among women than among men, especially for women <60 years, among whom smoking increased from 37.3% to 73.1% and obesity increased from 17.6% to 27.1%. Prof. Danchin noted that these findings indicate the crucial need to target future preventive measures toward younger women. Overall, significantly fewer patients had a CV history (p<0.001), but significantly more had typical risk factors, such as hypertension (p=0.006) and hypercholesterolemia (p=0.001) compared with 15 years ago.

The study also demonstrated significant increases in the use of reperfusion therapy compared with 15 years ago, with the rate of percutaneous coronary intervention increasing from 11.9% to 60.8% (p<0.001). The use of evidence-based interventions within the first 48 hours, such as treatment with β-blockers, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, and statins, also increased significantly (p<0.001). In addition, the time from onset of symptoms to first medical contact significantly decreased over time (p<0.001). All of these factors likely contribute to the decreasing mortality rate observed over time.

Filippo Crea, MD, PhD, Institute of Cardiology, Catholic University of the Sacred Heart, Rome, Italy, noted that the study had several strengths, but its weaknesses included potential bias related to a prevalent inclusion of large-volume hospitals and a lack of information on infarct size, microvascular obstruction, and ejection fraction at discharge; and lack of follow-up data on recurrence of acute coronary events.

Results from the PURE Study

Written by Maria Vinall

Results from the Prospective Urban Rural Epidemiology [PURE] study, presented by Salim Yusuf, MD, McMaster University, Hamilton, Ontario, Canada, indicated that different strategies are needed to influence health behaviors in countries, depending upon their socioeconomic status. In relatively low-income countries, key strategies include making healthy foods accessible and affordable, and promoting smoking cessation. Among relatively more high-income/industrialized countries, efforts should be focused on increasing physical activity and decreasing fat consumption, while continuing to promote smoking cessation.

Diet, physical activity, and smoking account for 50% to 60% of the risk for cardiovascular disease (CVD) [Yusuf S et al. *Lancet* 2004; Tu JV. *Lancet* 2010]; however, these factors vary markedly both across and within countries, due to environmental and societal factors. The PURE study

was designed to create an understanding of these factors in order to develop contextually appropriate strategies for CVD prevention.

The PURE study was comprised of 153,996 individuals (aged 35 to 70 years; 42.1% men) from 348 urban and 280 rural communities in 17 low-, middle-, and high-income countries for whom data on diet, physical activity, and smoking were collected during 2003-2010. Validated food frequency questionnaires were used to record diet; physical activity (recreational and nonrecreational/obligatory) was collected using the International Physical Activity Questionnaire. These factors, plus smoking prevalence (ever, current, and quitting) were then related to country gross domestic product (GDP; World Bank statistics) and household wealth (wealth index) overall and separately for individuals from urban and rural areas.

Results from the PURE study showed that among those living in low-income countries there is less consumption of fruits, vegetables, proteins and fats, and a higher consumption of carbohydrates, which researchers attributed to the affordability of different foods. Activity levels were higher in low-income countries due to a higher level of obligatory physical activities (mostly work and transportation-related). Smoking was also more prevalent among individuals in low-income countries. As country GDP increased, there was an increased consumption of fruits and vegetables, accompanied by a higher percentage of energy obtained from total (but not saturated) fats and proteins, with a lower percentage of energy from carbohydrates. Physical activity declined with increasing GDP mostly because of a marked decline in obligatory/nonrecreational activity that was not compensated for by an increase in recreational physical activity. In all categories studied, the association of household wealth to diet, physical activity, and quitting smoking were similar to that observed for GDP.

"Policies to prevent CVD need to focus on different aspects of lifestyle among the rich versus the poor and between rich and poor countries," said Prof. Yusuf. "In particular, healthy foods need to become more affordable."

PURE: Treatment and Control of Hypertension

Written by Lori Alexander

Hypertension is a global epidemic; yet rates of awareness, treatment, and control are lower than expected around the world, according to the results of the Prospective

Urban Rural Epidemiology [PURE] study. Reporting on the study, Rafael Diaz, MD, Estudios Cardiológicos Latinoamérica, Rosario, Argentina, noted that the overall prevalence of hypertension was approximately 41%, with fewer than half of people with hypertension being aware of the diagnosis or being treated for it, and only 13% of those with a diagnosis of hypertension having controlled blood pressure (BP).

