





A CITY OF HOPE ORANGE COUNTY REPORT:

THE YOUNGER FACE OF CANCER







ORANGE COUNTY HAS ONE OF THE HIGHEST CANCER INCIDENCE RATES IN PEOPLE UNDER 50 IN SOUTHERN CALIFORNIA¹

Historically, cancer has been associated with aging. The median age of a cancer diagnosis is 66² and the risk of cancer increases with age. Yet, data reveals an alarming trend: the incidence of cancer among people under 50 around the world is projected to increase by 31% in 2030.³ Diet, alcohol use and tobacco consumption are among the main risk factors.⁴

Environmental carcinogens pose additional risk: the government's most recent Report on Carcinogens lists 256 substances and exposure circumstances known or reasonably anticipated to cause cancer in humans.⁵

Across the United States, early-onset cancer — defined as disease occurring between ages 18 and 49 — is on the rise for cancers of the uterus, colon and rectum, breast, pancreas, stomach, kidney and renal pelvis, and cervix⁶. The surge has cancer researchers and providers concerned, especially because cancer in younger people tends to be more aggressive, as seen in breast cancer.⁷

Colorectal cancer is on a particularly steep incline — so steep that by the year 2030, it is projected to be the leading cause of cancer death for young adults in the United States.⁸

Another perplexing trend is an increase in the incidence of lung cancer in younger and middle-aged women than in men of the same age — a shift not explained by differences in smoking.⁹

Orange County, California, with its reputation for healthy living, is not immune from this upswing. In fact, Orange County has the highest overall rate of cancer incidence in people under 50, compared to Los Angeles, Riverside, San Diego and San Bernardino counties.¹⁰

The incidence rates for cancer in people under 50 in Orange County are the most pronounced in breast, colon and lung cancer:

- Breast cancer rates are increasing for women under 50 in Orange County. Orange County has the 13th highest incidence rate in the state with this disease type. By comparison, Los Angeles County ranked 26th in the state.¹¹
- Orange County ranks 25th in the state for colon cancer incidence rates under 50, above Los Angeles,
 San Bernardino and San Diego counties. The rate of early-onset colon cancer is rising and threatening to nudge Orange County even higher.¹²
- Orange County has one of the highest incidence rates of lung cancer in women under 50 in California, ranking fifth in the state although data suggests a downward trend.¹³

"This is a startling paradigm shift," says Edward S. Kim, M.D., M.B.A, physician-in-chief, City of Hope Orange County. "We are seeing a deeply concerning rise in adult early-onset cancer. It is imperative to identify the reasons behind this trend, educate the public, advance prevention and early diagnosis, and develop more effective treatments."

What's Behind the Increase

Both puzzling and concerning, the increase in cancer rates among younger adults is linked to several possible causes.

First, we're somewhat better at cancer screening. That means some cancers are being caught more often among the general population than in the past. This is actually good news, as screenings typically detect cancer in earlier stages when it is more treatable. However, better screening is just one factor. There is substantial evidence indicating more troubling environmental causes for early-onset cancers.

"We cannot deny that a wide range of environmental factors — called 'the exposome' — have rapidly changed in developed countries since the mid-20th century. Admittedly, controlling some of these environmental conditions is difficult. There is evidence that some toxic exposures happen as early as in the womb or even in preconception germ cells. However, we have reason to believe changes to diet and lifestyle, especially in youth and early adulthood, could make a significant difference," Kim says.

The sharp increase in colon cancer — which accounts for the highest cause of cancer death in men under 50 and the second highest cause of cancer death in women in that age group — isn't exactly clear, but researchers at the American Cancer Society say it likely reflects lifestyle exposures that began with generations born after 1950.

About 1 in 3 people diagnosed with colorectal cancer before age 50 have a family history or genetic predisposition, according to the American Cancer Society.

"Sedentary lifestyles and consumption of processed foods and alcohol are likely contributing factors," said Misagh Karimi, M.D., a medical oncologist at City of Hope Orange County Lennar Foundation Cancer Center who specializes in colon cancer. "We see that about half of our younger patients diagnosed with colon cancer are overweight."

