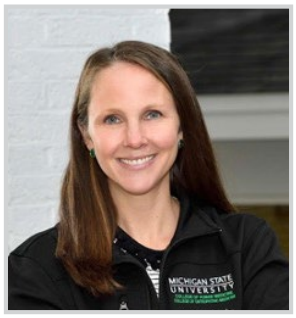
Interview

Kelly Hirko discusses disparities in the treatment of breast cancer, and in the wider field of oncology during their exclusive interview with EMJ. Hirko also discusses their current research which focuses on modifiable lifestyle risk factors, particularly obesity and nutrition.



Kelly Hirko

Assistant Professor of Epidemiology and Biostatistics, Department of Epidemiology and Biostatistics, College of Human Medicine, Michigan State University, Traverse City, USA

Citation: EMJ. 2023; DOI/10.33590/emj/10305342. https://doi.org/10.33590/emj/10305342.

Q1 What initially sparked your interest to pursue a career in this field, and motivated you to continue researching?

My interest in cancer research was sparked during my experience in the Undergraduate Research Opportunity Program (UROP) as an undergraduate at the University of Michigan, in Ann Arbor, USA. Through that experience, I worked in a prostate cancer pathology laboratory focused largely on biomarker discovery. My work centred on creating a tissue microarray from prostate cancer tissue for immunohistochemical analysis. As a member of the lab, I enjoyed participating in the research team meetings to discuss interesting findings and future directions for the research.

During my time in the lab, I had the opportunity to read and discuss medical literature on prostate cancer aetiology, and to discover epidemiologic research describing patterns of prostate cancer occurrence and outcomes. At that time, I was particularly intrigued by several recently published migration studies showing the increased risk of prostate cancer among individuals, after they moved from a low-risk to a high-risk country. These findings suggested that cancer risk is modifiable, and that cancer could be prevented. Through my experience working in this pathology laboratory, I discovered epidemiology, and this set me on my path to pursue my MPH and PhD in Epidemiology, focused on cancer prevention and disparities.

I am now a community-based researcher and epidemiologist at Michigan State University's College of Human Medicine's rural campus in Northern Michigan. Being on the ground in a rural community oncology setting has been particularly illuminating, given that most of my training was in high-resource academic medical centres. In this role as a community-based researcher, I can better understand the multiple factors that may contribute to rural cancer disparities. For example, there are many unique challenges and barriers to delivering cancer care in rural community oncology settings, which often serve expansive geographic regions. Individuals in rural regions tend to travel long distances to receive cancer care, and public transportation options are limited.

These circumstances can place an undue and excessive burden on rural residents seeking to receive guideline-concordant cancer care. Moreover, cancer care is complex and challenging to deliver, even in high-resource academic medical centres. These challenges can be compounded in rural oncology settings, which are often under-resourced, and serve populations that tend to be older, sicker, and poorer. I am extremely motivated to continue my research focused on addressing cancer disparities, by engaging clinical and community partners to identify optimal approaches and strategies to improve cancer outcomes in this under-served population where I live, work, and play.

Q2 Your current research focuses on understanding the aetiology of cancer through the investigation of modifiable lifestyle risk factors, particularly obesity and nutrition. How big is the impact of these modifiable risk factors on the risk of developing cancer?

My research seeks to identify modifiable factors that contribute to the unequal burden of cancer, of which diet, physical activity, and obesity play an important role. Diet and physical activity are strongly linked with obesity, so we can think about these factors as interconnected, and each are related to cancer risk and prognosis.

Obesity-related cancers comprise around 40% of all the cancer diagnoses in the USA each year and, given the rising prevalence worldwide, obesity is a significant contributor to the overall cancer burden. When evaluating obesity-related factors in isolation, around 8% of cancers in the USA are attributed to obesity alone, another 3% are attributed to physical inactivity, and about 2% are attributed to low fruit and vegetable consumption. Therefore, consuming a healthy diet and living a healthy active lifestyle can reduce obesity, and have a dramatic impact on reducing cancer risk, and the risk of many other chronic diseases. More work is certainly needed at the policy level to ensure that the environments where people live support healthy lifestyle habits, including ensuring access to affordable healthy foods, and plentiful opportunities for physical activity.

Q3 You also research the use of biomarkers, such as sex steroid concentrations and tumour marker characteristics, to explore how exposures to certain lifestyle factors may result in the development of breast cancer. What are some of the main findings of this research?

Much of this research was conducted during my postdoctoral fellowship, when I was working with data from the Nurses' Health Study, a large prospective cohort study following study participants over several decades. Data from this study are extremely rich, with multiple measures of lifestyle factors assessed from surveys conducted every 2 years over a long period of time, as well as biospecimens collected for biomarker assessment. In the studies I worked on using the Nurses' Health Study data, we sought to understand how alcohol consumption contributes to breast cancer risk. Alcohol intake has been consistently linked to increased breast cancer risk, but there is not a clear understanding of biological mechanisms underlying the observed association.

