating that younger patients are more likely to have AA. The regression curves for sex (AUC=0.57), race (AUC=0.53), ethnicity (AUC=0.54), and statins (AUC=0.54) are not much better than random.

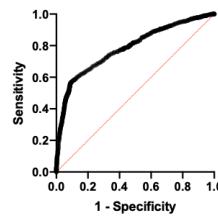
ROC curve: Multiple logistic regression of alopecia vs age and sex



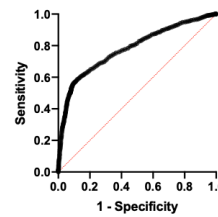
ROC curve: Multiple logistic regression of alopecia vs age, sex, race, ethnicity



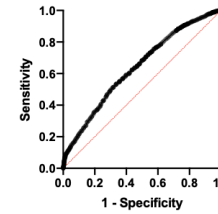
ROC curve: Multiple logistic regression of alopecia vs age, sex, statin, injection



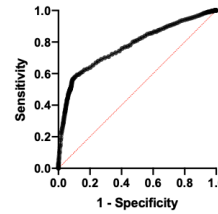
ROC curve: Multiple logistic regression of alopecia vs age, sex, injection



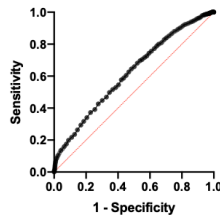
ROC curve: Multiple logistic regression of alopecia vs age, sex, statin



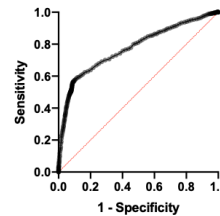
ROC curve: Multiple logistic regression of alopecia vs age, statin, injections



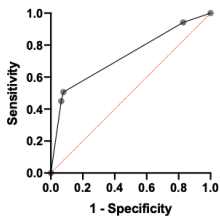
ROC curve: Multiple logistic regression of alopecia vs age and statin



ROC curve: Multiple logistic regression of alopecia vs age and injections



ROC curve: Multiple logistic regression of alopecia vs statin and injections



ROC curve: Multiple logistic regression of alopecia vs sex and statin

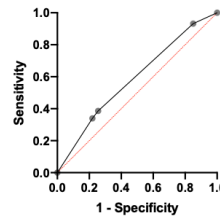
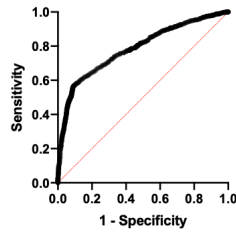
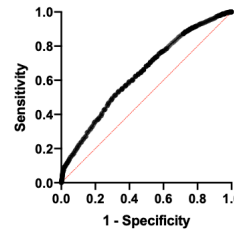


Figure 4. Alopecia areata. Multiple logistic regressions: ROC curves. This is a sample of curve fitting of various prediction models utilizing various factors. Patient data are plotted in accordance to AA outcome and multiple variables (not shown). Multiple logistic regression curves are calculated from each data set. ROC curves are plotted to measure the predictive ability of each multiple logistic regression curve (shown). Overall, the predictive ability is higher for AA vs age, sex, statins, injections (AUC=0.78), AA vs age, sex, injections (AUC=0.78), AA vs age, statins, injections (AUC=0.78), AA vs age and injections (AUC=0.78), and AA vs statins and injections (AUC=0.73). The predictive ability is lower for AA vs age and sex (AUC=0.63), AA vs age, sex, race, ethnicity (AUC=0.64), AA vs age, sex, statins (AUC=0.64), AA vs age and statins (AUC=0.62), and AA vs sex and statins (AUC=0.59).

ROC curve: Multiple logistic regression of alopecia vs age, sex, statin, injection



ROC curve: Multiple logistic regression of alopecia vs age, sex, statin



ROC curve: Multiple logistic regression of alopecia vs age, sex, injection

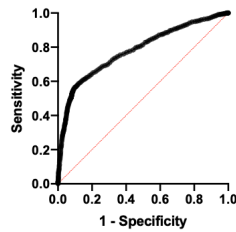
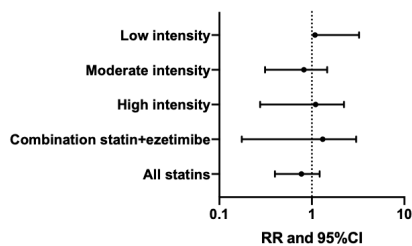


Figure 5. Alopecia areata. Statins do not affect model fit. Multiple logistic regressions (not shown) and their ROC curves (shown) are calculated from AA vs multiple variables. AA vs age, sex, statin, injection has good predictive ability (AUC=0.78). Removing injections from the variables decreases the model's predictive ability (AUC=0.64). Removing statins from the variables has no effect on model's predictive ability (AUC=0.78).

