Lack of Progress in Teen and Young Adult Cancers Concerns Researchers, Prompts Study

Mounting evidence suggests that adolescents and young adults are not getting the best that cancer treatment can offer. Spurred by data showing that cancer mortality rates among adolescents have barely budged for decades, scientists and others have called for heightened efforts to improve their clinical outcomes.

The most recent evidence comes from the National Cancer Institute’s Surveillance, Epidemiology, and End Results (SEER) program, which in April published a monograph claiming that a diagnosis of cancer among adolescents and young adults during the mid-1970s carried a better prognosis relative to other age groups than it does today. Yet since then, cancer mortality rates among this population have mysteriously flattened, while those of children and older adults have steadily improved.

Experts are now trying to determine why young adult cancers haven’t made the strides common in other age groups and what can be done about it. A collaboration of the Lance Armstrong Foundation (known as Livestrong) and NCI recently concluded that the single greatest current challenge facing young adults and older adolescents with cancer is the lack of progress in their outcomes, a deficit that has spanned nearly a quarter of a century. That is the conclusion of a 108-page report titled Closing the Gap: Research and Care Imperatives for Adolescents and Young Adults with Cancer, which was published by Livestrong and NCI in September. The report’s recommendations topped the agenda at a recent Livestrong conference, held Nov. 10–12 in Austin, Texas. At the conference, participants from hospitals and research groups throughout the United States developed a range of strategies to promote adolescent and young adult cancer research and awareness. Details were unavailable at press time.

“As a group, adolescents and young adults are understudied in cancer research,” stresses Crystal Mackall, M.D., who heads the pediatric oncology branch of the NCI’s immunology section. “Our feeling in the research community is that we’re glad folks are taking this on and putting together programs that target this particular segment of the population.”

Evidence Emerges

The initial evidence for flattened success rates came from Archie Bleyer, M.D., now a clinical research professor at Oregon Health and Sciences University in Portland. Bleyer noticed the discrepancy while poring over SEER data during the late 1990s, when he was chair of the adolescent and young adult committee of the Children’s Oncology Group (COG), a multinational research consortium. His own observations triggered a round of NCI studies in this area, culminating in the 2006 SEER monograph Cancer in 15-29 Year-Olds, U.S. SEER, 1975-2000.

That document, the first devoted exclusively to adolescents and young adults, comes down to one key finding. Among older adults, the controversial measure of 5-year cancer survival rates (see sidebar) have gone up by as much as 2% per year, while among children younger than 15, the annual rate of increase has averaged 1.6%. Meanwhile, survival improvements among adolescents and young adults have accrued more slowly. Among those aged 15–20, the annual rate of improvement barely reaches 1%, whereas among those aged 25–30, the annual improvement rate is 0.03%. The report also presents a limited amount of mortality data that appear to support these findings.

Pediatric cancer patients experienced a 3% annual decline in mortality for all invasive cancers between 1975 and 2000, while comparable declines among adolescents and young adults were substantially lower, reaching just 1.5% per year among those aged 20–24. Interestingly, the differences appear to be a global problem, the SEER monograph reports.

What’s behind those deficits? “This is an unanswered question,” Mackall says. “We don’t know how much of it is biological or how much has to do with psychosocial and financial factors, including access to health care and treatment compliance. It’s likely a collusion of several factors.”

Bleyer attributes the discrepancy in part to a widespread gap between pediatric and adult health care services that, he says, leaves many adolescents and...
young adults vulnerable. That’s particularly true in countries where universal health care coverage doesn’t exist, he adds. In the United States, adolescents and young adults constitute the most underinsured age group, falling between their parent’s policies or government-funded childhood insurance programs on the one hand and coverage supplied by full-time jobs on the other.

“Evidence from our studies suggests that cancer diagnoses are delayed among the underinsured, and that’s a real issue with this population,” Bleyer says. “Our assumption is that delays in diagnosis make it harder to improve outcomes… Moreover, underinsured and uninsured individuals also tend to get lesser care. So, a lack of insurance doesn’t just delay diagnosis—it also affects the quality of care afterward.”

Attacking Adolescent Cancer
A recent Lance Armstrong Foundation–National Cancer Institute report outlines five recommendations for how to provide better care for adolescent and young adult (AYA) cancer patients.

- Identify the characteristics that distinguish unique cancer burdens in the AYA patient.
- Provide education, training, and communication to improve awareness, prevention, access, and quality care for AYAs.
- Create the tools to study the AYA cancer problem, such as large prospective databases of AYA cancer patients, additional tumor samples, and instruments for assessing quality-of-life factors tailored to their age groups.
- Ensure excellence in service delivery across the cancer control continuum.
- Strengthen and promote advocacy and support of the AYA cancer patient.

A compounding problem, adds Ronald Barr, M.D., a professor of pediatrics at McMaster University in Hamilton, Ontario, is that adolescents and young adults typically don’t concern themselves with cancer risk. “They say, ‘That will never happen to me; I’m going to live forever,’” he explains. That invincibility complex, he stresses, also contributes to delays in diagnosis.

Are Teen Tumors Different?
Apart from these social factors, scientists say that age-specific differences in cancer biology might also play a role. According to Bleyer, most cancers among adolescents and young adults occur spontaneously, with few recognized contributions from genetics or the environment. Karin Albritton, M.D., an instructor in pediatrics at Harvard Medical School and the Dana-Farber Cancer Institute, and current director of the COG’s adolescent and young adult program, says knowledge of how genetic factors contribute to cancer in these age groups is “pretty much a blank slate. Almost all cases diagnosed under the age of 30 have unexplained causation. We can’t point to any known environmental or inherited factors. I believe that in time we’ll find that many of the cancers that occur in young adults have higher rates of genetic predisposition, but we can’t say that right now.”

