

Susan R. Heckbert, MD, PhD
Contribution to Science

1. Atrial fibrillation (AF) risk factors and outcomes. The Institute of Medicine, AHA, and NHLBI have all identified AF management as a top priority for research. In particular, relatively little is known about AF risk factors and outcomes in representative elderly populations and in race/ethnic groups other than whites. Central findings of our investigations in AF include: in patients with diabetes, poor glycemic control and longer diabetes duration are associated with higher AF risk; despite having more AF risk factors, blacks have lower rates of incident AF than whites; among elderly individuals at a given age, cognitive function declines faster over time in those with AF than in those without AF, even in the absence of stroke; and in the US Medicare population, during the first 5 years after a new AF diagnosis, mortality was the most frequent major outcome and new heart failure was the most common nonfatal event (as opposed to stroke). These findings have direct clinical relevance for the care of patients with AF and raise new questions about pathophysiology that inspire further research.

- a. Dublin S, Glazer NL, Smith NL, Psaty BM, Lumley T, Wiggins KL, Page RL, **Heckbert SR**. Diabetes mellitus, glycemic control, and risk of atrial fibrillation. *J Gen Intern Med* 2010;25:853-8. PMC2896589.
- b. Jensen PN, Thacker EL, Dublin S, Psaty BM, **Heckbert SR**. Racial differences in the incidence of and risk factors for atrial fibrillation in older adults: the Cardiovascular Health Study. *J Amer Geriatr Soc* 2013;61:276-80. PMC3878638.
- c. Thacker EL, McKnight, B, Psaty BM, Longstreth WT Jr, Sitlani CM, Dublin S, Arnold AM, Fitzpatrick AL, Gottesman RF, **Heckbert SR**. Atrial fibrillation and cognitive decline: a longitudinal cohort study. *Neurology* 2013;81:1-7. PMC3770176.
- d. Piccini JP, Hammill BG, Sinner MF, Hernandez AF, Walkey AJ, Benjamin EJ, Curtis LH, **Heckbert SR**. Clinical course of atrial fibrillation in older adults: the importance of cardiovascular events beyond stroke. *Eur Heart J* 2014;35:250-6. PMC3896863.

2. Genomics of AF. Previously, inherited forms of AF were considered rare, but recent research suggests that AF, and in particular AF with onset at an early age, is heritable. I co-chair the Atrial Fibrillation/PR interval Working Group of the Cohorts for Heart and Aging in Genomic Epidemiology (CHARGE) Consortium and am an active participant in the AFGen Consortium. My colleagues and I have published a series of articles establishing genetic associations with AF and electrocardiographic PR interval using genome-wide association analysis, examining the role of European ancestry to explain the observed lower AF incidence in African Americans, and using targeted sequencing to follow up on GWAS hits. Our current collaborative work focuses on using exome sequencing and whole genome sequencing to study the genetic basis of AF. The goal of this highly collaborative genetic work is increase understanding of the mechanisms of AF initiation and persistence, and to identify potential targets for drug development.

