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Representation of Older Adults in the Late-Breaking Clinical Trials American Heart Association 2011 Scientific Sessions

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To the Editor

Increasingly, the practice of medicine has relied on applicable and available evidence to deliver quality care. Cardiovascular medicine has led the way using numerous clinical trials as the basis of clinical practice guidelines. However, despite the strong association of aging with the development of cardiovascular disease, randomized clinical trials rarely enroll a substantial proportion of older adults, leading experts to question the applicability of the evidence base to the typical patient with cardiovascular disease (1). We sought to document the inclusion of older adults in contemporary high-profile, recently conducted clinical trial populations in cardiovascular disease and compare the age characteristics of the clinical trials with the age characteristics of the diseases being studied.

All late-breaking clinical trials (LBCTs) at the 2011 American Heart Association (AHA) Scientific Sessions were included in this study (2). For each LBCT, a brief summary of the important results, with all available age information, was extracted. This represented inclusion or exclusion characteristics on the basis of age and the age information of the baseline characteristic (means, medians, and proportions above and below age cut points). The LBCTs were divided into disease-based categories, and results were tabulated by category. When available, the published report for each LBCT was used. In cases in which the reports were not published, information was obtained from the LBCT slide set on the AHA Web site (2) and supplemented with information from ClinicalTrials.gov as needed. To compare the clinical trial cohort with the community population, the prevalence of older adults in each disease category was ascertained.

The 22 LBCTs at the 2011 AHA Scientific Sessions were divided by category: coronary artery disease (5 trials), acute coronary syndromes (5), chronic heart failure (3), atrial fibrillation (3), cardiac surgery and intervention (4), peripheral artery disease (1), and venous thromboembolism (1). Among those trials, 8 did not include older adults (age >60 to 80 years, depending on the study). In trials in which the percents of older adults were available, adults age >75 years constituted 9% to 55% of the enrolled subjects. In the remaining trials, the mean age was 54 to 66 years. This contrasts with the prevalence of older age among those with cardiovascular diseases in the general population, in which older adults represent one-third to one-half of patients with the cardiovascular diseases studied in these trials. See Table 1 (3–25) for details.

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With aging of the United States population and the evolving demographics of cardiovascular disease, we reviewed the LBCTs at the 2011 AHA Scientific Sessions to determine the ages of enrolled subjects and, when available, the percent of older adults included each trial. Our findings show that in the current era of clinical cardiovascular research, the demographics of those enrolled in the LBCTs are inconsistent with those of the community population and inadequately represent older adults with cardiovascular disease.

This report is not the first to raise concern about the enrollment of older adults in clinical trials in cardiovascular disease (26). Lee et al. (27) documented the low representation of older adults in randomized trials of acute coronary syndromes. Kitzman and Rich (28) identified the low percent of older adults in heart failure research in comparison with the advanced ages of most patients with heart failure. The gap in the evidence base for cardiovascular care in older adults has led experts to call for a new paradigm in the way we provide cardiac care and in the way we study cardiovascular disease (1). Nonetheless, this review of LBCTs at the 2011 AHA Scientific Sessions confirms that current high-profile cardiovascular clinical research still does not address the challenges of an aging society.

There are several disadvantages to systematically excluding older adults from clinical trials. When caring for older adults, we are forced to apply therapies that have not been proven effective in this vulnerable population. Second, by failing to enroll older and more complicated patients, the generalizability of the trial results to the broad population can be questioned. If a therapy shows a small benefit in the context of a highly selected clinical trial population, how can we reliably translate those results to the patients we care for, young and old?

In conclusion, the enrollment of older adults in the LBCTs at the 2011 AHA Scientific Sessions is low and does not reflect the representation of older adults with cardiovascular disease in the general population. Despite multiple calls to generate more age-specific data to better guide management for the older adults most vulnerable to cardiovascular disease and to cardiovascular disease management complexities, this need is still not being prioritized in cutting-edge, premier cardiovascular research efforts.

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Table 1

Older Adults With Cardiovascular Disease Compared With Older Adults Included in Cardiovascular Clinical Trials With Cardiovascular Disease Compared With Older Adults Included in Cardiovascular Clinical Trials

