

BIOGRAPHICAL SKETCH

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NAME: Rosner, Bernard

eRA COMMONS USER NAME (credential, e.g., agency login): ROSNER

POSITION TITLE: Professor of Medicine (Biostatistics), Senior Biostatistician, Brigham and Women's Hospital

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

| INSTITUTION AND LOCATION | DEGREE (if applicable) | Completion Date MM/YYYY | FIELD OF STUDY |
|--|---------------------------|----------------------------|----------------|
| Columbia University, New York, New York | B.A. | 1967 | Mathematics |
| Stanford University, Palo Alto, California | M.A. | 1968 | Statistics |
| Harvard University, Cambridge, Massachusetts | Ph.D. | 1971 | Statistics |

A. Personal Statement

Dr. Rosner has been involved with analyses of clustered data with application to ophthalmology for the past 30 years. In particular, his Biometrics 1982 and 1984 papers have each been cited over 200 times as one of the first papers to propose using the eye as the unit of analysis in ophthalmologic data analyses while adjusting for the cluster between outcomes for fellow eyes. More recently, in the past 8 to 10 years, he has been involved in applying clustering corrections to routinely used nonparametric tests which are widely used in ophthalmology. In addition, Dr. Rosner has collaborated with Dr. Eliot Berson for the past 30 years on statistical issues related to retinitis pigmentosa and has collaborated with Dr. Johanna Seddon on data analyses and statistical issues related to age-related macular degeneration for the past 15 years. In this application we focus on use of clustered data and methods in the context of AMD and diabetic retinopathy. Furthermore, in 2011, Dr. Rosner participated in a course on correlated data methods at the ARVO meeting to further disseminate clustered data and methods to the ophthalmic community and has written a paper on this subject which has been published in the journal Ophthalmic Epidemiology. Finally, Dr. Rosner was the senior author on two Tutorial in Biostatistics papers published in the journal Ophthalmic Epidemiology in 2017.

B. Positions and Honors**Positions**

1971–1974 Instructor in Preventive Medicine, Harvard Medical School, Boston, MA
 1972–1975 Lecturer on Statistics, Harvard University, Cambridge, MA
 1974–1976 Assistant Professor of Biostatistics, Harvard School of Public Health, Boston, MA
 1974–1977 Assistant Professor in Preventive Medicine, Harvard Medical School, Boston, MA
 1977–1991 Associate Professor in Preventive Medicine (Biostatistics), Harvard Medical School, Boston, MA
 1982–1991 Biostatistician, Brigham and Women's Hospital, Boston, MA
 1991– Professor of Medicine (Biostatistics), Harvard Medical School, Boston, MA
 1992– Senior Biostatistician, Brigham and Women's Hospital, Boston, MA

Honors and Prizes

1980– Fellow of the American Epidemiological Society
 1995 Fellow of American Statistical Association

C. Contribution to Science

I have worked on clustered data methods with application to ophthalmology for the past 30 years. In addition, I have worked on clinical studies and associated statistical issues related to glaucoma, macular degeneration, retinitis pigmentosa and diabetic retinopathy for the past 30 years. A sample of publications in these areas is provided below.

1. For clustered data:
 - a. Rosner B. (1982) Statistical methods in ophthalmology: an adjustment for the intraclass correlation between eyes. *Biometrics* 38(1): 105-14.
 - b. Rosner B. (1984) Multivariate methods in ophthalmology with application to other paired-data situations. *Biometrics* 40(4): 1025-35.
 - c. Rosner B, Glynn RJ, Lee ML. (2003) Incorporation of clustering effects for the Wilcoxon rank sum test: a large-sample approach. *Biometrics* 59(4): 1089-98.
 - d. Rosner B, Qiu W, Lee ML. (2013) Assessing discrimination of risk prediction rules in a clustered data setting. *Lifetime Data Anal.* Apr;19(2):242-56. doi: 10.1007/s10985-012-9240-6. PMID: PMC3622772

