In patients who received first- or second-generation DES, outcomes failed to show a benefit of DAPT treatment for 24 months. According to Prof. Valgimigli, "While we cannot rule out the possibility that a smaller-than-previously anticipated benefit may exist, the clear increase in bleeding, transfusion, and net adverse clinical events suggests that current recommendations may have overemphasized the benefit over the risk of long-term treatment with aspirin and clopidogrel."

These findings question the validity of current guideline recommendations, which were based on registry data. According to Prof. Valgimigli, if the risk of morbidity due to bleeding outweighs the anticipated benefit that is afforded by thienopyridine therapy, earlier discontinuation should be considered [Duke Heart Registry; *JAMA* 2007].

PURE: CV Drugs Underused for Secondary Prevention in Poor and Rural Populations

Written by Anne Jacobson

Despite proven efficacy and relatively low cost, key secondary prevention medications are widely underused in populations with prevalent cardiovascular disease (CVD), particularly in poor countries and rural areas, according to findings from the Prospective Urban Rural Epidemiological (PURE) study.

PURE is the first prospective study to evaluate the use of cardiovascular (CV) drugs for secondary prevention across countries with differing levels of economic development. Salim Yusuf, MD, McMaster University, Hamilton, Ontario, Canada, presented results from the PURE study.

From 2003 to 2009, the PURE study enrolled 153,996 adults from 628 urban and rural communities in 17 countries, with a subset of 5650 patients who reported a prior coronary heart disease (CHD) event and 2292 who reported a prior stroke. Participating countries were classified as high-income (Canada, Sweden, and United Arab Emirates), upper-middle-income (Argentina, Brazil, Chile, Malaysia, Poland, South Africa, and Turkey), lower-middle-income (China, Colombia, and Iran), and low-income (Bangladesh, India, Pakistan, and Zimbabwe), based on World Bank criteria at the beginning of the study. Medical history and use of key secondary preventive medications were assessed with a combination of telephone interviews, home visits, and clinic visits.

Across all countries, only a minority of patients aged 35 to 70 years with a history of CHD or stroke reported taking key secondary preventive drugs, including antiplatelet drugs, aspirin (25.3%), angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs; 19.5%), β-blockers (17.4%), or statins (14.6%).

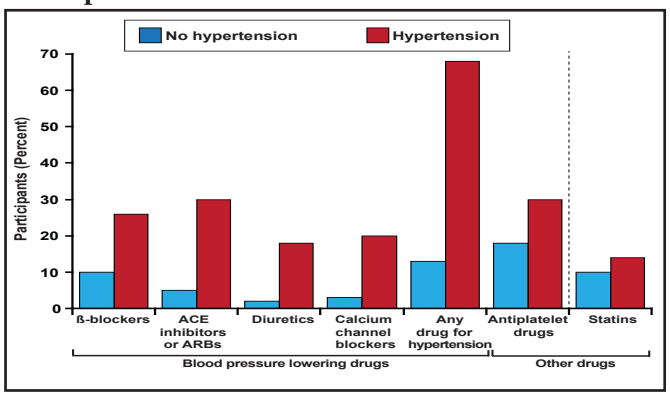
Between-country variations in medication use were twice as large as patient-level variability due to age, sex, education, smoking, obesity, hypertension, and diabetes, suggesting that national policies and health system structures have a predominant role in secondary prevention.

Medication use was highest in high-income countries and decreased with country income (p-trend <0.0001 for every drug type). Gaps between low-income and high-income countries were approximately 7-fold for aspirin and 20-fold for statins. Although 88.8% of patients in high-income countries took at least 1 drug for secondary prevention, far fewer patients received any medication in upper-middle-income countries (54.9%), lower-middle-income countries (30.7%), and low-income countries (19.8%).

There were also differences that were observed between types of communities, with patients in urban areas more likely than those in rural communities to take antiplatelet drugs (28.7% vs 21.3%), β-blockers (23.5% vs 15.6%), ACE inhibitors or ARBs (22.8% vs 15.5%), and statins (19.9% vs 11.6%), regardless of the economic status of the country (p<0.0001 for all drugs). However, gaps between urban and rural medication use were widest in the poorest counties (p interaction<0.0001).

Among patient-level factors, patients with CVD and hypertension were more likely than those with CVD alone to receive drugs that also lowered blood pressure, including β-blockers (28% vs 10%) and ACE inhibitors or ARBs (30% vs 5%; Figure 1). Conversely, younger patients; women; smokers; and those who were less educated, nonobese, or nondiabetic were less likely to use drugs for secondary prevention.

Figure 1. Drug Use by History of Hypertension in Participants with CVD.



