Guideline Concordance of New Statin Prescriptions: Who Got a Statin?

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ABSTRACT

OBJECTIVES: Statins are recommended to reduce serum cholesterol in patients at risk for atherosclerotic cardiovascular disease. Despite the prevalence of statin use, little is known about the indications for new prescriptions. We assessed the concordance of new statin prescriptions in the Veterans Health Administration (VHA) compared with the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III, or ATP III) guidelines (the guidelines in force in 2012) and the American College of Cardiology (ACC)–American Heart Association (AHA) 2013 guidelines.

STUDY DESIGN: Cross-sectional study.

METHODS: We identified every patient who received a new prescription (no statin use in the prior year) in the VHA in 2012. Patients were excluded if they had incomplete data, triglycerides greater than 400 mg/dL, or fewer than 2 primary care visits to ensure adequate baseline data to calculate Framingham and ACC-AHA 2013 risk scores.

RESULTS: We identified 250,243 new statin prescriptions in 2012 in the VHA, with 121,081 meeting inclusion criteria. Among new prescriptions, 68% were prescribed for primary prevention and 32% were prescribed for secondary prevention. Among patients receiving new statins for primary prevention, 48% did not have an indication supported by the ATP III guideline and 20% did not have an indication supported by the ACC/AHA guideline. Overall, approximately 19% of patients may have received a statin for an indication not supported by either guideline.

CONCLUSIONS: Veterans are commonly prescribed statins for indications not supported by professional society guidelines. The finding of common use of statins outside established guidelines represents an opportunity to improve the quality and value of the healthcare delivery.

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Statins are recommended for the lowering of serum cholesterol levels in individuals at risk for, or who have, atherosclerotic cardiovascular disease (ASCVD). The Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III [ATP III]) has been issuing guidelines since 1988, and its last report was in 2004.[1-3] The American College of Cardiology (ACC)–American Heart Association (AHA) updated the ATP guidelines in 2013.[4]

Compared with ATP III, the ACC-AHA guidelines focused on evidence-based recommendations and expanded the number of people recommended to receive statin therapy. The greatest increase was among individuals without known ASCVD with lower levels of cardiovascular risk who would be taking statins for primary prevention.[5,6] This expansion of the population recommended for statin prescriptions occurred at a time of controversy about the benefits of statins for primary prevention and during the focus on the elimination of unnecessary procedures, tests, and medications through the Choosing Wisely Campaign.[7-9] The Veterans Health Administration (VHA), in particular, has also made a commitment to reduce misuse and overuse.

Several studies have shown undertreatment of patients recommended to receive statins by both the ATP III and ACC/AHA guidelines.[10-16] Prior examination of statin use in countries outside the United States suggests that overuse is also likely high.[17,18] Much less is known about the indications for new prescriptions and the concordance of statin prescriptions to guidelines, with only 1 small single-center study from 2001 that found high rates of overuse.[19]

To better understand the characteristics of patients receiving a new statin prescription, we set out to assess the concordance of new statin prescriptions in the VHA compared with the ATP III guidelines (the guidelines in force in 2012) and the ACC-AHA guidelines.

METHODS

Overview

We performed a national retrospective study of new statin prescriptions in the VHA in 2012 and examined concordance with the ATP III and ACC-AHA guidelines.

Data Sources

The VHA Pharmacy Benefits Management (PBM) database collects information on inpatient and outpatient medications dispensed at the VHA The Corporate Data Warehouse (CDW) non-VHA medications database includes provider-entered information about medications provided to patients outside the VHA. Data on comorbidities, habits (eg, tobacco abuse), laboratory data, and vital statistics were obtained from the CDW, MedSAS, Decision Support System, and VHA Fee Basis files.

Study Population

All patients 18 years or older who received any statin prescription at the VHA in 2012 were identified using the PBM database. Statins included lovastatin, simvastatin, fluvastatin, atorvastatin, pravastatin, rosuvastatin, and pitavastatin. At this stage, the identified cohort included both patients with new statin prescriptions and patients with longstanding statin prescriptions. Next, to identify new users, patients were excluded if they had been on any statin dispensed in the VHA in the prior 12 months. Patients were also excluded if they had ever, according to data from the CDW database, received a statin outside the VHA. Patients who were on any other cholesterol agent including gemfibrozil, fenofibrate, nicotinic acid, cholestyramine, colestipol, colesevelam, ezetimibe, neomycin, or probucol in the prior 12 months were also excluded to ensure an accurate assessment of each patient's baseline lipid profile.

