Effectiveness of statins in Medicare-eligible patients and patients < 65 years using clinical practice data*

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SUMMARY

Objective: This study compared effectiveness of rosuvastatin (RSV) with other statins on lowering LDL-C and LDL-C goal attainment among Medicare-eligible patients (age ≥ 65 years) and patients with age < 65 years treated in usual clinical practice to provide evidence of real-world effectiveness of statins. Methods: Retrospective cohort study was conducted in patients, newly prescribed statin therapy during August 2003 to May 2005. Patient inclusion criteria: no prior prescription for dyslipidaemic medication in the preceding 12 months, continuously enrolled for ≥ 15 months and ≥ 90-day supply of statin. Effectiveness of RSV in reducing LDL-C and attaining LDL-C goal when compared with other statins was evaluated using multivariate regression, adjusting for baseline LDL-C, age, gender, smoking, hypertension, coronary heart disease (CHD), systolic blood pressure and therapy duration. Results: Adjusted percent LDL-C reduction was significantly greater (p < 0.05) with RSV (24.3% for ≥ 65 and 28.5% for < 65) compared with ATV (17.5%, 21.3%), SMV (14.8%, 18.4%), PRV (11.3%, 15.8%), FLV (10.7%, 20.6%) and LOV (13.3%, 14.4%). Among patients in both age groups at high or moderate CHD risk, a greater proportion of RSV patients attained LDL-C goal (76.0% for age group ≥ 65 years and 78.4% for age group < 65 years) vs. 50.5–73.0% for ≥ 65 and 51.3–71.5% for < 65 years of age on other statins (p < 0.0001). Conclusions: Rosuvastatin is more effective in lowering LDL-C in Medicare-eligible patients and patients < 65 years of age when compared with other statins in usual clinical practice. Moreover, RSV patients had higher LDL-C goal attainment rates when compared with other statins in high- and moderate-risk patients. The study results have implications for clinicians in selecting the optimal statin to meet individual patient care needs.

Introduction

Management of patients with hyperlipidaemia remains an important healthcare issue as coronary heart disease (CHD) continues to be the leading cause of mortality and morbidity in the United States (US) affecting 13 million Americans and costing $130 billion annually (1). The National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) guidelines highlighted the importance of aggressive hyperlipidaemia treatment by recommending LDL-C goal < 100 mg/dl for high-risk patients (2). In July 2004, an optional LDL-C goal < 70 mg/dl for very high-risk patients was recommended (3).

Investigations of patients treated with statins by community-based physicians are limited and indicate that treatment for hyperlipidaemia may be suboptimal (4–6) compared with clinical trial efficacy data (7–11). Reports indicate that many patients are not managed aggressively to reach ATP III goals, only 38–48% of patients in different health plans achieved goal (12,13) while only 23–24% of high-risk patients reached goal (14,15). With this gap in goal attainment, there is a need to determine if one statin is more effective than others in reducing LDL-C and attaining LDL-C goal so that physicians may optimise their patient outcomes.

Moreover, with the advent of Medicare D pharmacy benefits, older patients will potentially have greater access to statin therapy. Thus, clinicians need evidence regarding which statin is more effective for their Medicare-eligible patients (age ≥ 65 years) and patients < 65 years of age. This study was designed...
to determine the differential effectiveness of rosuvastatin (RSV) compared with other statins in reducing LDL-C and reaching ATP III LDL-C goal among Medicare-eligible patients and patients < 65 years of age treated by physicians in usual clinical practice. This study provides evidence of how effective statins are in routine clinical practice and whether the effectiveness is similar for younger vs. older patients.

**Methods**

A retrospective cohort study was conducted utilising the General Electric Medical System (GEMS) electronic medical records database of patients treated in physician practices. The study objective was to examine the effectiveness of statins under usual care at reducing LDL-C and ATP III goal attainment by comparing RSV with atorvastatin (ATV), simvastatin (SMV), pravastatin (PRV), fluvastatin (FLV) and lovastatin (LOV). Older patients, 65 years and older, were examined separately from patients < 65 years of age to identify the most effective statin for the Medicare and non-Medicare population.

Patients who were newly prescribed statin therapy during August 2003 to May 2005 and had no prior prescription for dyslipidaemic medication, including bile acid sequestrants, fibrin, niacin, ezetimibe or statin, in the preceding 12 months were included in the study. The GEMS database included the electronic medical records (EMR) of patients treated in usual clinical practice for over 3000 physicians across the US. The EMR was utilised largely by primary care physicians (85%) and cardiology practices (~5%). All patient care activities (outpatient medical and procedures, prescriptions, laboratory) in the physician’s office are captured in the EMR.

