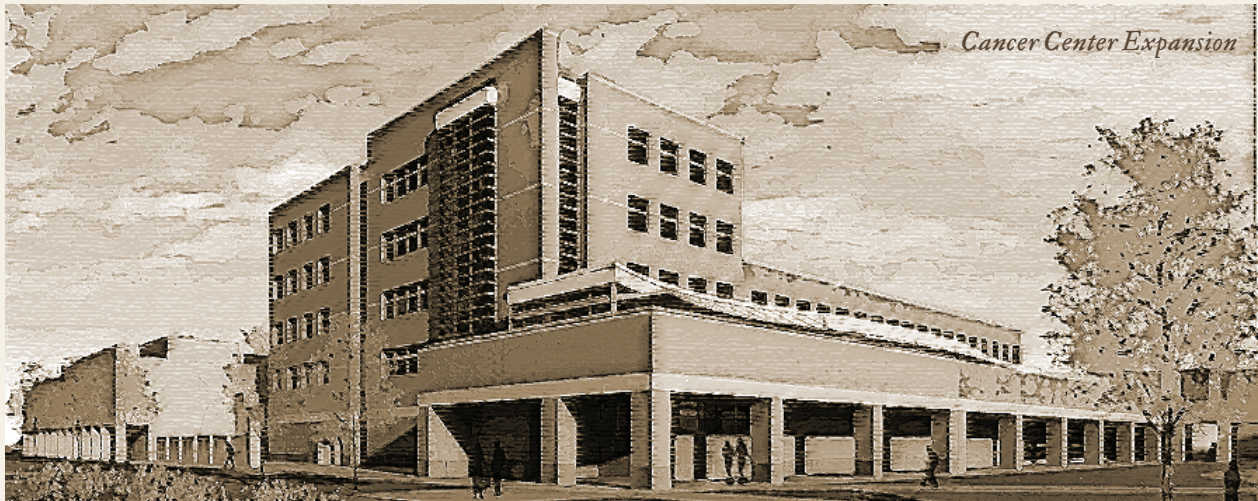

**University of
Colorado Hospital**
ANSCHUTZ MEDICAL CAMPUS
*An enduring PASSION for EXPLORATION
in the pursuit of NEW DISCOVERIES.*
CANCEREXPLORERS.COM

CANCER OUTCOMES

2011

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Dear Friends,

The University of Colorado Cancer Center's sole purpose is to discover, develop and deliver the most effective treatment for those diagnosed with cancer. This booklet highlights just a handful of ways we're doing this work in adult cancer, including innovative methods of testing tumors for gene anomalies, developing new drugs for pancreatic, colon, lung and bladder cancer, one of the few translational research and care programs for young women with breast cancer and providing survivors of all ages with programs to help the transition from oncology care to primary care.

Our adult clinical care program is the busiest in Colorado, with nearly 100,000 outpatient cancer visits to University of Colorado Hospital each year. The remarkable growth of the center since its opening in 2002 explains why University of Colorado Hospital is expanding the Anschutz Cancer Pavilion, adding two radiation vaults and nearly doubling the number of infusion bays. This expansion will be completed in April this year.

Our clinical trials program—hands down the most robust in the Rocky Mountain region—continues to grow, with 1,110 people enrolled in therapeutic trials and nearly 9,000 people enrolled in prevention trials last year. The Anschutz Cancer Pavilion expansion will also increase our clinical research space by nearly 12,000 square feet. And we're expanding our clinical outreach program, bringing clinical trials to people with cancer in rural and mountain Colorado towns.

But all of this activity doesn't mean much if it's not positively impacting our patients. You can turn to page 8 to see our center's 5-year survival rates for major cancer types. We can confidently say that most people treated by our physicians have better 5-year survival rates, especially those with late-stage cancers.

Everything we do in cancer at University of Colorado Hospital is backed by over 400 basic and translational and clinical scientists working at the University of Colorado Anschutz Medical Campus, University of Colorado at Boulder and Colorado State University. And as one of our nation's elite cancer centers—just one of 40 designated as a comprehensive cancer center by the National Cancer Institute—University of Colorado Cancer Center will continue to lead in our battle against cancer.

Sincerely,

Dan Theodorescu, MD, PhD

Director, University of Colorado Cancer Center

BREAKTHROUGHS in BLADDER CANCER genetics

Research teams at the University of Colorado Cancer Center were responsible for two major advancements in bladder cancer genetics in 2011:

- Identification of the first genetic sequencing of urothelial carcinoma
- Development of a gene expression model for bladder cancer metastasis

Genetic Sequencing

A CU Cancer Center team, in partnership with universities in China and Denmark, reported the first genetic sequencing of transitional cell carcinoma of the bladder in **Nature Genetics**. A set of the identified mutations also has been recently discovered in a host of other cancers, implying a possible common denominator in the cause of cancer in general.

In 59 percent of 97 patients with urothelial carcinoma, the team found mutations in genes responsible for chromatin remodeling.

“The discovery of mutation in the UTX gene and seven similar

chromatin remodeling genes is a major step toward detection and treatment of bladder cancer,” says Dan Theodorescu, MD, PhD, director of the CU Cancer Center and an author on this work.

The CU Cancer Center team is now working to confirm the sequencing in Caucasian subjects that was found in this study’s Asian subjects. After confirmation, the task will be twofold: designing genetic tests for these mutations that may allow easy, early, accurate diagnosis of bladder cancer, and developing therapies that recognize these mutations and kill the cancerous cells that hold them.