5-Year Survival Data Not Always a Good Measure of Progress

The 5-year survival rate used to measure progress in the current SEER analysis of adolescent and young adult cancer prognosis is controversial. Although the statistic is common in cancer research, many experts suggest that it can also be prone to biases and misleading results.

Of chief concern is that 5-year survival rates are heavily influenced by the time of diagnosis, says H. Gilbert Welch, M.D., who codirects the Veterans Administration Outcomes Group at Dartmouth Medical School in New Hampshire. To illustrate how that skews their interpretation, he offers the following example: Consider two individuals who both contract cancer at age 42 and then die from it at the age of 50. However, one isn’t diagnosed until age 47, while the other is diagnosed at age 42. The first patient lives 3 years with a cancer diagnosis and contributes nothing to 5-year survival, while the second patient lives with the diagnosis for 8 years. Nevertheless, both patients live with cancer for the same duration and die from it at the same age.

“The data would lead you to think the second patient had a big improvement, but the reality is that the patient just lived with a diagnosis for a longer period,” Welch explains.

Another problem, he says, is that some cancers meet pathological definitions for the disease and yet progress slowly or not at all. “And those cases inflate the statistic and distort its meaning,” Welch says.

A recent JNCI panel of scientists from NCI and academia suggested that survival rates have biases that “…may result in apparent trends in survival over time that do not reflect meaningful changes to the population.” Echoing Welch’s view, that same panel wrote, “Mortality rates remain the most important measure of progress against cancer.”

Crystal Mackall, who currently heads the immunology section at NCI’s pediatric oncology branch, emphasizes that 5-year survival rates have limitations that vary by disease. For rapidly progressing cancers, she says, the measure has more value than it does for indolent cancers that progress slowly.

Nonetheless, Mackall stresses that despite their reliance on 5-year survival data, the SEER conclusions on adolescent and young adult cancer prognoses are compelling. “The data aren’t perfect, but to me it looks like their outcomes are substantially reduced,” she says. “I think this is a wonderful starting point, and I’m now more convinced than ever that more work needs to be done.”

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Scientists know little about how cancer among adolescents and young adults differs from that of other age groups, in part because young people rarely contribute tumor samples for research. Most tumor samples are collected by academic treatment centers that specialize in either pediatric or adult cases, Albritton says. But for unknown reasons, community doctors rarely refer adolescents and young adults to these centers. According to Albritton, that limits the number of tumor samples obtained from these age groups. Exacerbating the shortage, she adds, is that academic centers almost never collect samples from patients who haven’t been enrolled in clinical trials.

Meanwhile, mounting evidence shows that clinical trials rarely include adolescents and young adult patients. The Livestrong–NCI collaborative report notes that just 1%–2% of adolescent and young adult oncology patients participate in clinical trials, compared with roughly 40% of pediatric cases under the age of 14 and roughly 5%–10% of those aged 40 years or more, according to Mackall.

“There are probably many reasons for this,” says Stephanie Elsea, a Livestrong spokesperson, “not the least of which is too few physician referrals.”

“This is an area that’s crying out for clinical investigation. We need to get more adolescents into clinical trials and we need more biological studies of the diseases for which they’re being treated,” Barr adds. “If we could get a handle on how adolescent tumors differ from those of children and adults on a cellular or molecular level, we might be able to produce new targets for intervention.”

**Children or Adults?**

That would be useful because evidence shows that adolescents and young adults fall into a gray area with respect to care—some wind up as pediatric patients, while others are treated as adults. Meanwhile, treatment practices directed at either age group can differ substantially. For instance, pediatric cancer patients are deemed stronger and healthier than their adult counterparts, so they generally receive higher-intensity treatments, with larger doses of chemotherapy. Bleyer suggests that some young cancer patients treated with adult doses would do better under higher-intensity, pediatric regimens.

“This is controversial and it treads on adult oncology, but I’m willing to take that on,” says Bleyer, a 2006 recipient of the American Society of Pediatric Hematology/Oncology’s distinguished career award. “There’s clear evidence that pediatric treatments [can be more] effective in this age group for acute lymphoblastic leukemia,” which is among the more common cancers in adolescents and young adults.

Mackall stresses that choices governing pediatric or adult treatments should be disease specific—Ewing sarcoma, for instance, is more common among younger patients and should therefore be treated by pediatric oncologists, she says. Testicular cancer, on the other hand, occurs more often among older adolescents, so it should be treated by oncologists who focus on adults. Even so, Mackall acknowledges that doctors who typically treat much older cancer patients might feel uncomfortable delivering high-intensity doses, even to young patients who might otherwise tolerate them.

Eugenie Kleinerman, M.D., professor and head of pediatrics at the University of Texas M. D. Anderson Cancer Center in Houston, agrees. Some adolescent and young adult patients are better off when treated with pediatric regimens, she said. In the late 1990s, M. D. Anderson created an adolescent and young adult program where patients can be treated by pediatric and adult oncologists working collaboratively. That approach, which is found in just a few cancer centers nationwide, tends to benefit patients most, Kleinerman says. “We have
multidisciplinary teams that consider the dosages we should use,” she explains. Kleinerman also emphasizes that adolescent and young adult patients often prefer being cared for in pediatric settings, where age differences with other patients aren’t as stark as they are in adult oncology facilities.

In short, research and treatment of cancer in adolescents and young adults as a unique population will probably gain momentum in the coming years. Mackall acknowledges the data on outcomes are preliminary, but the conclusions thus far appear compelling.

“In general, I think that this is a significant problem, and we’re now taking some important first steps,” she says. “We’ve stated the situation as it currently stands and we’re poised to make a lot of progress in the not-too-distant future.”

—Charlie Schmidt

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