Titration of statin therapy was allowed but patients switching to other statins during the study period were excluded as the effect of the initial statin could not be isolated in patients switching statins. Patients had to be continuously enrolled for a minimum of 15 months; 12 months prior to and 3 months after initiation of statin therapy. Additionally, patients were required to have a minimum of a 90-day supply of statin therapy (either a 90-day prescription or three 30-day prescriptions), and lipid results within 90 days prior to and >30 days after initiating statin therapy. The lipid value closest to the date of statin therapy initiation was defined as the baseline lipid measure. The follow-up lipid value was defined as the average of all lipid measures during the follow-up period, from 30 days after initiation of statin therapy to the date of the last statin prescription at the time of discontinuation or end of study (August 2005). The average LDL-C was used to obtain stable estimates using all available data and followed the methodology by Bullano et al. (16).

Therapy discontinuation was defined as the lack of a prescription or refill order within a 50% time period of the prescription supply. Thus, if a 30-day statin supply was ordered then the prescription must be refilled or a new order written within 45 days of the initial prescription to consider the patient persistent on statin therapy. Similarly, if a 90-day statin supply is ordered then the second prescription or refill must be written within 135 days of the initial prescription date to consider the patient persistent.

Two effectiveness outcomes were assessed: (1) per cent reduction in LDL-C and (2) percentage of patients attaining NCEP ATP III LDL-C goal. The outcome measures were computed for each individual statin and then compared with RSV. Change in total cholesterol, high-density lipoprotein (HDL-C) and triglycerides was also computed. For LDL-C goal attainment assessment, patients were stratified based upon NCEP CHD risk groups (2). CHD and CHD risk equivalent was defined as myocardial infarction, ischaemic heart disease, acute coronary syndrome, cerebral vascular accident, transient ischaemic attack, peripheral vascular disease, abdominal aortic aneurysm, angina pectoris, atherosclerosis and diabetes mellitus based on ICD-9 codes. The GEMS EMR (outpatient data only) did not contain information on inpatient procedures so the classification of patients with coronary artery bypass graft, angio-plasty or other revascularisation into the high-risk category was not possible. A count of risk factors was done to assign patients to moderate or low risk. Moderate-risk patients were defined by the presence of two or more CHD risk factors including current cigarette smoking, hypertension diagnosis or blood pressure ≥140/90 mmHg, low HDL-C < 40 mg/dl and age ≥45 for men and ≥55 for women. Low-risk patients were those with one or no CHD risk factors.

Given the lack of inpatient procedures data and data from non-primary care settings, there was a potential for misclassifying high-risk patients as moderate risk. The fact that physicians started these patients with LDL-C < 130 mg/dl on a statin treatment was considered a strong indicator of their underlying high-risk status or a more aggressive LDL-C target goal (<100 mg/dl). LDL-C goal was defined as <100 mg/dl for high-risk patients as well as those moderate-risk patients who were already at goal <130 mg/dl at baseline. Moderate-risk patients not at LDL-C goal at baseline had a goal of <130 mg/dl (2). Low-risk patients’ LDL-C goal was <160 mg/dl (2). Moreover, family history of premature CHD was not available in the EMR and was not included as one of the risk factors. Thus, some
patients may have been classified as low risk instead of moderate risk.

Linear regression analyses were conducted to compare effectiveness of RSV with other statins in lowering LDL-C while adjusting for age, gender, smoking, hypertension, CHD, systolic blood pressure, baseline LDL-C and therapy duration. Logistic regression analyses were undertaken to compare LDL-C goal attainment between RSV and other statins while adjusting for the same baseline characteristics. The goal attainment analyses were stratified by CHD risk level, high plus moderate risk and low risk. The sample mean of predicted probabilities from the logistic regression models was used as an estimate of the expected rate of goal attainment adjusted for patient characteristics. All statistical analyses were conducted using SAS version 9.1 (SAS Institute, Inc., Cary, NC).