Researchers point to the importance of taking care of our gut's microbiome — the internal mechanism responsible for absorption of vitamins, regulation of the immune system, and assistance with food digestion. We

can improve our microbiome health by not eating ultra-processed foods (processed foods bought from stores are now 60% of most American adult diets¹⁴), exercising to prevent obesity, and avoiding alcohol and smoking.

Additionally, it is crucial for health care providers to expand the accessibility of cancer screening options for younger individuals. All too often, primary care physicians may not recommend early screenings, because cancer has traditionally been associated with older age and the screening guidelines have thus focused on age-based strategies. For some younger adults, even having timely access to health care provider appointments is difficult, particularly among the economically disadvantaged.

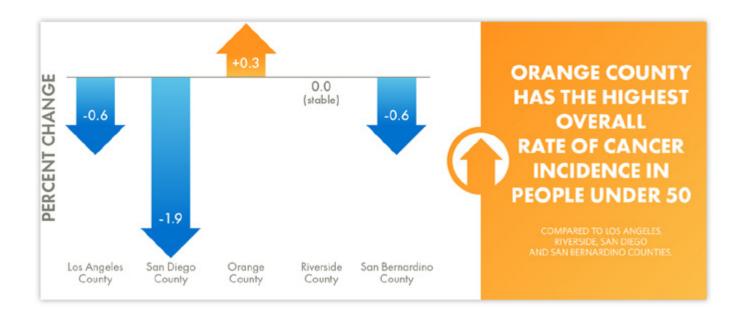
Expanding cancer research efforts focused on younger individuals is another critical area for improvement. Existing restrictions, including age-related criteria and other factors, frequently exclude certain populations from clinical studies. These exclusions limit our comprehension of cancer in these groups, especially among younger adults. By broadening access to clinical trials and increasing the focus on this demographic, we can enhance our understanding of the early-onset cancer phenomenon.

"This is a concern to all of us at City of Hope, and it's a concern to me as a member of this community and as a mother and a grandmother," said Annette M. Walker, president, City of Hope Orange County. "It is counterintuitive to our goal of reducing cancer risk for each successive generation. As the region's most advanced cancer treatment and research organization, City of Hope is as focused on preventing cancer as we are on treating and curing it. We know the best way to treat cancer is to prevent it in the first place."

Walker says she is encouraged by changes to screening guidelines that have lowered the recommended age for colon cancer screenings from 50 to 45 for people of average risk and mammograms from 50 to 40.

Irene Morae Kang, M.D., medical director, women's health medical oncology at City of Hope Orange County, specializes in breast cancer. She says younger patients face additional challenges.

"Younger people often face issues such as fertility preservation, managing employment and child care duties, changes in physical function and body image," Kang says. "These can be significant issues for our patients across the age spectrum but may specifically impact younger patients."



Stories of Hope From Younger Survivors

A cancer diagnosis is difficult to handle, and when it comes early in life, it hits patients and their families particularly hard. Many face obstacles to obtaining a diagnosis. Then, they experience the shock of learning that they are seriously ill.

However, even with these difficult journeys, there are those who have found hope and are reclaiming their lives.

Brandon: Cancer not on his radar



Brandon Arbini of Costa Mesa, California, 44, was busy with his business start-ups and raising three children when a few nagging symptoms sent him to his physician. Arbini was 41 and living a healthy lifestyle devoid of smoking and drinking. The doctor, just to be on the safe side, ordered a colonoscopy, which began his highly unexpected cancer journey.

The tumor in Arbini's colon was so large the colonoscopy could not be completed. A biopsy revealed Stage 4 cancer, which had spread to his liver. Arbini and his family were stunned,

and a consultation with a surgeon made the situation even worse. Instead of providing a clear treatment path, the surgeon's grim outlook and lack of guidance left Arbini and his wife confused and despondent.

A recommendation to go to City of Hope changed Arbini's story and saved his life. After surgery and chemotherapy, he is now in remission. "Remission is a word I didn't expect to hear," he says.