We were interested in examining whether alcohol may increase breast cancer risk by elevating sex steroid concentrations, including oestrogen, which is a known breast cancer risk factor. Using blood samples that were timed during a female's menstrual cycle, we assessed whether sex steroid concentrations in both the follicular and luteal phase of the menstrual cycle were associated with breast cancer risk in pre-menopausal females. In this cross-sectional study, we observed positive associations between alcohol consumption and oestrogen concentrations measured during the luteal phase of the menstrual cycle, but not with oestrogen levels during the follicular phase. We did not observe any significant associations with androgen levels in either phase of the menstrual cycle. Findings from this study suggested that differences in pre-menopausal oestrogen levels may contribute to the association of alcohol and breast cancer.

We followed this up by looking at associations between alcohol and breast cancer molecular subtypes, with the understanding that the luminal subtypes of breast cancer have oestrogen receptors expressed. Our hypothesis was that if oestrogen pathways linked to alcohol

were contributing to the increased risk of breast cancer, we would expect to see stronger positive associations between alcohol and the oestrogen receptor positive (luminal) subtypes. Our results from this study showed that alcohol was associated with an increased risk of luminal A breast cancer, but also an increased risk that was suggested to be stronger in human epidermal growth factor receptor 2 (HER2) breast cancer, which is oestrogen receptor negative. We did not observe significant associations between alcohol and the other breast cancer subtypes, including luminal B and triple negative. However, the sample size was quite small for the less common oestrogen receptor negative subtypes. Therefore, we cannot say that alcohol consumption is not associated with those subtypes. Given that alcohol consumption was significantly associated with both oestrogen receptor positive luminal A and oestrogen receptor negative HER2-type breast cancer, our findings suggest that mechanisms other than hormonal pathways may play a role in the association between alcohol and breast cancer.

During my postdoctoral research fellowship, I also evaluated associations between dietary patterns and sex hormone concentrations, and those findings were not consistent. For example, the Alternative Healthy Eating Index (AHEI) was inversely associated with pre-menopausal oestrogen concentration, suggesting that adherence to this healthy dietary pattern may reduce breast cancer risk by lowering oestrogen concentrations in pre-menopausal women. However, the associations were not similarly observed in the other healthy dietary patterns that we examined, including the Dietary Approaches to Stop Hypertension (DASH) and the alternative Mediterranean dietary patterns. We then also looked at associations between adherence to dietary patterns with risk of breast cancer by molecular subtype, and did not observe consistent associations; however, we observed a suggested inverse association between the DASH diet and a lower risk of HER2 breast cancer.

Overall, this research suggested that hormonal pathways may play a role in explaining some of the observed association between alcohol and risk of oestrogen receptor positive breast cancer subtypes, but the role of dietary patterns and hormonal pathways in breast cancer risk were not substantiated.

Q4 You wrote an article entitled, 'The impact of race and ethnicity in breast cancer—disparities and implications for precision oncology'. What are the disparities in the treatment of breast cancer?

In breast cancer, we have seen an increased survival over the past several decades, due largely to improved treatment and early detection; however, disparities in survival across geographic regions and racial and ethnic groups have persisted. From a health equity perspective, it is imperative to conduct research to better understand what factors contribute to these disparities. I believe that differences in access to, and utilisation of, guideline-contribute breast cancer treatment plays an important role in these disparities. Breast cancer treatments have evolved and can be very effective, but the advances many not reaching all of the populations in need.

Globally, there are extreme disparities in terms of access to comprehensive cancer treatment, with comprehensive cancer treatment available in more than 90% of high-income countries, but less than 15% of low-income countries. Even within middle- and high-income countries, it is often the case that where a person resides unfortunately predicts likelihood of survival after cancer diagnosis. So, individuals diagnosed with the same tumour type and stage in different geographical locations may have varying access to care, and drastically different outcomes.

> **"There are extreme disparities in terms of access to comprehensive cancer treatment."**

In our recent EMJ article, we discuss how the emphasis on precision oncology approaches and targeted therapies hold tremendous potential to improve outcomes, by creating treatment pathways based on specific tumour characteristics that vary across patient populations. However, these targeted drug therapies are costly, and often require additional testing and follow-up to determine eligibility based on the presence of specific mutations. This adds complexity and cost to the process, which disproportionately impacts under-resourced populations.

Additionally, oncology workforce and infrastructure limitations in under-resourced settings create additional barriers for delivery of these effective therapies, often resulting in suboptimal care. Thus, the utilisation of many targeted cancer therapies is inequitable with lower access and uptake among many disadvantaged populations.

It is also important to consider that these targeted therapies were developed largely from clinical studies with little to no enrolment of minority and disadvantaged populations. Introducing cancer therapies that were developed in a select population of participants may inadvertently exacerbate disparities if disadvantaged populations are excluded from the research that demonstrated the therapy's effectiveness. Many of these targeted therapies have proven extremely beneficial for those who can get them; however, we need to focus efforts on increasing access to these therapies, and including globally representative and under-served populations in clinical trials that develop these targeted therapies, so that the reach of the benefits are equitable across populations. We also need to learn more about how to effectively implement evidence-based cancer prevention and treatment programmes for all populations, and not just those who are treated in academic cancer centres.