2. For glaucoma:
 - a. Pasquale LR, Willett WC, Rosner BA, Kang JH. (2010) Anthropometric measures and their relation to incident primary open-angle glaucoma. *Ophthalmology* 117(8): 1521-9. PMID: PMC2904416
 - b. Kang JH, Wiggs JL, Rosner BA, Haines J, Abdrabou W, Pasquale LR. (2011) Endothelial nitric oxide synthase gene variants and primary open-angle glaucoma: interactions with hypertension, alcohol intake, and cigarette smoking. *Arch Ophthalmol.* Jun;129(6):773-80. PMID: PMC3337676
 - c. Kang JH, Loomis SJ, Rosner BA, Wiggs JL, Pasquale LR. Comparison of risk factor profiles for primary open angle glaucoma subtypes defined by pattern of visual field loss: a prospective study. *Invest Ophthalmol Vis Sci.* 2015 Mar 10. pii: IOVS-14-16088. doi: 10.1167/iovs.14-16088. [Epub ahead of print] PMID: PMC4408886
 - d. Kang JH, Willett WC, Rosner BA, Buys E, Wiggs JL, Pasquale LR. Association of Dietary Nitrate Intake With Primary Open-Angle Glaucoma: A Prospective Analysis From the Nurses' Health Study and Health Professionals Follow-up Study. *JAMA Ophthalmol.* 2016 Jan 14:1-11. doi:10.1001/jamaophthalmol.2015.5601. PMID: PMC4966649

3. For macular degeneration:
 - a. Reynolds R, Rosner B, Seddon JM. Dietary omega-3 fatty acids, other fat intake, genetic susceptibility, and progression to incident geographic atrophy. *Ophthalmology.* 2013 May;120(5):1020-8. doi:10.1016/j.ophtha.2012.10.020. Epub 2013 Mar 5. PMID: PMC3758110
 - b. Seddon JM, Reynolds R, Yu Y, Rosner B. Validation of a prediction algorithm for progression to advanced macular degeneration subtypes. *JAMA Ophthalmol.* 2013 Apr;131(4):448-55. doi:10.1001/jamaophthalmol.2013.2578. PMID: 23411794 (exempt from public access policy).
 - c. Seddon JM, Silver RE, Kwong M, Rosner B. Risk Prediction for Progression of Macular Degeneration: 10 Common and Rare Genetic Variants, Demographic, Environmental, and Macular Covariates. *Invest. Ophthalmol. Vis. Sci.* 2015 Feb 5. pii: IOVS-14-15841. doi: 10.1167/iovs.14-15841. [Epub ahead of print] PMID: PMC4405097
 - d. Seddon JM, Silver RE, Rosner B. Response to AREDS supplements according to genetic factors: survival analysis approach using the eye as the unit of analysis. *Br J Ophthalmol.* 2016 Jul 28. pii: bjophthalmol-2016-308624. doi: 10.1136/bjophthalmol-2016-308624. [Epub ahead of print]

4. For retinitis pigmentosa:
 - a. Berson EL, Rosner B, Sandberg MA, Weigel-DiFranco C, Moser A, Brockhurst RJ, Hayes KC, Johnson CA, Anderson EJ, Gaudio AR, Willett WC, Schaefer EJ. (2004) Clinical trial of cosahexaenoic acid in patients with retinitis pigmentosa receiving vitamin A treatment. *Arch Ophthalmol* 122(9): 1297-305.
 - b. Berson EL, Rosner B, Sandberg MA, Weigel-DiFranco C, Brockhurst RJ, Hayes KC, Johnson EJ,
 - c. Anderson EJ, Johnson CA, Gaudio AR, Willett WC, Schaefer EJ. (2010) Clinical trial of lutein in patients with retinitis pigmentosa receiving vitamin A. *Arch Ophthalmol* 128(4): 403-11. PMID: PMC2987594

5. For diabetic retinopathy:
 - a. Glynn RJ, Rosner B. Multiple imputation to estimate the association between eyes in disease progression with interval-censored data. *Stat Med*. 2004 Nov 15;23(21):3307-18.
 - b. Rosner B, Glynn RJ, Lee ML. Incorporation of clustering effects for the Wilcoxon rank sum test: a large-sample approach. *Biometrics*. 2003 Dec;59(4):1089-98.
 - c. Glynn RJ, Rosner B. Methods to quantify the relation between disease progression in paired eyes. *Am J Epidemiol*. 2000 May 15;151(10):965-74.
 - d. Hartnett ME, Stratton RD, Browne RW, Rosner BA, Lanham RJ, Armstrong D. (2000) Serum markers of oxidative stress and severity of diabetic retinopathy. *Diabetes Care* 23(2): 234-40.

