

Yale University

Patrick G. O'Connor, M.D., M.P.H.

*Professor of Medicine
Chief, Section of General Internal Medicine
School of Medicine
333 Cedar Street
P. O. Box 208025
New Haven, Connecticut 06520*

Campus address:

*Primary Care Center
789 Howard Avenue
Phone: 203-688-6532
Fax: 203-688-1198
E-Mail: patrick.oconnor@yale.edu*

Section of General Internal Medicine Yale University School of Medicine

Research Programs and Priorities 2005

Research in the Yale University Section of General Internal Medicine is focused on selected interrelated areas at the core of General Internal Medicine utilizing the principles and methods of Clinical Epidemiology and Health Services Research. Faculty in the Section apply these principles and methods to specific content areas including research methods and policy, HIV-related comorbid behaviors and conditions, occupational and environmental medicine, substance abuse, cerebral vascular disease, cognitive dysfunction in the elderly, cancer in the elderly, healthcare utilization and outcomes, medical education, international health. This work includes epidemiological studies, randomized clinical trials, case control studies, studies using large databases, and qualitative research. Faculty have also written several papers in the area of health care policy and have provided national leadership on topics such as ethical considerations in research and international health, the provision of substance abuse services, conflict of interest in research, and the care of underserved populations.

Several Section faculty are principal investigators and/or co-investigators in peer-reviewed research funded through federal and private agencies. In addition, a number of faculty hold federal or foundation-supported career awards to support their work. Along with their leadership roles in research activities related to the Yale Robert Wood Johnson Clinical Scholars Program, Section faculty have major leadership roles in research activities of the Yale Occupational and Environmental Medicine Program, and the Clinical Epidemiology Research Center at the VA Connecticut Healthcare System.

On the pages that follow, please find summaries of selected research programs and priorities in the Yale Section of General Internal Medicine including an overview of each program, a listing of the faculty involved in the programs, and a listing of program funding sources.

Patrick G. O'Connor MD, MPH
Professor and Chief,
Section of General Internal Medicine
January 7, 2005

I. The Insulin Resistance Intervention after Stroke (IRIS) Trial (www.iris-trial.org)

Overview: The IRIS trial is a randomized, double blind, placebo controlled clinical trial that will enroll 3136 participants at 93 hospitals. The primary aim is to determine if pioglitazone, an agent that reduces insulin resistance and has other potent vasoprotective effects, is effective in lowering the risk for stroke or myocardial infarction among non-diabetic men and women with a recent ischemic stroke and insulin resistance. Eligible subjects will be at least 45 years of age. Insulin resistance will be defined using an index based on fasting insulin and glucose values. Recruitment will be completed in 3 years and all patients will be followed for a minimum of 3 years (average of 4). Assuming an outcome rate of 27% at 4 years for placebo recipients, IRIS has 90% power to detect a 20% reduction in risk for the primary endpoints of fatal and non-fatal stroke and myocardial infarction.

The IRIS trial will determine the effectiveness of a new strategy, the treatment of insulin resistance in non-diabetic subjects, for preventing recurrent stroke and myocardial infarction after ischemic stroke. Since insulin resistance is estimated to affect 50% of stroke patients, this innovative treatment has the potential to benefit a large number of patients. If effective, pioglitazone will be comparable to carotid endarterectomy for symptomatic disease or anticoagulation for atrial fibrillation in terms of vascular events prevented.

Faculty:

Sandra L. Alfano, Pharm.D.	YNHH Pharmacy
Lawrence M. Brass, M.D.	Neurology
Dawn M. Bravata, M.D.	General Internal Medicine
Mark Gorman, M.D.	Neurology
Peter D. Guarino, M.P.H.	VA Cooperative Studies Program
Silvio E. Inzucchi, M.D.	Endocrinology
Walter N. Kernan, M.D. (PI)	General Internal Medicine
Peter N. Peduzzi, Ph.D.	Epidemiology and Public Health
Catherine M. Viscoli, Ph.D.	General Internal Medicine
Lawrence H. Young, M.D.	Cardiology

Funding: The study is a Cooperative Program funded by the National Institutes of Neurological Disorders and Stroke.

