BIOGRAPHICAL SKETCH

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NAME: Farzin Khosrow-Khavar

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

POSITION TITLE: Instructor

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
University of Victoria, Victoria, Canada	BSc	05/2002	Biochemistry
University of British Columbia, Vancouver, Canada	MSc	05/2011	Biochemistry & Molecular Biology
McGill University, Montreal, Canada	PhD	06/2020	Epidemiology
Brigham and Women's Hospital and Harvard Medical School	Postdoc	08/2022	Pharmacoepidemiology

A. Personal Statement

I am an epidemiologist with a focus on applying rigorous study designs and methods to assess benefits and harms of cancer therapeutics among patients who are receive care in clinical practice. I completed my doctoral degree in Epidemiology at McGill University. The body of work from my thesis examined the short-term and long-term safety of endocrine drugs among patients diagnosed with breast cancer. I also conducted real-world evidence (RWE) studies which examined the long-term safety of androgen deprivation therapy among patients diagnosed with prostate cancer. These studies have been published in prominent medical and epidemiology journals including Circulation, Journal of Clinical Oncology, Annals of Oncology, and American Journal of Epidemiology. I am also a co-investigator on a multi-center clinical trial funded by Canadian Institutes of Health Research which examines the effect of omission of radiation therapy among women diagnosed with breast cancer who achieve pathological complete response after neoadjuvant chemotherapy. I pursued my postdoctoral fellowship in the Division of Pharmacoepidemiology and Pharmacoeconomics at Brigham and Women's Hospital and Harvard Medical School. My postdoctoral fellowship was focused on examining the safety of biologics and targeted treatments, including long-term risk of malignancies, among patients diagnosed with autoimmune diseases.

As a new investigator at Rutgers School of Public Health and Institute for Health, Healthcare Policy and Aging Research, I examine the benefits and harms of cancer drugs among patients who are underrepresented in clinical trials including patients with multimorbidity, frail patients, older patients, and minorities. I am currently a principal investigator of a pilot study assessing the real-world effectiveness of endocrine therapy in breast cancer using novel oncology electronic medical record data sources in United States. I also assess disparities in access to novel cancer therapeutics and healthcare resources by ethnicity and socioeconomic status.

Finally, I conduct multi-level studies to identify facilitators and barriers of access to novel cancer therapeutics among minorities diagnosed with breast and prostate cancer.

I would like to highlight ongoing funded projects in breast cancer:

Rutgers Cancer Institute of New Jersey, Cancer Prevention and Control (CPC) Pilot Award
PI (Khosrow-Khavar)
Funding period: 02/2023-01/2024
Validation of Real-World Evidence Studies in Oncology by Calibration Against Randomized Controlled Trials

Canadian Institutes for Health Research
PI (Muanza, Basik, Parvez)
Funding period: 04/2021-04/2031
A prospective trial of radiation omission in patients with clinically node negative breast cancer and pathologic complete response after neoadjuvant chemotherapy

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

Sep. 2022- Instructor
Rutgers School of Public Health, Department of Biostatistics and Epidemiology
Center for Pharmacoepidemiology and Treatment Science
Institute for Health, Healthcare Policy and Aging Research
New Jersey, United States

2021-2022 Postdoctoral Research Fellow
Division of Pharmacoepidemiology and Pharmacoeconomics
Brigham and Women's Hospital and Harvard Medical School
(funded by Québec Health Research Fund postdoctoral fellowship)

Honors

2020-2022 Québec Health Research Fund Postdoctoral Fellowship (110,000 CAD)
2017-2019 Québec Health Research Fund Doctoral Award (40,000 CAD)
2017-2019 Canadian Institutes of Health Research Drug Safety and Effectiveness Training Award (20,000 CAD)
2018 McGill University, Department of Epidemiology Excellence in Teaching Award
2016 McGill University Faculty of Medicine Studentship (12,000 CAD)
2016 Novartis Young Oncology Investigator Award (5,000 CAD)
2014 McGill Graduate Excellence Award (10,000 CAD)
2014 Lady Davis Institute Graduate Studentship (10,000 CAD)
2013 RQRUM/Pfizer Graduate Studentship (7,500 CAD)
2013 McGill University Graduate Excellence Award (4,000 CAD)
2008 Canadian Institutes of Health Master's Research Award (20,000 CAD)
2005 Natural Sciences & Engineering Research Council Industrial Research Award (4,500 CAD)
2002 University of Victoria Presidential Entrance Scholarship (4,500 CAD)

C. Contributions to Science

1. The body of work generated from my doctoral thesis assessed the cardiovascular safety of therapeutics in breast cancer. Aromatase inhibitors and tamoxifen are the two classes of drugs that are commonly used to treat patients diagnosed with hormone receptor-positive breast cancer. Current clinical guidelines recommend treatment of hormone receptor-positive breast cancer with either aromatase inhibitors or tamoxifen for up to ten years. Women diagnosed with breast cancer represent an older patient population who are at an increased risk of cardiovascular disease, the leading cause of mortality among patients diagnosed with breast cancer. Thus, the differential effects of aromatase inhibitors and tamoxifen on cardiovascular disease is an important safety consideration. The findings from this body of work indicate that aromatase inhibitors, in comparison with tamoxifen, are associated with increased risk of cardiovascular disease in randomized controlled trials and among patients who receive care in clinical practice. The increased risk of cardiovascular outcomes with aromatase inhibitors was observed when these drugs were used either as monotherapy or in sequential treatment with tamoxifen. This body of work made a significant contribution to the net clinical benefit of aromatase inhibitors for treatment of hormone receptor-positive breast cancer. The assessment of cardiovascular risk of aromatase inhibitors in RCTs has been included in a scientific statement by American Heart Association on cardiovascular disease and breast cancer treatment (Mehta LS et al., Circulation, 2018).

