

Be-Well STUDY

Bladder Cancer Epidemiology, Wellness and Lifestyle

Thank you for being a part of the Be-Well (Bladder Cancer Epidemiology, Wellness and Lifestyle) Study, one of the largest and most comprehensive cohort studies of people with a history of non-muscle invasive bladder cancer (NMIBC).

We are reaching out to let you know that we have exciting news to share! The study launched in January 2015 and will continue with NEW FUNDING from the National Cancer Institute through May 2028.

The Be-Well Study includes participants from throughout the Kaiser Permanente Northern California and Southern California regions originally enrolled in the study from 2015-2019.

The study was designed to bridge the knowledge gaps in NMIBC clinical care and survivorship. Funded by the National Cancer Institute, Be-Well collected detailed information on occupational history, environmental exposures, diet, and lifestyle, and blood and urine samples from you and other patients with newly diagnosed NMIBC. By analyzing these samples and data, our goal is to find answers to at least two key questions, along with other new questions that may come up during the study:

1. Are there any biomarkers or genetic factors that can be used to predict risk of disease recurrence, and survival?
2. Does the choice of lifestyle influence effectiveness of treatment, prognosis, overall health, and quality of life?

We have made progress to answer these questions and are happy to share study findings in this newsletter. We sincerely thank you for your contributions and participation in making a difference in the lives of people, like yourself, with bladder cancer!

Be-Well Study: At-A Glance

PARTICIPANTS

Total **1472**

Age (years) **21-102**

GENDER

Male **77%**

Female **23%**

CHARACTERISTICS

White **79%**

Hispanic **8%**

Black **6%**

Asian **5%**

Other **2%**

STUDY STATUS

Baseline completed **1472**

Baseline Blood samples received **1137**

Baseline Saliva samples received **746**

Baseline Urine samples received **965**

12 month or 24 month follow ups completed **1091**

Meet the Be-Well Study Investigators



Marilyn Kwan, PhD

Marilyn is one of the Principal Investigators of the Be-Well Study and co-leads the study with Dr. Li Tang. She is a Senior Research Scientist at the Division of Research, Kaiser Permanente Northern California with expertise in cancer epidemiology and survivorship studies.

Her current research focuses on breast and bladder cancer prognosis and survival. She also studies the long-term health effects of cancer treatment in breast cancer survivors, including cardiovascular disease, osteoporosis and fractures, and lymphedema. Her devotion to Be-Well comes from the fact that bladder cancer is an understudied Top 10 cancer which can impact a patient's quality of life and has high cost of clinical care. She hopes to improve the long-term overall health of people living with a history of cancer.

In her free time, Marilyn enjoys exploring local sites and watching movies with her teenage daughter and son and husband, and coaching CrossFit classes at her local gym.



Li Tang, PhD

Li is one of the Principal Investigators of the Be-Well Study and continuously co-leads new research activities in the Be-Well Study along with Dr. Kwan. She oversees the Be-Well research activities at Roswell Park Comprehensive Cancer Center in Buffalo, New York. She is a Professor of Oncology in the Department of Cancer Prevention and Control, and has expertise in Nutritional and Molecular Epidemiology.

Her research is focused on the interactive roles of genetic and dietary factors in cancer treatment and prognosis. In addition to epidemiology, she has over twenty years of experience in laboratory-based research in bladder cancer. She is devoted to translating laboratory research findings into health practice and guidance. Her goal is to provide evidence-based recommendations for cancer survivors.

In her free time, Li enjoys exploring local cuisines and trail hiking in the beautiful Buffalo region with her daughter and husband. She also preserves a little private time for herself for reading and crafting.



Reina Haque, PhD

Reina is the lead investigator at Kaiser Permanente Southern California for the Be-Well Study. She is a senior cancer epidemiologist in the Department of Research & Evaluation and a professor in the Department of Health Systems Science at the Kaiser Permanente Bernard J. Tyson School of Medicine. She is also the scientific advisor to the Kaiser Permanente Southern California cancer registry and assists the Southern California Permanente Medical Group with quality improvement projects.

Reina's work encompasses cancer screening, etiology, treatment, and survivorship. She has led several large studies funded by the NIH/National Cancer Institute and the state of California on long-term outcomes of cancer treatments, molecular markers of breast and prostate cancer recurrence, comorbidities in cancer survivors, and how lifestyle factors influence cancer mortality.

