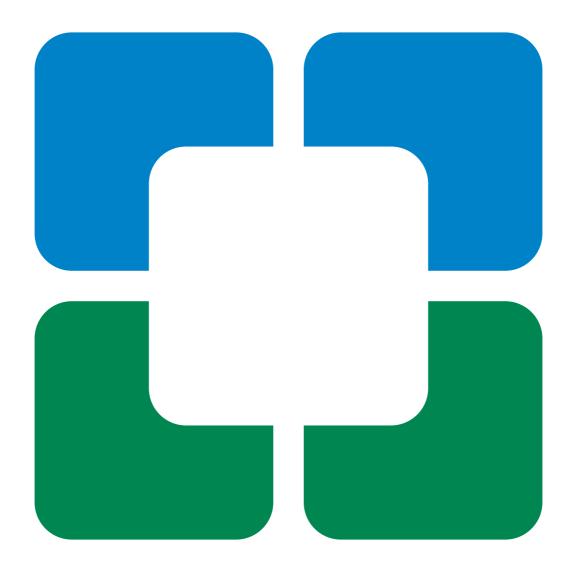
Taussig Cancer Institute









Measuring and understanding outcomes of medical treatments promotes quality improvement. Cleveland Clinic has created a series of Outcomes books similar to this one for its clinical institutes. Designed for a physician audience, the Outcomes books contain a summary of many of our surgical and medical treatments, with a focus on outcomes data and a review of new technologies and innovations.

The Outcomes books are not a comprehensive analysis of all treatments provided at Cleveland Clinic, and omission of a particular treatment does not necessarily mean we do not offer that treatment. When there are no recognized clinical outcome measures for a specific treatment, we may report process measures associated with improved outcomes. When process measures are unavailable, we may report volume measures; a relationship has been demonstrated between volume and improved outcomes for many treatments, particularly those involving surgical and procedural techniques.

In addition to these institute-based books of clinical outcomes, Cleveland Clinic supports transparent public reporting of healthcare quality data. The following reports are available to the public:

- Joint Commission Performance Measurement Initiative (qualitycheck.org)
- Centers for Medicare and Medicaid Services (CMS) Hospital Compare (medicare.gov/hospitalcompare), and Physician Compare (medicare.gov/PhysicianCompare)
- Cleveland Clinic Quality Performance Report (clevelandclinic.org/QPR)

Our commitment to transparent reporting of accurate, timely information about patient care reflects Cleveland Clinic's culture of continuous improvement and may help referring physicians make informed decisions.

We hope you find these data valuable, and we invite your feedback. Please send your comments and questions via email to:

OutcomesBooksFeedback@ccf.org.

To view all of our Outcomes books, please visit clevelandclinic.org/outcomes.



Dear Colleague:

Welcome to this 2016 Cleveland Clinic Outcomes book. Every year, we publish Outcomes books for 14 clinical institutes with multiple specialty services. These publications are unique in healthcare. Each one provides an overview of medical or surgical trends, innovations, and clinical data for a particular specialty over the past year. We are pleased to make this information available.

Cleveland Clinic uses data to manage outcomes across the full continuum of care. Our unique organizational structure contributes to our success. Patient services at Cleveland Clinic are delivered through institutes, and each institute is based on a single disease or organ system. Institutes combine medical and surgical services, along with research and education, under unified leadership. Institutes define quality benchmarks for their specialty services and report on longitudinal progress.

All Cleveland Clinic Outcomes books are available in print and online. Additional data are available through our online Quality Performance Reports (clevelandclinic.org/QPR). The site offers process measure, outcome measure, and patient experience data in advance of national and state public reporting sites.

Our practice of releasing annual Outcomes books has become increasingly relevant as healthcare transforms from a volume-based to a value-based system. We appreciate your interest and hope you find this information useful and informative.

Sincerely,

DMO

Delos M. Cosgrove, MD CEO and President

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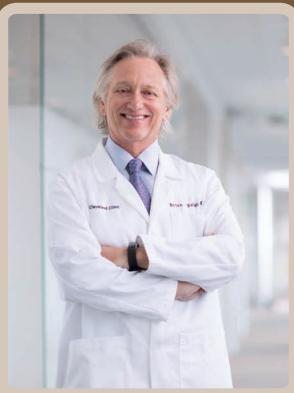
Chairman's Letter

Dear Colleagues,

Thank you for your interest in the annual outcomes data from the Taussig Cancer Institute. Our cancer center is home to more than 450 top cancer specialists, researchers, nurses, and technicians who are dedicated to delivering the right treatment at the right time, providing access to the latest research and clinical trials, and ensuring the highest-quality experience for our patients.

In early 2017, we began seeing patients in the new Cleveland Clinic Taussig Cancer Center building. Designed, built, and staffed with empathy at the forefront, the building brings together multidisciplinary cancer specialists, leading scientists, clinical support, and psychosocial services to deliver an exceptional patient experience. The new building reflects our vision of unified cancer care at Cleveland Clinic. That same vision and high standards apply at our 17 locations in northern and central Ohio, and Florida.

In the pages that follow, you will find examples of the clinical excellence, innovation, and patient-centered care we are proud to deliver. It is our patients who inspire us to provide the best care possible and work diligently toward our ultimate goal of beating cancer.



© Russell Lee Photography

We welcome your feedback, questions, and ideas for collaboration. Please contact me via email at OutcomesBookFeedback@ccf.org and reference the Taussig Cancer Institute book in your message.

Sincerely,

Brian J. Bolwell, MD, FACP

Chairman, Taussig Cancer Institute

Bia & Bowell mo

Professor, Cleveland Clinic Lerner College of Medicine

Institute Overview

Cleveland Clinic Taussig Cancer Institute is a multidisciplinary, comprehensive cancer center committed to providing patients with personalized care based on revolutionary research.

As the hub of cancer care at Cleveland Clinic, Taussig Cancer Center physicians and specialists collaborate to deliver coordinated care with other cancer specialists throughout Cleveland Clinic. The combined clinical experience and expertise of more than 450 top cancer specialists, researchers, nurses, and technicians ensures that each patient receives the best care, including:

- Accurate diagnosis and customized therapy
- Access to clinical trials of the newest drugs, and integration with translational research that brings discoveries in the laboratory to patient care
- Evidence-based disease management, including genetic and molecular pathology studies as indicated to inform treatment
- Support programs to promote physical and psychological well-being throughout treatment and into survivorship

Cleveland Clinic's multidisciplinary approach brings specialists together throughout northern Ohio and in Weston, FL, enabling collaboration and coordination among world-renowned surgical oncologists, plastic surgeons, gastroenterologists, interventional radiologists, pathologists, and genetic counselors. Multidisciplinary teams at the institute include clinicians who specialize in medical and radiation oncology, bone marrow transplantation, palliative care, oncology nursing, cancer research, and psychosocial support.

Taussig Cancer Institute offers patients and families a range of programs, along with survivorship services, to enhance quality of life and provide support as they cope with the challenges of cancer and its treatment.



Institute Overview

Therapies and Volumes

Provided below is an overview of the number of patients seen and the range of therapies available at Taussig Cancer Institute in 2016.