Ashly: The nurse who lets her patients know she's "been there"



Ashly Grafton, R.N., 38, is a clinical research nurse at City of Hope Orange County who feels a special bond with her patients. Grafton was diagnosed with triple-negative Stage 2 breast cancer at age 32.

Fortunately, her medical knowledge and self-advocacy helped save her life. When she felt a lump in her breast, she had it checked by a doctor, even though a well-woman exam a few weeks prior found nothing wrong. Grafton says she trusted her instincts and lobbied

to get an immediate mammogram and ultrasound appointment, and again for a biopsy as soon as possible. "If you feel something is wrong with your health, you have to push for what you need.

"That's especially true for younger women because there is a misconception that breast cancer only affects women older than 40, and that mindset needs to change. I would not have gotten things done if I hadn't voiced my concerns and insisted on getting my tests," says Grafton, who now helps advocate for younger people with cancer.

Will: The athlete works to rebound



Will Godoy of Mission Viejo, California, was in the best shape of his life — a runner with 0.8 percent body fat. When he experienced abdominal pains at age 35, doctors immediately thought it was colitis and put him on antibiotics. But the pain returned, especially when he ate. Not long after, doctors found a golf ball-sized tumor in his colon.

After several surgeries and chemotherapy, Godoy's cancer is under control. He remains

active and started participating in triathlons again in 2022. "Even though it's been a struggle, it's really molded me into this person who I am today," says Godoy, now 44. "Cancer is not a joke, and I feel like people should be aware of it. They should understand that you can prevent it ... if you get enough information early enough."

Juliette: "Too young for cancer"



When Juliette Landgrave of Mission Viejo, California, found a lump in her breast in the shower, she thought it could be a cyst. After all, she was only 38. She wanted to be sure and got a mammogram. She was shocked by the results: she had two malignant masses in her breast and was diagnosed with triple-negative breast cancer, (TNBC) which occurs more often in younger women and in African American women and tends to be more aggressive.¹⁵

Given her age and the fact that she has always wanted children, Landgrave, 40, underwent fertility treatments to preserve her eggs before starting chemotherapy. She underwent surgery, reconstruction, radiation therapy and immunotherapy, and she is cancer-free today. "People would tell me I'm too young to have cancer. And obviously, cancer doesn't care about your age."

Alisa: A heartbreaking conversation with her children



Alisa Secaida of La Verne, California, received a shocking Stage 4 lung cancer diagnosis at age 35, which necessitated an agonizing discussion about her illness with her two young children. "Having to tell them about this was heartbreaking," she says.

Secaida, 38, was also forced to advocate for her care, as her health care providers, not believing lung cancer would appear in a nonsmoker and someone so young, held off referrals to specialists. After considerable insistence from her family, things turned

around, and Secaida was referred to City of Hope.

And then came a revelation — her cancer turned out to be a rare variety called ALK+, in which the ALK (anaplastic lymphoma kinase) gene undergoes a rearrangement, or "translocation," and fuses with another gene, triggering cancer. Only about 5% of non-small cell lung cancers are ALK+. It was great news because ALK + can be treated with targeted therapies specifically designed for that genetic mutation. Secaida knows her persistence paid off and, had she not insisted on seeing a specialist, her prognosis would not be positive.

Camilla Row: Grateful for a second chance



When Camilla Row, formerly of Orange County, California, was diagnosed with stomach cancer at age 39, the mother of two was in shock and disbelief. Cancer was an "old person's" disease, she thought. However, studies have found a concerning increase in gastric cancer in people under 50; and as a person of Asian descent, Row was unknowingly at higher risk. The reasons why are not fully understood, but Asian Americans have three times the risk of stomach cancer as non-Asian, non-Hispanic white people.

Following several intensive years of treatment, including multiple surgeries and chemotherapies, Row, 45, tested cancer-free in 2023. Her survivorship journey continues, and Row remains committed to fighting for her life and for her family. "Everything came together for me," Row says. "But I worked really hard. I didn't take no for an answer."

