It is estimated that >30 million American adults, or 9.4% of the U.S. population, had diabetes in 2015, of which ~7.2 million were undiagnosed (1). In 2015, diabetes was the seventh leading cause of death in the United States, with atherosclerotic cardiovascular disease (ASCVD) being the primary reason for morbidity and mortality among patients with diabetes. ASCVD, defined as a history of myocardial infarction (MI), stable or unstable angina, acute coronary syndromes, coronary or other arterial revascularization, stroke or transient ischemic attack, or peripheral arterial disease (PAD) presumed to be of atherosclerotic origin, is the greatest contributor to the direct and indirect costs of diabetes (2). The absolute risk of cardiovascular disease (CVD) more than doubles in patients diagnosed with diabetes, and ~80% of patients with diabetes die of CVD (3–5). Of patients diagnosed with diabetes, women have a 25% greater risk of...
stroke and a 40% greater risk of developing heart disease than men (6).

The HMG-CoA (3-hydroxy-3-methylglutaryl-coenzyme) reductase inhibitors, commonly known as statins, have been proven in several studies to decrease LDL cholesterol and major cardiovascular events in patients with diabetes with or without preexisting vascular disease (7–9). The CARDS (Collaborative Atorvastatin Diabetes Study) trial showed a 37% reduction in the primary prevention of cardiovascular events among patients with diabetes (8). The PROSPER (Pravastatin in Elderly Individuals at Risk of Vascular Disease) trial demonstrated significant reductions in LDL cholesterol, coronary heart disease (CHD) death, and nonfatal MI risk in patients with and without preexisting vascular disease (10). Statins have been shown to reduce the progression of PAD, amputations, and ischemic ulcers (7).

Literature suggests that statins may have a role in the prevention or treatment of microvascular complications associated with diabetes (11–15), but large prospective studies on this subject area are lacking.

The American Diabetes Association’s (ADAs) Standards of Medical Care in Diabetes—2017, similar to the 2013 American College of Cardiology (ACC)/American Heart Association (AHA) Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults (16), began recommending statin therapy for the majority of patients with diabetes, shifting away from targeting specific LDL cholesterol levels. The 2017 ADA standards defined “ASCVD risk factors” to help determine a recommended statin intensity for individual patients. These risk factors included LDL cholesterol ≥100 mg/dL, high blood pressure, smoking, chronic kidney disease (CKD), albuminuria, and family history of premature ASCVD. The only group of patients for which these guidelines did not recommend a statin was patients <40 years of age with no ASCVD risk factors. The guidelines recommended either a moderate- or high-intensity statin with or without ezetimibe in all patients with diabetes ≥40 years of age. The statin intensity and recommendation for ezetimibe depended on certain risk factors and age. For patients with a previous acute coronary syndrome and LDL cholesterol ≥50 mg/dL and those with a history of ASCVD who could not tolerate high-dose statin therapy, the use of ezetimibe was recommended. Patients with previous ASCVD were recommended to have a high-intensity statin regardless of age (2).

Studies have shown that pharmacist-led interventions are associated with significantly improved glycemic control in patients with diabetes (2,17–26), although research assessing pharmacists’ effects on appropriate statin prescribing in this patient population is lacking. The primary objective of this study was to assess the differences in statin prescribing between patients with diabetes who were managed by the pharmacy team and those managed by internal medicine providers at a large multispecialty private practice.

Secondary objectives were to assess the differences in statin prescribing between male and female patients, patients with and without ASCVD, patients 40–75 and >75 years of age, patients with and without a documented statin intolerance, and patients with and without a reason for a lack of appropriate statin therapy.

**Methods**

This retrospective observational study was conducted using the electronic health record at a large multispecialty outpatient practice. This privately owned medical practice includes internal medicine, cardiology, and family practice providers and also serves as a practice site for pharmacy faculty and residents from a nearby college of pharmacy. Patients of this practice were enrolled in pharmacy services by medical doctors, physician assistants, and nurse practitioners. Patients being referred for diabetes management have a wide range of glycemic control; some need general diabetes education and counseling, some are newly diagnosed and need initiation of therapy, and others have more complicated and established disease requiring more intensive medication dose titration and follow-up. Patients were included in the analysis if they were ≥40 years of age and had a diagnosis of diabetes. Patients in the pharmacy group had had at least two pharmacy visits during the previous 12 months and had a signed collaborative practice agreement (CPA). The CPAs permitted the pharmacist to initiate, adjust, or discontinue cholesterol medications as part of a comprehensive approach to diabetes management. Similarly, patients in the internal medicine group had had at least two internal medicine visits during the previous 12 months and had not participated in pharmacy diabetes services.