Stable coronary heart disease		
Population	Coronary heart disease prevalence	29% age >75 yrs (3)
Clinical trials	"Comparison of the Progression of Coronary Atherosclerosis for Two High Efficacy Statin Regimens With Different HDL Effects: SATURN Study Results" (4)	Excluded subjects age >75 yrs
	"Lipid-Modulating Effects of Evacetrapib, a Novel CETP Inhibitor, Administered as Monotherapy or in Combination With the Most Commonly-Used Statins" (5)	Mean age 56 yrs
	"Extended-Release Niacin Does Not Reduce Clinical Events in Patients With Established Cardiovascular Disease Whose LDL-Cholesterol is Optimally Controlled With Statin Therapy: Results From the AIM-HIGH Trial" (6)	Mean age 64 yrs
	"ELEVATE-TIMI 56: Escalating Clopidogrel by Involving a Genetic Strategy-TIMI 56" (7)	Excluded subjects age >75 yrs
	"Practice-Based Opportunities for Weight Reduction (POWER)" (8)	Mean age 54 yrs
Acute coronary syndromes		
Population	Incident heart attacks	45% age >75 yrs (9)
Clinical trials	"Intracoronary Compared With Intravenous Bolus Abciximab Application During Primary Percutaneous Coronary Intervention: AIDA STEMI Trial" (source: presentation slides)	18% age ≥75 yrs
	"Abciximab Plus Unfractionated Heparin Versus Bivalirudin in Patients With Non-ST-Segment Elevation Myocardial Infarction Undergoing Percutaneous Coronary Intervention. The ISAR-REACT 4 Randomized Trial" (10)	Excluded subjects age >80 yrs
	"The Thrombin Receptor Antagonist for Clinical Event Reduction in Acute Coronary Syndrome (TRA*CER) Trial" (11)	17% age ≥75 yrs
	"Anti-Xa Therapy to Lower Cardiovascular Events in Addition to Standard Therapy in Subjects With Acute Coronary Syndrome-Thrombolysis in Myocardial Infarction 51 (ATLAS ACS 2-TIMI 51) Trial: A Randomized, Double-Blind, Placebo Controlled Study to Evaluate the Efficacy and Safety of Rivaroxaban in Acute Coronary Syndrome" (12)	9% age ≥75 yrs
	"The Impact of Full Coverage for Preventive Medications After Myocardial Infarction on Recurrent Vascular Events: The Post-MI Free Rx Event and Economic Evaluation (Post-MI FREEE) Trial" (13)	Excluded subjects age ≥65 yrs
Chronic heart failure		
Population	Incident heart failure	23% age ≥ 80 yrs (14)
Clinical trials	"Effect of Cardiac Stem Cells in Patients With Ischemic Cardiomyopathy: Interim Results of the SCIPIO Trial" (15)	Excluded subjects age >75 yrs
	"Double Blind Placebo Controlled Dose Ranging Study of the Efficacy and Safety of Celivarone 50, 100 or 300 mg OD With Amiodarone as Calibrator for the Prevention of ICD Interventions or Death (ALPHEE)" (16)	Mean age 64 yrs
	"Pharmacist Intervention to Prevent Hospitalization and Death in Patients With Heart Failure: A Prospective Cluster Randomised Controlled Trial" (17)	55% of subjects age ≥70 yrs
Atrial fibrillation		
Population	Atrial fibrillation prevalence	37% age ≥80 yrs (18)
Clinical trials	"Atrial Fibrillation Catheter Ablation Versus Surgical Ablation Treatment: A multi-Center Randomized Clinical Trial" (19)	Excluded subjects age >70 yrs
	"A Randomized Multicenter Comparison of Radiofrequency Ablation and Antiarrhythmic Drug Therapy as First-Line Treatment in 294 Patients With Paroxysmal Atrial Fibrillation" (source: presentation slides)	Excluded subjects age >70 yrs
	"The Results of the PALLAS Study: PALLAS Was Designed to Test Whether Dronedarone Could Reduce Major Vascular Morbidity and Mortality in Patients	Enrolled subjects age ≥65 yrs, 52% age ≥75 yrs

	With Permanent Atrial Fibrillation and Previous Vascular Disease or Multiple Risk Factors" (20)	
Cardiac surgery and intervention		
Population	Cardiac procedures	52% age >65 yrs (9)
	Percutaneous coronary intervention	26% age ≥75 yrs (21)
Clinical trials	"Randomized Trial of Early Surgery Versus Conventional Treatment for Infective Endocarditis (EASE)" (source: presentation slides)	Excluded subjects age >80 yrs
	"Colchicine Reduces Post-Operative Atrial Fibrillation. Results of the COPPS Atrial Fibrillation Study" (22)	Mean age 66 yrs
	"Testing an Evidence-Based, Individualized Informed Consent Form to Improve Patients' Experiences With PCI" (source: presentation slides)	No information available
	"Outcomes of Non-Primary PCI at Hospitals With and Without On-Site Cardiac Surgery: A Randomized Study" (source: presentation slides)	Mean age 64 yrs
Peripheral vascular disease		
Population	Peripheral artery disease prevalence	57% age >70 yrs (23)
	Incident venous thromboembolism	26% age ≥75 yrs (24)
Clinical trials	"Claudication Treatment Comparative Effectiveness: 6 Month Outcomes From the CLEVER Study" (source: presentation slides)	Mean age 64 yrs
	"Extended Anticoagulant Prophylaxis in Initially Hospitalized Medically Ill Patients: Results of the ADOPT (Apixaban Dosing to Optimize Protection From Thrombosis) Trial" (25)	30% age ≥75 yrs

AIDA STEMI = Abciximab Intracoronary Versus Intravenously Drug Application in ST-Elevation Myocardial Infarction; AIM-HIGH = Atherothrombosis Intervention in Metabolic Syndrome With Low HDL/High Triglycerides: Impact on Global Health; CETP = cholesterol ester transfer protein; CLEVER = Claudication: Exercise Versus Endoluminal Revascularization; COPPS = Colchicine for Prevention of the Postpericardiotomy Syndrome; HDL = high-density lipoprotein; ISAR-REACT 4 = Intracoronary Stenting and Antithrombotic Regimen: Rapid Early Action for Coronary Treatment 4; MI = myocardial infarction; OD = once daily; PALLAS = Permanent Atrial Fibrillation Outcome Study Using Dronedarone on Top of Standard Therapy; SATURN = Study of Coronary Atheroma by Intravascular Ultrasound: Effect of Rosuvastatin Versus Atorvastatin; SCIPIO = Stem Cell Infusion in Patients With Ischemic Cardiomyopathy.