In her free time, she enjoys going on urban hikes and reading, particularly novels by South Asian writers.

Be-Well in the Research News

Associations of Dietary Isothiocyanate Exposure From Cruciferous Vegetable Consumption with Recurrence and Progression of Non-Muscle-Invasive Bladder Cancer

Cruciferous vegetables, such as broccoli, cauliflower, and kale, among others, have long been thought to help prevent bladder cancer and improve bladder cancer prognosis due to strong laboratory evidence. These vegetables have unique phytochemicals called dietary isothiocyanates. Using data and biospecimens from the Be-Well Study, we found that high intake of dietary isothiocyanates from eating cruciferous vegetables is associated with delayed NMIBC recurrence, reduced risk of multiple recurrence, and importantly, reduced risk of NMIBC progression to advanced disease. Overall, Be-Well participants reported eating on average 0.7 servings (< ½ cup) per day of cruciferous vegetables, leading to generally low isothiocyanate levels in the bladder. This analysis suggests that higher exposure to dietary isothiocyanates that comes from eating cruciferous vegetables could be a promising strategy to lower risk of recurrence and progression in patients with NMIBC.

Wang Z, Kwan ML, Haque R, Goniewicz M, Pratt R, Lee VS, Roh JM, Ergas IJ, Cannavale KL, Loo RK, Aaronson DS, Quesenberry CP, Zhang Y, Ambrosone CB, Kushi LH, Tang L. Associations of dietary isothiocyanate exposure from cruciferous vegetable consumption with recurrence and progression of non-muscle-invasive bladder cancer: findings from the Be-Well Study. *Am J Clin Nutr.* 2023 Jun;117(6):1110-1120. doi: 10.1016/j.ajcnut.2023.04.006. Epub 2023 Apr 11. PMID: 37044209.



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Perioperative Intravesical Chemotherapy for Patients with Non-Muscle-Invasive Bladder Cancer: Understanding the Extent of and Sources of Variation in Guideline-Recommended Use

We assessed the relationship between disease risk group of the patient (low, intermediate, or high), which is defined based on tumor characteristics at diagnosis according to the American Urological Association, and receipt of intravesical chemotherapy in 988 NMIBC patients diagnosed at Kaiser Permanente Northern California. Our analysis found no statistically significant association between disease risk group and receipt of intravesical chemotherapy. However, when analyzing the data across Kaiser Permanente service area, patients treated in high-volume service areas had lower odds of receiving IVC, compared with patients treated in low-volume service areas. These findings highlight opportunities to improve use of IVC for eligible patients.

Check DK, Aaronson DS, Nielsen ME, Lee VS, Ergas IJ, Roh JM, Kushi LH, Tang L, Kwan ML. Perioperative Intravesical Chemotherapy for Patients With Non-Muscle-invasive Bladder Cancer: Understanding the Extent of and Sources of Variation in Guideline-recommended Use. *Urology.* 2019 Feb;124:107-112. doi: 10.1016/j.urology.2018.10.016. Epub 2018 Oct 23. PMID: 30359712; PMCID: PMC7202079.



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Be-Well in the Research News

Natural History of Multiple Recurrences in Intermediate-Risk Non-Muscle Invasive Bladder Cancer

According to American Urological Association guidelines, NMIBC at diagnosis is classified as either low-risk (low grade Ta and tumor size ≤ 3 cm), high-risk (high grade T1, or tumor size > 3 cm, or with carcinoma in situ), or intermediate-risk (all others). There is no consistent understanding on the prognosis of intermediate-risk NMIBC. Our team described the risk of multiple recurrences in intermediate-risk NMIBC and their impact on disease progression in participants in the Be-Well Study. In 291 patients, the 5-year risk of initial recurrence was 54.4%. After initial recurrence (n=137), 60.1% of patients had a second recurrence by 2 years. After second recurrence (n=70), 51.5% of patients had a third recurrence by 3 years. We found that female sex, increasing tumor size, and number of prior recurrences were associated with multiple recurrences. Receiving maintenance BCG treatment was associated with reduced recurrences. The 5-year risk of progression was higher for patients with more than one recurrence. This analysis found that multiple recurrences are common in intermediate-risk NMIBC and are associated with higher risk of progression.

