THE RANCHO BERNARDO STUDY OF HEALTHY AGING

A Rich Resource for Studying Women's Health in Aging and Sex Differences

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Disclosures

No relevant commercial relationships to disclose.

Our website contains detailed study description and access to data

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The Rancho Bernardo Study of Healthy Aging
University of California, San Diego

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## Study Description

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Overview

The Rancho Bernardo Study (RBS) of Healthy Aging began in 1972-74 as a population-based heart disease risk factor screening survey of all residents of the southern California community of Rancho Bernardo, a suburb of San Diego. The original study, including the first two research clinic visits, was part of the nation-wide Lipid Research Clinic (LRC) Prevalence program, a multi-centered collaborative study funded by the National Heart, Lung and Blood Institute (NHLBI). Subsequent RBS visits have been supported by grants from the National Institute of Aging (NIA), the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), the Agency for Healthcare Policy and Research (AHCPR), and the National Institute on Alcohol Abuse and Alcoholism (NIAAA). The RBS archive includes data on 6726 participants; most (76%) were age 40 or older at the time of enrollment; 51% were age 60 and older. Overall, 94% of participants were enrolled in the RBS cohort at its inception in 1972-74 (Visit 1); the remaining 387 were recruited from the Rancho Bernardo community and enrolled at subsequent visits as detailed in the descriptions of each research clinic visit below. Each RBS participant was assigned a 9-digit subject ID code at entry into the cohort, which is used to link all participant data in the RBS Archive.

The Rancho Bernardo Study: The Beginning

Initiated in 1972 by Dr. Elizabeth Barrett-Connor as part of the Lipid Research Clinic Prevalence Study
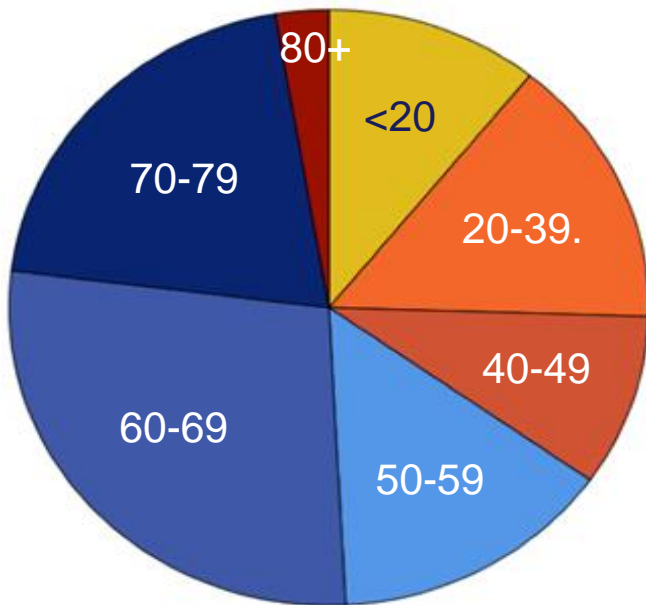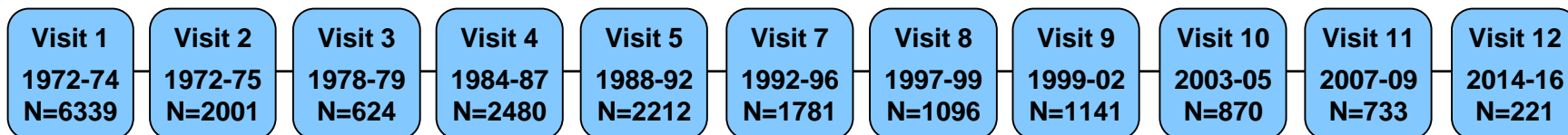

Age at entry

- ❖ > 6300 residents of RB volunteered at the initial visit – this included 82% of adults aged 30-79, as well as younger & older residents

- ❖ Cohort eventually enrolled 6726 participants; 54% women; average age of entry 54.

RBS Data & Timeline

32 annual mailers – health and psychosocial assessments

Follow-up for Vital Status – including cause of death

Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 7	Visit 8	Visit 9	Visit 10	Visit 11	Visit 12
1972-74	1972-75	1978-79	1984-87	1988-92	1992-96	1997-99	1999-02	2003-05	2007-09	2014-16
N=6339	N=2001	N=624	N=2480	N=2212	N=1781	N=1096	N=1141	N=870	N=733	N=221

CVD / Diabetes / Health Status & Health Behaviors / Physical Characteristics / Psychosocial Measures

Sex-Specific Questionnaires

Biomarkers and Lab Measures

Verified Medications

Cognitive and Physical Function Tests

Bone Scans

Vital Status (Nov, 2019):
- 71% mortality (DC for 90%)
- Average age at death 82.7
- 1353 have lived to 90 or older
- 85 centenarians …. so far!