When patients were followed up on their SALT score, number of patches, or size of patches, between 1 month to 4 years, statins were not associated with improvement in AA (RR=0.73, 95%CI=[0.38, 1.4]; multiple logistic regression: AA vs age, sex, statins, injections: AUC=0.58) (Figure 6, Figure 7).

Probability of improvement of patients taking statins



Probability of improvement of patients receiving injections

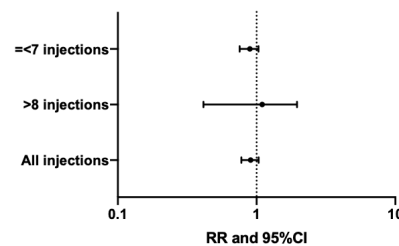
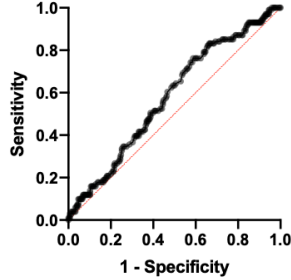
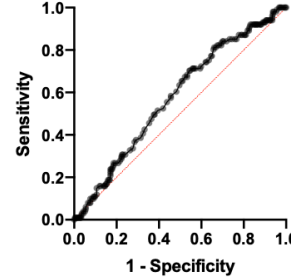


Figure 6. Alopecia areata. Probability of improvement of AA in those taking statins or receiving injections. Patients are split into categories. Two by two contingency tables are created from observed frequencies of those improved with intervention and those not improved (0=no, 1=yes). RR and 95%CI are calculated with the dot representing RR and line segment representing 95%CI. Overall, there is no significant difference in improvement of AA patients for those on statins of any intensity (RR=0.71, 95%CI=[0.4,1.2]) or those receiving injections (RR=0.92, 95%CI=[0.78, 1.1]).

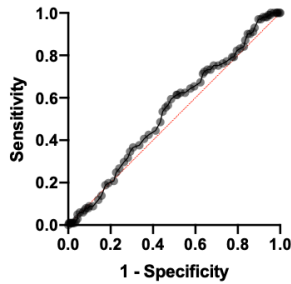
ROC curve: Multiple logistic regression of improvement vs age, sex, statins, injections



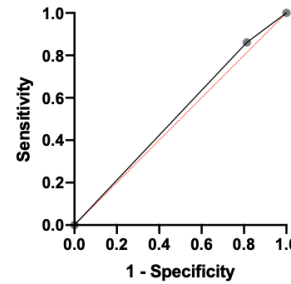
ROC curve: Multiple logistic regression of improvement vs age, statins, injections



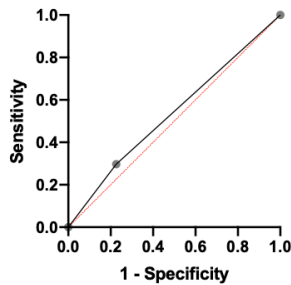
ROC curve: logistic regression of improvement vs age



ROC curve: logistic regression of improvement vs statins



ROC curve: logistic regression of improvement vs injections



ROC curve: logistic regression of statins vs injections

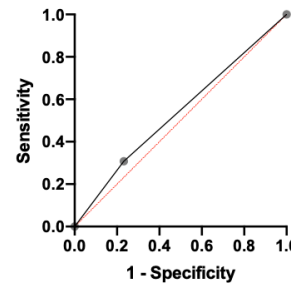
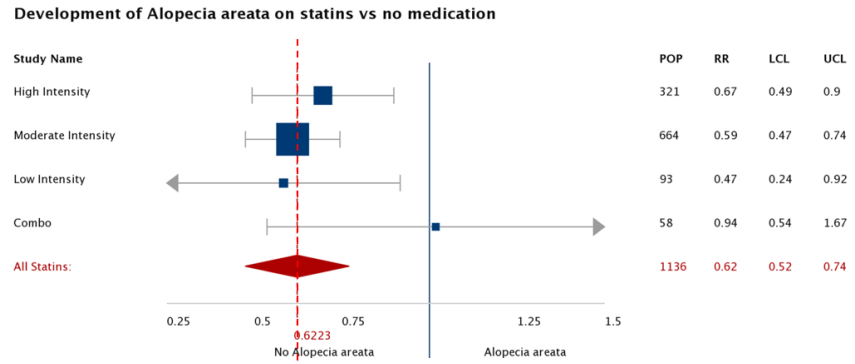