		Location					
		Hematology & Medical Oncology		Radiation Oncology		Cleveland Clinic Cancer Centers	
	Total	Main Campus	Regional	Main Campus	Regional	Sandusky	Mansfield
Total visits	381,152	91,180	132,882	52,810	48,087	33,561	22,632
Professional visits Main campus (%) Regional (%)	200,999 105,086 (52) 95,913 (48)	96,225	65,012	8861	4236	16,579	10,086
New outpatient visits/consults	20,124	7667	5692	3168	1821	1161	705
Outpatient visits	148,383	58,046	52,969 ^a	8370	4025 ^a	15,764	9209
Inpatient visits	52,616	38,179	12,043 ^a	491	211 ^a	815	877
Inpatient admissions	6949	3978	2274	282	122	259	34
Treatment visits Main campus (%) Regional (%)	183,386 59,876 (33) 123,510 (67)	29,420	65,497 ^b	30,456	33,323 ^b	15,456	9234
Chemotherapy treatment visits Main campus (%) Regional (%)	106,150 29,420 (28) 76,730 (72)	29,420	65,497 ^b	_	_	6420	4813
Radiation therapy treatment visits Main campus (%) Regional (%)	77,236 30,456 (39) 46,780 (61)	-	-	30,456	33,323 ^b	9036	4421

^aIncludes Cleveland Clinic regional hospitals

Total visits represent all outpatient visits with a clinical provider or resource; professional visits are for evaluation and management; inpatient admissions represent patients discharged at main campus by institute physician staff. Patients were seen by Taussig Cancer Institute staff at main campus, family health/cancer centers, and during professional visits at Cleveland Clinic regional hospitals unless otherwise noted.

^bIncludes treatment (chemotherapy and radiation) volumes at Cleveland Clinic regional hospitals

Outpatient and Inpatient Visits by Disease Group or Site (N = 202,664) 2016

Disease/Site	Number of Visits
Benign hematology	21,648
Breast	30,001
Central nervous system	5088
Endocrine	1171
Gastrointestinal	27,856
Genitourinary	17,045
Gynecological	2832
Head and neck	6676
Leukemia/MDS	24,610
Lung	19,134
Lymphoma	17,738
Melanoma	3615
Myeloma	13,431
Sarcoma	6591
All others	5228

MDS = myelodysplastic syndromes

Patients seen by Taussig Cancer Institute staff at main campus, family health centers/cancer centers, and during professional visits at Cleveland Clinic regional hospitals.

Radiation Oncology Treatment Procedures (N = 1721)

2016

Procedure Type	N (%)
Gamma Knife [®]	610 (35)
High-dose-rate brachytherapy	216 (13)
Low-dose-rate brachytherapy	270 (16)
Eye plaques	63 (4)
Hyperthermia	75 (4)
Stereotactic body radiosurgery (total)	487 (28)
Lung	232
Spine	150
Liver	67
Other	38
Total	1721

In 2016,
4274 patients
participated in 407
cancer-related clinical
trials conducted at
Cleveland Clinic,
including 516 patients
who participated in
84 clinical trials at
community locations.

National Cancer Institute (NCI)-Designated Cancer Center

Cleveland Clinic is a member of the Case Comprehensive Cancer Center (Case CCC), an NCI-designated partnership organization supporting all cancer-related research efforts at Case Western Reserve University, University Hospitals Case Medical Center, and Cleveland Clinic.

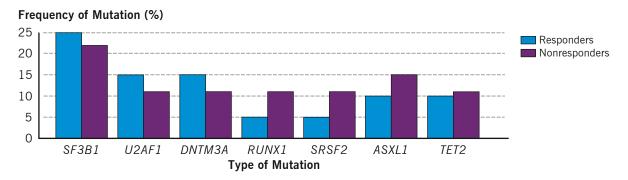
American College of Surgeons (ACoS) Commission on Cancer (CoC) — Cleveland Clinic's cancer program is CoC-accredited with commendation in all 4 areas possible for an NCI-designated cancer center.

Cleveland Clinic's Leukemia and Myeloid Disorders Program is one of the largest and best respected in the world. A multidisciplinary team of leukemia specialists, pharmacists, nurses, advanced practice providers, and research professionals in Cleveland Clinic Cancer Center explore all options and tailor the most appropriate treatment plan for each patient — offering the greatest chance of curing the condition and enabling patients to live long and healthy lives.

Using Molecular Mutation Informatics to Optimize Predictive Algorithms for Response to Erythropoietic Stimulating Agents in Patients With Low-Risk Myelodysplastic Syndromes

Erythropoietic stimulating agents (ESAs) are the initial therapy for many patients with low-risk myelodysplastic syndromes (LR-MDS) and can predictably benefit patients with low transfusion burden and a low erythropoietin (EPO) level. However, only about 40% to 50% of patients respond to ESAs. To better understand the impact of EPO stimulation/treatment on the clonal dynamics of LR-MDS and improve the prognostic model, Taussig Cancer Institute researchers analyzed DNA from the marrow or peripheral blood samples of LR-MDS patients using a targeted multiamplicon deep next-generation sequencing panel of all open reading frames of the top 60 most commonly mutated genes in myeloid malignancies.

Frequency of Mutations and ESA Responsiveness in Patients With Low-Risk Myelodysplastic Syndromes (N = 50) 2002 - 2016



Analysis of molecular profiles of LR-MDS patients identifies mutations possibly associated with ESA failure. Certain mutations, such as *ASXL1*, *RUNX1*, and *ETV6*, may be more indicative of high risk disease due to the lack of response to ESA therapy and require alternative therapy.

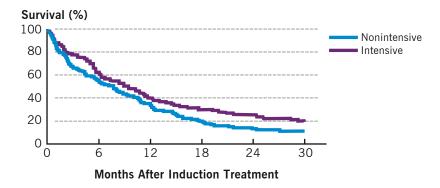
Reference

¹Hellström-Lindberg E, van de Loosdrecht A. Erythropoiesis stimulating agents and other growth factors in low-risk MDS. *Best Pract Res Clin Haematol*. 2013 Dec;26(4):401-410.

Intensive vs Non-Intensive Induction Therapy for Patients With Newly Diagnosed Acute Myeloid Leukemia (AML) Using 2 Different Novel Prognostic Models

Nonintensive therapies are increasingly used in patients older than 65 due to concerns about their ability to tolerate intensive chemotherapy. To better understand the relative benefit-risk ratios associated with intensive vs nonintensive therapies, researchers from Cleveland Clinic's Leukemia and Myeloid Disorders Program, along with colleagues from several other institutions, analyzed data from 1295 patients with newly diagnosed acute myeloid leukemia.

Survival of Patients With Newly Diagnosed Acute Myeloid Leukemia, Aged 70–79 Years, Receiving Intensive vs Nonintensive Induction Therapy (N = 242)



Patients treated with intensive therapy in this age range had higher survival rates at 2 years, suggesting that intensive therapy could be considered for most patients, up to 80 years of age.

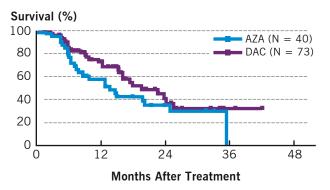
Taussig Cancer Institute

9

A Randomized Phase 2 Study of Low-Dose Decitabine vs Azacitidine in Patients With Low- or Intermediate-1-Risk Myelodysplastic Syndromes

The outcome of patients with LR-MDS is heterogeneous, with some patients having a particularly poor prognosis. We evaluated the relative safety and efficacy of low-dose decitabine (DAC) and azacitidine (AZA) in patients with LR-MDS.