Patients were further excluded if they had fewer than 2 primary care visits in the 12 months prior to the index prescription, because we wanted to focus on patients receiving primary care in the VHA and because these patients did not have enough baseline data for characterization. Patients were also excluded if they either did not have a complete lipid panel in the 6 months prior to entering the cohort or had triglycerides over 400 mg/dL, to ensure that patients did not have an alternative indication for a statin as a result of elevated triglycerides.

Clinical Characteristics

Individuals were classified as receiving statins for secondary prevention if they had coronary artery disease (CAD), angina, stroke, transient ischemic attack (TIA), or peripheral artery disease (PAD). The *International Classification of Disease, Ninth Revision, Clinical Modification* (*ICD-9-CM*) and Current Procedural Terminology (CPT) were used to identify patients with CAD and PAD in the prior 10 years. A high-sensitivity stroke algorithm developed for VHA administrative data was used to identify patients with a history of stroke and TIA.[20] The presence of diabetes and hypertension in the 2 years prior to receipt of statins was identified using a combination of receipt of medications and *ICD-9-CM* codes.[21] The presence of other vascular risk factors, including carotid disease and abdominal aortic aneurysm, was identified using a combination of CPT codes and *ICD-9-CM* codes.[22,23] The *ICD-9-CM* codes, CPT codes, and medications used to construct these comorbidities are provided in the **eAppendix** [**eAppendices** available at **ajmc.com**]. We used several sources of data to assess current smoking status. Patients were considered current tobacco smokers if they had evidence of current smoking from the electronic clinical reminders data (VHA health factors file), consults related to smoking services, or outpatient clinic visits related to smoking cessation programs in the year prior to receiving a statin.

Risk Calculators

We used age, sex, race, systolic blood pressure (SBP), presence of diabetes, use of blood pressure medication, total cholesterol, high-density lipoprotein cholesterol, and smoking status to calculate 10-year ASCVD risk at time of statin initiation using both the Framingham risk calculator (used in ATP III) and the ACC-AHA 2013 cardiovascular risk calculator.[24,25] Patients were classified as black, white, or unknown race. Thirty percent of patients had an unknown race and were categorized as white for the purpose of ASCVD risk calculation. The ACC-AHA calculator was developed for patients aged 40 to 79 years. Among our cohort, 10% of patients were older than 79 years. We classified these patients as being aged 79 years for the purpose of calculating a 10-year risk score. If more than 1 SBP measurement was available, an average of the 2 most recent values was used. If more than 1 lipid panel had been performed, the most recent in terms of time to the statin prescription was used. Smoking status was determined as described above.

Determination of Guideline Eligibility

Eligibility for statin therapy for primary prevention was assessed using the ATP III and ACC-AHA guidelines (**Table 1**), using

TAKEAWAY POINTS

New statin prescriptions at the Veterans Health Administration were reviewed using a cross-sectional study design. We found that statins are often prescribed for indications not supported by either the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) or the American College of Cardiology–American Heart Association 2013 guidelines.

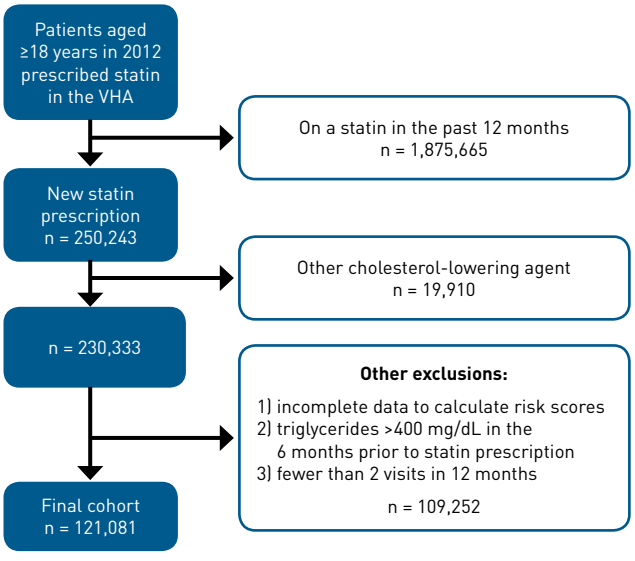
- Despite being commonly prescribed, little is known about indications for new statin prescriptions.
- Veterans are commonly prescribed statins for indications not supported by professional society guidelines.
- The identification of the use of statins outside established guidelines represents an opportunity to improve the quality and value of healthcare delivery.