II. Veterans Aging Cohort Study (www.vacohort.org)

Overview: An observational cohort study of >6,000 veterans in care at 8 VA medical centers with and without HIV infection focused on the role of alcohol and other important comorbid behaviors and conditions in determining survival and quality of life for people with and without HIV infection. The study works with data from the VA national electronic medical record system supplemented with patient and provider surveys; blood and DNA banked specimens; and telephone interviews. It is now in the planning and feasibility stages of a large intervention trial targeted at changing provider and patient behaviors through the

use of a tailored electronic medical record and targeted behavioral interventions. The study is primarily funded by the NIAAA with supplemental funding from the VA (clinical and research dollars), NIDA, NIMH, NIA, Robert Wood Johnson Foundation, and grants from industry.

Faculty:

Amy Justice, MD, Ph.D. (PI)	General Internal Medicine
Shawn Fultz, M.D., M.P.H.	General Internal Medicine
Scott Braithwaite, M.D.	General Internal Medicine
Joseph Goulet, Ph.D.	General Internal Medicine
Joseph Erdos, M.D.	Psychiatry
Patrick O'Connor, M.D.	General Internal Medicine
David Fiellin, M.D.	General Internal Medicine
Perry Miller, M.D.	Anesthesiology
Seth Powsner, M.D.	Psychiatry
David Paltiel, Ph.D.	School of Public Health
Kristina Crothers, M.D.	Pulmonary
Lydia Chwastiak, M.D.	Psychiatry and General Internal Medicine
Bridget Martel, M.D.	General Internal Medicine
Peter Peduzzi, Ph.D.	Epidemiology and Public Health and General Internal Medicine

III. Occupational and Environmental Medicine

Research activities in Yale Occupational and Environmental Medicine Program include epidemiologic, clinical and experimental laboratory investigations. Current research interests are focused primarily on: risk factors for injury and diseases among aging workers in an industrial work force (Alcoa); isocyanate asthma, and noise-induced hearing loss, and animal sentinel research

a. Alcoa Studies

Overview: This is a cluster of epidemiologic research projects sharing a common study population (40,000 US employees of Alcoa), common databases (including the real time safety data system of all injuries and health claims data) and a common core research staff. The following are the major ongoing studies:

- 1) Root causes of the major chronic diseases in a working age population
- 2) Risk factors for injury and illness in this population, including psychosocial factors, physical job stress, gender, work organization, and quality of health care services
- 3) Causes of airways disease in aluminum potroom workers
- 4) Risk factors for hearing loss in this population, including co-exposure to noise and neurotoxic chemicals, demographic and other risk factors

Faculty:

Mark Cullen, M.D.	Occupational Medicine
Peter Rabinowitz, M.D.	Occupational Medicine
Oyebode Taiwo, M.D.	Occupational Medicine

Funding: Alcoa, MacArthur Foundation, NIOSH R01 (Solvents, noise, hearing loss), NIH NIA RO1 pending

b. Isocyanate Asthma Studies

Overview: This group of multidisciplinary interrelated clinical, epidemiological, and laboratory studies is investigating the pathogenesis of isocyanate asthma, risk factors, diagnosis, and preventive strategies. This research includes a longitudinal study of a unique population of isocyanate-exposed workers (autobody shop workers), a field intervention study to reduce exposures, controlled human isocyanate exposures using our exposure chamber located on the GCRC (H-5), laboratory studies characterizing effects of isocyanates and human immunologic responses, and an isocyanate mouse model.