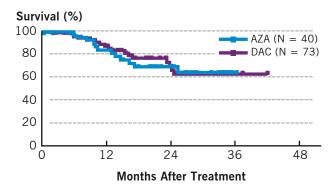
Event-Free Survival in Patients With Low- or Intermediate-1-Risk Myelodysplastic Syndromes Treated With Low-Dose Decitabine vs Azacitidine (N = 113) 2012 – 2016



AZA = azacitidine, DAC = decitabine

Overall Survival in Patients With Low- or Intermediate-1-Risk Myelodysplastic Syndromes Treated With Low-Dose Decitabine vs Azacitidine (N=113)

2012 - 2016



AZA = azacitidine, DAC = decitabine

While both treatments are effective and well-tolerated in patients with lower-risk MDS, early results indicate that low-dose DAC may result in superior event-free survival compared with low-dose AZA. A randomized trial comparing low-dose AZA, low-dose DAC, a 5-day course of AZA treatment, and the best supportive care in LR-MDS is ongoing.

Novel Geno-Clinical Model Uses Machine Intelligence to Predict Hypomethylating Agent Response/Resistance in Patients With Myelodysplastic Syndromes

While treatment with hypomethylating agents (HMAs) improves cytopenia and prolongs survival in patients with MDS, only 30% to 40% of patients respond to this treatment. The ability to predict which patients are more likely to respond to HMAs could prevent prolonged exposure to ineffective therapy, avoid toxicities, and decrease unnecessary treatment costs. To enhance the efficacy of a proposed geno-clinical model that uses machine learning algorithms to predict responses to HMAs, 5 popular algorithms were used individually and in combination to analyze the HMA responsiveness of a multiinstitutional cohort of patients with MDS.

Accuracy in Predicting Hypomethylating Agent Response in Patients With Myelodysplastic Syndromes (N = 443)



DT = decision tree, HR = high risk, NB = naive Bayes, RF = random forest, SVM = support vector machine, TE = tree ensemble

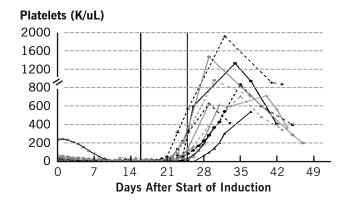
When applying machine learning algorithms to random samples from the cohort, the accuracy in predicting HMA responses was 62% to 66%. However, when the results of each model were combined in a "bag of models" approach, predictive accuracy increased to 69%. When the analysis was limited to patients with high-risk disease, the predictive accuracy increased to 60% to 76%.

Single Arm, Phase 2 Study of Eltrombopag to Enhance Platelet Count Recovery in Older Patients With Acute Myeloid Leukemia Undergoing Remission Induction Therapy

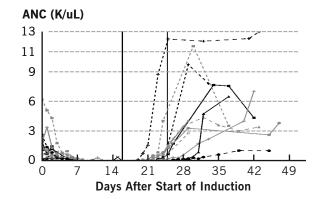
In patients with acute myeloid leukemia (AML) undergoing 7+3 induction chemotherapy (IC), incomplete platelet recovery can lead to increased risks of adverse effects. This phase 2 study evaluates the efficacy of eltrombopag, a thrombopoietin receptor agonist, in accelerating platelet count recovery in patients with AML who are at least 60 years old and receiving IC. Trends in levels of hemoglobin, absolute neutrophil count, and platelet count over time, along with median eltrombopag start and stop times, are shown in the following figures.

Platelet Count Over Time From Start of Eltrombopag in Older Patients With Acute Myeloid Leukemia Undergoing Remission Induction Therapy (N = 13)

2014 - 2016



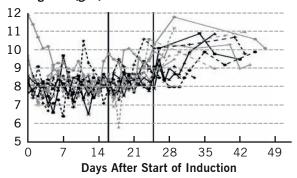
Absolute Neutrophil Count Over Time From Start of Eltrombopag in Older Patients with Acute Myeloid Leukemia Undergoing Remission Induction Therapy (N = 13) 2014 - 2016



ANC = absolute neutrophil count

Hemoglobin Level Count Over Time From Start of Eltrombopag in Older Patients With Acute Myeloid Leukemia Undergoing Remission Induction Therapy (N = 13) 2014 - 2016

Hemoglobin (g/dl)



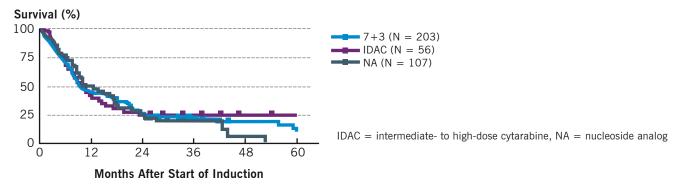
This analysis suggests that eltrombopag can hasten platelet recovery, potentially reduce platelet transfusions, and increase complete remission rates in older AML patients undergoing IC without any limiting toxicities. The study is currently accruing patients.

Impact of Salvage Induction Chemotherapy Regimens in Higher-Risk Myelodysplastic Syndromes and Acute Myeloid Leukemia After Hypomethylating Agent Treatment Failure

Prognosis is poor for patients with higher-risk MDS and AML following the failure of hypomethylating agents. Second-line intensive chemotherapy (IC) can reduce disease burden and serve as a bridge to allogeneic stem cell transplantation; however, there is no standardized induction regimen.

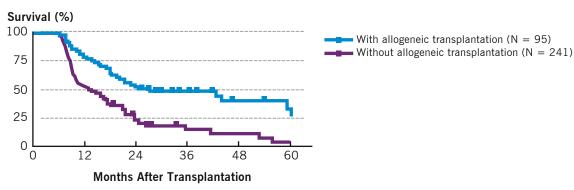
Impact of Induction Chemotherapy Regimens on Overall Survival of Patients With Myelodysplastic Syndromes and Acute Myeloid Leukemia Following Hypomethylating Agent Failure (N=366)

2005 - 2015



Comparison of the 3 IC regimens reveals that no one strategy is superior in terms of outcomes or toxicity. IC post-HMA is a valid treatment option, with rates of response and transplantation exceeding that of other treatment modalities.

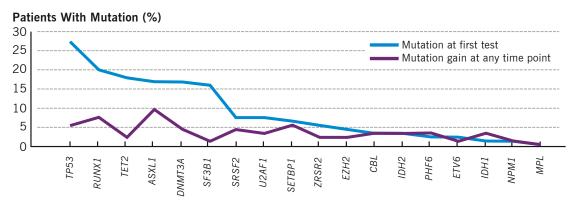
Impact of Allogeneic Transplantation After HMA Failure on Overall Survival of Patients With MDS or AML (N = 95) 2005 - 2015



Serial Monitoring of Myeloid Mutations Found Clinically Relevant in Patients With Myelodysplastic Syndromes

Taussig Cancer Institute is 1 of 5 institutions in the Myelodysplastic Syndromes Clinical Research Consortium, the first privately funded MDS research consortium in the United States. In 2016, the consortium presented the results of its analysis of the impact of serial mutation monitoring of myeloid mutations in patients with MDS.

Serial Mutation Profiling in Patients With Myelodysplastic Syndromes (N = 94) 1994 – 2016



Type of Mutation

Independent of age or prognostic score at baseline, a higher number of mutations present at diagnosis was associated with poor overall survival. The acquisition of additional mutations in any gene was associated with worse overall survival. Serial mutation profiling identified a small number of patients who had acquired "actionable" mutations for which clinical trials were potentially available, but did not substantively alter treatment choices.

A small number of patients who underwent allogeneic stem cell transplantation, offered at Cleveland Clinic, lost the diagnostic mutations at the time of transplant.

Through 2016,
Cleveland Clinic's
Blood & Marrow
Transplant Program
had performed
1231 allogeneic
transplants.

40

Cleveland
Clinic's Blood
and Marrow
Transplant
Program
celebrates
40 years of
providing
blood and
marrow
transplants.