The first two papers use clustered data methods applied to data from the Sorbinil Retinopathy Trial.

Complete List of Published Work in My Bibliography:

<http://www.ncbi.nlm.nih.gov/sites/myncbi/bernard.rosner.1/bibliography/40637828/public/?sort=date&direction=ascending>

D. Additional Information: Research Support and/or Scholastic Performance

Active: Brigham and Women's Hospital Administered Grants

P01CA87969

(Stampfer)

05/11/2010 – 06/30/2020

NIH

Dietary and Hormonal Determinants of Cancer in Women

The long-term objective of this Program Project is to identify novel hormonal, dietary and genetic determinants of cancer risk, specifically breast, colorectal, and ovarian cancers, in women, with the aim of finding means for prevention and improved survival. The availability of questionnaire data, blood and urine samples, and tumor tissue from women with cancer, coupled with the long-term (up to 36 years) follow-up, affords a unique opportunity to better understand the time course, as well as mechanisms of cancer development.

R01CA050385

(Eliassen/Willett)

02/01/2015-01/31/2021 (NCE)

NIH/NCI

Risk Factors for Breast Cancer in Younger Nurses

The goal of this grant is to examine plasma metabolites in relation to breast cancer risk, assess the interrelation of diet and metabolomics in breast cancer etiology, and explore the role of potentially modifiable risk factors in activation of the PI3K pathway. We will investigate how the interplay between diet, host microbiome, and metabolism influences risk of breast cancer. The aims will be conducted within the Nurses' Health Study cohort of 116,430 women followed since 1989.

R01EY022445

(Rosner)

09/01/2013 – 03/31/2021

NIH

Nonparametric and Survival Methods in Ophthalmology

This proposal will consider (a) more efficient use of longitudinal data in ophthalmic treatment trials with non-normal outcome variables, (b) more valid estimates of accuracy of risk prediction rules for EMD so as to identify high risk subjects for possible future intervention trials, (c) more accurate assessment of long-term disease course in RP patients and (d) innovative approaches for dissemination of correlated data methods.

UL1TR002541

(Nadler)

05/01/2018 - 04/30/2023

(CTSC)

Harvard Clinical and Translational Science Center

The Harvard Clinical and Translational Science Center brings together the intellectual force, technologies, and clinical expertise of Harvard University and its affiliates and partners to reduce the burden of human illness. Dr. Rosner's participation involves providing biostatistical consultations. Role: biostatistical consultations

R01EY015473 (Pasquale) (Kang) 04/01/2014 - 05/31/2022
NIH/NEI
Gene-Environment Interactions in Glaucoma
The major aim of the proposal is to determine whether specific gene-environment interactions are determinants of primary open-angle glaucoma (POAG) in the Nurses' Health Study and Health Professionals Follow-up Study.

1U01CA182367-01A1 (Chan) 08/01/2015-07/31/2020
NIH
Molecular Risk Stratification for Colonoscopic Surveillance
Data and tumor tissue specimens from several cohorts including the Nurses' Health Study (NHS), the Health Professionals Follow-up Study (HPFS), and the Adenoma Prevention with Celecoxib Trial will be collected and analyzed for genomic markers to improve colonoscopic surveillance in patients after resection of adenoma.

2R01OH009803 (Schernhammer) 09/01/2015 - 08/31/2020
NIH
Adverse Health Effects of Shift Work
Given how frequent shift work is among pregnant women in the United States, we need a better understanding of whether and how exposure of the baby in the womb to any level or pattern of shift work may increase its risk for chronic diseases later in life. We are in the unique position to have data that simultaneously provide information on a mom's shift work history and follow their child until later in life, which allows us to study the effects of shift work, particularly during pregnancy, on the health of women's children. The results from our study have the potential to change the practice of shift work schedules for pregnant women, as this may ultimately mean that women who work night shifts should be switched to day shifts as soon as they become (or plan to become) pregnant.

UM1CA176726 (Willett-HSPH) (Eliassen) 06/01/2013 – 08/31/2023
NIH/NCI
Life Course Cancer Epidemiology Cohort in Women
The purpose of this project is to continue the prospective follow-up of over 116,000 women, born 1946 to 1964, who were enrolled in the Nurses' Health Study II in 1989. We aim to maintain the quality of the Nurses' Health Study II follow-up and associated data, as well as to pilot new technologies and sample types that would provide novel dimensions to the cohort.