Gene Expression Model

Another CU Cancer Center team this year developed a gene expression model that can help determine whether a bladder patient should undergo chemotherapy prior to removal of the bladder and lymph nodes.

In about 25 percent of patients, the bladder cancer already has spread to the lymph nodes by the time of detection. In these patients,

chemotherapy prior to surgery can improve outcomes. Until now, however, the only way to know if the cancer had spread was to surgically remove the lymph nodes for examination.

“The concept behind the test is like a signature—some genes go up and some genes go down, and the signature defines whether or not the lymph nodes are likely to be involved,” says Dara Aisner, MD, PhD, investigator at the cancer center and molecular pathologist at University of Colorado School of Medicine, who co-authored the article with Theodorescu and Garrett Dancik, a postdoctoral fellow in the Theodorescu laboratory.

Depending on the results of this quick and easy 20-gene test, a treatment team can decide whether to complete a round of chemotherapy prior to lymph node and bladder removal or to proceed with surgery.

This research was presented in **PLoS Currents** and **The Lancet Oncology**.

COLORADO TEAM works to DETECT COLORECTAL cancer BIOMARKERS

University of Colorado Cancer Center researchers are working to identify genetic biomarkers that are necessary for Src inhibitors to work effectively in colorectal cancer patients.

The research team, led by Wells Messersmith, MD, received a \$1.25 million grant from the National Institutes of Health in 2011 to fund this work. The award is a five-year RO1 grant, one of the highest levels awarded by the National Institutes of Health.

“The new class of anticancer drugs to block Src most likely will benefit only a small subset of patients,” says Messersmith, associate professor of medical oncology at the University of Colorado School of Medicine and director of the gastrointestinal medical oncology program. “The goal is to identify those patients who won’t benefit prior to treatment so that time and money is not wasted.”

The researchers are using a novel technique developed at the CU Cancer Center to implant surgically resected human tumors into mice. They will test drugs that are

designed to shut down the genetic mutations causing the cancer on those tumors. The goal is to find genetic biomarkers that can be used to screen patients prior to treatment to avoid prescribing costly drugs that ultimately have no chance of working.

If biologically targeted drugs are given to patients who lack the appropriate genetic mutations, they can cause harmful side effects, delay the use of effective treatment and add unnecessary and sometimes exorbitant costs to a patient’s treatment.

Two years ago, researchers found that two drugs used commonly to treat colorectal cancer for several years had no benefit in at least 40 percent of patients. The drugs targeted the epidermal growth factor receptor (EGFR) but were found to be ineffective and possibly harmful in patients with mutated copies of the K-ras gene.

It has been estimated that more than \$3 billion was spent on giving these drugs to patients who had no chance of benefit, Messersmith says.

UCH ADVANCES lung cancer treatment

University of Colorado Hospital researchers and clinicians are at the forefront of uncovering biological therapies that halt the progress of lung cancer in tiny subsets of patients. These teams have been pivotal in understanding and treating ALK and EGFR genetic mutations that affect approximately 15 percent of non-small-cell lung cancer patients.

ALK-fusion

Last August, the FDA approved crizotinib for commercial use in ALK-positive patients just 10 months after Phase I safety trials. CU led these trials after developing a genetic test to identify ALK-positive patients. The drug was fast-tracked to approval after showing it stabilized or shrunk tumors in 90 percent of ALK-positive patients in the trial.

But by the time the drug was approved for commercial use, the cancer already had returned in some of the initial patients. While disappointing, the news was fully expected by the CU team that was already at work on other drugs to knock the cancer back again.

“When your first miracle stops working, you start looking for the second one,” says D. Ross Camidge, MD, PhD, director of the lung cancer clinical program at the University of Colorado Hospital.

Doctors, for instance, have found that Alimta is a successful follow-up drug if patients did not receive it prior to crizotinib.

EGFR

Meanwhile, on a parallel path, other CU researchers have been hunting a different form of lung cancer, this one with the EGFR mutation.

Last fall, CU researchers reported that they had successfully developed a biomarker test that helped substantially reduce death rates in EGFR-positive patients. The test identified patients that would benefit from a combination of chemotherapy and the drug cetuximab. When patients with an over expression of EGFR are given the combination treatment, they experienced a 36 percent reduction in death.

CU also is one of just four hospitals in the United States now conducting a clinical trial on a combination of drugs to treat lung cancer patients with the EGFR mutation whose cancer has become resistant to the first line therapy drug Tarceva. The two drugs being tested in combination are Afatinib and Cetuximab.

“It’s the combination which seems magical here,” Camidge says.

Meanwhile, in the lab, CU researchers this year identified the

Lung/Head and Neck Cancer Program at the University of Colorado Hospital

- *Lung Cancer Specialized Program of Research Excellence [SPORE] grant: One of initial three centers to receive this grant, CU has received it continuously since 1992 and is now one of just seven cancer centers nationally*
- *One of largest trial accrualers in the National Lung Screening Trial, which demonstrated CT scans can reduce lung cancer death by 20 percent in high-risk subjects*
- *CU’s Colorado Molecular Correlates Laboratory is one of 14 labs nationally testing 1,000 lung cancer patients for 10 known genetic mutations as part of the Lung Cancer Mutation Consortium*

Get a more in-depth look at the program with this editorial by York Miller, MD, co-leader.

next pathway that the cancer is likely to use when the EGFR mutation is shut down—a pathway that depends on the sister protein fibroblast growth factor receptor.