Results
There were 5989 patients with age ≥ 65 years, and 5326 patients who were < 65 years of age who met the study inclusion criteria. RSV patients comprised 4% of the ≥ 65 age group and 6% of the < 65 age group (Table 1). RSV Medicare-eligible patients (age ≥ 65 years) and patients < 65 years of age had higher baseline LDL-C (p < 0.05) and total cholesterol (p < 0.05) than other statin patients except for LOV (Table 1). RSV patients also had shorter therapy duration (p < 0.05) than all other statin patients likely because of relatively recent availability when compared with other statins. Medicare-eligible RSV patients were younger than other statin patients (p < 0.05) except for ATV and SMV (Table 1). For patients < 65 years of age, RSV patients were significantly younger than SMV and LOV patients (Table 1). For both Medicare-eligible and patients < 65 years of age, initial statin dose did not vary by CHD risk level (Table 1).

Lipid changes
Medicare-eligible RSV patients had significantly greater (p < 0.05) LDL-C reduction (29.8%) compared with other statins (11.3–19.1%), despite differences in age and therapy duration (Table 2). For patients < 65 years of age, RSV patients had significantly greater (p < 0.05) observed LDL-C reduction (33.6%) compared with other statins (17–23.6%) (Table 2). After adjustment for differences in baseline characteristics, both Medicare-eligible patients and patients < 65 years of age, RSV patients had significantly greater LDL-C reduction than other statins (p < 0.05) (Table 2). After adjustment, patients < 65 years of age who were treated with RSV had a 28.5% LDL-C reduction compared with 14.4–21.3% for other statins. Similarly, Medicare-eligible RSV patients had a greater adjusted (24.3%) per cent LDL-C reduction compared with other statins (10.7–17.5%).

Medicare-eligible patients and patients < 65 years of age treated with RSV had significantly greater reduction in total cholesterol than other statin patients (Table 3). Medicare-eligible RSV patients had an adjusted 17.5% reduction in total cholesterol compared with 7.0–12.2% for other statins, p < 0.05. Among patients < 65 years of age, RSV had an adjusted 22.1% total cholesterol reduction compared with 17.2% for ATV (p ≥ 0.05) and 10.8–14.1% for other statins (p < 0.05). The average change in HDL-C for each statin was 0.8–3.4% for Medicare-eligible and −1.3% to 1.7% for < 65 patients (Table 3). There was no difference in the change in triglycerides between RSV and other statins for either the Medicare-eligible patients or patients < 65 years of age.

ATP III goal attainment
ATP III goal attainment was computed by CHD risk level and patients who were at LDL-C goal level at baseline were excluded. A greater proportion of moderate- and high-risk RSV patients compared with other moderate- and high-risk statin patients, both Medicare-eligible patients and < 65, attained ATP III LDL-C goal after adjusting for baseline differences (Table 4). After adjustment, approximately 78% of < 65 years of age moderate- and high-risk patients and 76% of high- and moderate-risk Medicare-eligible patients attained LDL-C goal on RSV compared with 51–71% of < 65 years age patients and 50–73% of older patients taking other statins (Table 4).

There was little difference across statins in LDL-C goal attainment among the low-risk patients for both Medicare-eligible patients and patients < 65 years of age (Table 4). After adjustment, a significantly greater proportion of low-risk RSV patients < 65 years of age had attained LDL-C goal compared with PRV and LOV (p < 0.05). For Medicare-eligible low-risk patients, a significantly greater proportion of RSV patients attained LDL-C goal than PRV (p < 0.05) after adjustment for baseline covariates.

Discussion
Rosuvastatin is more effective in lowering LDL-C in this sample of Medicare-eligible patients and patients < 65 years of age than other statins. These greater LDL-C reductions resulted in better goal attainment among RSV patients, both < 65 and
≥ 65 age groups. For moderate- and high-risk RSV patients, 76% attained ATP III LDL-C goals compared with 50–73% of other statin patients. There was no difference in goal attainment across statins for low-risk patients. RSV was also more effective (p < 0.05) in lowering total cholesterol among Medicare-eligible patients and patients < 65 years of age than other statins.