Sharma V, Chamie K, Schoenberg M, Lee VS, Fero K, Lec P, Munneke JR, Aaronson DS, Kushi LH, Quesenberry CP, Tang L, Kwan ML. Natural History of Multiple Recurrences in Intermediate-Risk Non-Muscle Invasive Bladder Cancer: Lessons From a Prospective Cohort. *Urology*. 2023 Mar;173:134-141. doi: 10.1016/j.urology.2022.12.009. Epub 2022 Dec 24. PMID: 36574911.



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Smoking Behaviors and Prognosis in Patients with Non-Muscle-Invasive Bladder Cancer in the Be-Well Study

We examined the impact of tobacco smoking and marijuana use on risk of recurrence in patients in the Be-Well Study. Overall, 67% of study participants were former or current cigarette smokers at NMIBC diagnosis. Duration of cigarette smoking and amount of cigarettes smoked over time (also called pack-years) were associated with higher risk of recurrence, with up to twice the risk for longer duration (>40 years of smoking) and higher amount of cigarettes smoked over time (>40 pack-years). Pipe, cigar, marijuana, and e-cigarette use were not associated with recurrence risk. This analysis suggests that duration and lifetime pack-years of cigarette smoking are associated with NMIBC recurrence risk in a dose-dependent fashion.

Kwan ML, Haque R, Young-Wolff KC, Lee VS, Roh JM, Ergas IJ, Wang Z, Cannavale KL, Ambrosone CB, Loo RK, Aaronson DS, Quesenberry CP, Kushi LH, Tang L. Smoking Behaviors and Prognosis in Patients With Non-Muscle-Invasive Bladder Cancer in the Be-Well Study. *JAMA Netw Open*. 2022 Nov 1;5(11):e2244430. doi: 10.1001/jamanetworkopen.2022.44430. PMID: 36449286; PMCID: PMC9713602.



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What to Expect Next

In the upcoming months, our research team will be sending you a packet in the mail asking for your permission for our team to obtain samples of the surgical specimens from your bladder cancer surgeries.

With our new research funding, we plan to use the specimens to examine genetic and molecular factors that may be related to developing bladder cancer. We will obtain these surgical specimens from your past surgeries that removed the cancer. These specimens are routinely stored at Kaiser Permanente facilities for clinical purposes, including research, so this activity will not require any new procedures on your part. Also, we will be asking you to complete a follow up questionnaire over the telephone with a member of our research team. This questionnaire will cover any updates to your general health, diet, lifestyle, and quality of life.

We would greatly appreciate your continued participation in these activities for this new phase of the Be-Well Study! If you have any questions, feel free to call us toll-free at **1-800-627-2067** or email at **Be-Well@kp.org**.

Spotlight on our Be-Well Interviewer

Diane Lott-Garcia is a Research Associate/ Research Interviewer for the Be-Well Study. She has been with the Division of Research, Kaiser Permanente Northern California for over 31 years and brings with her a tremendous amount of experience and quality to her work. She has worked on multiple studies including cardiovascular health, diabetes, breast cancer, and pathology, among many others. She is a seasoned research interviewer with extensive experience working with research study participants. For the Be-Well Study, she will conduct follow up telephone correspondence with study participants as well as administer telephone interviews.



In her free time, Diane enjoys traveling to Iowa to see her family and renovating her old farmhouse, as well as taking pride in her garden. She loves traveling with her adult children and loving on her English and French bulldogs.

A Word of Thanks from Our Clinician Advisors

On behalf of the KP Northern and Southern California urologists involved in bladder cancer care, we would like to extend our heartfelt thanks for your participation in this important study. We are extremely excited to continue partnering with you and the Be-Well Study team to increase our understanding of bladder cancer and help improve bladder cancer research and clinical care.



David Aaronson, MD
South San Francisco Medical Center
Kaiser Permanente Northern California



Ron Loo, MD
Downey Medical Center
Kaiser Permanente Southern California

New Contact Information?

To keep in touch with you, we need your latest contact information. Please let us know if your phone number or home address has changed. You can reach us by calling our toll-free number at **1-800-627-2067** or by email at **Be-Well@kp.org**.

For the Most Up-to-Date Be-Well Study Information



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Word Search Cruciferous Vegetables

R E W O L F I L U A C F G P Z
W A T E R C R E S S U X M H X
J D I V V F P B L N P G F M T
U K S G O I Y L E K N R M I Q
G F O F N A G A B A T U R L F
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WORD BANK

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