“We know that patients treated with EGFR inhibitors invariably relapse,” says CU researcher Lynn Heasley, PhD, who is leading the work into FGFR. “We’ve now shown that when lung cancers respond to EGFR inhibitors, FGFR becomes induced and active.”

continued...

As the research team works to develop an effective FGFR inhibitor, it will use a revolutionary approach available at the university to screen these agents against the entire human genome to identify the new pathways that will be activated as a result. This will allow them to almost

simultaneously develop therapies to target those next pathways.

Heasley's team has been studying the role of FGFRs for the past five years. Two years ago, it reported that FGFRs were the dominant proteins driving some types of lung cancer.

This new work shows that FGFRs can also “rise up” in response to drugs that shut down other oncoproteins, such as the mutated EGFR, to help the cancer survive.

Translational RESEARCH SPEEDS drug development

The University of Colorado Cancer Center Developmental Therapeutics Program has three aims: to discover new agents and test them in preclinical models; to bring those agents to patients through Phase I Clinical Trials; and to bring them to the greater population—and ultimately to the market—through Phase II and III Clinical Trials.

Recent successes include:

- **Bench to Bedside:** Gail Eckhardt, MD, division chief of medical oncology at the University of Colorado School of Medicine and co-director of the developmental therapeutics program, had a drug in the lab and in the clinic that was known to inhibit a gene called IGFR-1. Working with other CU researchers and bioinformatics specialists, the team found a biomarker that can determine which patients will get the most benefit from the drug. Stephen Leong, MD, a clinical drug developer at CU wrote a clinical trial for this drug using this biomarker that is now enrolling patients.
- **And back to bench:** CU's nationally acclaimed translational research program quickly moves drugs from the lab to the clinic, but it also allows movement in reverse—a critical feature in today's war on cancer

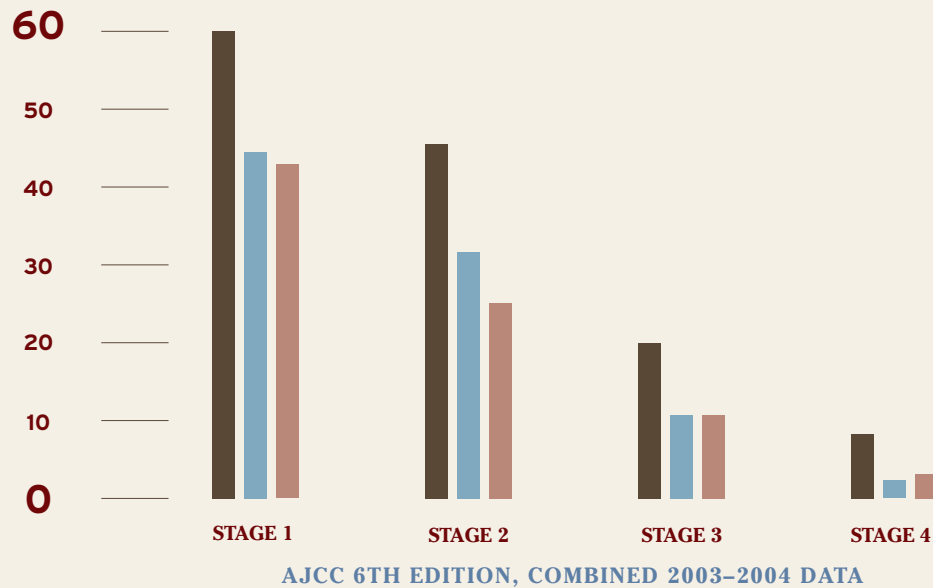
since so many drugs work on very small subsets of a particular cancer. A recent example of this model occurred in the case of lung cancer with the ALK translocation. Ross Camidge, MD, PhD, a member of the CU Lung/Head and Neck Cancer Program, was in clinical trials testing the drug crizotinib against the MET genetic mutation when he noticed that a certain subset of patients were responding better than others. He turned to a team of CU researchers who were able to develop a test and find that these patients had the ALK-fusion mutation.

- **Move to market:** The CU Cancer Center plays a leading role in clinical trials to help take new drugs to market quickly. One of the best examples is GlobelImmune, a company formed by UCCC members Don Bellgrau, PhD, and Rick Duke, PhD. They discovered a vaccine for Hepatitis C—the main cause of liver cancer—which was worked out in preclinical studies at CU Cancer Center and has since moved into clinical trials.

This brief summarizes a recent editorial by Wells Messersmith, MD, co-leader of the University of Colorado Cancer Center Developmental Therapeutics Program.