### Table 1: Baseline characteristics of Medicare-eligible patients and < 65 years of age patients newly initiated on statin therapy

| Characteristics                                  | Rosuvastatin | Atorvastatin | Simvastatin | Pravastatin | Fluvastatin | Lovastatin |
|--------------------------------------------------|--------------|--------------|-------------|-------------|-------------|------------|
| **Medicare-eligible patients (≥ 65 years)** (n = 5989) |              |              |             |             |             |            |
| Number of subjects                               | 235 (4%)     | 3195 (54%)   | 1432 (24%)  | 495 (8%)    | 256 (4%)    | 376 (6%)   |
| Age (mean ± SD)                                  | 73.3 (5.1)   | 73.5 (5.0)   | 74.0 (4.9)  | 74.1 (5.0)* | 74.9 (5.0)* | 74.5 (5.0)* |
| Male (%)                                         | 42           | 44           | 49          | 46          | 42          | 38         |
| Smoker (%)                                       | 7            | 5            | 5           | 4           | 2           | 4          |
| Hypertension (%)                                 | 55           | 52           | 50          | 53          | 50          | 56         |
| CHD (%)                                          | 13           | 14           | 14          | 12          | 12          | 12         |
| **NCEP risk group, n (%)**                       |              |              |             |             |             |            |
| CHD/CHD risk equivalent†                         | 96 (41%)     | 1557 (49%)   | 703 (49%)   | 216 (44%)   | 124 (48%)   | 146 (39%)  |
| Mean statin dose                                 | 11.1         | 17.9         | 24.1        | 34.8        | 60.8        | 24.2       |
| Moderate risk                                    | 78 (33%)     | 728 (23%)    | 301 (21%)   | 124 (25%)   | 61 (24%)    | 123 (33%)  |
| Mean statin dose                                 | 13.3         | 17.8         | 23.1        | 34.8        | 61.3        | 24.3       |
| Low risk                                         | 61 (26%)     | 910 (28%)    | 428 (30%)   | 155 (31%)   | 71 (28%)    | 107 (28%)  |
| Mean statin dose                                 | 10.7         | 16.9         | 23.8        | 33.9        | 63.9        | 24.7       |
| **Baseline lipids, mean ± SD**                   |              |              |             |             |             |            |
| LDL-C                                           | 143.5 (47.0) | 124.4 (43.5)*| 118.9 (39.7)*| 127.8 (39.7)*| 126.8 (35.6)*| 139.3 (38.6) |
| Total cholesterol†                               | 217.8 (47.9) | 202.0 (44.6)*| 195.5 (41.6)*| 204.1 (39.4)*| 206.8 (42.2)*| 220.5 (40.6) |
| HDL-C‡                                           | 52.1 (14.9)  | 52.8 (13.9)  | 52.8 (14.4) | 52.7 (13.9) | 53.3 (15.1) | 55.0 (14.3) |
| Triglycerides‡                                    | 148.1 (79.6) | 144.8 (75.6) | 140.1 (75.5)| 138.9 (67.3)| 146.9 (74.9)| 145.3 (79.4)|
| **Statin therapy, mean (SD)**                    |              |              |             |             |             |            |
| Initial daily dose                                | 12.2 (7.2)   | 17.5 (12.9)  | 23.5 (11.5) | 34.5 (14.7) | 62.0 (24.8) | 24.4 (11.0) |
| Therapy duration§, days                          | 199.5 (123.0)| 265.8 (160.4)*| 266.1 (161.0)*| 263.5 (158.6)*| 287.0 (165.3)*| 251.1 (158.9)*|
| **< 65 years of age patients (n = 5326)**         |              |              |             |             |             |            |
| Number of subjects                               | 353 (6%)     | 3340 (63%)   | 944 (18%)   | 322 (6%)    | 143 (3%)    | 224 (4%)   |
| Age (mean ± SD)                                  | 53.9 (7.7)   | 53.8 (7.9)   | 54.9 (7.4)* | 54.7 (7.3)  | 55.0 (7.6)  | 55.2 (7.2)*|
| Male (%)                                         | 46           | 52           | 52          | 50          | 50          | 47         |
| Smoker (%)                                       | 9            | 10           | 9           | 12          | 12          | 9          |
| Hypertension (%)                                 | 42           | 37           | 40          | 39          | 36          | 46         |
| CHD (%)                                          | 9            | 9            | 8           | 9           | 6           | 9          |
| **NCEP risk group, n (%)**                       |              |              |             |             |             |            |
| CHD/CHD risk equivalent†                         | 78 (22%)     | 969 (29%)    | 264 (28%)   | 91 (28%)    | 31 (22%)    | 45 (20%)   |
| Mean statin dose                                 | 10.5         | 19.6         | 24.9        | 31.8        | 51.4        | 24.1       |
| Moderate risks                                   | 123 (35%)    | 735 (22%)    | 208 (22%)   | 77 (24%)    | 36 (25%)    | 67 (30%)   |
| Mean statin dose                                 | 11.9         | 17.2         | 24.5        | 37.5        | 65.3        | 23.0       |
| Low risk                                         | 152 (43%)    | 1636 (49%)   | 472 (50%)   | 154 (48%)   | 76 (53%)    | 112 (50%)  |
| Mean statin dose                                 | 10.6         | 16.2         | 24.3        | 33.6        | 74.4        | 24.0       |
| **Baseline lipids, mean ± SD**                   |              |              |             |             |             |            |
| LDL-C                                           | 163.5 (48.1) | 142.2 (46.4)*| 140.3 (46.2)*| 142.2 (38.4)*| 147.9 (37.5)*| 153.8 (40.6)*|
| Total cholesterol†                               | 239.8 (43.7) | 219.1 (46.1)*| 216.6 (44.7)*| 218.4 (36.9)*| 226.9 (32.2)*| 230.5 (41.8)*|
| HDL-C‡                                           | 48.8 (12.7)  | 50.1 (13.0)  | 51.4 (13.5) | 50.3 (12.5) | 53.3 (13.5) | 51.0 (14.6) |
| Triglycerides‡                                    | 179.6 (99.5) | 160.2 (89.2) | 156.5 (86.0)| 155.8 (80.1)| 145.7 (75.7)| 157.3 (81.9)|
| **Statin therapy, mean ± SD**                    |              |              |             |             |             |            |
| Daily dose                                       | 11.3 ± 5.3   | 16.5 ± 12.0  | 24.3 ± 11.3 | 35.7 ± 15.0 | 66.4 ± 21.7 | 23.5 ± 11.7 |
| Therapy duration§, days                          | 196.7 (121.0)| 264.5 (159.4)*| 266.0 (158.2)*| 288.5 (159.6)*| 276.0 (158.8)*| 248.9 (153.1)*|