Faculty:

Carrie Redlich, M.D.	Occupational Medicine
Adam Wisnewski, Ph.D.	Occupational Medicine
Youcheng Liu, M.D.	Occupational Medicine
Meredith Stowe, M.D.	Occupational Medicine
Mark Cullen, M.D.	Occupational Medicine
Kim Bottomly, M.D.	Immunobiology
Christina Herrick, M.D.	Dermatology
Susan Woskie, M.D.	Umass – Industrial Hygiene
Ellen Eisen, M.D.	Umass – Statistics

Funding – Active grants: “Longitudinal Study of Isocyanate Asthma in Body Shops”, NIOSH R01, “Isocyanate Exposure Intervention Study in Body Shops”, NIOSH R01, “Program for Patient-Oriented Environmental Health Research and Training”, NIEHS K24, “Isocyanate Antigens and T-cells that Cause Asthma”, NHLBI, R01, “Human Lung Gamma/Delta T Cells, Antigens and Functions”, NHLBI, R01

c. Noise-Induced Hearing Loss:

Overview: Gene-environment interactions in noise-induced hearing loss: genetic polymorphisms predisposing to noise-induced hearing loss

Faculty:

Peter Rabinowitz, M.D.	Occupational Medicine
Adam Wisnewski, M.D.	Occupational Medicine

Funding: Alcoa, RO1 pending

d. Animal Sentinel Research:

Overview: An ongoing medical informatics project is assembling the scientific literature regarding animals as sentinels of human environmental health hazards. This literature is being identified, classified, and curated into an interactive online database for use by the scientific community (see <http://canarydb.med.yale.edu/>). The database is allowing for evidence-based assessment of the relevance of animal sentinel events to human health.

Related to this animal sentinel work are several collaborative epidemiologic studies investigating the relationship between environmental hazards and outcomes, including pollution sources, parasites and amphibian limb deformities.

Faculty:

Peter Rabinowitz, M.D.

Occupational Medicine

David Skelly, M.D.

Biology

Funding: “Animals as Sentinels of Human Environmental Hazards” National Library of Medicine, G08

IV. Substance Abuse Core

Overview: The Yale Primary Care Substance Abuse Core conducts observational and randomized clinical trials of addiction treatment designed to transfer effective strategies from specialty to primary care and HIV clinical sites. Current funded research includes trials of medications (e.g. buprenorphine) and counseling (e.g. cognitive behavioral therapy) for the treatment of heroin and prescription opiate addicted patients. These trials are funded by the National Institute on Drug Abuse and the Health Resources Service Administration and are conducted at Yale-New Haven Hospital’s Primary Care Center and HIV specialty Nathan Smith Clinic. Augmenting these trials is Robert Wood Johnson Foundation supported research on the development of instruments for patient and provider satisfaction with this type of treatment. In addition, faculty from the Substance Abuse Core have partnered with the New York Academy of Medicine to form the National Evaluation Center for a 10 site observational study of the use of buprenorphine in HIV specialty clinics. Additional research funded by the National Institute of Alcohol Abuse and Alcoholism investigates the efficacy of brief counseling interventions for problem drinkers in the Emergency Department. Finally, the Substance Abuse Core conducts and publishes evidence-based systematic reviews of the impact of substance abuse disorders on common medical conditions funded by the Robert Wood Johnson Foundation and research on the impact of synthetic opiates on cardiac function funded by the Department of Veterans Affairs and the National Institute on Drug Abuse.

Faculty:

Patrick O'Connor, M.D., M.P.H	General Internal Medicine
David Fiellin, M.D.	General Internal Medicine
Lynn Sullivan, M.D.	General Internal Medicine
Bridget Martell, M.D.	General Internal Medicine
Amy Justice, M.D., Ph.D.	General Internal Medicine
Richard Schottenfeld, M.D.	Psychiatry
Thomas Kosten, M.D.	Psychiatry
Marek Chawarski, Ph.D.	Psychiatry
Michael Pantaloni, Ph.D.	Psychiatry
Brent Moore, Ph.D.	Psychiatry
Declan Barry, Ph.D.	Psychiatry
Gail D'Onofrio, M.D.	Surgery
Linda Degutis, Ph.D.	Surgery
Susan Busch, Ph.D.	Epidemiology and Public Health
Jody Sindelar, Ph.D.	Epidemiology and Public Health

Funding: National Institute on Drug Abuse, National Institute of Alcohol Abuse and Alcoholism, Robert Wood Johnson Foundation, Health Resource Service Administration, Department of Veteran's Affairs, Substance Abuse and Mental Health Services Administration.

