



without diabetes (RR, 0.71; 95% CI, 0.56 to 0.91 vs RR, 0.92; 95% CI, 0.77 to 1.09; $P_{\text{interaction}} = .04$).

Limitations of VISION included its observational design (statin use clearly might be a surrogate for another confounder related to 30-day outcome when the associated risk for survival is substantially lower than the primary outcome), the presence of some baseline differences, and the lack of data on statin type/dose, liver function, and muscle function.

Nonetheless, the data from this large cohort of patients undergoing noncardiac surgery indicate the potential value of statin use before surgery in lessening CV complications 30 days postoperatively. Dr Berwanger noted that these findings need to be confirmed in large perioperative randomized controlled trials.

Low Adherence/Discontinuation of Statin Therapy Is Common and Detrimental in MI Patients

Written by Brian Hoyle

Examination of hospital records of over 45 000 Medicare beneficiaries aged ≥ 66 years has revealed that high adherence to statin therapy, regardless of statin intensity, is beneficial following discharge after hospitalization for myocardial infarction (MI). Yet, low adherence to therapy or discontinuation is common.

The researchers, including Robert S. Rosenson, MD, Mount Sinai Icahn School of Medicine, New York City, New York, USA, and Paul Muntner, PhD, University of Alabama Birmingham, Birmingham, Alabama, USA recently reported that only 27% of 8762 randomly sampled Medicare beneficiaries hospitalized for coronary heart disease events received high-intensity statins [Rosenson RS et al. *J Am Coll Cardiol.* 2015]. The present study was undertaken as a further exploration of the finding.

The study initially enrolled 969 040 Medicare beneficiaries aged ≥ 66 years and < 110 years who were hospitalized at the aforementioned institutions for MI between 2006 and 2012. This initial population was whittled down to 45 629 individuals whose first statin prescription following discharge was for a high-intensity statin (atorvastatin, 40 or 80 mg; rosuvastatin, 20 or 40 mg; or simvastatin, 80 mg). The pattern of statin use at 182 days following discharge was ascertained, with maintenance of therapy for $\geq 80\%$ of the time deemed high adherence and $< 80\%$ of the time reflecting low adherence. Other patterns analyzed included down-titration and subsequent high adherence to moderate- or low-intensity statins; low adherence to high-, moderate-, or

low-intensity statins; and complete discontinuation of statin therapy (> 60 days with no statin supply and no prescription refills).

Outcomes included recurrent MI, hospitalization for cardiovascular diseases (CVD) and non-CVD, and all-cause mortality beginning 182 days after discharge and ending on December 31, 2012.

The majority of the 45 629 individuals displayed high adherence to high-intensity statin therapy at 182 days (57.4%), followed by those whose adherence was low (18.8%), those who discontinued therapy (14.1%), and those with high adherence to a down-titrated regimen (9.7%). These groups were similar in age (mean age, 76 years), sex (female, 53%), and race (white, $> 80\%$).

Similarities extended to the prevalence of diabetes (44.6%, 49.4%, 45.7%, and 43.3% in the same respective order) and a history of coronary heart disease (58.7%, 64.7%, 59.1%, and 54.8% in the same respective order).

Recurrent MI within 182 days following hospital discharge occurred in 1324 (5.1%) patients with high adherence to high-intensity statins, 334 (7.5%) patients with high adherence to low- or moderate-intensity statins, 796 (9.3%) patients with low adherence to statins, and 484 (7.6%) patients who discontinued statins.

Patients with high adherence to either high-intensity statins or low-/moderate-intensity statins experienced fewer MI recurrences, fewer CVD-related hospitalizations, and fewer all-cause mortalities. The pattern was less clear for non-CVD hospitalization but still favored high-adherent individuals.

Analyses of results adjusting for calendar year, age, race/ethnicity, and sex and for these parameters plus a battery of factors concerning patient care and history of comorbidities confirmed the lower occurrence of recurrent MI, CVD hospitalization, non-CVD hospitalization, and all-cause mortality in individuals with high adherence, be that to low-, moderate-, or high-intensity statins. Individuals whose adherence was low or who discontinued statin use had worse outcomes.