Biorepository of remaining serum, plasma, urine samples

Ideal cohort for the study of Sex Differences

Homogenous cohort in terms of ....

- ❖ Race/ethnicity – almost all white, northern European
- ❖ Socioeconomic status – middle to upper-middle class
- ❖ Education – 60% have at least some college
- ❖ Health care – almost all have access to quality health care

Limits generalizability, but <u>greatly reduces confounding</u> due to these factors, maximizing the ability to identify sex differences.

Uncovering sex differences in risk factors and symptoms of common conditions of aging is a primary contribution of existing RBS studies.

Clinical and Subclinical Cardiovascular Disease

❖ Up to 47 years of follow-up for CVD events, including CVD mortality

❖ Clinical CVD events queried ~biannually via mailers, ~every 4 years at clinic visits

A) No Diabetes
Higher Fetuin-A
Low Fetuin-A

B) Diabetes
Low Fetuin-A
Higher Fetuin-A

Cumulative CVD Survival vs Follow-up Time (years)

Laughlin et al. J Am Coll Cardiol, 2012

Subclinical CVD assessments
- Coronary artery calcification
- Carotid atherosclerosis
- Peripheral arterial disease

Longitudinal CVD risk factors
- Lipids, BP, fasting glucose

Novel CVD biomarkers
- Endothelin 1
- LP-PLA2
- Fetuin-A
- OPG/RANKL
- IGF1 system
- Inflammation markers
- Adipocytokines
- Sex and adrenal hormones
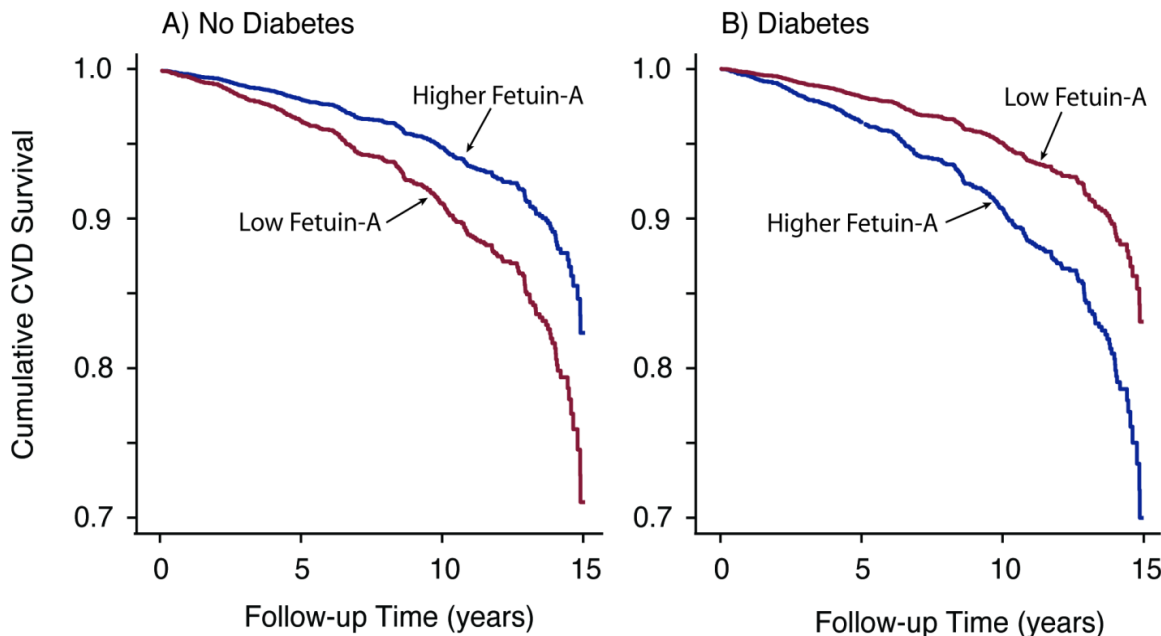
A great resource for studying cognitive aging

- ❖ Brief battery of cognitive tests in 2600 participants up to 7 times over 28 years
- ❖ Up to 15 years of health history prior to first cognitive assessment