The mission of the Blood and Marrow Transplant (BMT) program in the Taussig Cancer Institute is to provide high-quality, specialized patient care that emphasizes innovation, collaboration, research, and empathy. The leading edge 22-bed BMT floor features elements specifically designed for an immune-compromised patient population, including a centralized air-handling system, dedicated facilities for caregivers, and amenities to ease the burden of a 3- to 6-week average hospital stay. Cleveland Clinic's BMT program is accredited by the Foundation for the Accreditation of Cellular Therapy, and maintains associations with the National Marrow Donor Program, the Blood and Marrow Transplant Clinical Trials Network, the Chronic Graft vs Host Disease Consortium, the Radiation Injury Treatment Network, the SWOG, and the Center for International Blood and Marrow Transplant Research[®].

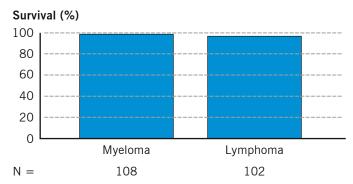
In the 2016 Transplant Center-Specific Survival Report, a publicly reported outcomes analysis by the Center for International Blood and Marrow Transplant Research¹ for all centers in the United States that perform allogeneic hematopoietic cell transplantation (HCT), Cleveland Clinic's 1-year actual survival probability was 64.5% and was within the predicted survival probability for the program (69.0%, 95% confidence interval, 63.4-75.2).

Reference

¹D'Souza A, Zhu X. Current Uses and Outcomes of Hematopoietic Cell Transplantation (HCT): CIBMTR Summary Slides, 2016. Available at: http://www.cibmtr.org. Accessed April 4, 2017.

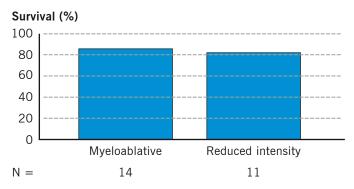
Survival 100 Days After Autologous Hematopoietic Cell Transplantation for Patients With Myeloma and Lymphoma

2015 - 2016



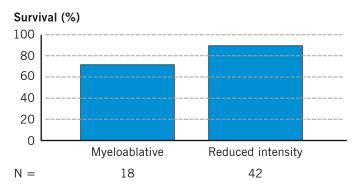
Cleveland Clinic's 100-day survival outcomes of 99% for patients with myeloma and 97% for patients with lymphoma are similar to national benchmarks.

Survival 100 Days After Allogeneic Hematopoietic Cell Transplantation Using Related Donor for Patients With Acute/Chronic Leukemia and Myelodysplastic Syndromes 2015 – 2016



Cleveland Clinic's 100-day survival outcomes of 86% for patients receiving myeloablative conditioning and 82% for patients receiving reduced intensity conditioning for related donor allogeneic HCT for acute/chronic leukemia and myelodysplastic syndromes are similar to national benchmarks.

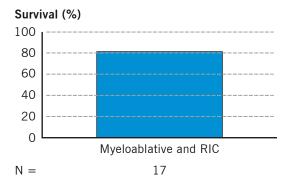
Survival 100 Days After Allogeneic Hematopoietic Cell Transplantation Using Unrelated Donor for Patients With Acute/Chronic Leukemia and Myelodysplastic Syndromes 2015 – 2016



Cleveland Clinic's 100-day survival outcomes of 72% for patients receiving myeloablative conditioning and 90% for patients receiving reduced intensity conditioning for unrelated donor allogeneic HCT for acute/chronic leukemia and myelodysplastic syndromes are similar to national benchmarks.

Survival 100 Days After Allogeneic Hematopoietic Cell Transplantation Using Haploidentical Donor for Patients With Acute/Chronic Leukemia and Myelodysplastic Syndromes

2015 - 2016

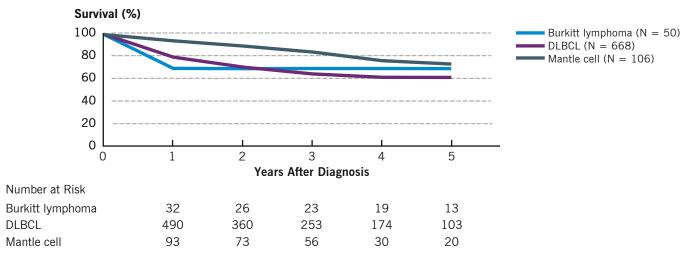


RIC = reduced intensity conditioning

Cleveland Clinic's 100-day survival outcome of 82% for patients receiving myeloablative conditioning or reduced intensity conditioning for haploidentical donor allogeneic HCT for acute/chronic leukemia and myelodysplastic syndromes is similar to the national benchmark.

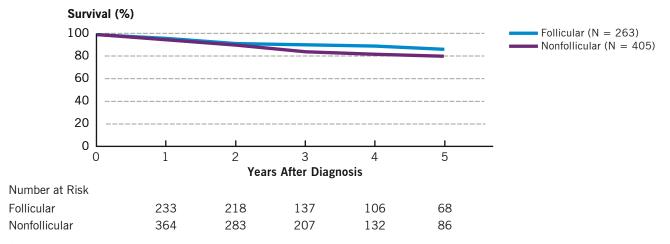
As part of Taussig Cancer Institute's mission to improve patient outcomes, lymphoma program staff constantly update and review standard-of-care treatments, participate in clinical trials of new treatment strategies, and work closely with the bone marrow transplant program. The results of this carefully coordinated approach are reflected in the outcomes shown in the survival curves below.

Five-Year Overall Survival of Patients With Aggressive Non-Hodgkin Lymphoma by Disease Type (N = 824) 2007 - 2015



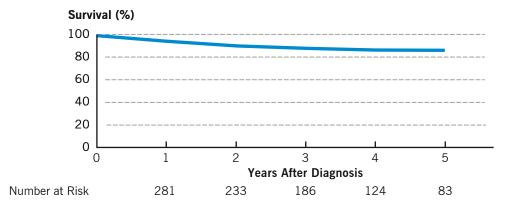
DLBCL = diffuse large B-cell lymphoma

Five-Year Overall Survival of Patients With Follicular vs Other Types of Indolent Lymphoma^a (N = 668) 2007 - 2015

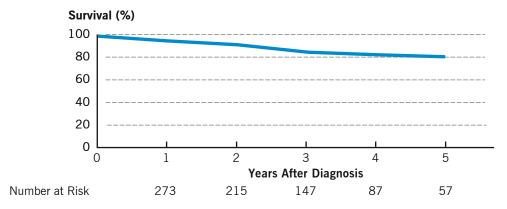


^aIncludes small cell lymphocytic lymphoma, Waldenstrom macroglobulinemia, and lymphoplasmacytic lymphoma

Five-Year Overall Survival of Patients With Hodgkin Lymphoma (N = 323) 2007 - 2015



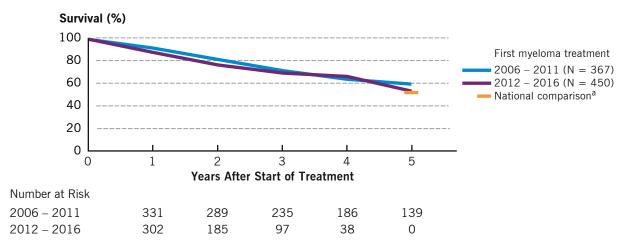
Five-Year Overall Survival of Patients With Chronic Lymphocytic Leukemia a (N = 302) 2007 - 2015



^aB-cell chronic lymphocytic leukemia/small lymphocytic lymphoma

Outcomes for patients with multiple myeloma treated at Taussig Cancer Institute compare favorably with other reported outcomes. Life expectancy has not significantly changed since 2006, but there are too few patients in long-term follow-up for the cohort of patients who may derive benefit from recently approved drugs. Overall favorable data may reflect care by a specialized healthcare team, common use of maintenance therapy in myeloma, and access to novel therapies, including within the context of clinical trials.