*p < 0.05 for comparison with rosuvastatin; †CHD risk = high risk + moderate risk with baseline LDL-C < 130 mg/dl; ‡Number of subjects for total cholesterol, LDL-C and triglycerides were slightly less than that of LDL-C; Medicare-eligible, n = 207 for RSV, 2714 for ATV, 1201 for SMV, 452 for PRV, 219 for FLV and 350 for LOV; < 65 years of age, n = 303 for RSV, 2873 for ATV, 853 for SMV, 298 for PRV, 135 for FLV and 215 for LOV; §Therapy duration was shorter for RSV because of its more recent commercial availability compared with other statins.

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A 6% difference in per cent LDL-C is considered to be clinically meaningful (17,18). A greater than 6% difference in LDL-C reduction between RSV and other statins as observed in the present study indicated clinical meaningfulness of the study findings. A definition for clinically meaningful difference in LDL-C goal attainment has not been established, so clinicians and payers may need to define their own clinically significant threshold. However, one could hypothesise that the clinically and statistically

Table 2 Observed changes in LDL-C levels for Medicare-eligible patients and < 65 years of age patients newly initiated on statin therapy

| LDL-C | Rosuvastatin | Atorvastatin | Simvastatin | Pravastatin | Fluvastatin | Lovastatin |
|-------|-------------|--------------|-------------|-------------|-------------|------------|
| < 65 years of age patients | | | | | | |
| Number of subjects | 353 | 3340 | 944 | 322 | 143 | 224 |
| Baseline (mg/dl) | 163.5 ± 48.1 | 142.2 ± 46.4* | 140.3 ± 46.2* | 142.2 ± 38.4* | 147.9 ± 37.5* | 153.8 ± 40.6* |
| Follow-up (mg/dl) | 102.3 ± 36.6 | 102.1 ± 31.2 | 106.7 ± 31.4* | 113.6 ± 27.6* | 109.4 ± 27.1* | 118.8 ± 31.5* |
| Per cent change (%) | 33.6 ± 27.9 | 22.5 ± 29.4* | 19.0 ± 25.6* | 17.0 ± 20.2* | 23.6 ± 20.1* | 20.2 ± 19.9* |
| Adjusted per cent change* (%) | 28.5 ± 15.7 | 21.3 ± 15.7* | 18.4 ± 15.7* | 15.8 ± 15.7* | 20.6 ± 15.7* | 14.4 ± 15.7* |
| Medicare-eligible patients | | | | | | |
| Number of subjects | 235 | 3195 | 1432 | 495 | 256 | 376 |
| Baseline (mg/dl) | 143.5 ± 47.0 | 124.4 ± 43.5* | 118.9 ± 39.7* | 127.8 ± 39.7* | 126.8 ± 35.6* | 139.3 ± 38.6 |
| Follow-up (mg/dl) | 93.8 ± 32.6 | 97.4 ± 29.3 | 107.3 ± 32.8* | 108.0 ± 30.5* | 107.9 ± 27.3* | 107.9 ± 27.3* |
| Per cent change (%) | 29.8 ± 26.6 | 17.2 ± 28.8* | 12.3 ± 33.0* | 12.5 ± 23.7* | 11.3 ± 25.1* | 19.1 ± 22.0* |
| Adjusted per cent change* (%) | 24.3 ± 16.6 | 17.5 ± 16.6* | 14.8 ± 16.6* | 11.3 ± 16.6* | 10.7 ± 16.6* | 13.3 ± 16.6* |