V. Clinical Epidemiology Research Center (www.cercva.org)

Overview: The Clinical Epidemiology Research Center (CERC) is a new patient-oriented research unit on the West Haven VA campus. The CERC broadens the capability of the Cooperative Studies Program Coordinating Center by providing expertise in observational (non-randomized) studies. Examples of CERC-related projects include determining the effectiveness of screening tests; evaluating prognosis in cancer and cardiovascular disease; assessing health effects of Gulf War military service; measuring quality of care; determining patient preferences for the site of care at the end-of-life; examining new therapies for stroke and infectious diseases; and exploring patient decision-making regarding treatment options. In addition, the CERC fosters collaboration among physician investigators by providing research and career mentorship, as well as grant funding for pilot projects—in a new research building that allows for co-localization of faculty and staff. The CERC also represents an important link between the statistical expertise of Coordinating Center staff and the clinical expertise of Medical Center staff, creating a fertile environment for conducting cutting-edge patient-oriented research.

Faculty:

John Concato, M.D., M.S., M.P.H. (Director)	General Internal Medicine
Mihaela Aslan, Ph.D. (Associate Director)	General Internal Medicine
Joseph V. Agostini, M.D.	Geriatrics

Lawrence Brass, M.D.	Neurology
Dawn M. Bravata, M.D.	General Internal Medicine
Jeptha Curtis, M.D.	Cardiology
Liana Fraenkel, M.D., M.P.H.	Rheumatology
Terri R. Fried, M.D.	Geriatrics
Barbara I. Gulanski, M.D.	Endocrinology
Kalpana Gupta, M.D.	Infectious Diseases
Douglas Leslie, M.D.	Psychiatry
Richard A. Marottoli, M.D., M.P.H.	Geriatrics
Richard Martinello, M.D.	Infectious Diseases
Chirag Parikh, M.D.	Nephrology
Lisa M. Walke, M.D.	Geriatrics
Carolyn K. Wells, M.P.H.	General Internal Medicine
H. Klar Yaggi, M.D., M.P.H.	Pulmonary

Funding: The Center is funded through the VA Clinical Science Research Service; grants to individual faculty are from NIH, VA, and private (e.g., Robert Wood Johnson Foundation) sources.

VI. Cancer in the Elderly Working Group

The utility of clinical research is limited by overemphasis on “proof of concept” studies, studying a narrow spectrum of outcomes among homogenous, young, and relatively healthy participants. This is particularly apparent in oncology, as older patients account for the majority of cancer patients yet are frequently excluded from trial participation. To confront these challenges, this working group has focused on two overlapping domains. We are conducting observational studies of older cancer patients who are representative of patients in the “real world”, and we are also exploring barriers to enrolling older (and more heterogeneous) patient samples into cancer trials.

First, we are using observational studies on answer relevant clinical questions have not or could not be addressed by clinical trials. Our main focus is on how comorbid, chronic disease affects the care and outcomes of elderly patients with colorectal cancer. We are also identifying hospital and physician characteristics associated with better quality outcomes. Secondly, we are identifying barriers to trial enrollment and have demonstrated that elderly minority patients are particularly underserved in cancer trials. This work is complementary to recent collaborative efforts with colleagues in the Yale Program on Aging, which include a qualitative study addressing barriers to research participation for elderly minorities. We are also identifying health system and institutional characteristics associated with success in recruiting elderly patients into cancer studies, and have been consulted by the leadership of the Yale Cancer Center to help construct a strategy to increase enrollment into therapeutic trials.