TABLE 1. Summary of Guideline Eligibility Criteria Used to Assess Indications for New Statin Prescriptions

ATP III[a]	1. Secondary prevention and LDL-C of ≥100 mg/dL 2. LDL-C of ≥190 mg/dL 3. Diabetes and LDL-C ≥100 mg/dL 4. Framingham risk score and LDL-C level a. Risk of ≥20% and LDL-C of ≥100 mg/dL b. Risk of 10%-20% and LDL-C of ≥130 mg/dL with ≥2 risk factors including tobacco use, HTN, HDL-C <40 mg/dL, and age ≥45 for men and ≥55 for women c. Risk of <10% and LDL-C of ≥160 mg/dL with ≥2 risk factors
ACC/AHA	1. Secondary prevention 2. LDL-C of ≥190 mg/dL 3. Diabetes and LDL-C ≥70 mg/dL 4. ACC/AHA 10-year ASCVD risk of ≥7.5% and LDL-C of ≥70 mg/dL

ACC indicates American College of Cardiology; AHA, American Heart Association; ASCVD, atherosclerotic cardiovascular disease; ATP III, Adult Treatment Panel III; HDL, high-density lipoprotein cholesterol; HTN, hypertension; LDL, low-density lipoprotein cholesterol.
[a]The presence of earlier ASCVD in relatives could not be captured by our data to use when determining ATP III eligibility.

FIGURE. Patient Selection



VHA indicates Veterans Health Administration.

previously described hierarchical criteria.[2-4,6] Patients were classified as receiving a statin for secondary prevention if they had a history of CAD, TIA, PAD, or stroke.[2-4,6]

Statistical Analysis

Data analysis was descriptive in nature with means and standard deviations reported (R version 3.1, R Development Core Team). Patients who received statins for primary and secondary prevention were described. The patients who received a statin for primary prevention were further classified as to whether they would have been eligible based on the ATP III guideline, ACC/AHA guideline, only the ATP III or ACC/AHA guideline but not both, or neither guideline.

RESULTS

New Statin Prescriptions in the VHA

There were 2,125,908 patients at the VHA who received a statin in 2012, of whom 121,081 met the inclusion and exclusion criteria for analysis as a new statin prescription (**Figure**). Sixty-eight percent (82,600) of new statins were prescribed for primary prevention and 32% (38,481) for secondary prevention of ASCVD (**Table 2**). Patients receiving statins for primary prevention were, on average, younger than patients receiving statins for known ASCVD, and they had a lower incidence of diabetes and hypertension. Among patients who received a new statin for primary prevention, 6% were younger than 40 years and 8% were older than 75 years.

Guideline Concordance of Statins

Of the patients receiving new statins for primary prevention, 48% did not meet the ATP III guidelines and 20% did not fulfill the new ACC-AHA guidelines (**Table 3**). Twenty-eight percent of patients met ACC-AHA guideline recommendations but not the ATP III guidelines, and only 0.3% of patients met the ATP III guidelines and not the ACC-AHA guidelines. About one-third (31%) of the patients recommended by only the ACC-AHA guidelines had low-density lipoprotein cholesterol (LDL-C) levels of 70 to 99 mg/dL. No patients older than 75 years were recommended by only the ATP III guidelines. Nineteen percent of new statin prescriptions were for patients who were not recommended by either guideline to receive statin therapy. About a fifth (19%) of these patients were younger than 40 years, and 19% had a baseline LDL-C level of less than 70 mg/dL.

DISCUSSION

We found that, among veterans, the majority of new statins are prescribed for primary prevention. We found that a substantial proportion of new statin prescriptions would be considered outside the scope of current and former guideline recommendations.