Q5 What are the current disparities that are faced in the field of oncology care, and how do these healthcare disparities affect different patient populations?

One of the biggest challenges that I see is that some of the important cancer care advances are not accessible to everybody. Research is needed to develop effective strategies for implementing evidence-based cancer care in under-resourced settings, and to ensure that under-represented populations participate in research studies. This equity focus is critical to ensure that the scientific advancements reach the under-served populations who often face worse cancer outcomes, and may benefit most. There are many existing evidence-based cancer treatments available, but we need to focus efforts on ensuring that these interventions are acceptable, accessible, and feasible for delivery in under-resourced settings across the globe. Implementation science approaches and outcomes should be prioritised from the onset of research studies, to ensure broad reach and sustainability of cancer control and treatment programmes in multiple settings and contexts. To effectively mitigate disparities, it will also be critical to engage with community partners throughout the research process, including guiding research questions and approaches based on community input and priorities.

It is important to consider the unique challenges and barriers to receiving quality cancer care across populations and settings. As a rural community-based researcher, transportation barriers are stark, with some individuals travelling 200 miles each way to receive cancer care, which often requires daily treatments over multiple weeks. This travel can be extremely costly and challenging for individuals, particularly with those who have other comorbidities, those with inflexible jobs, and other family responsibilities. At the rural cancer centre where I am based, this transportation barrier became a pressing issue, with patients parking their recreational vehicles in the cancer centre parking lot and camping out for the duration of treatment because they could neither commute back and forth from home, or afford to stay in a hotel for the treatment duration. Elevating the awareness around how these barriers impact cancer care delivery and contribute to disparities is critical, given that the bulk of cancer research reflected in the medical literature is conducted at academic medical centres, largely in urban settings. There are plentiful examples of specific challenges related to receiving quality guideline-concordant cancer care from across the globe, and these contextual barriers need to be addressed to ensure that scientific advances are equitably implemented across diverse settings.

Q6 Which initiatives exist to combat existing disparities?

The good news is that more emphasis is being placed on conducting research to address cancer disparities, and we are making progress. Much of the progress has been accomplished due to the tireless work of patient advocates, cancer survivors, and community organisations advocating for outreach efforts to promote cancer screening, and/or providing resources to address specific barriers to preventive and treatment services. Ongoing efforts to standardise the collection of social determinants of health information in the medical record, in order to enhance referrals to support services, and leveraging technology tools, such as telehealth, to overcome healthcare access barriers hold tremendous potential to reduce persistent cancer disparities. Additionally, the use of resource-stratified phased implementation to address cancer control efforts in the context of available resources, similar to those developed by the Breast Health Global Initiative, are also promising, and potentially sustainable over the longer term.

Q7 Could you share some insights from your 2022 *EMJ Innovations* feature, entitled, 'Addressing Global Cancer Care Inequities Using Implementation Science and Community-Engaged Research Approaches'?

Our feature article highlights the importance of using implementation science approaches to develop feasible, appropriate, sustainable, and affordable cancer care delivery pathways in resource-constrained settings, and to identify priorities that can ensure maximum gains with the limited resources available. This approach requires recognition of the practical considerations for implementing the healthcare advances that are the focus of clinical trials in real-world oncology settings (outside of academic medical centres), where the bulk of cancer care is delivered. Importantly, in this article, we also advocate for community-engaged research approaches, to ensure that cancer research is relevant and important for the communities we serve; and to develop and tailor our approaches for cancer care delivery, as needed, to make them work in real-world oncology centres. We cannot just assume that what works in a highly-controlled clinical trial setting can automatically be translated into real-world settings, especially in resource-constrained settings. Researchers should recognise the multiple contextual factors that influence the implementation and dissemination of research findings into practice. To ensure that our approaches are equitable, we need to include the community voice, and that includes people who are treated for cancer in different cancer settings across the globe.

Q8 What changes do you hope to see in the future to fight disparities in healthcare?

The change that I would most like to see is to prioritise community-engaged research, including community members, patient advocates, and providers serving under-resourced populations, in research efforts to develop and test cancer care interventions. Community members most

burdened by the disease should have an elevated voice to raise concerns about what is working, what is not working, and how we can work together to create acceptable and appropriate interventions to reduce the burden of cancer in under-served populations. As such, it is critical to increase diversity in our clinical trials, and have global access to clinical trials for cancer. We need to move away from a system of self-selection in clinical trials, which often results in a uniform study population in terms of race, ethnicity, and socioeconomic status.

This selection bias into trials can influence the findings of these studies, and the treatments that are developed and approved for use. Increasing access and diversity of participants in clinical trials can help to ensure that our advancements are equitable, and have broad reach across all populations.

"It is critical to increase diversity in our clinical trials."