Faculty:

Cary P Gross, M.D. (PI)	General Internal Medicine
Elizabeth Bradley, Ph.D.	Epidemiology and Public Health
Ted Holford, Ph.D.	Epidemiology and Public Health
Sharon Inouye, M.D.	General Internal Medicine
Harlan Krumholz, M.D.	Cardiology
Susan Mayne, Ph.D.	Epidemiology and Public Health
Ruth McCorkle, R.N., Ph.D.	Yale School of Nursing
Lynn Tanoue, M.D.	Pulmonary
Mary Tinetti, M.D.	Geriatrics

Funding: Past and current sources of funding have included grants from the National Cancer Institute and National Institute on Aging, industry (Boehringer Ingelheim and Astra Zeneca), as well as a contract from the Department of Clinical Bioethics at the NIH. Future potential funding sources include the NIH and private foundations.

VII. Delirium Prevention Research: Project Recovery

Overview: Project Recovery conducts a large variety of patient-oriented research projects pertaining to understanding risk factors, pathophysiology, intervention strategies, cost-effectiveness, and clinical outcomes of delirium prevention in older hospitalized persons. This program project brings together interdisciplinary faculty collaborators to address delirium prevention. Specific projects have included the development and validation of the Confusion Assessment Method (the most widely used delirium instrument internationally); identification of predisposing and precipitating risk factors for delirium; testing of a multicomponent targeted intervention strategy; evaluation of the cost-effectiveness of delirium prevention strategies; determination of outcomes related to delirium; assessment of barriers to translating research into real-world clinical programs for delirium prevention; evaluation of the pathophysiology of delirium using SPECT scanning; determination of caregiver burden associated with delirium; examination of delirium superimposed on dementia; and measurement of the incidence and risk factors for delirium in the ICU. This large-scale program project has resulted in over 89 published studies to date. In addition, this project has generated an international collaboration of over 300 clinicians and researchers in delirium prevention (The Hospital Elder Life Program National Dissemination Project) at over 40 hospitals in 13 states and 3 countries. An integrated website is under development, funded by the National Library of Medicine, to support the delirium prevention project. Future directions will include the development of the Aging Brain Program, a new program project to expand this work to investigate the relationship of delirium and dementia.

Faculty:

Sharon K. Inouye, M.D., M.P.H. (PI)	General Internal Medicine
Sidney T. Bogardus, Jr., M.D.	Geriatrics
Joseph V. Agostini, M.D.	Geriatrics

Dorothy Baker, Ph.D., RN	Geriatrics
Peter Charpentier, M.PH.	Geriatrics/Epidemiology and Public Health
Gail McAvay, Ph.D.	Geriatrics
Peter Van Ness, Ph.D.	Geriatrics
Hal Blumenfeld, M.D.	Neurology
Ruth McCorkle, Ph.D., RN	Nursing
Douglas Leslie, Ph.D.	Psychiatry
Christopher van Dyck, M.D.	Psychiatry
Margaret Pisani, M.D.	Pulmonary
Elizabeth Bradley, Ph.D.	Epidemiology and Public Health
Theodore Holford, Ph.D.	Epidemiology and Public Health
Mark Schlesinger, Ph.D.	Epidemiology and Public Health
Aditya Daftary, M.D.	Diagnostic Imaging
Sanjay Saluja, M.D.	Diagnostic Imaging
John Seibyl, M.D.	Diagnostic Imaging/Psychiatry

Extensive collaborations outside of Yale are involved with this program project, including Brown University, Case Western Reserve University, Harvard Medical School, Johns Hopkins University, Pennsylvania State, University of Illinois, University of Michigan, and Vanderbilt University

Funding: Project Recovery is funded by the National Institutes of Health/National Institute on Aging, National Library of Medicine, Commonwealth Fund, Retirement Research Foundation, Donaghue Medical Research Foundation, Samuels Foundation, and other public and private sources.