*p < 0.05 for comparison of rosuvastatin vs. each other statin; †Adjusted for age, gender, smoking, hypertension, CHD, systolic blood pressure, therapy duration and baseline LDL-C.

Table 3 Per cent change in total cholesterol, HDL-C and triglycerides for Medicare-eligible patients and < 65 years of age patients newly initiated on statin therapy

| Lipid change | Rosuvastatin | Atorvastatin | Simvastatin | Pravastatin | Fluvastatin | Lovastatin |
|-------------|-------------|--------------|-------------|-------------|-------------|------------|
| < 65 years of age patients | | | | | | |
| Total cholesterol | | | | | | |
| Number of patients | 303 | 2873 | 853 | 298 | 135 | 215 |
| Per cent total cholesterol change | –23.6 (19.9) | –17.0 (18.2)* | –13.6 (16.7)* | –12.0 (13.3)* | –16.3 (13.6)* | –15.0 (13.7)* |
| Per cent total cholesterol change adjusted† | –22.1 (13.9) | –17.2 (13.9) | –14.1 (13.9)* | –10.8 (13.9)* | –16.0 (13.9)* | –13.6 (13.9)* |
| HDL-C | | | | | | |
| Number of patients | 303 | 2770 | 822 | 292 | 134 | 203 |
| Per cent HDL-C change | 1.7 (15.8) | 0.8 (14.5) | 1.2 (14.2) | –0.7 (13.8)* | 0.6 (13.2) | –1.3 (11.9)* |
| Triglyceride | | | | | | |
| Number of patients | 301 | 2764 | 821 | 294 | 135 | 205 |
| Per cent triglyceride change | –2.9 (62.5) | –4.5 (45.5) | –2.6 (39.3) | 2.8 (40.2) | –2.1 (33.7) | –4.8 (30.8) |
| Medicare-eligible patients | | | | | | |
| Total cholesterol | | | | | | |
| Number of patients | 207 | 2714 | 1201 | 452 | 219 | 350 |
| Per cent total cholesterol change | –19.3 (18.6) | –12.3 (18.6)* | –8.9 (17.2)* | –9.3 (14.1)* | –7.9 (16.4)* | –13.2 (14.8)* |
| Per cent total cholesterol change adjusted† | –17.5 (10.6) | –12.2 (10.6)* | –10.7 (10.6)* | –8.8 (10.6)* | –7.0 (10.6)* | –8.8 (10.6)* |
| HDL-C | | | | | | |
| Number of patients | 206 | 2696 | 1203 | 450 | 217 | 347 |
| Per cent HDL-C change | 3.4 (14.6) | 1.2 (15.0)* | 1.7 (14.6) | 1.6 (18.8) | 1.8 (15.3) | 0.8 (13.0)* |
| Triglyceride | | | | | | |
| Number of patients | 204 | 2698 | 1202 | 450 | 219 | 346 |
| Per cent triglyceride change | 15.7 (142.3) | 2.0 (64.2) | 9.8 (100.2) | 5.4 (61.2) | 5.0 (50.5) | 4.9 (65.2) |

*p < 0.05 for comparison of rosuvastatin vs. each other statin; †Adjusted for age, gender, smoking, hypertension, CHD, systolic blood pressure, therapy duration and baseline LDL-C.
meaningful difference in LDL-C reduction as observed in this study should equate to a clinically meaningful difference in goal attainment.