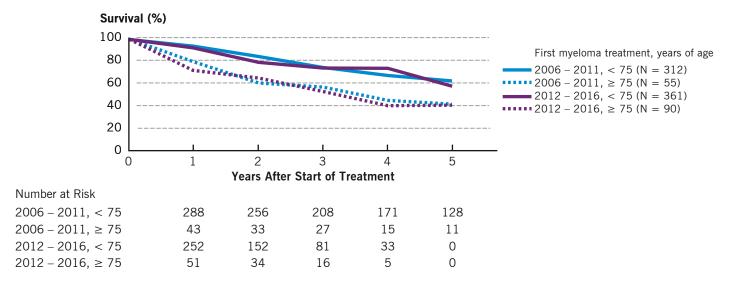
Five-Year Overall Survival of Patients With Multiple Myeloma After Start of Treatment (N = 817) 2006 - 2016



^a National comparison represents relative survival after diagnosis from Fast Stats: An interactive tool for access to Surveillance, Epidemiology, and End Results (SEER) cancer statistics. Surveillance Research Program, National Cancer Institute. http://seer.cancer.gov/statfacts/html/mulmy.html. Accessed March 3, 2017.

Based on SEER 18 data, patients with multiple myeloma diagnosed between 2006 and 2012 have a 5-year relative survival rate of 48.5% from time of diagnosis, meaning death from other causes is not counted in this number, whereas it is counted in our analysis.

Five-Year Overall Survival of Patients With Multiple Myeloma by Age at First Treatment (N = 818) 2006 - 2016



The improvement of outcomes for myeloma patients in recent years is still limited to patients < 75 years of age at the start of therapy who had 5-year survival estimates of around 60% compared to around 40% for patients age 75 or older at the start of myeloma therapy. Although these data are not adjusted for age-related life expectancy, lack of improvement in relative survival has been reported for this age group.¹

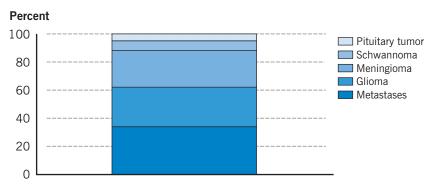
Reference

1. Sant M, Minicozzi P, Mounier M, et al. Survival for haematological malignancies in Europe between 1997 and 2008 by region and age: results of EUROCARE-5, a population-based study. *Lancet Oncol*. 2014 Aug;15(9):931-942.

The Rose Ella Burkhardt Brain Tumor and Neuro-Oncology Center (BBTC) of the Neurological Institute is one of the largest and most comprehensive programs in the country and is dedicated to providing exceptional patient care including surgery, radiation, chemotherapy, and clinical research trials for brain tumor patients. Patient care is provided by a multidisciplinary team consisting of neurosurgeons, radiation oncologists, neuro-oncologists, medical oncologists, psychiatrists, and neuropsychologists, along with nurses, physician assistants, case managers, and social workers who all specialize in treating patients with brain tumors. The BBTC is dedicated to bringing patients novel treatment options emerging from the institute's extensive basic and translational research programs. The primary mission is to offer excellent care through surgical intervention, as well as conducting clinical research to enhance patient outcomes. The BBTC enrolled 342 patients in therapeutic research trials in the past 5 years (2012–2016).

Brain Tumor Diagnosis Distribution (N = 2015)

2016

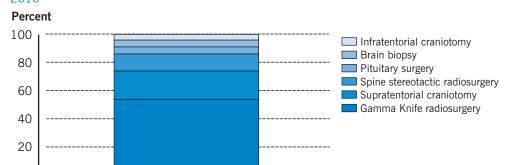


In 2016, gliomas remain the most common brain tumor for patients treated in the BBTC.

Brain Tumor Procedures (N = 1136)

2016

0



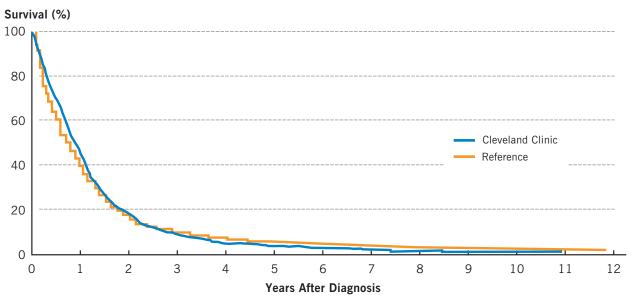
Gamma Knife[®] radiosurgery is the most common procedure performed, followed by supratentorial craniotomy and spine stereotactic radiosurgery.

Glioblastoma

In 2016, 76 patients with newly diagnosed glioblastoma, the most common type of malignant primary brain tumor, underwent initial surgical resection and treatment at Cleveland Clinic. Approximately 12,000 cases of glioblastoma are diagnosed each year in the United States.

Glioblastoma Treatment: Survival (N = 826)

2001 - 2012



Reference = Software: Surveillance Research Program, National Cancer Institute SEER*Stat software (seer.cancer.gov/seerstat) version 8.3.3. Data: Surveillance, Epidemiology, and End Results (SEER) Program (seer.cancer.gov) SEER*Stat Database: Incidence - SEER 18 Regs Research Data + Hurricane Katrina Impacted Louisiana Cases, Nov 2015 Sub (1973-2013 varying) - Linked To County Attributes - Total U.S., 1969-2014 Counties, National Cancer Institute, DCCPS, Surveillance Research Program, Surveillance Systems Branch, released April 2016, based on the November 2015 submission.

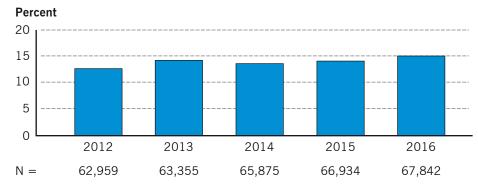
24

Cleveland Clinic's Breast Center is committed to providing patients with the best possible prevention, detection, and treatment options for breast disease. A multidisciplinary team comprising surgeons, medical oncologists, radiation oncologists, nurses, and social workers collaborates with each patient to develop a tailored care plan at 4 accredited breast centers throughout northeast Ohio.

Prevention and Screening

Percentage of Screening Mammograms Resulting in Callback

2012 - 2016



Cleveland Clinic offers a diagnostic callback program for patients with abnormal screening mammograms.

Victory in Pink

In partnership with local churches, Taussig Cancer Institute's Community Outreach department provides programs to increase breast health awareness and encourage women to get regular mammograms.

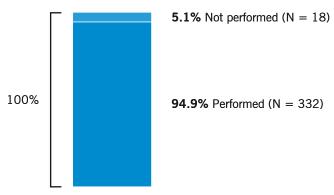
In 2016, 1500 women participated in these education sessions, and 357 women received mammograms.

¹Accreditation by the National Accreditation Program for Breast Centers (NAPBC), a program administered by the American College of Surgeons

Quality Measures

Needle Core or Fine Needle Aspirate Biopsy Prior to Surgical Treatment of Breast Cancer (N = 350)

2015

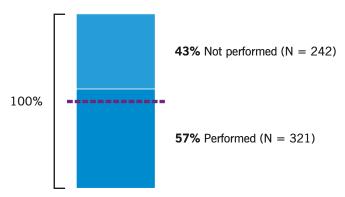


Cleveland Clinic's performance was 94.9% (332 of 350 patients) in 2015 for this Commission on Cancer standard of care quality measure (95% confidence interval [CI], 92.5-97.2). Cleveland Clinic performs within the acceptable range for biopsy prior to surgical treatment of breast cancer.