Approximately 20% of patients with an LDL-C less than 70 mg/dL or who were currently smoking were prescribed statins, despite not meeting either guideline recommendation. In these instances, it is possible that clinicians overestimated the risk of, for example, tobacco use alone, and prescribed a statin regardless of overall risk. Although guideline-discordant prescriptions appear relatively common in this sample, the challenges are that not all clinical scenarios can be included in the guidelines and that clinical

judgment and clinician–patient shared decision making, including independent risk factor assessment, may explain a proportion of prescriptions outside guidelines.

The rates of potential statin overuse appear high, but the possible harms to the patient from overuse of statins are difficult to assess and highly debated. Until recently, there was not a consensus definition of statin intolerance.[26] The most commonly reported adverse effects (AEs) are muscle pains and weakness without elevations in creatinine kinase. The prevalence of these AEs in clinical practice is quite high (~20%), and these AEs are higher than those reported in randomized controlled trials.[27-29] A high rate of statin discontinuation has been reported, including approximately 50% of patients who stop statins within the first year of prescription; intolerance has been suggested to be the primary source of discontinuation.[28,30,31] Thus, the overall perception of negligible harms and the potential for a reduction in cardiovascular deaths may lead clinicians to overprescribe statins.[32,33]

For some individuals currently taking statins without guideline-based indications, there may be no clear benefits, and there are potential unintended consequences of these prescriptions that should also be taken into account.[34-36] For example, it has been documented that statin users experience more weight gain and become more sedentary than statin nonusers, possibly from the false sense of protection from taking a statin, leading individuals to ignore their diet and physical activity.[37] In these patients, efforts that are focused on reduction of risks including exercise, weight loss, tobacco cessation, and management of hypertension, rather than initiation of a cholesterol medication, should be the primary focus.[36]

Overprescribing statins certainly may also have financial implications for the health system, given the widespread use and the potentially long time horizon for younger patients prescribed statins for primary prevention. Currently, the "Choosing Wisely" campaign of the American Board of Internal Medicine Foundation, building on the work of the National Physicians Alliance, aims to list procedures, tests, and medications whose use should be questioned.[7,38,39] With an estimated $750 billion annually spent on unnecessary and inefficient care, identification and reduction of potential overuse is imperative.[40,41] However, de-implementation of statin use, even in populations not recommended by current guidelines, may be very challenging because of the perceived lack of harm and potential promise of long-term clinical benefit. Patients 40 years or younger may be committed to primary prevention for life. It is not at all clear whether such long-term use will be as effective or as harmless as is generally assumed.

Limitations and Strengths

This study has several limitations. We initiated this study in 2013 using 2012 data and planned to use existing guidelines. The issuance of new guidelines by the AHA in 2013 complicated our study but also provided an opportunity to use both guidelines in assessing care. Second, our study is based on national VHA data and there

TABLE 2. Characteristics of Patients Receiving New Statin Prescription in the VHA

Patient Characteristics	Patients Who Received Statin for Primary Prevention	Patients Who Received Statin for Secondary Prevention
Overall N	82,600 (68%)	38,481 (32%)
Age in years, mean	59	67
Male, %	92	97
Race, %		
White	50	72
Black	13	13.5
Unknown	37	14.5
Total cholesterol level, mean	216.3	188.7
HDL-C level, mean	45.7	43.6
LDL-C, %		
>190	8.8	4.4
160-190	21.8	10.5
130-159	33.5	21.7
100-129	22.7	27.7
70-99	9.5	22.5
<70	3.6	13
CAD, %	0	84
Stroke/TIA, %	0	6
Peripheral vascular disease, %	0	28
Diabetes, %	32	44
HTN, %	55	75
Other vascular risk factors, %		
AAA	1	1.5
Carotid disease	1	1.5
CHF, %	0.02	0.2
Tobacco abuse, %		
Current	32	33
Former	17	20
Never	22	17
Unknown	28	30
Framingham Risk Score, mean (SD)	14.5 (7.8)	–
2013 ACC/AHA Risk Score, mean, (SD)	19.8 (14)	–

AAA indicates abdominal aortic aneurysm; ACC, American College of Cardiology; AHA, American Heart Association; CAD, coronary artery disease; CHF, congestive heart failure; HDL-C, high-density lipoprotein cholesterol; HTN, hypertension; LDL-C, low-density lipoprotein cholesterol; SD, standard deviation; TIA, transient ischemic attack; VHA, Veterans Health Administration.