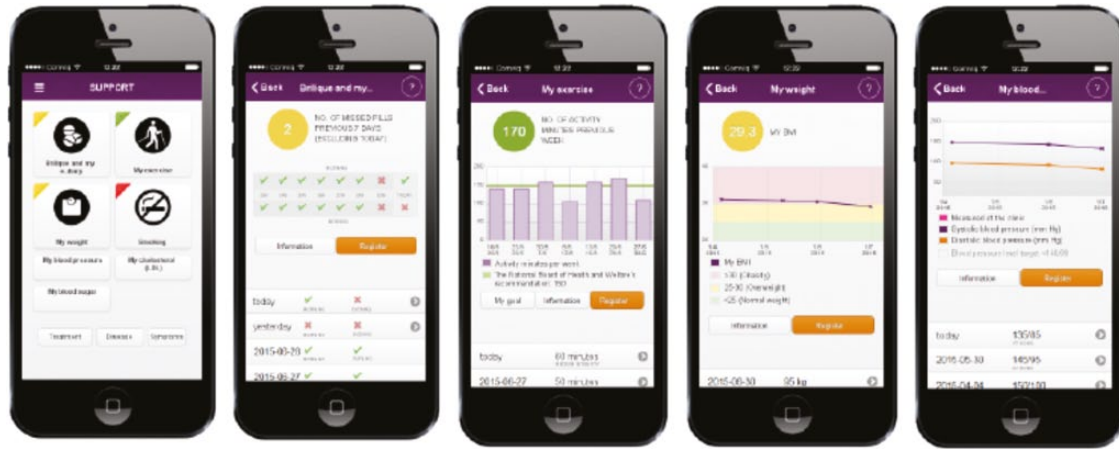
Thus, down-titration and discontinuation of high-intensity statins are both common and detrimental.

SUPPORT Findings: Smartphone App Bolsters Drug Adherence and Beneficial Lifestyle Changes in Myocardial Infarction Patients

Written by Brian Hoyle

A smartphone app that provides interactive feedback in response to patient input can be beneficial in

Figure 1. Example Screen Views of the Interactive App



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motivating patients who have suffered a myocardial infarction (MI) to maintain or improve drug adherence and adopt/continue healthy cardiovascular lifestyle changes. The SUPPORT trial [NCT01874262], headed by Christoph Varenhorst, MD, PhD, Uppsala Clinical Research Center and Department of Medical Sciences, Cardiology, Uppsala University, Sweden, may herald the use of disease-specific apps to complement conventional secondary cardiovascular care.

In the SUPPORT trial, 166 patients (mean age, 58 years; 81% men; 21% current smokers) being treated with ticagrelor for acute MI were randomized to use the interactive smartphone app (active group, n=86) or a simpler, noninteractive app that tracked only adherence to the ticagrelor regimen (control group, n=80).

The study lasted about 6 months. Cardiovascular risk factors that were assessed at baseline, 6 to 10 weeks, and 23 to 25 weeks included body mass index, physical activity, blood pressure, low-density lipoprotein cholesterol, and smoking cessation. Quality of life, self-reported ticagrelor use, patient satisfaction, and safety were also assessed.

In the interactive version of the app, patient entry of data prompted visual feedback and messages that were intended to boost motivation concerning adherence to the ticagrelor regimen, to increase awareness of cardiovascular disease, and to enhance resolve to make and maintain healthy lifestyle changes in aspects including physical activity and quitting smoking (Figure 1).

At baseline, the active and control groups were similar in demographic and clinical characteristics (Table 1).

The primary end point was patient-registered drug nonadherence, defined as a composite end point

Table 1. Patient Characteristics

	Active Group (n = 86)	Control Group (n = 80)	Total (n = 166) ^a
Men, %	83	79	81
Age, y	56.8 ± 8.0	58.4 ± 8.6	57.5 ± 8.3
Smokers, %	26	15	21
Body mass index, kg/m ²	28.9 ± 5.6	28.4 ± 4.7	28.7 ± 5.2
LDL-C, mmol/L	3.9 ± 1.2	3.3 ± 0.9	3.6 ± 1.1
Blood pressure, mm Hg			
Systolic	131.1 ± 14.6	125.2 ± 17.9	128.2 ± 16.5
Diastolic	78.8 ± 11.0	75.5 ± 11.0	77.2 ± 11.1
Diabetes	8 (9.3)	13 (16.3)	21 (12.7)
Hypertension	40 (46.5)	38 (47.5)	78 (47.0)

Data presented as n (%) or mean ± SD unless noted otherwise.

LDL-C, low-density lipoprotein cholesterol.

^aOut of 174 patients randomized, 166 were evaluable and included in analyses.

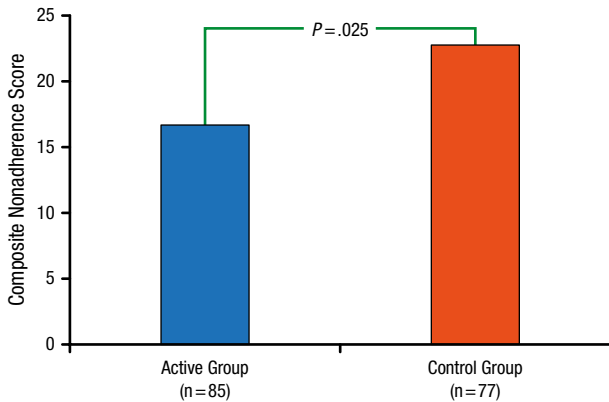
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of treatment failure (2 missed doses during a 7-day period) and a gap in treatment consisting of 4 consecutive missed doses. Self-reported adherence to the ticagrelor regimen at 6 months was significantly higher ($P = .025$) in the active group (16.6 ± 42.9 missed events) than in the control group (22.8 ± 41.3 missed events; Figure 2).