Breakthroughs and New Hope

While the news that the incidence of certain cancer types is impacting younger patients is not encouraging, innovative treatments continue to emerge from research at leading cancer research and treatment organizations like City of Hope. Here is a sampling of the research and new therapies offering tremendous promise.

- A blood test that may screen for early-onset colorectal cancer This research by scientists at City of Hope is a first step to noninvasively and inexpensively detect colorectal cancer at an earlier and more treatable stage. "More research is needed, but this finding could help fill a void in the cancer prevention and early detection field, which does not currently have a noninvasive and accurate way to detect the presence of nonhereditary colorectal cancer in people younger than 50 years old," said Ajay Goel, Ph.D., M.S., professor and chair of the Department of Molecular Diagnostics and Experimental Therapeutics at City of Hope. "The study is significant because it is the first time a novel microRNA biomarker has been identified, developed and validated to detect early-onset colorectal cancer."
- Answers in an unexpected place: The gut Recent insights into gut microbiome health are revolutionizing our approach to preventing and treating colorectal and other cancers. A healthy gut microbiome acts as a protective shield against intestinal infections, while an imbalanced microbiome can trigger inflammation, potentially contributing to tumor development. Additionally, the gut microbiome plays a pivotal role in augmenting the effectiveness of cancer immunotherapy, particularly with checkpoint inhibitors, a treatment increasingly recommended for specific colorectal cancer subtypes. This microbiome-immunotherapy interplay may also extend to helping with the adverse effects of immunotherapy, and is believed applicable across various cancer types, such as melanoma.
- The investigational pill with enormous potential punch An experimental pill that has eliminated malignant cancer cells and prevented their resurgence in laboratory and mouse models is in human safety testing in a Phase 1 clinical trial. The newly discovered, cancer-inhibiting investigational medicine known as AOH1996 has been shown in preclinical research to bring all cancer growth to an abrupt standstill. Researchers describe the agent as capable of zeroing in on proliferating cell nuclear antigen (PCNA), a key factor fueling cancer progression. Linda Malkas, Ph.D., a scientist at City of Hope and the M.T. & B.A. Ahmadinia Professor in Molecular Oncology, leads the laboratory that pioneered this breakthrough research. She emphasizes that AOH1996 has the capability to halt the growth of cancer cells across more than 70 diverse solid tumor cell lines. This includes not only breast cancer but also cervical, lung, skin, and ovarian cancer cells. Its capabilities in humans will be discovered in later-stage clinical trials.
- A breakthrough for difficult to treat colon cancers In a recent medical breakthrough, City of Hope's Marwan G. Fakih, M.D., the Judy & Bernard Briskin Distinguished Director of Clinical Research, has unveiled a pioneering combination immunotherapy regimen that shows good outcomes for treating colon cancer that is chemotherapy-resistant and microsatellite stable (a biomarker of certain colon cancer types). Fakih's Phase 1 clinical trial has yielded positive results, with more than 50% of patients whose cancer hadn't spread to the liver surviving after 20 months of treatment. The regimen, which includes a combination immunotherapy treatment consisting of ipilimumab and nivolumab plus the targeted therapy regorafenib, offers new-found hope to those with this challenging form of cancer. Fakih's groundbreaking research underscores the importance of personalized treatment approaches and continues to inspire further investigation into innovative therapies.
- A cancer-killing virus A City of Hope-developed virus has been shown to shrink colon, lung, breast, ovarian and pancreatic tumors in preclinical laboratory and animal models. "Our previous research demonstrated

that oncolytic viruses can stimulate the immune system to respond to and kill cancer, as well as stimulate the immune system to be more responsive to other immunotherapies, including checkpoint inhibitors," said Daneng Li, M.D., principal investigator and associate professor of City of Hope's Department of Medical Oncology & Therapeutics Research. "Now is the time to further enhance the power of immunotherapy, and we believe CF33-hNIS has the potential to improve outcomes for our patients in their battle with cancer."