Patients enrolled in pharmacy services were reviewed for inclusion in the analysis. Once eligible pharmacy patients were identified, an equal number of internal medicine patients were randomly reviewed and matched for inclusion. Patients in the pharmacy group were seen by pharmacists or pharmacy residents, whereas those in the internal medicine group were seen by one of seven medical doctors or their respective physician assistants or nurse practitioners. Data were assessed to determine the appropriate-ness of statin prescribing per the 2017 ADA standards (Table 1). Statistical analysis was completed using SPSS Statistics, version 25.0 (IBM Corp., Armonk, N.Y.). Descriptive statistics were used to analyze patient characteristics and demographics, χ2 was used to analyze nominal data and between-group differences regarding appropriate statin prescribing, and unpaired t tests were used to analyze continuous variables, with statistical significance set at a P value of <0.05. Unless otherwise specified, the analysis included all patients in a
given subgroup, including those with and without a documented statin intolerance or a reason for a lack of appropriate statin therapy.

Results

A total of 176 patient charts were examined, with 88 patients in the pharmacy group and 88 patients in the internal medicine group. Baseline characteristics were similar between groups, except significantly more patients in the internal medicine group than in the pharmacy group were >75 years of age (24 vs. 11 patients, respectively, \( P = 0.023 \)) (Table 2). No patients received a PSCK9 (protein convertase subtilisin/kexin type 9) inhibitor either before or during the study.

More patients in the pharmacy group were prescribed a statin of appropriate intensity per the 2017 ADA standards, although this difference was not statistically significant (47.7 vs. 34.1%, \( P = 0.092 \)). A majority of patients in both groups were indicated to receive a high-intensity statin (Table 3). Of the patients indicated for a high-intensity statin, significantly more patients in the pharmacy group than in the internal medicine group received an appropriate high-intensity statin (44.3 vs. 27.4%, \( P = 0.03 \)).

Of the total patient population, significantly more males than females were prescribed appropriate statin therapy, regardless of ASCVD history. Significantly more patients from the pharmacy group who were either female, aged 40–75 years, or had no history of ASCVD received appropriate statin therapy compared to patients in the internal medicine group (Table 4). Of the total patient population, patients with a history of ASCVD were more likely to be prescribed an appropriate statin than those without a history of ASCVD (50.8 vs. 35.7%, \( P = 0.074 \)), although this difference was not statistically significant. No statistically significant differences were observed between the internal medicine and pharmacy groups regarding documented statin intolerance or a reason for a lack of appropriate therapy (Table 5). However, if patients who were prescribed inappropriate statins for documented reasons (e.g., the patient had an acceptable lipid panel while taking a lower-than-recommended statin intensity) or because of statin intolerances were counted as receiving an appropriate statin, significantly more patients with ASCVD received an appropriate statin (78.7 vs. 62.6%, \( P = 0.044 \)).
**Discussion**

This study demonstrated that pharmacist-managed patients were more likely to receive appropriate statin therapy according to the 2017 ADA standards than those managed by internal medicine providers, although this difference was only statistically significant for patients for whom high-intensity statins were indicated. The lack of a statistically significant difference could potentially be the result of the study’s small sample size. However, there was a trend toward improved statin prescribing in the pharmacy group compared to the internal medicine group that we feel is meaningful. This trend shows that pharmacists are valuable additions to the diabetes treatment team, not only for glycemic control but also for improvement of statin prescribing practices. These findings indicate that more research is needed on this topic.

This analysis also demonstrated that males treated at this practice were significantly more likely to receive appropriate statin therapy than females. These results are consistent with a previous study by Virani et al. (27), who used the Department of Veterans Affairs administrative data sources and found sex-related disparities in the receipt of statin and high-intensity statin therapy in patients with CVD. Virani et al. found that females with CVD were less likely to receive statin therapy (57.6 vs. 64.8%, \(P < 0.0001\)) and less likely to receive high-intensity statin therapy (21.1 vs. 23.6%, \(P < 0.0001\)) than males, although the appropriateness of statin therapy was not reported (27).