Reas et al Am J Geriatr Psychiatry, 2017
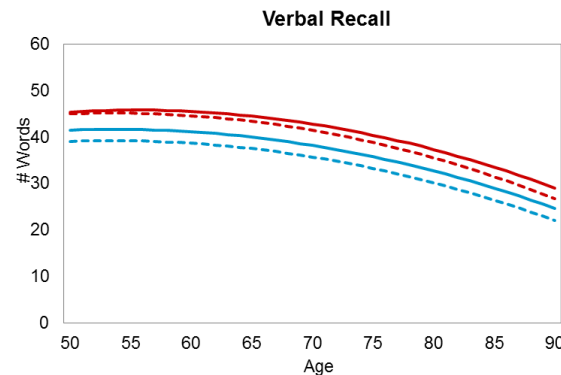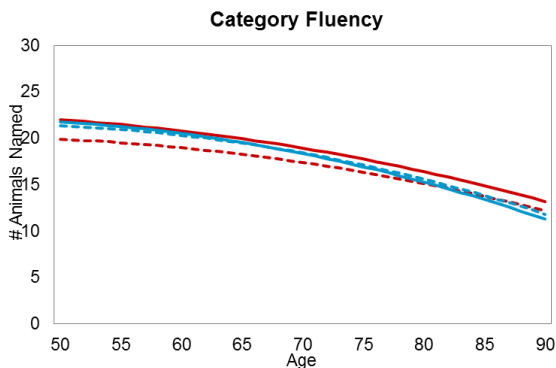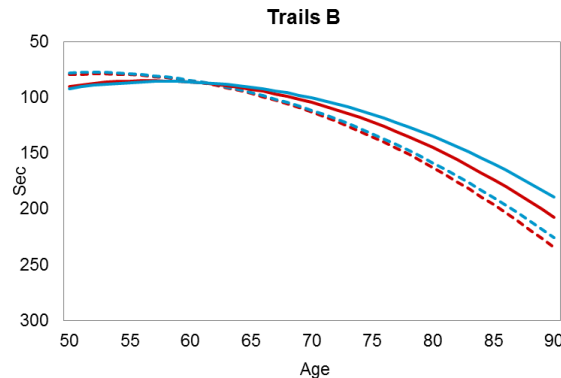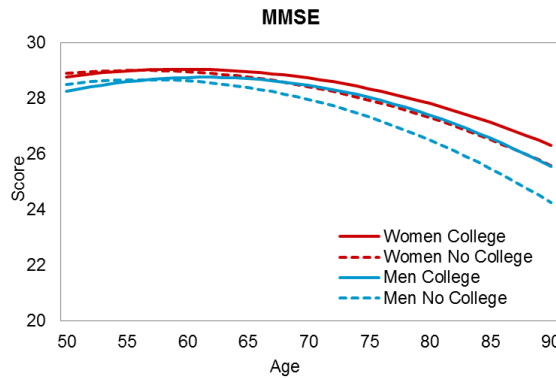
Factors that affect age-related change in cognitive performance:

- Gender
- Education level
- Hearing impairment
- Cardiovascular risk
- Metabolic disorders
- Physical activity
- Vitamin D insufficiency
- Alcohol use
- Diet
- APOE ε4 genotype

Can take into account competing risk of death; have time-varying covariates; dual trajectories

Diabetes – Sex Differences

Diabetes has been a major focus of RBS since it's start in 1972

❖ 47 years of follow-up for incident diabetes

❖ Fasting glucose available at 10 of 12 visits, 2hr OGTT at 2 visits

❖ Self-report of doctor's diagnosis at all visits and 20 mailers

❖ Biomarkers: glycosylated hemoglobin, insulin, proinsulin, c-peptide

RBS among the first to report many important sex differences in diabetes

❖ More than half of diabetes in older adults would be missed without an OGTT

❖ Women with diabetes have more classic CVD risk factors than men with diabetes ---- explains why diabetes is a stronger heart disease risk factor in women than men

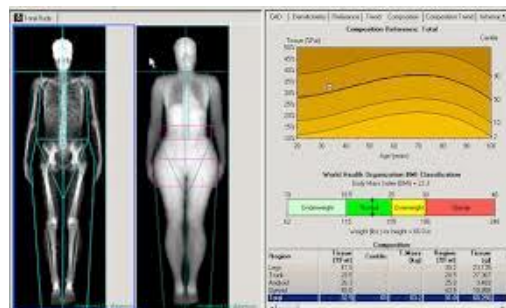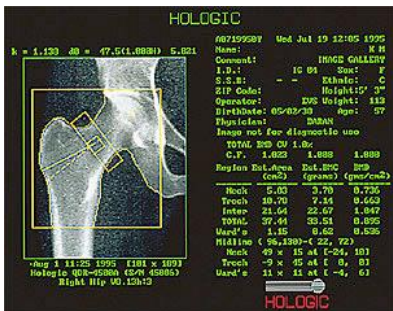❖ Low testosterone predicts diabetes in men, high testosterone in women

Elizabeth Barrett-Connor. Why Women Have Less Heart Disease than Men And How Diabetes Modifies Women's Usual Cardiac Protection. A 40-Year Rancho Bernardo Cohort Study. Global Hearth, 2013.