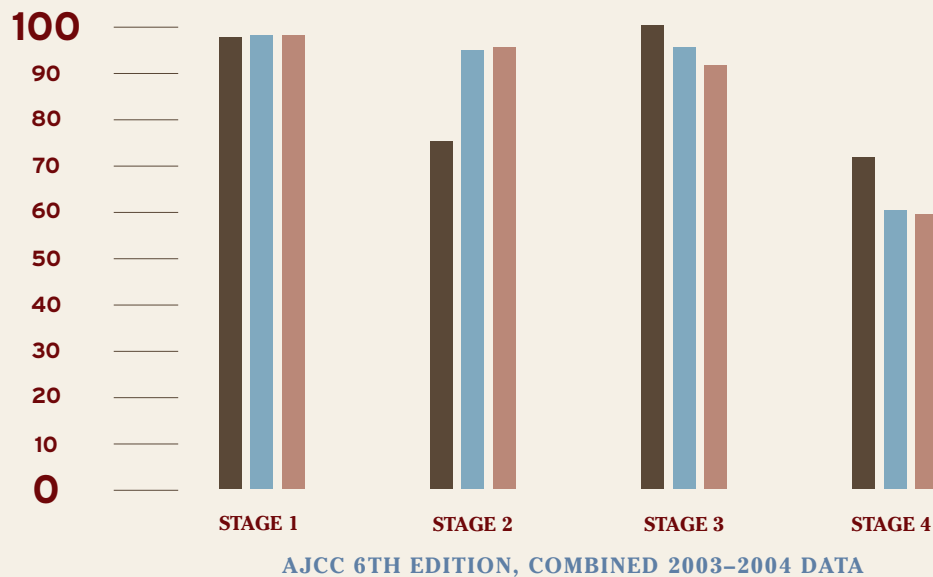
OUTCOMES data

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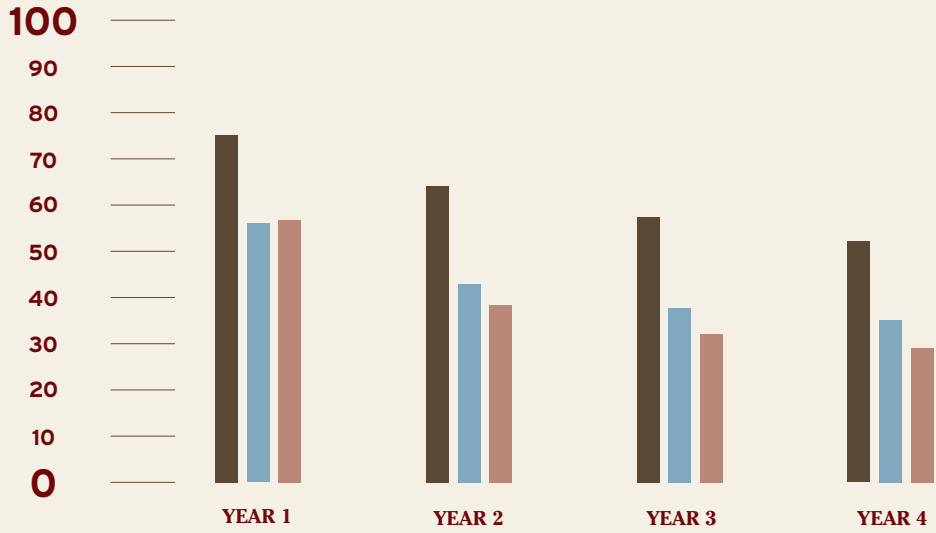


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THYROID CANCER 5-YEAR SURVIVAL



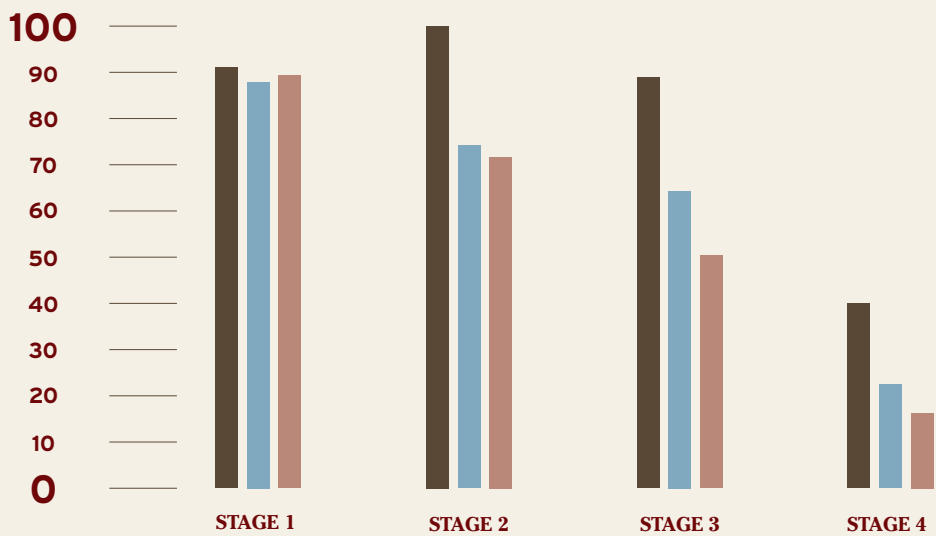
CENTRAL NERVOUS SYSTEM CANCER
5-YEAR SURVIVAL