- Answers in a blood test Liquid biopsies sound like a much bigger ordeal for the patient than they really are it's just a blood test. But these simple blood tests are being explored as effective methods to detect, analyze and track DNA, cells and other substances that tumors shed into bodily fluids, including blood and urine. Researchers believe the test can detect colorectal cancer early, measure treatment responses, identify treatment resistance, and monitor for recurrence. For example, the COBRA trial is studying liquid biopsies as a new way to identify patients with Stage 2A colon cancer, who may benefit from additional chemotherapy after surgery.
- Mobile cancer prevention and screening City of Hope is taking leading-edge clinical screening and care into Southern California communities with the launch of a new mobile cancer prevention and screening program. The program is the first in the U.S. to provide this level of mobile comprehensive cancer prevention and screening services. The program will feature two highly advanced mobile clinics with a full staff, including nurse practitioners, nurses, mammography technologists and support staff. The mobile clinic assesses the risk and screens for at least 15 different types of cancer, including state-of-the-art mammography technology. If a mobile clinic client receives a positive finding from their screening, a nurse navigator will guide them through the diagnostic process and provide appropriate resources.
- Addressing Hispanic and Latino cancer incidence The ENLACE study, supported by the Cancer Moonshot initiative, is a groundbreaking research project aimed at understanding the molecular characteristics of colorectal cancer in Hispanic and Latino populations. As the first study of its kind to use advanced genomic tools for this purpose, ENLACE is analyzing tumor samples and blood for genetic mutations associated with the disease. This effort not only highlights the importance of personalized medicine but also addresses the gap in cancer research, focusing on Hispanic and Latino communities.

Is Prevention Possible? Advice for Younger Adults

A host of factors can contribute to a cancer diagnosis, making it challenging to claim that altogether preventing early-onset is entirely possible. Nonetheless, many health care professionals agree that there are ways to help mitigate your risk.



Know your family history. This may mean difficult conversations for some, and for others who are adopted or estranged from their families, it's just not possible. However, being aware of the illnesses in a family tree makes it easier to assess one's risk and obtain advice on minimizing the chances of getting certain types of cancer. More information on genetic screening is available here.



Start moving. Adults should get 150 to 300 minutes of moderate intensity exercise or 75-100 minutes of vigorous intensity activity each week, according to the American Cancer Society. Getting more than 300 minutes of exercise is even better.



Diet improvements. To maintain a diverse gut microbiome, a healthy recommended diet includes high-fiber vegetables like spinach and broccoli, nuts, whole grains and whole fruits in a variety of colors. In addition, polyunsaturated fats found in fish, walnuts, pumpkin, flax and chia seeds, and sunflower, safflower and unhydrogenated soybean oils appear to produce a healthier gut.



Get screened. Unfortunately, many screening guidelines are tied to age, which means some health care providers and insurers may be averse to recommending screenings, such as mammograms for younger people. However, if there is clear evidence of risk, such as symptoms or family history, exceptions can be made. Most importantly, if a person feels something is wrong, it is always important to advocate for getting tested. More information on mammograms is available here, and lung cancer screening is available here. Finding cancer early – before it spreads and grows – improves treatment outcomes.



Get vaccinated. Beyond COVID-19 vaccine updates (which help keep you generally healthy), there are vaccines for preventing cancer. For example, the human papillomavirus (HPV) vaccine helps prevent most cervical cancers, as well as vagina, vulva, penis and anus cancers caused by HPV. Getting this vaccine is just as important for young men as young women.



Don't smoke. The bottom line is that quitting smoking is one of the best things you can do at any age to avoid cancer. This includes vaping. Also, it is highly recommended that you refrain from or limit alcohol consumption.

Finally, have a primary care provider who is your partner and listens to your concerns. Plot a strategy for prevention rather than waiting until something is wrong. If you find that you are not getting your concerns answered, do not shy away from being your own health advocate. Ask questions and, if needed, get a second opinion. It's also important to seek education and resources from cancer experts.

Taking charge of your health now is important for your physical and emotional well-being, and an important investment for your future.

Sources

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