In the present study, both pharmacy and internal medicine groups had low rates of appropriate statin prescribing in female patients, but significantly more female patients in the pharmacy group received appropriate therapy than in the internal medicine group. It is unclear why practitioners were less likely to prescribe appropriate statin therapy to female patients with diabetes. Providers may not be aware of recent literature indicating that, although women have a lower risk of CVD in the general population, women with diabetes are at a higher risk for CVD than their male counterparts. Meta-analyses conducted predominantly in patients with type 2 diabetes have concluded that women have a significantly higher risk of both CHD and stroke than males (28, 29). Another meta-analysis regarding patients with type 1 diabetes demonstrated that women have a greater risk of CHD, stroke, and all-cause mortality (30). Statins have demonstrated a similar benefit for primary and secondary prevention in both sexes (31), although past evidence has shown women receive poorer cardiovascular care than men (32). Our study did not examine whether female patients’ preferences or past reported side effects affected this prescribing practice disparity. Of note, previous studies have not demonstrated a higher incidence of side effects in females for either primary or secondary prevention (33, 34).

The findings of this study showed that significantly more patients aged 40–75 years and patients without a history of ASCVD in the pharmacy group received appropriate statin therapy than those in the internal medicine group. These patient populations may traditionally be seen as

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**TABLE 3. Statin Intensity Prescribed Appropriately**

<table>
<thead>
<tr>
<th>Statin Intensity</th>
<th>Pharmacy ((n = 88))</th>
<th>Internal Medicine ((n = 88))</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate</td>
<td>2 of 2 (100)</td>
<td>1 of 1 (100)</td>
<td>NA</td>
</tr>
<tr>
<td>Moderate or high</td>
<td>4 of 6 (66.7)</td>
<td>6 of 9 (66.6)</td>
<td>0.999</td>
</tr>
<tr>
<td>High or moderate plus ezetimibe</td>
<td>1 of 1 (100)</td>
<td>3 of 5 (60)</td>
<td>0.999</td>
</tr>
<tr>
<td>High</td>
<td>35 of 79 (44.3)</td>
<td>20 of 73 (27.4)</td>
<td>0.030</td>
</tr>
</tbody>
</table>

*Data expressed as \(n\)%.*

**TABLE 4. Percentages of Patient Subgroups Who Were Prescribed Appropriate Statin Therapy**

<table>
<thead>
<tr>
<th>Patient Subgroup</th>
<th>Pharmacy ((n = 88))</th>
<th>Internal Medicine ((n = 88))</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males</td>
<td>56.3</td>
<td>50.0</td>
<td>0.539</td>
</tr>
<tr>
<td>Females</td>
<td>37.5</td>
<td>15.0</td>
<td>0.022</td>
</tr>
<tr>
<td>Patients with ASCVD history</td>
<td>54.2</td>
<td>48.6</td>
<td>0.674</td>
</tr>
<tr>
<td>Patients without ASCVD history</td>
<td>45.3</td>
<td>23.5</td>
<td>0.015</td>
</tr>
<tr>
<td>Patients aged 40–75 years</td>
<td>46.8</td>
<td>29.7</td>
<td>0.039</td>
</tr>
<tr>
<td>Patients aged &gt;75 years</td>
<td>54.5</td>
<td>45.8</td>
<td>0.632</td>
</tr>
</tbody>
</table>

**TABLE 5. Documentation for Lack of Appropriate Statin Therapy**

<table>
<thead>
<tr>
<th>Reason for Lack of Appropriate Statin Therapy</th>
<th>Pharmacy ((n = 46))</th>
<th>Internal Medicine ((n = 58))</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Documented reasoning for lack of appropriate statin therapy</td>
<td>20 (43.5)</td>
<td>23 (39.7)</td>
<td>0.176</td>
</tr>
<tr>
<td>Documented intolerance to statin therapy</td>
<td>12 (23.9)</td>
<td>9 (15.5)</td>
<td>0.999</td>
</tr>
<tr>
<td>Neither documented reasoning for lack of appropriate statin therapy nor intolerance to statin therapy</td>
<td>24 (52.2)</td>
<td>32 (55.2)</td>
<td>0.761</td>
</tr>
</tbody>
</table>

*Data expressed as \(n\)%.*
having lower risk than older patients or patients with a history of ASCVD, despite guideline recommendations (2,16), and this belief could lead to a lower perceived urgency in prescribing recommended statin therapy. The pharmacy team at this practice may be more aggressive in following guideline recommendations for statin therapy than the internal medicine team. This may be the result of the pharmacy team having more appointment time to provide more comprehensive diabetes management, including cholesterol management.