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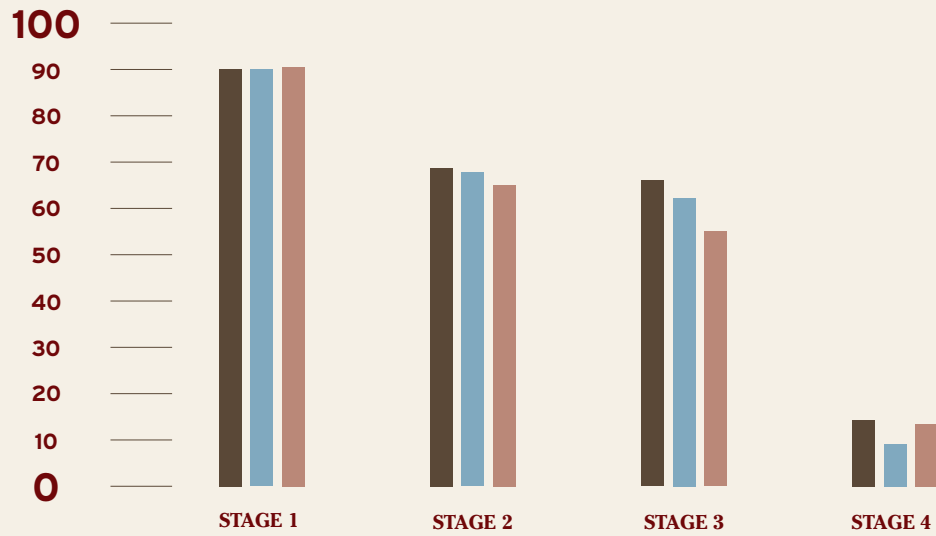
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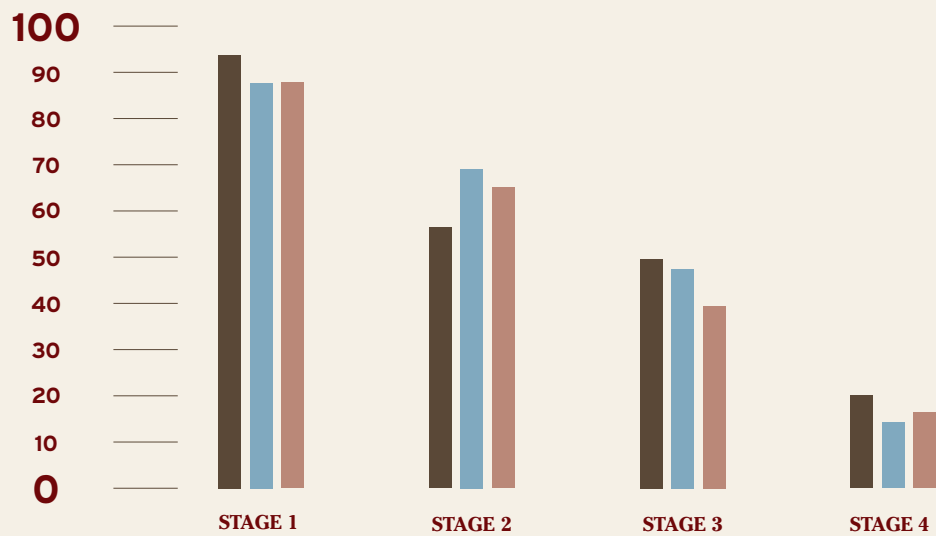
BREAST CANCER 5-YEAR SURVIVAL



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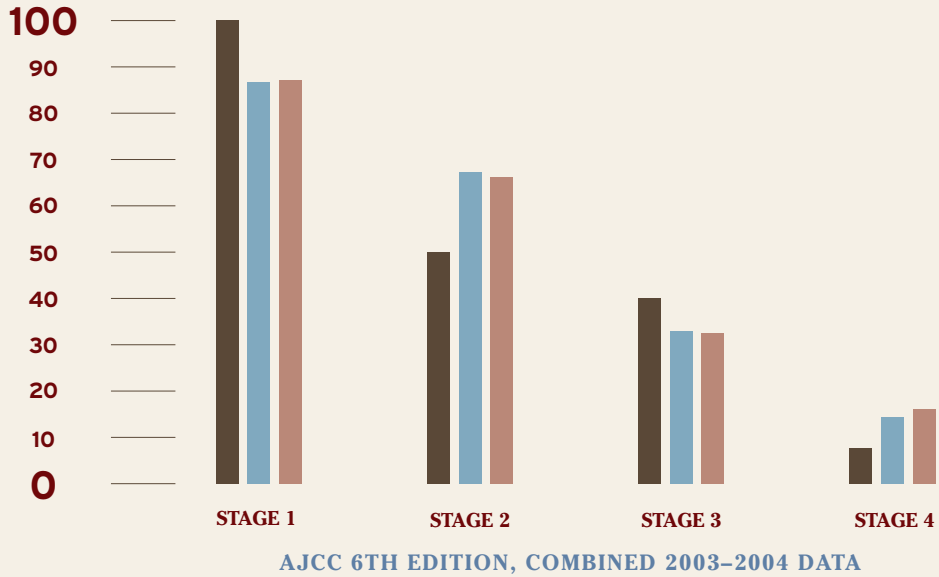
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FEMALE GENITAL SYSTEM 5-YEAR SURVIVAL



