

Let a healthy lifestyle be thy medicine

While cancer survivors often receive a wide range of advice about how to lead a healthy lifestyle in terms of diet, exercise, and dietary supplements, this advice is neither consistent, nor is it backed by empirical data. The Pathways Study aims to change this.

Increased longevity and more effective cancer therapies have led to a substantial rise in the number of cancer survivors. In the United States alone, it is estimated that there are over two million breast cancer survivors. Indeed, this large and growing population requires more advanced scientific knowledge with regards to the various factors that affect cancer outcomes, such as disease recurrence, risk of second malignant neoplasms, and the late effects of cancer treatments. Moreover, it is becoming more and more important to understand the potential role of modifiable lifestyle factors in cancer prognosis.

ETIOLOGY VERSES PROGNOSIS

Surprisingly, little is known about the effects of lifestyle factors on cancer survival. This is partly due to the standard approach to researching diet and breast cancer in human populations. Essentially, studies on food and nutrition have focused almost exclusively on cancer etiology and prevention, not on prognosis. Only a few epidemiologic studies have examined factors influential to cancer risk, and even fewer have addressed the extent to which demographic, lifestyle, genomic, clinical, and psychosocial factors play a role in cancer outcomes. Moreover, most of the knowledge derived from epidemiologic studies on the role of diet and other lifestyle factors on breast cancer recurrence or survival after primary breast cancer has come from small studies, or from studies that were not specifically designed to investigate such questions.

Although there have been investigations that focus on populations post-breast cancer diagnosis, much of the research has largely focused on therapeutic trials or diagnostic markers and has rarely considered lifestyle factors. The little research there is on lifestyle factors in relation to cancer prognosis is very basic and often aims at the question of whether they impact the quality of life, and not on whether they influence cancer survival or recurrence. Overall, this is an understudied area with substantial opportunity for progress. More studies specific to cancer prognosis and the influence of lifestyle factors would certainly help medical professionals to respond to the growing interest among breast cancer survivors in adopting alternative therapies and special diets beyond conventional therapy to improve their prognosis.

THE PATHWAYS STUDY

One such study does already exist. The Pathways Study is a prospective multi-institution study of 4,505 women diagnosed after the age of 21 years with invasive breast cancer at Kaiser Permanente Northern California (KPNC). Led by Dr Lawrence Kushi, Principal Investigator and nutritional epidemiologist in the Division of Research at Kaiser Permanente Northern California, this study began recruiting participants in early 2006. The Pathways Study is unique in that it enrolls women immediately after breast cancer diagnosis, using the initial diagnosis as a starting point to collect baseline data on food intake, dietary

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supplement intake, physical activity, impact of alternative therapies and other lifestyle factors in prognosis and outcome. This is a major distinction from the handful of other similar studies, which have generally enrolled women after completion of adjuvant therapy or much later.

While the Pathways Study places emphasis on examining the effects of lifestyle, its main focus is to consider all contextual aspects of breast cancer prognosis to arrive at more holistic findings. In addition to lifestyle factors, data are being collected on psychosocial factors, demographic and social environment characteristics, and biospecimens collected for measuring molecular and genetic factors, such as germline genetic disposition, inflammatory markers, and vitamin D levels. Of course, all domains are viewed in the context of each participant's family history, with breast cancer risks and relevant prognostic factors taken into consideration. "With Pathways, we want to provide some of the first objective information about how nutrition, exercise and other lifestyle factors impact breast cancer prognosis. We hope our collaborative work will set the example for future studies on healthy lifestyles as an element of all types of cancer prognosis," Dr Kushi explains.

BUILDING A SOLID INFRASTRUCTURE

The Pathways Study was recently renewed for a third five-year funding cycle and is now being boosted by the "Infrastructure for Pathways: Prospective Study of Breast Cancer Survivorship" – an infrastructure application project that supports the study by leveraging digital data. This infrastructure application allows Dr Kushi and his collaborators to continue active follow-ups of study participants, keep clinical and lifestyle data updated, and systematically document outcomes. Surely, a broader collection of data on lifestyle and psychosocial factors, blood and saliva samples, and tumour tissues linked to KPNC medical records and virtual neighborhood audits, as well as social and built environment databases, will greatly enhance the Pathways Study and make it an exceptional comprehensive resource for research on breast cancer survivorship and prognosis. "There has never been a better opportunity to conduct a study that leverages electronic medical records than now. The Pathways Study may still be in its infancy, but having a proper infrastructure to back it will contribute significantly to its progress," Dr Kushi concludes.

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Q&A

How well is the Pathways Study received by medical professionals and the medical research world?

From the start, the Pathways Study was developed in partnership with clinicians in Kaiser Permanente Northern California (KPNC). In informing potential study participants of our study, we worked with KPNC's breast care coordinators – patient navigators for women diagnosed with breast cancer. We have periodically provided updates to the KP clinical community about the study. Our KP clinical collaborators, including Dr Susan Kutner, a breast cancer surgeon who also leads KP's Breast Care Task Force, and Dr Lou Fehrenbacher, a medical oncologist and head of the KP Oncology Clinical Trials Program, have been highly supportive of the study. The biomedical research community has also recognised its importance, as indicated by our ongoing success in funding.