a. **Khosrow-Khavar F**, Filion KB, Al-Qurashi S, Torabi N, Bouganim N, Suissa S, Azoulay L. Cardiotoxicity of Aromatase Inhibitors and Tamoxifen in Postmenopausal Women with Breast Cancer: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *Annals of Oncology* 28(3): 487-496, 2017 **(159 citations)**.

b. **Khosrow-Khavar F**, Filion KB, Bouganim N, Suissa S, Azoulay L. Aromatase Inhibitors and the Risk of Cardiovascular Outcomes in Women with Breast Cancer: Population Based Cohort Study. *Circulation*; 141(7): 549-559, 2020 (**59 citations**).

c. **Khosrow-Khavar F**, Bouganim N, Filion KB, Suissa S, Azoulay L. Cardiotoxic Effects of Sequential Aromatase Inhibitors Use in Women with Breast Cancer. *American Journal of Epidemiology*, 189(10): 1086-1095, 2020.

2. This body of work assessed the long-term safety concerns with aromatase inhibitors and tamoxifen including the risk of Parkinson's disease and colorectal cancer. These studies were conducted using United Kingdom Clinical Practice Research Datalink which captures approximately 20,000 patients diagnosed with hormone receptor-positive breast cancer. The long-term safety concerns were based on signals from RCTs and mechanism of action of aromatase inhibitors countering potential neuroprotective effects of estrogen respectively. Overall, these studies indicated that aromatase inhibitors were not associated with an increased risk of Parkinsonism or colorectal cancer when compared tamoxifen among patients diagnosed with hormone receptor-positive breast cancer. The evidence generated from these RWE studies provide reassurance to clinicians and patients regarding long-term safety of aromatase inhibitors, particularly given that these drugs are recommended for treatment of hormone receptor-positive breast cancer for up to ten years.

We also conducted an RWE study which examined whether androgen deprivation therapy, a mainstay treatment for prostate cancer, is associated with increased risk of Alzheimer's disease or dementia. This RWE study included 30,903 men patients diagnosed with prostate cancer. Overall, we did not observe an association between androgen deprivation therapy and risk of dementia or Alzheimer's disease. This evidence supports the long-term safety of androgen deprivation therapy and provides reassurance to healthcare practitioners and patients regarding this long-term safety concern. This study was cited in a scientific committee report on management of patients with advanced prostate cancer (Caram M et al, European Urology, 2018).

a. **Khosrow-Khavar F**, Azoulay L, Montastruc F, Montastruc JL, Renoux C. Aromatase inhibitors and Risk of Parkinsonism in Women Diagnosed with Breast Cancer: Population Base Cohort Study. *Cancer*; 128(12):2339-2347, 2022.

b. **Khosrow-Khavar F,** Yin H, Barkun A, Bouganim N, Azoulay L. Aromatase Inhibitors and the Risk of Colorectal Cancer in Post-Menopausal Women with Breast Cancer. *Annals of Oncology*; 29(3); 744-748, 2018.

c. **Khosrow-Khavar F**, Rej S, Yin H, Aprikian A, Azoulay L. Androgen Deprivation Therapy and Risk of Dementia in Patients with Prostate Cancer. *Journal of Clinical Oncology;* 35(2): 201-207, 2017 **(67 citations)**

3. This body of work, which was conducted during my postdoctoral fellowship and examined the safety of tofacitinib, a novel targeted agent that is commonly used in management of rheumatoid arthritis. These studies were conducted after the ORAL Surveillance post-marketing safety trial, mandated by United States Food and Drug Administration, indicated an increased risk of malignancies and cardiovascular disease with tofacitinib when compared with other second line agents used in treatment of rheumatoid arthritis. The clinical trial population included patients diagnosed with rheumatoid arthritis who were at least 50 years of age and with cardiovascular risk factors. In contrast, the study population in our RWE studies encompassed the full spectrum of patients with rheumatoid arthritis who received care in clinical practice. Our study demonstrated a heterogeneity of treatment effect in clinical practice. We found that tofacitinib, in comparison with tumor necrosis factor inhibitors, was not associated with augmented risks of malignancies or cardiovascular disease among all patients who received care in clinical practice. However, consistent with trial results, our studies indicated that tofacitinib is associated with augmented risk of malignancies and cardiovascular disease among patients at least 50 years of age with cardiovascular risk factors. The heterogeneity of treatment effect suggests that these risk factors should be considered when considering tofacitinib as a treatment option for management of rheumatoid arthritis. These studies incorporated trial calibration in the RWE study against the ORAL Surveillance RCT. We demonstrated consistent results with the RCT when duplicating the trial eligibility criteria, exposure and outcome definition, and comparator.

a. **Khosrow-Khavar F**, Kim, SC, Lee H, Lee S, Desai RJ. Tofacitinib and Risk of Cardiovascular Outcomes: results from the Safety of TofAcitinib in Routine care patients with Rheumatoid Arthritis (STAR-RA) Study. *Annals of Rheumatic Diseases*; 81(6):798-804, 2022.

b. **Khosrow-Khavar F**, Desai RJ, Lee H, Lee S, Kim SC. Tofacitinib and Risk of Malignancy in Patients with Rheumatoid Arthritis with Rheumatoid Arthritis: results from the Safety of TofAcitinib in Routine care patients with Rheumatoid Arthritis (STAR-RA) Study. *Arthritis & Rheumatology*; 74(10):1648-1659, 2022.

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