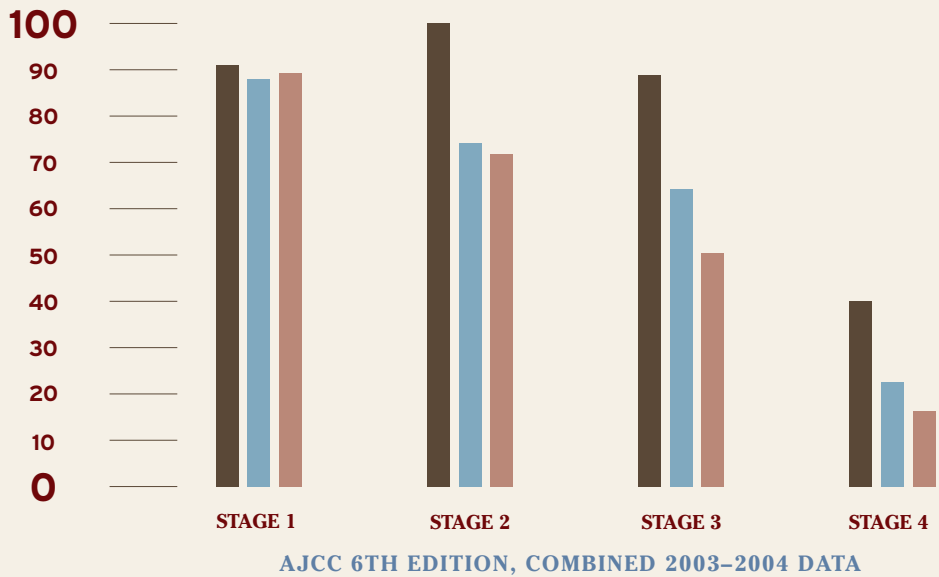
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OVARIAN CANCER
5-YEAR SURVIVAL



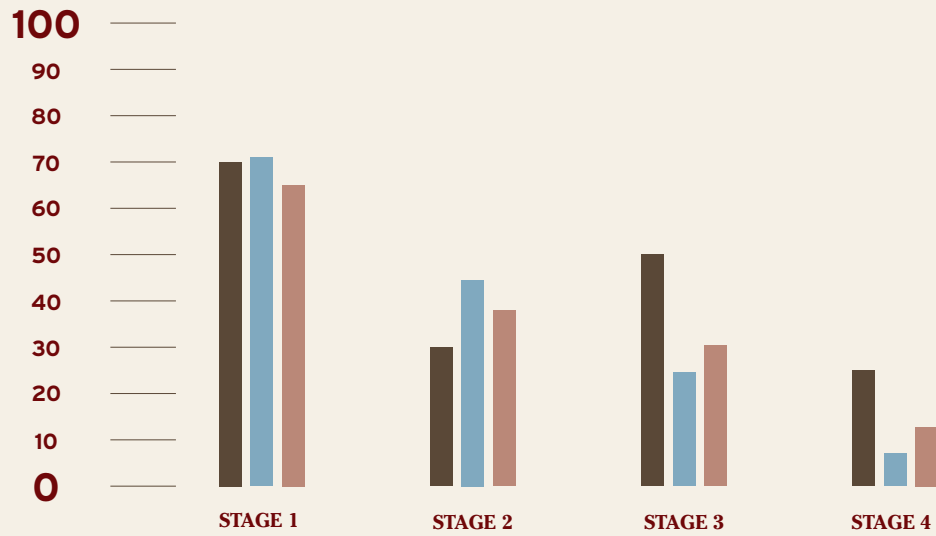
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CORPUS UTERI
5-YEAR SURVIVAL