The present study only focused on lipid changes and goal attainment comparisons of RSV with other statins and did not examine mortality or cardiovascular event differences as end-points. Clinical trials examining the impact of RSV on mortality and cardiovascular event outcomes are ongoing (19–21). A meta analysis of 14 randomised trials of statin therapy indicated that statins safely reduced the 5-year incidence of major coronary events, coronary revascularisation and stroke by about one-fifth per mmol/l (39 mg/dl) reduction in LDL-C (22). This analysis found an approximately linear relationship between the absolute reductions in LDL-C achieved and the proportional reductions in the incidence of coronary and other major vascular events and that larger LDL-C reductions produced larger reductions in vascular disease risk. These results cannot be directly applied to the current study findings as it is not a randomised trial and there are obvious differences in inclusion criteria and follow-up period between the trials included in the meta analysis when compared with the current observational study. However, one can use the results of the meta analysis to arrive at a general guidance of the expected benefits in terms of avoided cardiovascular events. Extrapolating to the study’s 49.7 mg/dl average absolute reduction in LDL-C for Medicare-eligible patients and 61.2 mg/dl average absolute reduction in LDL-C for < 65 years of age patients with RSV, it could be estimated that continued RSV therapy could reduce major vascular events by one-fourth and one-third respectively. Such estimates can also be projected for other statins in this study or for differences in LDL-C reduction observed between different statins.

This study provides evidence of greater effectiveness of RSV in usual care. The data reflect patients treated in the community, largely by primary care physicians, and represent clinicians’ treatment patterns for their statin patients. Moreover, this is the first investigation to provide effectiveness estimates of statins for the Medicare-eligible population. Other studies have derived estimates from clinical trial populations and managed care populations which tend to be predominantly younger and employed rather than ≥ 65 and retired. It is also important to recognise that many patients on statin therapy (both Medicare-eligible and < 65 years) were not achieving their LDL-C goal in usual care. As few as 51–65% of patients reached goal on LOV, PRV or FLV, leaving 34–49% of patients not attaining LDL-C goal. Thus, the selection of a statin that increases the likelihood of attaining goal is important. Future studies need to examine specific reasons for this low LDL-C goal attainment rate and limited adoption of guidelines.

Statin therapy utilisation patterns were different between patients with ≥ 65 and < 65 years of age, with more Medicare-eligible patients receiving

| Table 4 ATP III LDL-C goal attainment for rosuvastatin vs. other statins for Medicare-eligible patients and < 65 years of age patients by CHD risk group |
|---|---|---|---|---|---|---|
| | < 65 years of age | Medicare-eligible | | | | |
| | Number of subjects | Unadjusted percentage attaining LDL-C goal | Adjusted percentage attaining LDL-C goal | Number of subjects | Unadjusted percentage attaining LDL-C goal | Adjusted percentage attaining LDL-C goal |
| Moderate- and high CHD risk | | | | | | |
| Rosuvastatin | 187 | 73.6 (44.2) | 78.4 (8.6) | 136 | 74.1 (43.9) | 76.0 (7.1) |
| Atorvastatin | 1407 | 70.4 (45.6) | 71.5 (9.4)* | 1526 | 70.2 (45.7) | 73.0 (7.5)* |
| Simvastatin | 381 | 66.3 (47.3) | 66.9 (10.3)* | 623 | 62.0 (48.6)* | 64.1 (8.6)* |
| Pravastatin | 133 | 55.6 (49.8)* | 59.7 (11.5)* | 228 | 57.6 (49.5)* | 59.5 (8.9)* |
| Fluvastatin | 57 | 63.2 (48.6) | 65.8 (10.9)* | 118 | 48.6 (50.2)* | 50.5 (9.0)* |
| Lovastatin | 109 | 55.0 (50.0)* | 51.3 (11.5)* | 213 | 62.4 (48.5)* | 64.8 (8.3)* |
| Low CHD risk | | | | | | |
| Rosuvastatin | 90 | 90.0 (30.2) | 91.0 (7.7) | 24 | 89.5 (31.5) | 85.4 (11.0) |
| Atorvastatin | 713 | 90.2 (29.7) | 91.0 (7.6) | 205 | 91.3 (28.3) | 85.7 (10.9) |
| Simvastatin | 179 | 89.5 (30.7) | 90.1 (7.7) | 72 | 90.0 (30.2) | 83.0 (12.1) |
| Pravastatin | 58 | 83.6 (37.3) | 82.6 (12.0)* | 27 | 82.8 (38.4) | 74.7 (14.9)* |
| Fluvastatin | 28 | 92.6 (26.7) | 91.0 (7.1) | 8 | 81.8 (40.4) | 72.2 (15.5) |
| Lovastatin | 54 | 80.4 (40.1)* | 82.5 (12.0)* | 41 | 94.3 (23.5) | 88.8 (9.2) |