TABLE 3. Classification of Patients Receiving Statins by Guideline for Primary Prevention

	ATP III		AHA/ACC 2013		Limited Recommendation		Not Recommended by Either Guideline
	Recommended	Not Recommended	Recommended	Not Recommended	AHA/ACC Only, Not by ATP III	ATP III Only, Not by AHA/ACC 2013	
n (%)	43,296 (52%)	39,304 (48%)	66,286 (80%)	16,314 (20%)	23,259 (28%)	269 (0.3%)	16,045 (19%)
Male, %	94	90	94.8	80	96.2	85.5	79.9
Mean age, years (SD)	60.7 (11.4)	57.6 (12.5)	61.6 (10.7)	49.4 (12.3)	63.2 (0.1)	40.3 (6.7)	49.6 (12.4)
<40, %	4.3	8.3	2.9	19.8	0.7	52	19.3
40-75, %	85.9	84.7	87.6	76.2	90.3	48	76.7
>75 (%)	9.8	7	9.5	4	9	0	4
Total cholesterol level, mean (SD)	228 (40)	203 (42)	219 (42)	206 (47)	201 (38)	245 (24)	206 (47)
HDL-C level, mean (SD)	43 (12)	48 (14)	45 (13)	48 (15)	48 (14)	55 (21)	48 (15)
LDL-C level, %							
>190	16.8	–	11	–	–	–	–
160-190	21.1	22.7	20.2	28.3	19.1	61.7	27.8
130-159	33.7	33.2	33.2	34.6	32.3	37.1	34.6
100-129	28.4	16.5	24.8	13.9	18	1.1	14.1
70-99	–	19.9	10.7	4.5	30.5	–	4.6
<70	–	7.7	–	18.5	–	–	18.8
Diabetes, %	46.6	15.2	36.5	11.6	17.5	–	11.8
Current smoker, %	41	22.7	35.2	20.7	24.9	100	19.4
Framingham Risk Score, mean (SD)	17.9 (7.6)	10.7 (6.1)	16.3 (7)	6.7 (5.9)	13.4 (4.6)	14.2 (5.6)	6.61 (5.8)
2013 ACC/AHA Risk Score (mean)	25 (14)	14 (12)	22.8 (13)	7.8 (11)	18.2 (10.6)	5.9 (1.1)	7.9 (11)

ACC indicates American College of Cardiology; AHA, American Heart Association; ATP III, Adult Treatment Panel III; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; SD, standard deviation.

may have been some under-recognition of risk factors, including family history used to calculate risk in the ATP III guidelines, and race used to determine risk in the ACC/AHA guidelines, because individuals of unknown race were assumed to be white. However, the VHA health record information is among the richest data sources available and we used previously developed algorithms, when available, to characterize patients.[20,21,24] Third, we used VHA pharmacy data to ascertain new statin use. Some veterans may receive medications outside the VHA and may have been current users and not new users. In these patients, the cholesterol test may have been acquired while on a non-VHA statin, and therefore it would be incorrect to interpret the results as a baseline nonstatin value. We attempted to limit this possibility by requiring our cohort to have at least 2 VHA primary care visits prior to receipt of a statin prescription to largely confine our cohort to patients who receive primary care in the VHA. To assess how much non-VHA statin use affected our conclusions, we examined a random sample of 20 charts for patients whose receipt of statins was not concordant with either guideline. We did not identify any patients who received non-VA prescriptions in this group. To further evaluate non-VA statin use, we reviewed a random sample of 20 charts in patients with an LDL-C value of less than 70 mg/dL. We identified 4 patients (20%) in this select group who had evidence of non-VA statin use. These data suggest that the potential bias in the results related to missing data about non-VA medications is present but likely small in magnitude. Fourth, our sample is a predominantly male sample and may not be generalizable to statin use in the nonveteran US population. Finally, we have probably underestimated overuse of statins in the VHA because we did not examine statin use in populations that are unlikely to benefit, such as those who are receiving dialysis, have congestive heart failure, or have limited life expectancy. Overuse of statins among patients on established prescriptions—as opposed to new prescriptions—may be more common because there may be inertia related to stopping medications.[42]

A major strength of the study is the population-based analysis of statin use in a national health system. By examining statin

use across the entire VHA system, we gain an understanding of national prescribing patterns much more so than would be possible in smaller studies.[10-15,17-19] By understanding national prescribing patterns, we can potentially identify high-value areas of quality improvement. Based on our study, increasing awareness among physicians about the lack of efficacy of statin use in young patients without ASCVD, or in patients with an LDL-C value of less than 70 mg/dL, might reduce inappropriate prescriptions and is a potential target to decrease overuse.