Figure 7. Alopecia areata. Goodness of fit curves for multiple logistic regressions of AA improvement vs multiple variables. Overall, the goodness of fit for various models is not much better than random: improvement vs age, sex, statins, injections (AUC=0.58), improvement vs age, statins, injections (AUC=0.58), improvement vs age (AUC=0.54), improvement vs injections (AUC=0.54), statins vs injections (AUC=0.54), improvement vs statins (AUC=0.52).

Age is a confounder

In our data, we noticed that older patients are more likely to be taking statins (statins average age=65 yr vs no statins average age=44 yr, $p=0$). Age is strongly associated with statins (simple logistic regression: statins vs age: AUC=0.84) (Figure 2). Age was a better predictor for AA than statins (simple logistic regression: AA vs age: AUC=0.62; AA vs statins, AUC=0.54; multiple logistic regression: AA vs age, sex, statins: AUC=0.64, AA vs sex and statins: AUC=0.59) (Figure 3, Figure 4). After age matching AA patients with controls, the association between statins and AA became weaker (Figure 8).

Before Age Matching



After Age Matching
Match ratio of 2

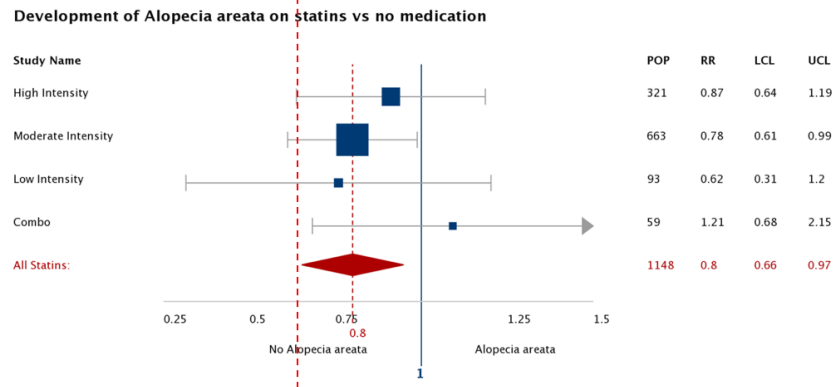


Figure 8. Alopecia areata. Age matching decreases effect of statins on AA. Before age matching, patients on statins are less likely to be diagnosed with AA (all statins RR=0.62, 95%CI 0.52-0.74). After age matching, patients on statins are less likely to be diagnosed with AA but the risk is approaching statistical non-significance (all statins RR=0.8, 95%CI 0.66-0.97). Patients on low and high intensity statins are not more or less likely to be diagnosed with AA. POP=population, RR=relative risk, LCL=lower confidence limit, UCL=upper confidence limit.

Discussion

The results of this large cohort study demonstrate that statins have no reliable therapeutic effect in alopecia areata, which is in favor of the null hypothesis that statins have no effect on AA. Based on this study, we therefore reject the alternative hypothesis that statins improve AA.

However, in this study, we also discovered that age can be a major confounder of the effect of statins on alopecia areata. Although statins do not appear to be associated with an improvement in alopecia areata, the implication is that it is not the whole story either. Older age affects AA chronicity and severity as older patients are more likely to have milder disease with higher chances of remission (Lyakhovitsky et al 2019). Older patients also tend to have decreased immune system responsiveness, statin metabolism, and medical comorbidities, which can affect statin pharmacokinetics (Fulop et al 2018). We should not conclude that statins do not work without controlling for age in previous or future studies.