*p < 0.05 for comparison of rosuvastatin vs. each other statin; †Adjusted for per cent LDL-C reduction needed to reach goal, age, gender, smoking, hypertension, CHD, systolic blood pressure and therapy duration.
Recent generic availability of SMV has provided further opportunities to achieve efficiency in management of patients with dyslipidaemia. To realise efficiencies without compromising quality of care, appropriate patient-specific selection for generic statins and branded statins is required. Our analysis of real-world clinical practice data indicated that high- and moderate-risk RSV patients were more likely to attain LDL-C goals when compared with other statins (including generic statins). However, no difference in goal attainment rate between RSV and SMV was observed in low-risk patients. This suggests that generic SMV may be used in low-risk patients and RSV may be used in high- and moderate-risk patients to achieve effective and efficient management of dyslipidaemia in the population. An extensive and formal cost-effectiveness evaluation of statins was beyond the scope of this study. However, using the observed effectiveness from this study and the wholesale acquisition costs for statin therapy (First DataBank National Drug Data File), a cost-effectiveness ratio (cost per LDL-C reduction) for RSV would be $3359 for patients < 65 years of age and $3683 for Medicare-eligible patients and $5251 and $6969 for ATV patients < 65 years of age and Medicare-eligible respectively. For generic SMV, a rough cost-effectiveness ratio would be between $373 and $458 for patients < 65 years of age and between $584 and $716 for Medicare-eligible patients when using $0.06–$0.10 (26) for generic SMV tablet. These cost-effectiveness data further demonstrate that RSV may be used as the branded statin for effective and efficient management of dyslipidaemia among patients requiring a large reduction in LDL-C and generic SMV may be the efficient and appropriate generic statin for patients requiring a smaller LDL-C reduction.

Our study has limitations that should be considered. The study population includes patients treated by physicians utilising an electronic medical record system in their clinical practice. Although over 3000 physicians across the US are included, there may be differences in clinical practice patterns between physicians who utilise GEMS and physicians who are not electronically equipped. However, our study population included a more heterogeneous group of patients with Medicare health insurance and those with Medigap and/or commercial insurance rather than investigations that focussed only on employed patient populations in managed care (4,19,20). Selection bias may have occurred because of the observational nature of the study. Yet, multivariate analyses were employed to control for differences in demographics and clinical characteristics. Moreover, the study pharmacy data is the physician prescription order and not pharmacy claims data. Therefore, it
was not possible to ascertain that all statin prescription orders were filled by the patient. To reduce introduction of potential bias because of non-filling of some prescriptions, only those patients with at least 90 days supply of statin therapy were included. An additional limitation is the lack of inpatient procedure data in the GEMS database. Patients with angioplasty, coronary artery bypass graft and other revascularisation procedures are classified as high-risk patients according to NCEP ATP III (2). These patients could not be distinguished in our dataset thereby reducing the size and composition of our high-risk group. Furthermore, diagnoses from specialists (e.g. cardiologists) were under-represented in our data as the majority of physicians were primary care clinicians. Cardiovascular events could not be ascertained completely in our dataset, so the impact of different statins on the incidence of cardiovascular events could not be assessed. Longer follow-up studies with availability of both inpatient and outpatient data are needed to address the potential differential impact of statins on cardiovascular events.

Conclusions

The study results indicated that RSV is more effective in lowering LDL-C and total cholesterol among elderly and non-elderly patients than other statins. RSV is also more effective in attaining LDL-C goal among high- and moderate-risk patients for both elderly and non-elderly patients than other statins. For low-risk patients, in general there were no substantial differences in LDL-C goal attainment across statins (in particular between RSV vs. ATV, SMV and FLV). Rosuvastatin effectiveness (LDL-C reduction and goal attainment) has implications for physicians in selecting the optimal statin agent to meet their individual patient needs in both the Medicare-eligible patients and patients < 65 years of age. For both Medicare-eligible patients and < 65 years of age patients, RSV may be used in moderate- and high-risk patients and generic statins may be used in low-risk patients to achieve effective and efficient management of dyslipidaemia. These findings provide physicians and healthcare plans with a better understanding of the differential effectiveness of statin therapy for patient care and formulary management.

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