Source: Data from Cleveland Clinic tumor registry for main campus and family health center locations

26

Breast Conservation Surgery Rate for Women With Clinical Stage a 0, I, or II Breast Cancer (N = 563) 2015



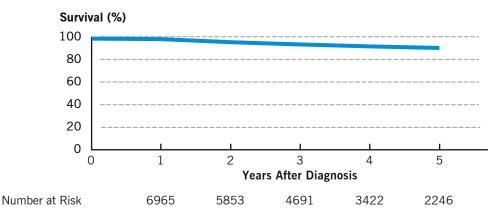
Source: Data from Cleveland Clinic tumor registry for main campus and family health center locations

Cleveland Clinic's performance was 57% (321 of 563 patients) in 2015 for this Commission on Cancer (CoC) standard of care quality surveillance measure (95% CI, 52.9-61.1). The CoC does not define a benchmark performance rate. The National Accreditation Program for Breast Centers standard is 50%. The rate at Cleveland Clinic reflects patient choice and referral bias of patients seeking surgery and reconstruction at Cleveland Clinic.

^aAmerican Joint Committee on Cancer (AJCC) stage I-IV breast cancer

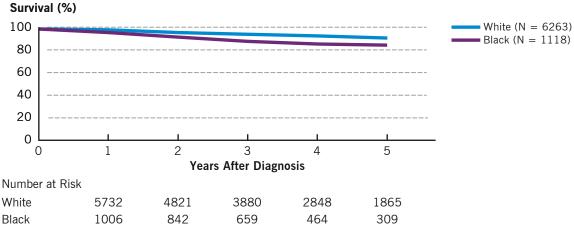
Treatment

Five-Year Overall Survival of Female Patients With All Stages a of Breast Cancer (N = 7632) 2007 - 2015



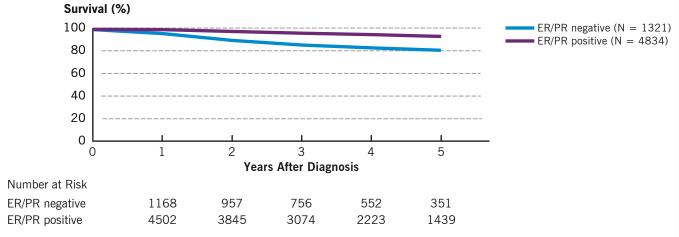
^aAJCC stage I–IV breast cancer

Five-Year Overall Survival of Female Patients With Breast Cancer by Race^a (N = 7381) 2007 - 2015



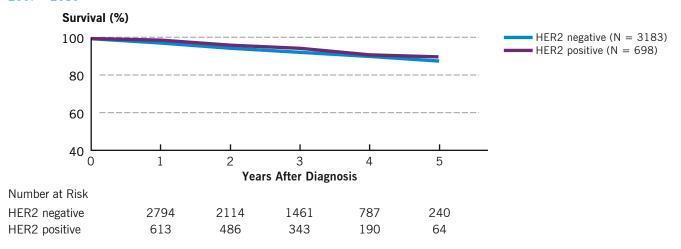
^aSelf-reported

Five-Year Overall Survival of Female Patients With Breast Cancer by Hormone Receptor Status (N = 6155) 2007 - 2015



ER = estrogen receptor, PR = progesterone receptor

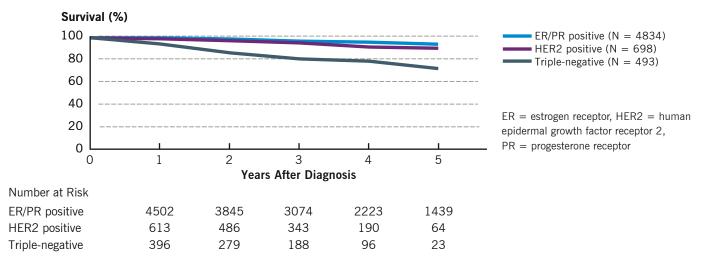
Five-Year Overall Survival of Female Patients With Breast Cancer by HER2 Status (N = 3881) 2007 - 2015



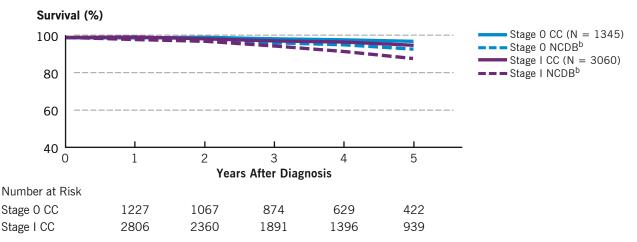
HER2 = human epidermal growth factor receptor 2

Five-Year Overall Survival of Female Patients With Breast Cancer by Estrogen Receptor, Progesterone Receptor, and HER2 Status (N = 6025)

2007 - 2015



Five-Year Overall Survival of Female Patients With Stage^a 0 and I Breast Cancer (N = 4405) 2007 - 2015



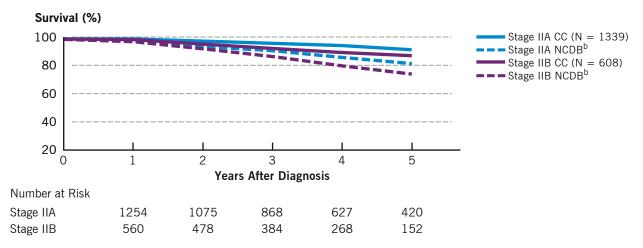
CC = Cleveland Clinic, NCDB = National Cancer Database

30

^aAJCC stage I–IV breast cancer

^bReference group data from the National Cancer Database (Commission on Cancer of the American College of Surgeons and the American Cancer Society) 2000–2002, as reported in: Edge SB, Byrd DR, Compton CC, Fritz AG, Greene FL, Trotti A. *AJCC Cancer Staging Manual*. 7th ed. New York, NY: Springer Science & Business Media; 2010.

Five-Year Overall Survival of Female Patients With Stage^a IIA and IIB Breast Cancer (N = 1947) 2007 - 2015

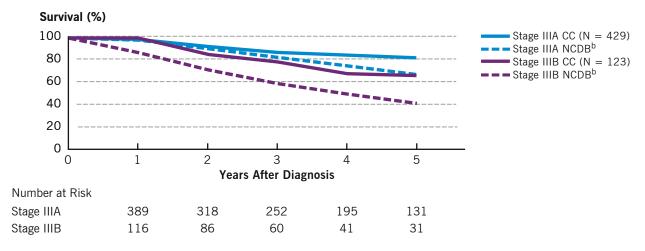


CC = Cleveland Clinic, NCDB = National Cancer Database

^aAJCC stage I–IV breast cancer

^bReference group data from the National Cancer Database (Commission on Cancer of the American College of Surgeons and the American Cancer Society) 2000–2002, as reported in: Edge SB, Byrd DR, Compton CC, Fritz AG, Greene FL, Trotti A. *AJCC Cancer Staging Manual*. 7th ed. New York, NY: Springer Science & Business Media; 2010.