The PURE study included 153,996 adults (ages 35 to 70 years; mean age, 50.4 years) from 628 rural and urban communities in 3 high–income countries (HIC), 10 upper- (UMIC) and lower–middle-income countries (LMIC), and 4 low-income countries (LIC). Hypertension was defined as an average systolic BP (SBP) ≥140 mm Hg or a diastolic BP (DBP) ≥90 mm Hg, the self-report of a medical diagnosis of hypertension, or the use of BP-lowering medications. The mean SBP for the study population was 131.23 mm Hg, and the mean DBP was 81.99 mm Hg. Most individuals (36.8%) had prehypertension; 21.9% had stage 1 hypertension, and 13.4% had stage 3 or 4 hypertension. Approximately 28% of the population had an optimal BP.

Awareness, treatment, and control of hypertension varied among rural and urban areas within the 3 categories of countries. In HIC and MIC, there was a greater prevalence of hypertension in rural areas than in urban areas; in LIC, the reverse was true, with a higher prevalence in urban areas. The prevalence of hypertension was greater among men in HIC and MIC, but was greater among women in LIC.

The investigators also assessed prevalence, awareness, treatment, and control among subgroups categorized by the presence of other cardiovascular risk factors (eg, diabetes, current or past smoking, obesity, age >65 years, and male sex). Rates were highest among individuals with ≥2 risk factors (compared with no or 1 risk factors). Hypertension was controlled in 15% of individuals with ≥2 risk factors, in 12% with 1 risk factor, and in 8% with no risk factors.

The low rates of BP control may be related to the low use of ≥2 BP-lowering medications. Although the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure notes that ≥2 medications are required for most people with hypertension, the control rates in PURE ranged from 15.7% in HIC to 13.1% in MIC to 1.6% in LIC.

Prof. Diaz noted that novel strategies to detect hypertension (such as systematic screening), simplified treatment algorithms, and facilitation of the early use of combination therapies may be helpful in improving the global control of hypertension, particularly in LIC.

The comparisons were adjusted for age and sex. The urban-rural differences in awareness (LIC and LMIC), treatment (LIC, LMIC, and UMIC), and control (LIC, LMIC, and UMIC) were significant (p<0.001).

Genetic Determinants of Variability in Dabigatran Exposure

Written by Lori Alexander

Genetic factors may be responsible for some of the inter-individual variability in dabigatran exposure, according to findings from the Randomized Evaluation of Long-Term Anticoagulation Therapy [RE-LY] Genetics study. The RE-LY trial demonstrated that dabigatran 150 mg BID was superior to warfarin, while the 110 mg dose was noninferior to warfarin in the reduction of stroke in patients with atrial fibrillation [Connolly SJ et al. *N Engl J Med* 2009]. The lower dose was associated with less major bleeding when compared with warfarin, while the higher dose (150 mg) had a similar rate of major bleeding.

Dabigatran etexilate is an oral prodrug that is rapidly converted by esterases (carboxylesterase-1 [CES1]) to the active agent dabigatran, explained Guillaume Pare, MD, McMaster University, Hamilton, Ontario, Canada, who presented the findings of the study. CES1 is a serine esterase that can activate or deactivate various drugs. Prof. Pare and colleagues hypothesized that genetic variability in the pathways required for bioactivation of dabigatran might be responsible for some of the 30% variability in dabigatran exposure.

In the first phase of the study, a genome-wide analysis (551,203 markers) was performed on biologic samples from 1490 patients of European ancestry enrolled in the RE-LY trial randomized to dabigatran to identify the genetic determinants of peak and trough concentrations of dabigatran. Another 807 patients from RE-LY treated with warfarin also underwent genotyping. Identified genetic determinants were tested for their association with efficacy and safety outcomes in an overlapping sample of 1694 patients. The primary efficacy endpoint was stroke or systemic embolism, and the primary safety endpoint was any bleeding (minor or major).

Genome-wide analysis demonstrated 2 variants associated with peak concentration of dabigatran, one at the ABCB1 locus (rs4148738) and one at the CES1 locus (rs8192935). The ABCB1 polymorphism was associated with a 12%