Bone Health: Osteoporosis, Fractures

A wealth of data with which to explore long-term changes in bone health (and body composition) in more than 2500 older adults over a 20+ year period

- ❖ Hip and spine DXA scans – up to 6

- ❖ Whole body DXA scans – up to 5

- ❖ Multi-site fracture history collected at each visit and bi-annually by mailer

Newer bone measures
- Quantitative CT of the hip
- Vertebral fracture assessment (VFA) by IVA
- Single photon absorptiometry of the radius
- Heel and finger BMD using portable ultrasound devices
- 3 measures of kyphosis

Bone-related biomarkers
- NTX (urine and serum)
- PINP
- OPG/RANKL
- Vitamin D, VDR genotype
- Sex and adrenal hormones

Other RBS data – available now or *coming soon!*

Demographic, lifestyle and health data available at 5 or more RBS clinic visits

Marital status, living arrangement	Disease history - personal, family	Body size & composition
Hormone use, reproductive history	Physical function tests –	Height, weight, waist & hip girth
Quality of life (SF12)	Grip strength, chair stand, gait	Body fat, lean body mass (DXA)
Health status (SF36)	Dietary intake	Comprehensive chem panel
Depressed mood (BDI)	Tobacco habit	Blood pressure: SBP, DBP
Self-assessed health status	Alcohol use	Total, HDL, LDL cholesterol
Hospitalizations, doctor visits	Physical activity, limitations	Triglycerides
Validated medications	ECG, angina, claudication	Fasting glucose

Biological measures available at 1 to 3 RBS clinic visits

Hearing / Vision	Vitamin D, PTH	IGF1, IGFBP1
Arthritis (by exam)	Fasting & post-challenge	Adipocytokines
ApoE genotype, VDR genotype	Insulin, glucose	Leptin, adiponectin, ghrelin
Subclinical CVD measures	HbA1c	Sex hormones, SHBG
Carotid IMT	Proinsulin, C-peptide	Testosterone, estradiol, estrone
Coronary artery calcium	Endothelin-1, LpPLA-2, OPG	Adrenal hormones
Peripheral arterial disease	Inflammatory markers	Cortisol, DHEA, DHEAS
Bone markers	IL-6, hsCRP, TNFα, fetuin-A	Trace minerals

Psychosocial measures available from clinic visits and/or yearly mailers

Standardized Questionnaires	Perceived Stress Score	Functional Activity Q'naire
Emotions	Life Satisfaction Index-Z	Economic Decision Making
Stress	Satisfaction with Life Scale	Self-assessed Numeracy
Beliefs, attitudes	Pittsburg Sleep Quality Inventory	BEM Sex Role Inventory
Social contact	Inventory Activities of Daily Living	Female Sexual Function Index
Optimism, Pessimism	Fatigue Scale	Male Sexual Function Inventory

Summary: Strengths of the RBS

❖ Up to 47 years of follow-up

❖ Availability of longitudinal exposure and outcome data & data files

❖ Continuing follow-up for vital status, death certificates

❖ Enhanced ability to examine sex-differences

❖ Detailed sex and reproductive health history

❖ Ability to compare mid-life and later-life risk factors

❖ Lifespan studies possible - based on early life self-report data

❖ Exceptional longevity studies possible, >1300 survived to 90+

❖ Ability to investigate biological factors linking major diseases of aging, e.g. diseases of the heart and those of the brain, breast and bone
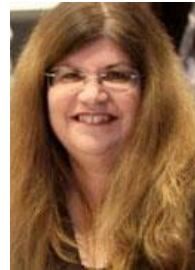
Acknowledgements

RBS Data Archiving Team

Linda McEvoy, PhD   **Gail Laughlin, PhD**   **Donna Kritz-Silverstein, PhD**   **Richele Bettencourt, MS**   **Jaclyn Bergstrom, MS**

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➤ Numerous foundations (e.g. American Diabetes Association; American Heart Association; AARP) and industry (e.g. Amgen, Orion Diagnostica)

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