Five-Year Overall Survival of Female Patients With Stage^a IIIA and IIIB Breast Cancer (N = 552) 2007 - 2015



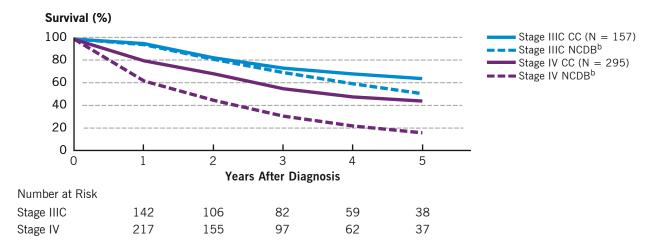
CC = Cleveland Clinic, NCDB = National Cancer Database

32

^aAJCC stage I-IV breast cancer

^bReference group data from the National Cancer Database (Commission on Cancer of the American College of Surgeons and the American Cancer Society) 2000–2002, as reported in: Edge SB, Byrd DR, Compton CC, Fritz AG, Greene FL, Trotti A. *AJCC Cancer Staging Manual*. 7th ed. New York, NY: Springer Science & Business Media; 2010.

Five-Year Overall Survival of Female Patients With Late Stage^a Breast Cancer (N = 452) 2007 - 2015



CC = Cleveland Clinic, NCDB = National Cancer Database

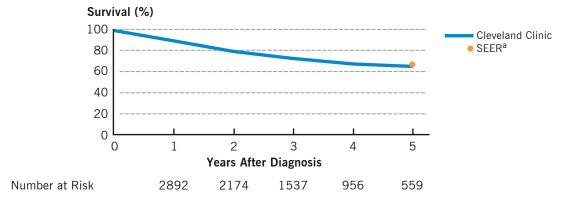
^aAJCC stage I–IV breast cancer

^bReference group data from the National Cancer Database (Commission on Cancer of the American College of Surgeons and the American Cancer Society) 2000–2002, as reported in: Edge SB, Byrd DR, Compton CC, Fritz AG, Greene FL, Trotti A. *AJCC Cancer Staging Manual*. 7th ed. New York, NY: Springer Science & Business Media; 2010.

Solid Tumor Oncology | Colorectal Cancer

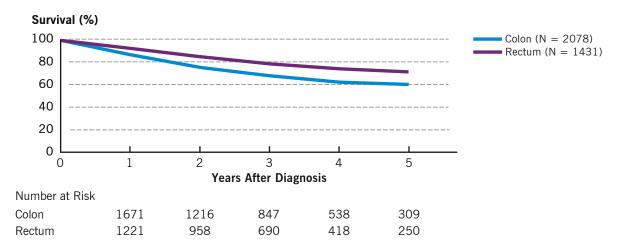
Patients with gastrointestinal cancer benefit from the coordinated efforts of Cleveland Clinic's multidisciplinary teams, comprising surgeons and physicians from the departments of Colorectal Surgery and General Surgery, Gastroenterology, Interventional Radiology, Medical Oncology, and Radiation Oncology. Tailored treatment regimens include adjuvant therapy following surgical resection for patients with tumors at risk for recurrence, as well as systemic therapies for patients with inoperable, incurable advanced disease. Clinical trials provide important treatment options to patients. The data shown below demonstrate superior outcomes in advanced-stage colorectal cancer.

Five-Year Overall Survival of Patients With All Stages of Colon and Rectal Cancer (N = 3510) 2007 - 2015

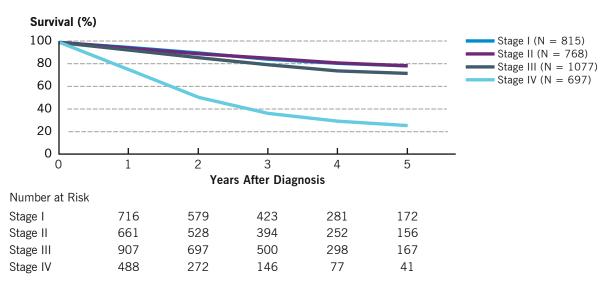


^aHowlader N, Noone AM, Krapcho M, Miller D, Bishop K, Altekruse SF, Kosary CL, Yu M, Ruhl J, Tatalovich Z, Mariotto A, Lewis DR, Chen HS, Feuer EJ, Cronin KA (eds). SEER Cancer Statistics Review, 1975-2013, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975 2013/, based on November 2015 SEER data submission, posted to the SEER website, April 2016. Accessed Feb. 28, 2017.

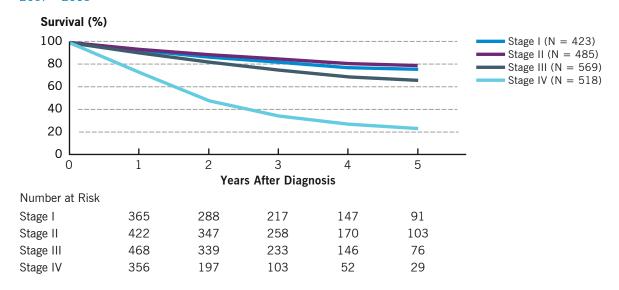
Five-Year Overall Survival of Patients With All Stages of Colon vs Rectal Cancer (N = 3509) 2007 - 2015



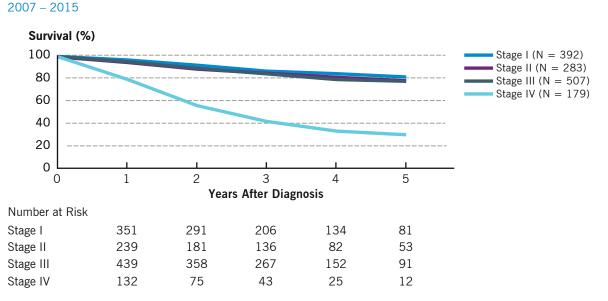
Five-Year Overall Survival of Patients With Colon and Rectal Cancer by Stage (N = 3357) 2007 - 2015



Five-Year Overall Survival of Patients With Colon Cancer by Stage (N = 1995) 2007 - 2015

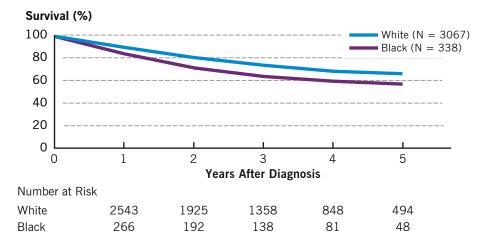


Five-Year Overall Survival of Patients With Rectal Cancer by Stage (N = 1361)



36

Five-Year Overall Survival of Patients With All Stages of Colon and Rectal Cancer by Race^a (N = 3405) 2007 – 2015



^aSelf-reported

Cleveland Clinic actively participates in efforts to address outcome disparities due to race and other factors. Taussig Cancer Institute has a unique model that combines community outreach and patient navigation to provide patients with a continuum of support, from screening to convenient appointment scheduling to removing other barriers to care to survivorship support. The institute's efforts include providing multiple access points in the community (e.g., beauty/barber shops, churches, community centers, libraries, and federally qualified health centers) where individuals are encouraged to complete the recommended cancer screenings that can lead to early detection and treatment of disease.

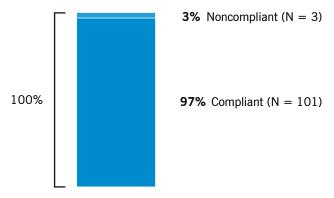
901

Cancer navigation episodes opened in 2016

Quality Measure

At Least 12 Regional Lymph Nodes Removed and Pathologically Examined for Patients Undergoing Resection for Colon Cancer (N = 104)

2015



Cleveland Clinic's performance was 97% (101 of 104; 95% CI, 93.9-100) for 2015 for this National Cancer Database^a standard of care quality measure, exceeding the 85% standard performance rate.