R01 CA193965 (Terry) 06/01/2016 – 05/31/2020
NIH/NCI
Redefining Normal: Personalized CA125 Cutpoints for Ovarian Cancer Screening
We propose to develop personalized CA125 cut points using individual characteristics to improve the sensitivity and specificity of this important ovarian cancer marker and lead the way to population screening that could save lives. Specific Aims: Develop and validate a predictive model of CA125 in women without ovarian cancer; Calculate personalized cutpoints and evaluate discriminatory ability compared to a single threshold in PLCO, NHS, and EPIC. Evaluate whether the addition of personalized CA125 improves ovarian cancer risk prediction by adding adjusted CA125 to established ovarian risk models.

P30CA006516 (Rosner) 12/01/2016 - 11/30/2021
DFHCC Biostatistics Core
The Dana Farber/Harvard Cancer Center is an inter-institutional research enterprise that unites the major clinical, population, and basic cancer research efforts of the Harvard medical and public health community. This Cancer Center links the efforts of a large cadre of cancer scientists. The goal of this proposal is to promote research advances that are aimed at lowering the burden of cancer. Role: Site PI

R01CA207369

(Hankinson)

06/15/2017-03/31/2022

NIH/NCI

Endogenous Hormones and Postmenopausal Breast Cancer: Etiologic Insights and Improving Risk Prediction

We propose to identify and validate biomarkers – particularly hormonal markers – that predict risk of invasive breast cancer in postmenopausal women. Using a prospective nested case-control design, we plan to analyze blood samples collected from the 32,826 participants in the Nurses' Health Study (NHS) who provided a blood sample in 1989-90 and, for 18,743 of these women, a second sample in 1999-2000. We propose to evaluate markers from several inter-related pathways (insulin, steroid hormone) to determine their role in cancer risk; we plan to validate a risk prediction model we are developing now and consider whether additional factors will improve the prediction.

579027

(Farvid)

01/01/2019 – 12/31/2020

American Institute for Cancer Research (AICR)

Beverage consumption and breast cancer survival by molecular subtypes and hormone receptor status
We will examine the associations of post-diagnostic beverage consumption including sugar-sweetened beverages (SSBs), artificially sweetened beverages (ASBs), coffee, tea, and plain water as well as post-diagnostic caffeine, added sugars, and natural sugars with breast cancer-specific and all-cause mortality. In addition, we will test which beverages should be considered as an alternative to improve survivorship among breast cancer patients. Further, these associations will be examined with pathological subgroups of breast cancer defined by hormone receptor status and molecular subtypes.

R01 DC017717

(Wang-HSPH)

09/13/2019 – 08/31/2022

NIH/NIDCD

What Causes Hearing Loss: Advancing the Methods

We will develop entirely novel analytical methods for quality control of hearing data, and validly and efficiently quantifying not only the exposure-hearing loss associations but also their causal relationships, while handling the various layers of correlation and multivariate outcomes arising from the measurement of multiple frequencies in audiometrically-assessed hearing data. In addition, we will develop statistical methods to correct for measurement error-induced bias in the estimates of the associations and causal effects in studies where hearing outcomes are evaluated in non-clinical settings.

1R01HL145813-01A1

(Abdi)

09/01/2019 - 06/30/2023

NIH/NHLBI

A novel approach to delivering therapeutics in heart transplantation

This proposal seeks to establish a nanodelivery system of immunomodulatory drugs in heart transplantation.

R01CA240341-01A1

(Yaghjian)

12/06/2019 – 11/30/2023

NIH/NCI

The Role of Breast Stem Cells in Breast Cancer Etiology and Risk Prediction

This study investigates 1) the association of selected early-life breast cancer risk factors with expression of stem cell markers (CD44, CD24, and ALDH1A1) in benign breast biopsies, 2) the association of stem cell markers' expression in benign breast disease with subsequent breast cancer risk, and 3) the association of circulating IGF1 and IGFBP-3 with expression of these markers.

BCRF Precision Prevention Initiative

(Lehman)

06/15/2019-06/14/2022

Breast Cancer Research Foundation

Precision Prevention through Artificial Intelligence-Based Risk Assessment

The goal of this project is to develop and implement AI-based risk models which predict the most aggressive breast cancers across the full diversity of women at risk.

End active other support for Rosner, Bernard