Despite differences between the internal medicine and pharmacy groups and sex disparities, overall appropriate statin prescribing per the 2017 ADA standards in patients with diabetes was low at this practice. We identified potential reasons for this finding. First, prescribers may not have been aware of current ADA recommendations due to the annual revision of these guidelines. To address this issue, perhaps the pharmacists at this practice could host an annual update on ADA guidelines for prescribers. Second, some prescribers may be following other cholesterol guidelines for their patients with diabetes, such as the 2013 ACC/AHA guidelines (16). However, both the ADA and the ACC/AHA guidelines agree that patients with ASCVD should be prescribed a high-intensity statin, yet this prescribing practice remains low. Some of the patients in this study may have been candidates for PSCK9 inhibitors, which may be another area of improvement for this practice. Additionally, we posit that some of the patients studied may have truly had a statin intolerance, or that their provider had a reason for a lack of appropriate statin therapy, but that these instances were not documented. Although a higher percentage of pharmacy patients who were not prescribed appropriate statin therapy had a documented intolerance or reason for a lack of appropriate therapy than the internal medicine patients, this was a nonsignificant trend, and both groups can improve their documentation in these scenarios.

This study is not without its limitations. First, it only examined statin prescribing and did not include analysis of adherence to statin therapy or outcomes related to these prescribing practices. Given the observational nature of our analysis, we cannot exclude the possibility of confounders. Because this study was completed at one private practice with a patient population that was largely white and older, these results are not necessarily generalizable to all practice settings. Furthermore, we did not show statistical significance in some areas of the study, potentially because of our limited sample size. For patients in the pharmacy group, we did not examine whether the appropriate statin was initiated by the pharmacist or by the internal medicine prescriber. The fact that significantly more patients in the internal medicine group versus the pharmacy group were >75 years of age could be a potential limitation of the analysis. However, statin recommendations per these guidelines were based on age, accounting for this difference. The number of patients with CKD at baseline was reported, but the stage of CKD was not, which could be another potential limitation. Of note, although these guidelines identify CKD as an ASCVD risk factor, they do not note how the stage of CKD would affect this risk. Additionally, the ADA updates its diabetes guidelines frequently, and this study was completed using the 2017 guidelines, which are now out of date. Of note, the ADA guidelines from 2018, the year the present data were reviewed, were less specific and left more decisions up to the provider, yet remained quite similar to those from 2017 (35). Finally, although all eligible pharmacy patients were included in the study, only a random sampling of the same number of internal medicine patients were examined, which may have affected results.

Conclusion
No statistically significant differences between the pharmacy group and the internal medicine group were observed in the appropriateness of overall statin use in patients with diabetes per the 2017 ADA Standards of Care guidelines. However, among patients for whom a high-intensity statin was indicated, female and younger patients and those who did not have a history of ASCVD were significantly more likely to receive an appropriate statin in the pharmacy group than the internal medicine group. By including pharmacy services in primary care practice settings and allowing pharmacists to help manage and maximize treatment of hyperlipidemia via comprehensive CPAs, prescribing practices could be improved. Overall, appropriate statin prescribing remains low in all studied patient groups, and improvement of statin prescribing practices should be a priority for diabetes treatment teams, especially for patients with diabetes and a history of ASCVD.

Acknowledgments
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Duality of Interest
No potential conflicts of interest relevant to this article were reported.

Author Contributions
J.M.H. researched and analyzed data and wrote the manuscript, including discussion. R.A.F. reviewed and edited the manuscript, contributed to discussion, and analyzed data. N.S. reviewed and edited the manuscript and contributed to discussion. J.M.H. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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