CONCLUSIONS

Low-value statin use is common in the VHA. The finding of common use of statins outside established guidelines represents an opportunity to improve the quality and value of the healthcare delivery. ■

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eAppendix

eAppendix Table 1. Identification of Comorbidities That Classified Patients as Receiving a Statin for Secondary Prevention

	***ICD-9-CM* Codes**	***ICD-9-CM* Procedure Codes**	**CPT Codes**
Coronary artery disease/Unstable angina/MI/CABG, Revascularization (any single code in prior 10 years).	410.xx, 411.xx, 412.x, 413.x, 414.x, 429.7, 429.71 429.79 996.03,	CABG codes 36.10, 36.11, 36.12, 36.13, 36.14, 36.15, 36.16, 36.17, 36.19, 36.2, v45.81 PCI codes 00.66, 36.06, 36.07, 36.09, v45.82 36.01-36.04	CABG codes 33510, 33511, 33512, 33513, 33514, 33516, 33517, 33518, 33519, 33521, 33522, 33523, 33533, 33534, 33535, 33536, 33572, 4110F, s2205, s2206, s2207, s2208, s2209 PCI codes 92973, 92980, 92981, 92982, 92984, 92995, 92996, G0290 G0291
Peripheral Vascular disease (any single code in prior 10 years).	440.2, 440.3, 440.4, 443.9	38.08, 38.09, 38.13 38.18, 38.19 39.25, 39.26 39.29, 39.50, 39.90	37220, 37221, 37222, 37223, 37224, 37225, 37226, 37227,37228, 37229,37230, 37231, 37232,37233, 37234, 37235
Stroke or TIA (Reker's high sensitivity algorithm adapted to include TIA)			
Admission or discharge primary diagnosis	362.32, 362.33, 362.34, 430.xx, 431.xx 432.xx 433.01 433.11, 433.21, 433.31, 433.81 433.91, 434.01,434.11, 434.91, 435.x 436.xx, 997.02		
Rehab Admission or discharge primary diagnosis is V57.xx (Rehabilitation) and any secondary diagnosis	342.xx 362.31 362.32 362.33 362.34 430.xx, 431.xx 432.xx 433.01, 433.11, 433.21, 433.31, 433.81, 433.91,		

	434.01,434.11, 434.91, 435.x, 436.xx, 997.02		
Admission or discharge primary diagnosis is 433.xx and 434.xx and any secondary diagnosis code	342.xx 362.31 362.32 362.33 362.34 430.xx, 431.xx 432.xx 433.01, 433.11, 433.21, 433.31, 433.81, 433.91, 434.01,434.11, 434.91, 435.x 436.xx, 997.02		

eAppendix Table 2. Other Vascular Risk Factors (Any Single Code in Prior 10 Years)

	***ICD-9-CM* Codes**	***ICD-9-CM* Procedure Codes**	**CPT Codes**
Carotid artery disease	433.1	00.61, 00.63, 38.12	35301, 37215, 37216
Abdominal aortic aneurysm	441.3, 441.5, 441.4, 441.9	38.34, 38.40, 38.44, 38.64, 39.52, 38.60, 39.25, 39.71, 39.78	

eAppendix Table 3. Comorbidities Constructed With *ICD-9-CM* Codes and Medications

Variables Extracted Using a Combination of Medications and *ICD-9-CM* Codes			
Diabetes	250.xx, 357.2, 366.41, 362.0, 962.3, E932.3	Insulin, Acarbose, Acetohexamide, Chlorpropamide, Exenatide, Glimepiride, Glipizide, Glyburide, Miglitol, Nateglinide, Pioglitazone, Pramlintide, Repaglinide, Rosiglitazone, Sitagliptin, Tolazamide, Tolbutamide	Evidence of *ICD-9-CM* code in 2 years prior to statin prescription or any medication fill.
Hypertension	401.x, 402.x, 403.x, 404.x, or 405.x		2 outpatient *ICD-9-CM* codes or 1 admission in prior 2 years or 1 *ICD-9-CM* code in past year and prescription of any antihypertensive listed below