VIII. Sleep Apnea and Cerebrovascular Disease Working Group

Overview: A working group formed to examine the relationship between sleep apnea and the development of stroke and transient ischemic attacks. Members of this group have identified the prevalence of sleep apnea post-stroke (Mohsenin) and have established that sleep apnea is a risk factor for stroke (Yaggi). This group (Bravata, PI) is currently conducting two randomized controlled trials to evaluate the safety and feasibility of diagnosing and treating sleep apnea in patients with either acute ischemic stroke or transient ischemic attacks. The overall goal of this research is to evaluate if diagnosing and treating sleep apnea can improve stroke symptom severity and reduce the occurrence of stroke, TIA, myocardial infarction or death in cerebrovascular disease patients.

Faculty:

Dawn Bravata, M.D.	General Internal Medicine
John Concato, M.D.	General Internal Medicine
Lawrence M. Brass, M.D.	Neurology
H. Klar Yaggi, M.D.	Pulmonary/Sleep Medicine
Vahid Mohsenin, M.D.	Pulmonary/Sleep Medicine

Francoise Roux, M.D.
Mark Gorman, M.D.

Pulmonary/Sleep Medicine
Neurology

Funding: VA Health Services Research & Development (HSR&D) Service, the VA Cooperative Studies Program, the Robert Wood Johnson Generalist Physician Faculty Scholars Program, and the Yale Pepper Center.

IX. Media and Medicine

Overview: Ongoing and planned proposals in this priority area employ the visual media to explore healthcare from the perspective of individual patients.

a. *Ongoing Projects:*

Rolling, the 71 minute documentary on the experiences of individuals in wheelchairs is currently being re-edited for broadcast on PBS in 2005 (down to 56 minutes). The broadcast of the program will be coordinated with a large national outreach effort through the United States as well as with policy makers in Washington. Support for this effort will be underwritten by.

b. *Planned Projects:*

1. Coming Home from Iraq: A Visual Qualitative Study Exploring the Impact of Physical Injury on Patients and Their Families. A 5-year project focused on understanding the experiences of wounded soldiers and their families. It is now in the planning stages. Support from a private patron has been obtained, and a proposal is currently being considered by the.
2. An indepth-case study of the working poor living in Waterbury ,Connecticut. This is a 5 year project which will use qualitative methods and the visual medium to explore the perspectives of individuals who are living in Waterbury, Connecticut with marginal health status. It is now in the planning stages.

Faculty:

Gretchen Berland, M.D.
Kai Erikson, M.D.
Harlan Krumholz, M.D.
Jock Reynolds, M.D.

General Internal Medicine
Sociology
Cardiology
History of Art and School of Art

Funding: Pfizer, William T. Grant Foundation, The Donaghue Foundation, the Robert Wood Johnson Foundation and several private donors.

X. Medical Education Research

This group of investigators conducts research in medical education, often using the residents and medical students as research subjects. Many projects find immediate practical application in programmatic reform, adoption by the traditional program, translation to Yale medical student curricula, and dissemination to other institutions. In addition, since 1998, the group has produced 44 publications, including 29 reports of original research. Areas of inquiry include curriculum development, curriculum evaluation, teaching and evaluating evidence-based medicine skills, professionalism, evaluation of clinic competence, women's health, office preceptor teaching behaviors, hospitalism, house staff team structures, medical information needs, and minorities in medicine.

Faculty:

Michael Green, MD, MSc	General Internal Medicine
Stephen Huot, MD, PhD	General Internal Medicine
William Rifkin, MD	General Internal Medicine
Julie Rosenbaum, MD	General Internal Medicine
Eric Holmboe, MD	General Internal Medicine
Walter Kernan, MD	General Internal Medicine
Karen Brown, MD	General Internal Medicine
Laura Whitman, MD	General Internal Medicine
Janet Henrich, MD	General Internal Medicine
Daniel Tobin, MD	General Internal Medicine

Funding: Robert Wood Johnson Foundation, ACP foundation, Sorros foundation, Macy foundation