In our current understanding of alopecia areata, we know that it can be caused by a collapse of multiple immune signaling pathways involving hair follicles losing immune privilege, increased JAK/STAT signaling, and Th2 and Th17. Numerous immune cells: CD8, CD4, NK, and dendritic, are implicated as well as numerous cytokines such as IFN gamma, TNF alpha, and IL-12 (Sutic et al 2023). Epigenetics, gut microbiome, nutritional deficiencies, and exposome are also involved, making this disease a complex interplay of immune processes. In our current understanding of statins, we know that different types of statins exert various anti-inflammatory effects including reducing T cell proliferation, MHC2 presentation to CD4 T cells, modulating IFN gamma, IL-12, Th1, and Th2, leukocyte adhesion, and portions of JAK/STAT signaling, though there has been very little novel research on statin mechanisms of action in the past 10 years (Greenwood et al 2013). Thus, while statins may not have a significant effect on alopecia areata improvement, the disease may require more potent or more specific immune disruption, which is why JAK inhibitors have been working so well (Lambiase et al 2025). The external validity of this study is high in that it is conducted in a community based setting and its results can be generalized to the larger community.

This study has several limitations: since this study involves retrospective chart review, the study design has limited ability to determine causality, although mitigation was attempted by statistical methods. Another major limitation was that co-morbidities which could have affected statin efficacy were not considered given incomplete data. Finally, the duration of statins use was not followed up on given incomplete data from many patients.

In future studies about statins and alopecia areata, age must be controlled for before making causal claims.

Conclusion

Perceived improvement of statins on AA is confounded by age. Our data do not support statins as an effective therapy for AA. Some limitations of this study are that it cannot explain causality, and we did not consider comorbidities or duration of statin use. Further studies which control for age and consider comorbidities and duration of statin use are warranted to determine the effectiveness of statins on AA and explore shared pathophysiological mechanisms.

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Abbreviations and acronyms

AA=Alopecia areata

SALT= Severity of Alopecia Tool

DNCB=Dinitrochlorobenzene

JAK/STAT=Janus kinase / Signal Transducer and Activator of Transcription

PRP=platelet rich plasma

Treg=regulatory T cell

RR=relative risk

95%CI=95% confidence interval

AUC=area under the curve

LDL-C=low density lipoprotein-cholesterol

ROC=receiver operating characteristic

POP=population

LCL=lower confidence limit

UCL=upper confidence limit

Th1=T helper 1

Th17=T helper 17

Th2=T helper 2

CD8=cluster of differentiation 8" (cytotoxic T cells)

CD4="cluster of differentiation 4" (helper T cells)