How realistic is it that lifestyle, complementary and alternative therapies will be officially integrated into traditional breast cancer treatments or other cancer treatments?

There is growing evidence that lifestyle factors, such as the amount of physical activity one engages in, or the foods one chooses, can have substantial impact on cancer outcomes. While conventional medical care may acknowledge the role these choices may play, this is not an area that most physicians are trained to incorporate into their practice. Thus, despite the interest of guidelines organisations such as the American Cancer Society or World Cancer Research Fund in providing guidance in the lifestyle factors in cancer prognosis, it may require substantial cultural shifts in how medical care is delivered to have such knowledge translated into clinical care.

Once the Pathways Study has collected enough information, what are the next steps? Is there an awareness/implementation plan?

Aside from the usual professional dissemination strategies of presenting in professional conferences and publishing

in peer-reviewed journals, we hope to work closely with our KP clinical colleagues as well as the broader community of patient advocates to disseminate key findings. To this end, under our current funding, we have established a study participant and community advisory board. Membership includes study participants, clinicians, and breast cancer care advocates. We anticipate that this group will provide leadership in dissemination strategies, as well as providing guidance on future scientific directions for the study.

What can be done to inform and educate breast cancer physicians on the impact of lifestyle in cancer prognosis?

One of the first things is to conduct further research in these areas. Aside from the Pathways Study, there are half a dozen other studies of somewhat similar design that are examining diet and activity in breast cancer outcomes; indeed, we are hoping to create a consortium of these studies so we can learn from each other and leverage the power of combining knowledge across these studies. A substantial knowledge base can support clinical recommendations. This knowledge can be disseminated through clinical conferences, and through other educational opportunities, with perhaps the long-term impact of incorporating the importance of lifestyle choices in medical education.

What were some of the challenges you faced during the initial phases of the Pathways Study? What obstacles are to come?

Probably the most substantial challenge was identifying the appropriate setting for conducting the study. I first started to think about designing studies to examine food, nutrition, and physical activity in cancer prognosis and outcomes when I was at the University of Minnesota. It was partly to pursue these ideas that I left for Columbia University, thinking that the diverse population and many interested colleagues at NY institutions could help to create an outstanding study. Around the same time, I was approached to consider a job at Kaiser Permanente. Recognising that it would be difficult to follow patients diagnosed in most hospitals, given the fractured nature

of the US health care system, I realised that Kaiser Permanente's integrated health care setting would provide a relatively stable population with access to comprehensive medical care information, including key areas that we know are important in cancer prognosis, such as the specifics of diagnosis and details of treatments received. Thus, I chose to leave Columbia University and join the research group at KPNC, although those discussions in NYC were key in developing the study, with the ongoing collaboration with Dr Christine Ambrosone at Roswell Park Cancer Institute – she was at Mount Sinai School of Medicine at the time I was at Columbia – and our ongoing collaborations with colleagues at Columbia University.

Future challenges include the ongoing need to ensure that we continue the study as best we can, and make these data available to the broader research community so that knowledge to inform the care of women with breast cancer is generated and does not remain in untapped databases.

In what ways could the data collected in the Pathways Study be used to advance research in other areas?

The Pathways Study is a great example of a multidisciplinary and multi-level, perhaps ecologic or holistic approach, toward examining the question of identifying factors that may favorably impact breast cancer outcomes.

Although our primary focus has been on documenting food intake and physical activity patterns, we are collecting data ranging from germline DNA to the social and neighbourhood environment. We hope that this will allow us to examine factors in one domain while informed by those in others – something that is not necessarily possible in many other studies. If we demonstrate the interplay of factors in different areas, the Pathways Study can provide an example of the ways in which consideration of multi-level factors can influence health outcomes.

Detail

RESEARCH OBJECTIVES

Dr Kushi is a nutritional epidemiologist with research interests in cancer prevention and prognosis. He is Principal Investigator of the Pathways Study, a prospective cohort study of 4,505 women with breast cancer that is investigating diet, physical activity, and other factors in prognosis and outcomes.

FUNDING

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KEY COLLABORATORS

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- Dr Christine Ambrosone and Dr Song Yao, Roswell Park Cancer Institute, Buffalo, NY
- Dr Scarlett Lin Gomez, Cancer Prevention Institute of California, Fremont, CA
- Ms Catherine Thomsen, Zero Breast Cancer, San Rafael, CA
- Dr Al Neugut and Dr Dawn Hershman, Columbia University, NY, NY
- Dr Heather Greenlee and Fred Hutchinson Cancer Research Center, Seattle, WA
- Dr Jeanne Mandelblatt, Georgetown University, Washington, DC



BIO

A graduate of Amherst College and the Harvard School of Public Health, Larry has held research and faculty positions at the Fred Hutchinson Cancer Research Center, the University of Minnesota, and Columbia University, where he was the Vahlteich Professor of Human Nutrition. He joined the Division of Research, Kaiser Permanente Northern California, in 2002.

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