OUTCOMES data

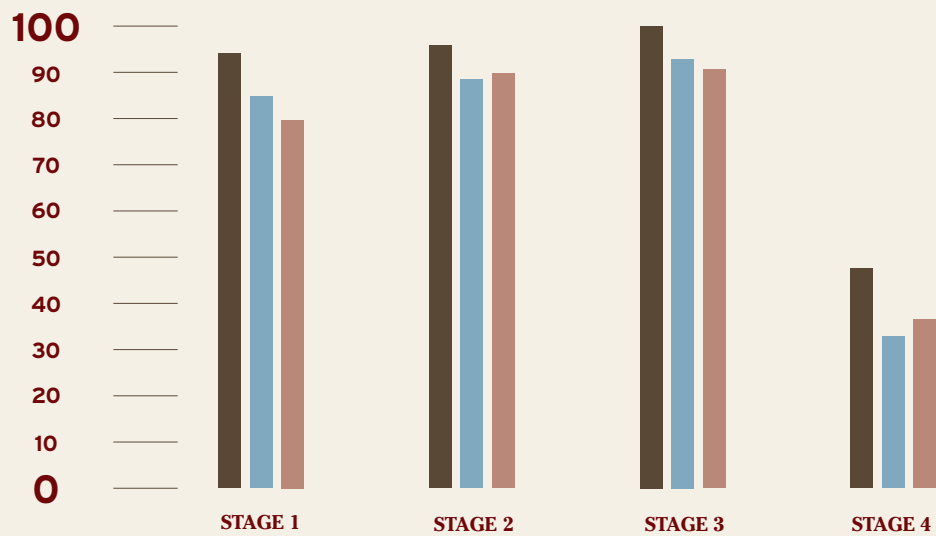
BLADDER CANCER 5-YEAR SURVIVAL



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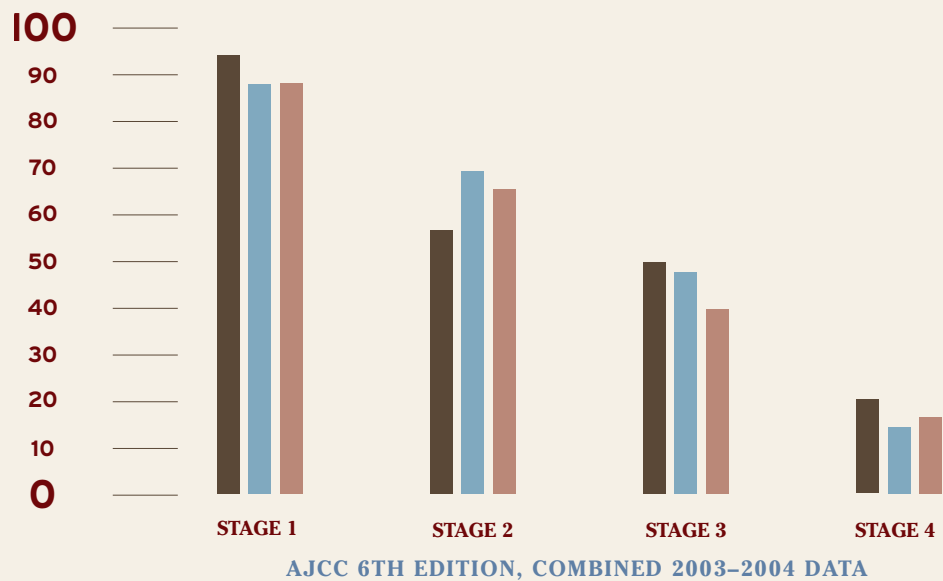
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PROSTATE CANCER 5-YEAR SURVIVAL



AJCC 6TH EDITION, COMBINED 2003-2004 DATA

COLORECTAL CARCINOMA
5-YEAR SURVIVAL



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COLORADO'S only FEDERALLY DESIGNATED CANCER CENTER tackles CANCER problem from all angles

The University of Colorado Cancer Center is the hub of cancer research in Colorado. We are a consortium of more than 400 researchers and physicians at three state universities and six institutions, all working toward one goal: translating science into cancer survivorship.

Through collaboration and innovation, UCCC members discover, develop and deliver breakthroughs that improve cancer care for people and companion animals. We focus on:

Personalized care that embraces the best clinical practices of prevention, diagnosis, treatment and survivorship.

- Innovative interdisciplinary research.
- Premier clinical and scientific training.
- Creative partnerships.

Founded in 1988, UCCC is the only comprehensive cancer center designated by the National Cancer Institute in Colorado and the Rocky Mountain region. Our founding director, Paul A. Bunn, Jr., MD, led the organization until 2009. In 2010, Dan Theodorescu, MD, PhD, ushered UCCC into a new era.

UCCC is headquartered on the Anschutz Medical Campus in Aurora, Colo., in the University of Colorado School of Medicine. Member institutions include University of Colorado Denver, University of Colorado at Boulder, Colorado State University, University of Colorado Hospital, The Children's Hospital, Denver VA, Denver Health, National Jewish Health and the Kaiser Permanente's Institute of Health Research. Our clinical outreach program extends through Colorado and neighboring states.

Highlights and Accomplishments

UCCC is known clinically for its robust and diverse Phase I clinical trials program and personalized cancer treatment. Our scientific expertise ranges from understanding how chromosome structure controls cancer cell behavior, to understanding how the immune system impacts cancer. Other strengths include:

Lung cancer care and research: UCCC is one of the world's best lung cancer research and treatment programs. We are the coordinating center for the Lung Cancer Mutations Consortium, funded by a \$5.3 million American Reinvestment and Recovery Act Grand Opportunities grant.