Reproduced with permission from *The Lancet*; Use of secondary prevention drugs for cardiovascular disease in the community in high-income, middle-income, and low-income countries (the PURE Study): a prospective epidemiological survey; Yusuf S et al. 2011.

Long-term follow-up of the PURE study is ongoing. Future reports from the PURE trial will examine specific barriers to effective health care delivery, with the intention of shaping national policies to increase access to medications that are vital for the secondary prevention of CVD.

The results of this large global study underscore the importance of efforts to increase the use of proven secondary preventive therapies and offer an opportunity to reduce CV morbidity and mortality using proven, available, and inexpensive therapies. While the greatest need appears to be in lower-income countries, there appears to be significant underuse in high-income countries as well. These data support the concept of a "polypill," which has the potential to deliver multiple proven therapies in a single pill in an attempt to close the large treatment gap that was observed in this analysis. The appeal of such an approach is the simplicity that it offers to deliver several drugs at once, which may outweigh the limited flexibility in the selection of the specific drugs and their doses.

Additional reading: Yusuf S et al. *Lancet* 2011.

Postprandial TG and Risk in Patients with CVD

Written by Anne Jacobson

The Homburg Cream and Sugar Study (HCS) provided additional information regarding the relationship of fasting and postprandial triglyceride (TG) levels and risk in patients with cardiovascular disease (CVD). The study was designed to determine whether the measurement of postprandial TG levels improved risk prediction of cardiovascular (CV) events over traditional risk markers in stable patients with CVD. Risk prediction using fasting serum TG in high-risk patients with normal impaired glucose tolerance remains uncertain. The role of postprandial serum TGs as a risk modifier in secondary prevention is unknown. Ulrich Laufs, MD, Universitätsklinikum des Saarlandes, Homburg, Germany, discussed the results of the prospective HCS study [NCT00628524].

A long-standing association exists between elevated TG levels and CVD [Miller M et al. *Circulation* 2011; Sarwar N et al. *Circulation* 2007; Austin MA et al. *Am J Cardiol* 1998]. However, the extent to which TG directly promotes CVD or represents an independent biomarker of risk has been debated for decades [Hulley SB et al. *N Eng J Med* 1980]. Serum concentrations of TG-rich lipoproteins are strongly correlated with the time and the type of food intake and therefore the within patient variability is large. In addition, concomitant metabolic factors such as insulin resistance and genetic predisposition affect the individual fasting TG and postprandial TG kinetics. Impaired glucose tolerance and diabetes remain undiagnosed in a significant proportion of patients which may be important for the epidemiologic association of TG with CVD. HCS is the first study that determines glucose tolerance and postprandial TGs concurrently in a larger cohort of individuals.

Basic science suggests that nonfasting TG may correlate more closely with atherogenic remnant lipoprotein particles. Hydrolysis of the postprandial TG-rich lipoproteins yields small cholesterol-enriched remnant lipoprotein particles that have been shown to exert atherogenic effects and the lipolysis of TG-rich lipoproteins along the vessel wall producing potentially toxic oxidized fatty acids. The concept that atherosclerosis was a postprandial phenomenon was suggested many years ago. Subgroup analyses of the Copenhagen City Heart Study and the Women's Health Study found that nonfasting TGs represent a superior predictor of incident CVD compared with fasting levels in primary prevention [Jackson KG et al. *Atherosclerosis* 2011].

The HCS study was therefore designed to determine whether characterization of postprandial TG kinetics may improve the prediction of CV events in addition to the assessment of glucose tolerance and traditional risk factors. The researchers developed an oral TG and glucose tolerance test to obtain standardized measurements of postprandial TG kinetics in 514 consecutive patients with angiographically confirmed coronary artery disease (CAD). Follow-up was 18 months, and the primary outcome was the composite of CV death and CV hospitalization, a broad endpoint that included hospitalization for acute coronary syndromes, unplanned (symptom-driven) coronary angiography, heart failure, ischemic stroke or transient ischemic attack, cardiac arrhythmia that required resuscitation, and unplanned cardiac device implantation.

Findings indicated that postprandial TG kinetics depended on glucose tolerance. Patients with normal glucose tolerance had lower fasting TG (n=126; mean TG 108±42 mg/dL) and a lower absolute postprandial TG increase compared with patients with pathological glucose metabolism (n=388; mean fasting TG 172±157 mg/dL), whereas the mean relative TG increase was similar.

Overall, postprandial TG level was not associated with CV risk (p=NS). Fasting TG level was associated with risk in univariate analysis; however, after adjustment, this relationship was no longer significant (p=NS).

Continued on page 20