- a. Pfeufer A, van Noord C, Marcianti KD, Arking DE, Larson MG, Smith AV, Tarasov KV, Müller M, Sotoodehnia N, Sinner MF, Verwoert GC, Li M, Kao WHL, Köttgen A, Coresh J, Bis JC, Psaty BM, Rice K, Rotter, JI, Rivadeneira F, Hofman A, Kors JA, Stricker BHC, Uitterlinden AG, van Duijn CM, Beckmann BM, Sauter W, Gieger C, Lubitz SA, Newton-Cheh C, Wang TJ, Magnani JW, Schnabel RB, Vasani RS, Najjar SS, Lakatta E, Schlessinger D, Uda M, Abecasis GR, Ehret GB, Boerwinkle E, Chakravarti A, Soliman EZ, Lunetta KL, Perz S, Wichmann HE, Meitinger T, Levy D, Gudnason V, Ellinor PT, Sanna S, Käb S, Witteman JCM, Alonso A, Benjamin EJ, **Heckbert SR**. Genome-wide association study of PR interval. *Nat Genet* 2010; 42: 153-9. PMC2850197.
- b. Ellinor PT, Lunetta KL, Glazer NL, Pfeufer A, Alonso A, Chung MK, Sinner MF, de Bakker PI, Mueller M, Lubitz SA, Fox E, Darbar D, Smith NL, Smith JD, Schnabel RB, Soliman EZ, Rice KM, Van Wagener DR, Beckmann BM, van Noord C, Wang K, Ehret GB, Rotter JI, Hazen SL, Steinbeck G, Smith AV, Launer LJ, Harris TB, Makino S, Nelis M, Milan DJ, Perz S, Esko T, Köttgen A, Moebus S, Newton-Cheh C, Li M, Möhlenkamp S, Wang TJ, Kao WH, Vasani RS, Nöthen MM, MacRae CA, Stricker BH, Hofman A, Uitterlinden AG, Levy D, Boerwinkle E, Metspalu A, Topol EJ, Chakravarti A, Gudnason V, Psaty BM, Roden DM, Meitinger T, Wichmann HE, Witteman JC, Barnard J, Arking DE, Benjamin EJ, **Heckbert SR**, Käb S. Common variants in KCNN3 are associated with lone atrial fibrillation. *Nat Genet* 2010;42:240-4. PMC2871387.

- c. Marcus GM, Alonso A, Peralta CA, Lettre G, Vittinghoff E, Lubitz SA, Fox ER, Levitzky YS, Mehra R, Kerr KF, Deo R, Sotoodehnia N, Akyzbekova M, Ellinor PT, Paltoo DN, Soliman EZ, Benjamin EJ, **Heckbert SR**. European ancestry as a risk factor for atrial fibrillation in African Americans. *Circulation* 2010;122:2009-15. PMC3058884.
- d. Boerwinkle E, **Heckbert SR**. Following-up genome-wide association study signals: lessons learned from the Cohorts for Heart and Aging Research in Genomic Epidemiology (CHARGE) Targeted Sequencing Study. *Circ Cardiovasc Genet* 2014 Jun;7(3):332-4. PMC4330964.

3. Medication effects and drug safety. I have a longstanding interest in medication effects and drug safety. My colleagues and I have conducted studies of medication use in relation to cardiovascular outcomes in the setting of Group Health, making use of the automated pharmacy data that records prescription medication use in an unbiased fashion for Group Health enrollees. I currently collaborate with Group Health investigators on the FDA Mini-Sentinel project, designed to develop methods for studying drug effects nationwide using large automated databases. I completed a recent term as a member of the US Food and Drug Administration (FDA) Drug Safety and Risk Management Advisory Committee, and am currently a member of the FDA Endocrinologic and Metabolic Drugs Advisory Committee. The goal of my contributions is to improve the safety and use of prescription medications in the US.

- a. **Heckbert SR**, Li G, Cummings SR, Smith NL, Psaty BM. Use of alendronate and the risk of incident atrial fibrillation in women. *Arch Intern Med* 2008;168:826-31.
- b. **Heckbert SR**, Wiggins KL, Glazer NL, Dublin S, Psaty BM, Smith NL, Longstreth WT Jr, Lumley T. Antihypertensive treatment with ACE inhibitors or beta-blockers and risk of incident atrial fibrillation in a general hypertensive population. *Am J Hypertens* 2009; 22:538-44. PMC2672972.
- c. Cook AJ, Tiwari RC, Wellman RD, **Heckbert SR**, Li L, Heagerty P, Marsh T, Nelson JC. Statistical approaches to group sequential monitoring of postmarket safety surveillance data: current state of the art for use in the Mini-Sentinel pilot. *Pharmacoepidemiol Drug Saf* 2012;21(Suppl 1):72-81.
- d. Drieling RL, LaCroix AZ, Beresford SA, Boudreau DM, Kooperbeg CL, **Heckbert SR**. Validity of self-reported medication use compared with pharmacy records in a cohort of older women: findings from the Women's Health Initiative. *Am J Epidemiol* (in press).