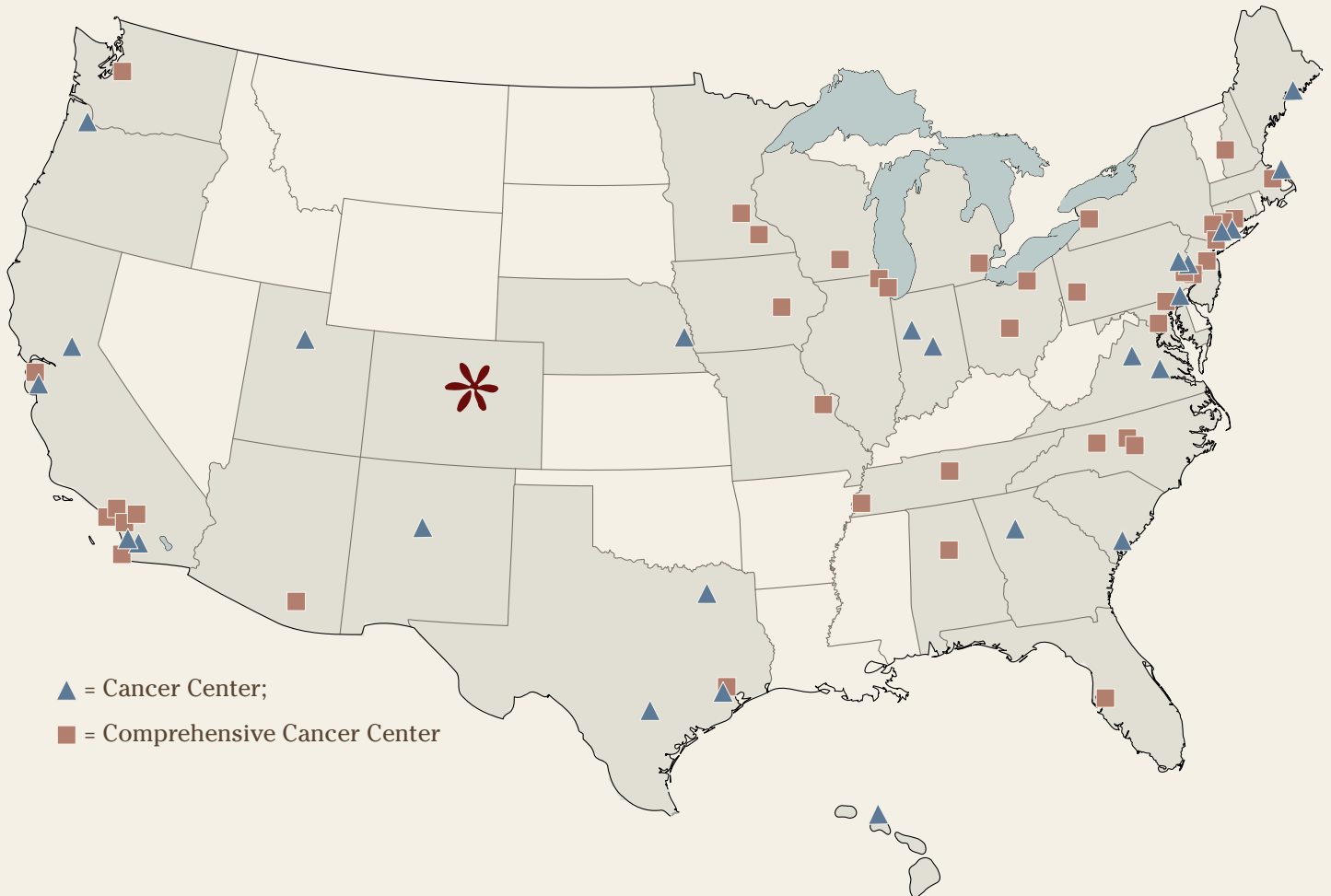
Cancer survivorship: one of 8 Lance Armstrong Foundation LIVESTRONG Survivorship Centers of Excellence, home to the region's three full-scale cancer survivorship clinics: The HOPE clinic for young adult survivors of cancer at The Children's Hospital, the TACTIC clinic for adult survivors of childhood cancer at University of Colorado Hospital, and the THRIVE clinic for transitioning adult cancer patients back to primary care.

Cancer Screening: The Colorado Colorectal Screening Program is a national model for ensuring uninsured Coloradoans who meet certain financial and risk criteria receive colon cancer screening and follow-up care at no cost to them.

Molecular tumor testing. UCCC has developed tests that find specific gene defects that can be targeted with new drugs and, positioned UCCC as a national leader for clinical trials of "targeted" drugs.

continued...

CANCER CENTERS *in the USA*



Tumor Explants. UCCC is on the cutting edge of personalized cancer treatment, developing laboratory methods to test cancer therapy by explanting living cancers from patients into a special breed of mice. The mice receive different treatments to identify the drug combination that the patient's tumor will best respond to.

Cancer Clinical Trials. With the largest human and companion animal cancer clinical trials programs in the region, UCCC provides patients across the state and region with access to cutting-edge cancer care UCCC's Phase I Trials program is the only program of its kind in the region.

Structural Biology. UCCC's NMR spectroscopy and X-Ray facilities are among the best in the world and have helped

recruit world-class scientists to use them. The machines, housed in UCCC's Structural Biology core, help scientists solve structures of cancer molecules to develop drugs with precise molecular targeting.

Animal Cancer Treatment and Clinical Trials. The Colorado State University Animal Cancer Center is the world leader in research and treatment of spontaneously occurring cancers in companion animals, especially dogs. UCCC's members at CSU collaborate with researchers in human cancers, and clinical trials in dogs have led to new treatments for people.

continued...

Stereotactic Body Radiation Therapy (SBRT). UCCC members Dr. Brian Kavanagh and Dr. Tracey Schefter led the development of SBRT, a highly precise, high dose radiation treatment that noninvasively targets tumors inside the liver and other organs.

Pregnancy-Associated Breast Cancer. Drs. Pepper Schedin and Ginger Borges are world experts on breast cancer that arises as a complication of pregnancy, which affects about 30,000 young women each year.

Learn more:

[*www.coloradocancercenter.org*](http://www.coloradocancercenter.org)

[*uch.edu*](http://uch.edu)

[*coloradocancerblogs.org*](http://coloradocancerblogs.org)

[*facebook.com/coloradocancercenter*](https://facebook.com/coloradocancercenter)



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UNIVERSITY OF COLORADO HOSPITAL is the Rocky Mountain region's *LEADING ACADEMIC MEDICAL CENTER*. It is recognized as the highest-performing academic hospital in the United States for delivering quality health care by the University HealthSystem Consortium, and is ranked as the best hospital in the Denver metro area and one of the best in the country by U.S. News & World Report. UCH is best known as an innovator in patient care and often as one of the first hospitals to bring new medicine to the patients' bedside. The hospital's physicians are affiliated with the University of Colorado School of Medicine, part of the University of Colorado system. Based on the expansive Anschutz Medical Campus in Aurora, CO, the hospital is where patient care, research and education converge to establish the future of health care delivery.