Secondary analyses revealed a positive trend in the active group vs the control group for smoking cessation (80% vs 46%; $P = .139$), increased physical activity in terms of median change in weekly exercise minutes (90 vs 65; $P = .612$), and quality of life as measured with the EQ5D-VAS (14.7 vs 8.4; $P = .059$). Patients'



Figure 2. Primary End Point: Patient-Registered Drug Noncompliance



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satisfaction was higher in the active group as compared with the control group (usability score of 100, 87 vs 78; $P = .001$).

The majority (68%) of active group participants would keep using the app if it were generally available, and most (97%) would recommend the app to other acute MI patients receiving drug therapy.

Among patients with acute MI, the interactive smartphone app was successful in enhancing motivation to continue drug therapy adherence and adopt healthy lifestyle changes. Thus, disease-specific apps could aid secondary prevention care.

Geneva Stairs Study Findings: Workplace Physical Activity Reduces Serum PCSK9 Levels

Written by Brian Hoyle

As described by Christel Kamani, MD, Geneva University Hospitals, Geneva, Switzerland, further blood analysis of participants in the Geneva Stairs Study [Meyer P et al. *Eur J Cardiovasc Prev Rehab.* 2010] has linked regular workplace physical activity in the form of stair climbing with decreased plasma level of proprotein convertase subtilisin/kexin type 9 (PCSK9). These results bolster the value of regular physical activity in the reduction of low-density lipoprotein cholesterol (LDL-C), suggesting a novel mechanism through the modulation of the PCSK9 pathway.

In the Geneva Stairs Study, 77 Geneva University Hospitals employees who were healthy but physically

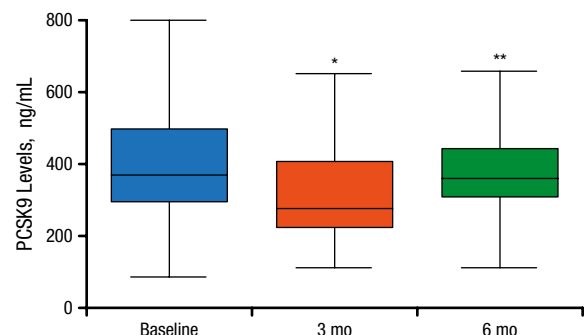
inactive regularly used stairs in their workplace instead of the elevator for a 6-month period. The use of stairs during the first 3 months was actively promoted, followed by another period of 3 months with no specific recommendations and where the use of stairs was less intensive. Monitoring over the 6 months revealed exercise-related improvements in a number of parameters usually associated with an increased risk of adverse cardiovascular events, including LDL-C (absolute change, $-0.13\% \pm 0.49\%$; relative change, $-3.0\% \pm 13.5\%$; $P = .026$). The findings implicated stair climbing as a simple means to reduce cardiovascular disease risk.

Presently, the blood samples from 67 of the study participants (mean age, 42.7 ± 8.8 years) were examined for PCSK9, a protein present in the liver as well as the kidney and tissues of the small intestine. PCSK9 functions to reduce the number of LDL receptors on the plasma surface of hepatocytes; thus, there is a correlation between plasma level of PCSK9 and plasma level of LDL-C.

In the first 3 months of the study, which was the period of peak stair-climbing activity, a significant decrease in PCSK9 levels was observed (baseline, 403.6 ± 166.0 ng/mL; 3 months, 324.3 ± 146.2 ng/mL; $P = .001$). In the final 3 months, when stair climbing was less intensive, serum PCSK9 levels rose to approximate the baseline condition (6 months, 381.8 ± 127.9 ng/mL; $P = .260$). A similar pattern was apparent for LDL-C, with a significant difference ($P = .010$) from baseline (3.5 ± 0.9 mmol/L) to 3 months (3.3 ± 0.9 mmol/L), with a return to the baseline value at 6 months ($P = .527$).

Plasma PCSK9 levels at baseline, 3 months, and 6 months are summarized in Figure 1.

Figure 1. Plot of Plasma PCSK9 Levels at Baseline, 3 Months, and 6 Months



PCSK9, proprotein convertase subtilisin/kexin type 9.

* $P < .011$ vs baseline; ** $P < .260$.

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