4. Use of electronic health record data in cardiovascular outcomes research. My colleagues and I have developed and validated methods for identifying cardiovascular disease outcomes using electronic health record data in large populations. My funded work in this area has been conducted in the settings of Group Health Cooperative, the Cardiovascular Health Study, Women's Health Initiative, Multi-Ethnic Study of Atherosclerosis, Jackson Heart Study, and in US Medicare enrollees. Through this work, we have identified cost-effective, validated methods for studying the determinants and outcomes of cardiovascular disease in large, representative populations.

- a. **Heckbert SR**, Kooperberg C, Safford MM, Psaty BM, Hsia J, McTiernan A, Gaziano JM Frishman WH, Curb JD. Comparison of self-report, hospital discharge codes, and adjudication of cardiovascular events in the Women's Health Initiative. *Am J Epidemiol* 2004;160:1152-1158.
- b. Piccini JP, Hammill BG, Sinner M, Jensen PN, Hernandez AF, **Heckbert SR**, Benjamin EJ, Curtis LH. Incidence and prevalence of atrial fibrillation and associated mortality among Medicare beneficiaries, 1993-2007. *Circ Cardiovasc Qual Outcomes* 2012;5:85-93. PMC3332107.
- c. Jensen PN, Johnson K, Floyd J, **Heckbert SR**, Carnahan R, Dublin S. A systematic review of validated methods for identifying atrial fibrillation using administrative data. *Pharmacoepi Drug Saf* 2012;21(Suppl 1):141-147. PMC3674852.
- d. Wallace ER, Siscovick DS, Sitlani C, Dublin S, Mitchell P, Odden M, Hirsch CH, Thielke S, **Heckbert SR**. Incident atrial fibrillation and disability-free survival in the Cardiovascular Health Study. *J Am Geriatr Soc* 2016 Mar 1. doi: 10.1111/jgs.14037. [Epub ahead of print]

5. Mentoring of trainees and junior faculty. I am committed to recruiting and training the next generation of highly skilled researchers. I teach the graduate course in Pharmacoepidemiology at the University of Washington (UW), and I have served as a mentor for trainees in the UW T32 Training Programs in Cardiovascular Epidemiology, Cardiovascular Biostatistics, and Pulmonary and Critical Care Medicine. I was chair of the UW K30 Clinical Research Curriculum Award from 2000-2007, took a lead role in the Education

Core of the UW Clinical and Translational Science Award from 2007-2010, and was Director of the UW Clinical Research Graduate Certificate Program in the UW Department of Epidemiology from 2008-2015. I am currently Associate Program Director of the UW T32 Palliative Care Training Grant. I have chaired 28 Epidemiology master's degree thesis committees and five PhD dissertation committees. Selected publications from my trainees are listed below, and several more are listed above in items 1-4 of "Contributions to Science".

- a. Rea TD, **Heckbert SR**, Kaplan RC, Psaty BM, Smith NL, Lemaitre RN. Smoking status and the risk of recurrent coronary events following myocardial infarction. *Ann Intern Med* 2002;137:494-500.
- b. Velicer CM, **Heckbert SR**, Lampe JW, Potter JD, Robertson C, Taplin SH. Antibiotic use in relation to the risk of breast cancer. *JAMA* 2004;291:827-35.
- c. Sotoodehnia N, Siscovick DS, Vatta M, Psaty BM, Tracy RP, Towbin J, Lemaitre RN, Rea TD, Durda JP, Chang J, Lumley TS, Cobb LA, Kuller LH, Burke GL, **Heckbert SR**. Beta2-adrenergic receptor genetic variants and risk of sudden cardiac death. *Circulation* 2006;113:1842-8.
- d. Glazer NL, Dublin S, Smith NL, French B, Jackson LA, Hrachovec J, Siscovick DS, Psaty BM, **Heckbert SR**. Newly detected atrial fibrillation and compliance with antithrombotic guidelines. *Arch Intern Med* 2007;167:246-52.

Complete list of published work in MyBibliography:

<http://www.ncbi.nlm.nih.gov/sites/myncbi/susan.heckbert.1/bibliography/41145634/public/?sort=date&direction=descending>