Antihypertensive Medications Used to Construct Comorbidities

Thiazide diuretics	chlorothiazide chlorthalidone hydrochlorothiazide polythiazide (Renese) indapamide (Lozol) metolazone (Mykrox) metolazone (Zaroxolyn)
Loop diuretics	bumetanide (Bumex) furosemide (Lasix) torsemide (Demadex)
Potassium-sparing diuretics	amiloride (Midamor) triamterene (Dyrenium)
Aldosterone receptor blockers	eplerenone (Inspra) spironolactone (Aldactone)
Beta blocker	atenolol (Tenormin) betaxolol (Kerlone) bisoprolol (Zebeta) metoprolol (Lopressor) metoprolol extended release (Toprol XL) nadolol (Corgard) propranolol (Inderal) propranolol long-acting (Inderal LA)

	timolol (Blocadren)
Beta blocker with intrinsic sympathomimetic activity	acebutolol (Sectral) penbutolol (Levatol) pindolol (generic)
Combined alpha- and BBs	carvedilol (Coreg) labetalol (Normodyne, Trandate)
ACE Inhibitors	benazepril (Lotensin) captopril (Capoten) enalapril (Vasotec) fosinopril (Monopril) lisinopril (Prinivil, Zestril) moexipril (Univasc) perindopril (Aceon) quinapril (Accupril) ramipril (Altace) trandolapril (Mavik)
Angiotensin II antagonists	candesartan (Atacand) eprosartan (Teveten) irbesartan (Avapro) losartan (Cozaar) olmesartan (Benicar) telmisartan (Micardis) valsartan (Diovan)
CCBs—nondihydropyridines	diltiazem extended release (Cardizem CD, Dilacor XR, Tiazac) diltiazem extended release (Cardizem LA) verapamil immediate release (Calan, Isoptin) verapamil long acting (Calan SR, Isoptin SR) verapamil (Coer, Covera HS, Verelan PM)
CCBs—dihydropyridines	amlodipine (Norvasc) felodipine (Plendil) isradipine (Dynacirc CR) nicardipine sustained release (Cardene SR) nifedipine long-acting (Adalat CC, Procardia XL) nisoldipine (Sular)
Alpha-1 blockers	oxazosin (Cardura) prazosin (Minipress) terazosin (Hytrin)
Central alpha-2 agonists and other centrally acting drugs	clonidine (Catapres) clonidine patch (Catapres-TTS) methyldopa (Aldomet) reserpine (generic) guanfacine (Tenex)
Direct vasodilators	hydralazine (Apresoline) minoxidil (Loniten)
ACEIs and CCBs	Amlodipine-benazepril hydrochloride Enalapril-felodipine

	Trandolapril-verapamil
ACEIs and diuretics	Candesartan-hydrochlorothiazide (Atacand HCT) Eprosartan-hydrochlorothiazide Teveten-HCT) Irbesartan-hydrochlorothiazide Avalide) Losartan-hydrochlorothiazide Hyzaar) Olmesartan medoxomil-hydrochlorothiazide (Benicar HCT) Telmisartan-hydrochlorothiazide (Micardis-HCT) Valsartan-hydrochlorothiazide
BBs and diuretics	Atenolol-chlorthalidone (50/25, 100/25) Tenoretic Bisoprolol-hydrochlorothiazide (2Ziac Metoprolol-hydrochlorothiazide (Lopressor HCT) Nadolol-bendroflumethiazide (Corzide) Propranolol LA-hydrochlorothiazide (Inderide LA) Timolol-hydrochlorothiazide
Centrally acting drug and diuretic	Methyldopa-hydrochlorothiazide (Aldoril) Reserpine-chlorthalidone (Demi-Regroton, Regroton) Reserpine-chlorothiazide (Diupres) Reserpine-hydrochlorothiazide (Hydropres)
Diuretic and diuretic	Amiloride-hydrochlorothiazide (Moduretic) Spironolactone-hydrochlorothiazide (Aldactazide) Triamterene-hydrochlorothiazide (Dyazide, Maxzide)