NK=natural killer

IFN=interferon

TNF=tumor necrosis factor

IL=interleukin

MHC2=Major Histocompatibility Complex class II molecules

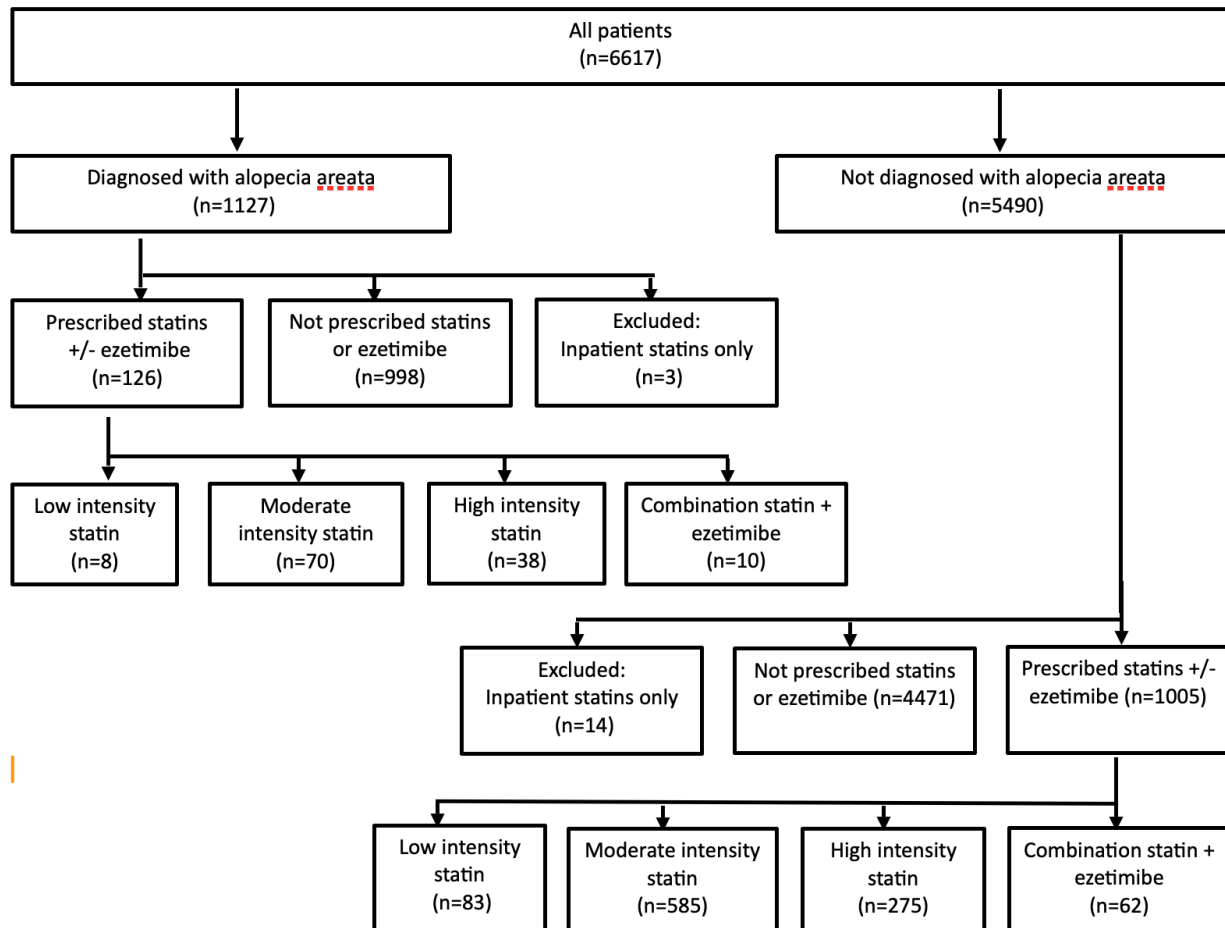
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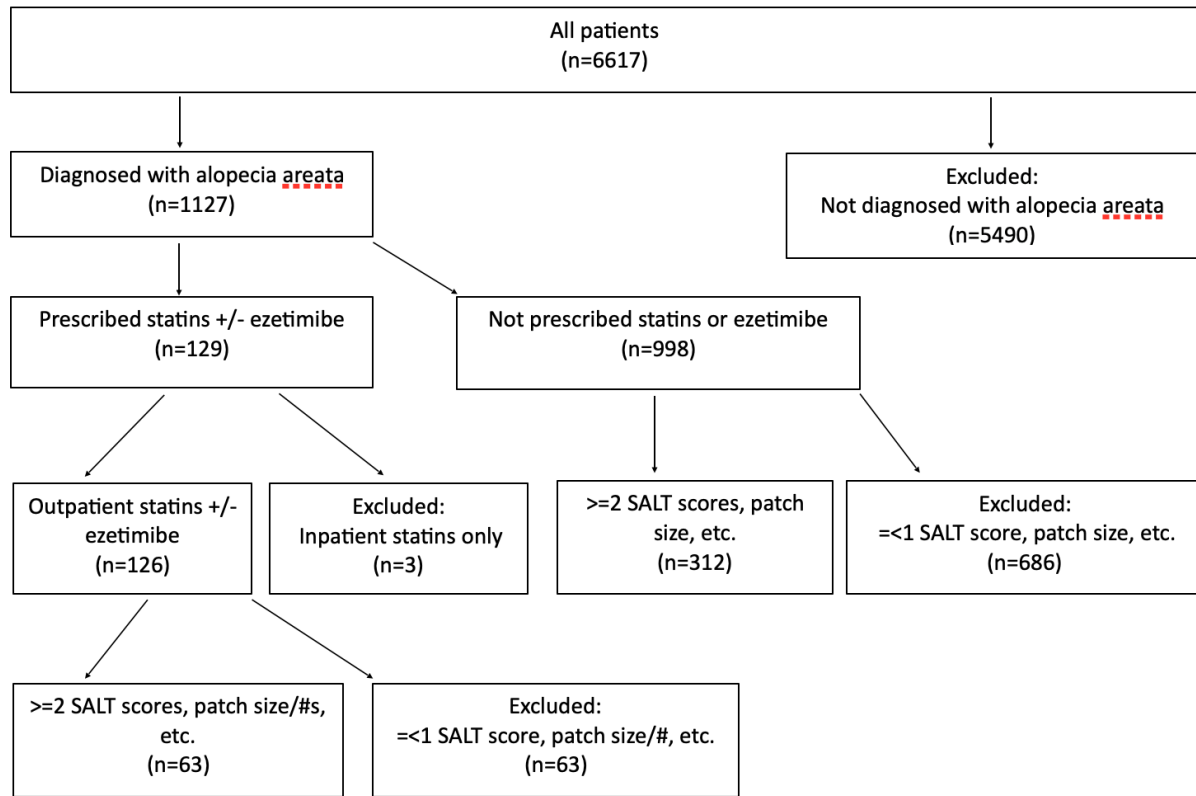
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Supplement



Supplemental Figure 1. Alopecia areata. Study design. Longitudinal retrospective cohort study. Patients are split into two groups: alopecia and no alopecia. Patients are observed to be on statin or no statins. Statins are categorized by intensity. Inpatient patients who only received statins while in the hospital are excluded because this study looks at outpatient statins over a longer duration.



Supplemental Figure 2. Alopecia areata. Study design of improvement of AA. Patients are split into those diagnosed with AA and those not diagnosed with AA. Patients without AA are excluded. Patients with AA are categorized according to whether they received statins. Patients who received inpatient statins only are excluded given that this study follows statin effects over a longer duration. Electronic medical records were reviewed for patients on outpatient statins and patients not on statins. Patients who had ≤ 1 SALT score, patch size (cm^2), patch number, or no qualitative descriptions of improvement are excluded because change cannot be calculated.

Prediction Model

$$\text{Logit}[P(Y=1)] = \ln\{P(Y=1)/P(Y=0)\} = \beta_0 + \beta_1*B + \beta_2*C + \beta_3*D + \beta_4*E + \beta_5*B*C + \beta_6*B*D + \beta_7*B*E + \beta_8*C*D + \beta_9*C*E + \beta_{10}*D*E + \beta_{11}*B*C*D + \beta_{12}*B*C*E + \beta_{13}*B*D*E + \beta_{14}*C*D*E$$

Parameter estimates	Variable	Estimate	Standard error	95% CI (profile likelihood)	P value	Significance
β_0	Intercept	-0.8568	0.1673	-1.187 to -0.5307	<0.0001	****
β_1	B : Age	-0.03376	0.003932	-0.04156 to -0.02614	<0.0001	****
β_2	C : Sex	-0.2344	0.2737	-0.7722 to 0.3011	0.3917	
β_3	D : Statins	-2.583	0.8873	-4.402 to -0.9235	0.0036	**
β_4	E : Injections	2.403	0.3071	1.807 to 3.012	<0.0001	****
β_5	B*C	0.01538	0.007079	0.001422 to 0.02918	0.0299	*
β_6	B*D	0.04209	0.01303	0.01718 to 0.06824	0.0012	**
β_7	B*E	0.004698	0.006560	-0.008239 to 0.01750	0.4739	
β_8	C*D	1.638	1.187	-0.6878 to 3.979	0.1676	
β_9	C*E	0.4630	0.5414	-0.5921 to 1.532	0.3925	
β_{10}	D*E	1.135	1.354	-1.510 to 3.821	0.4019	
β_{11}	B*C*D	-0.02500	0.01891	-0.06238 to 0.01188	0.1862	
β_{12}	B*C*E	-0.01667	0.01311	-0.04251 to 0.008936	0.2035	
β_{13}	B*D*E	-0.02357	0.02045	-0.06411 to 0.01635	0.2492	
β_{14}	C*D*E	0.7302	0.6062	-0.4547 to 1.925	0.2284	

<u>Model diagnostics</u>	Degrees of Freedom	AICc	Negative log likelihood value	Model deviance, G squared
Intercept-only model	6616	6042	3020	6040
Selected model	6602	4814	2392	4784

Area under the ROC curve

Area	0.7848
Std. Error	0.008221
95% confidence interval	0.7687 to 0.8009
P value	<0.0001

Pseudo R squared

Tjur's R squared	0.2338
McFadden's R squared	0.2080

Hypothesis tests

	Statistic	P value
Hosmer-Lemeshow	24.79	0.0017

Supplemental Table 1. Alopecia areata. Prediction model of best fit. The multiple logistic regression model of best fit (AUC=0.78) is AA vs age, sex, statins, and injections. The curve is based on log odds of AA (logit). Parameters and two- and three-way interactions are estimated and 95%CI calculated. The parameters contributing most to the prediction model are age ($p<0.0001$), injections ($p<0.0001$), statins ($p=0.0036$), age and statins ($p=0.0012$), and age and sex ($p=0.0299$).