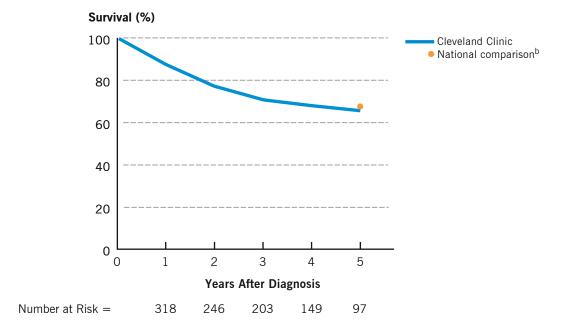
38

^aThe National Cancer Database is a nationwide oncology outcomes database and is a joint program of the Commission on Cancer and the American Cancer Society.

Radiation oncologists and medical oncologists at Cleveland Clinic work in close collaboration to treat patients with gynecologic cancers. Gynecologic tumor sites include the vulva, vagina, cervix, uterine body, and uterine adnexa. Standard radiation treatment employs high-dose-rate brachytherapy and external beam radiotherapy.

Cervical Cancer

Five-Year Overall Survival of Patients With Cervical Cancer^a (N = 386) 2007 – 2015

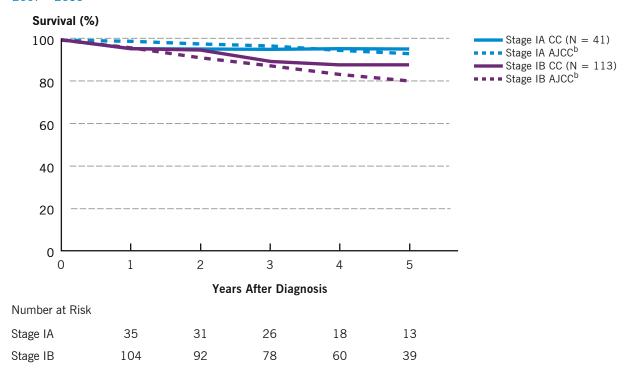


alncludes patients treated at main campus and Fairview Hospital, a Cleveland Clinic hospital

^bNational comparison represents relative survival after diagnosis from Fast Stats: An interactive tool for access to Surveillance, Epidemiology, and End Results (SEER) cancer statistics. Surveillance Research Program, National Cancer Institute. http://seer.cancer.gov/statfacts/html/cervix.html. Accessed on Mar. 29, 2017.

Historically cervical cancer was subdivided into stage IA (microinvasive carcinoma), which can be treated by a simple hysterectomy, and stage IB (more than microinvasive carcinoma), which is treated with radical surgery or radiation therapy.

Five-Year Overall Survival of Patients With Stage IA and IB Cervical Cancer^a (N=154) 2007-2015



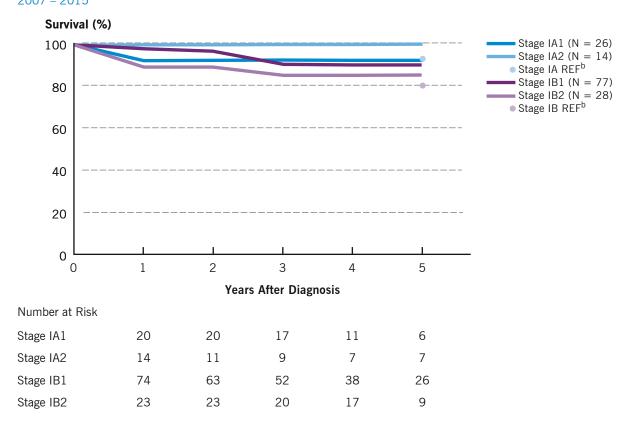
AJCC = American Joint Committee on Cancer, CC = Cleveland Clinic

^aIncludes patients treated at main campus and Fairview Hospital, a Cleveland Clinic hospital

^bComparison group data from the National Cancer Data Base (Commission on Cancer of the American College of Surgeons and the American Cancer Society) 2000–2002, as reported in: Edge SB, Byrd DR, Compton CC, Fritz AG, Greene FL, Trotti A. *AJCC Cancer Staging Manual*. 7th ed. New York, NY: Springer Science & Business Media; 2010.

In 1994, cervical cancer was further subdivided into stage IA1, IA2, IB1, and IB2 to better estimate the risk of recurrence and survival. This is reflected in the Cleveland Clinic data listed below.

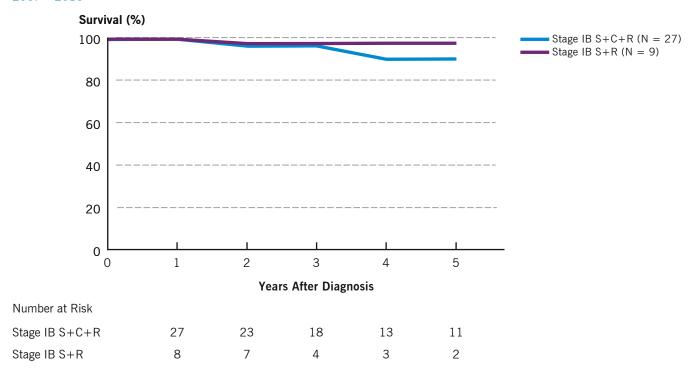
Five-Year Overall Survival of Patients With Stage IA1, IA2, IB1, and IB2 Cervical Cancer a (N = 145) 2 2007 – 2015



^aIncludes patients treated at main campus and Fairview Hospital, a Cleveland Clinic hospital

^bComparison group data from the American Cancer Society, as reported in: Survival rates for cervical cancer, by stage. American Cancer Society Web site. Retrieved from: https://www.cancer.org/cancer/cervical-cancer/detection-diagnosis-staging/survival.html#written_by. Updated Dec. 5, 2016. Accessed on Apr. 13, 2017.

Five-Year Overall Survival of Patients With Stage IB by Treatment Modality a (N = 73) 2007 - 2015

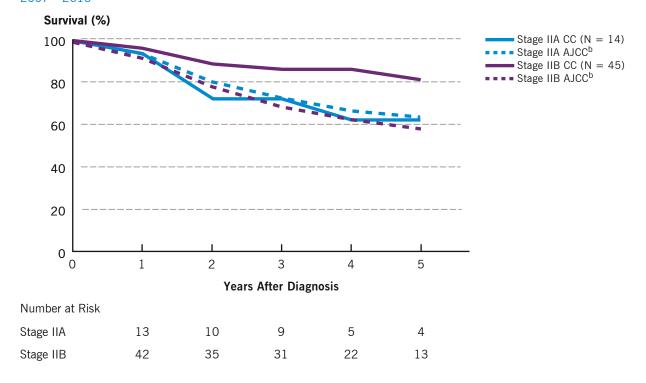


C = chemotherapy, R = radiation, S = surgery

Following surgery for stage I cervical cancer, certain patients have high risk factors (including lymph node metastasis, extension beyond the cervix, and positive margins) or intermediate risk factors (including large tumor size, presence of lymph-vascular space invasion, and extended cervical stromal invasion) that require radiation therapy of the pelvis. The graph above demonstrates that those patients with the lowest risk factors have the best outcomes. Patients treated with adjuvant radiation and concurrent chemotherapy had a better overall survival rate than those treated with radiation only.

^aIncludes patients treated at main campus and Fairview Hospital, a Cleveland Clinic hospital

Five-Year Overall Survival of Patients With Stage IIA and IIB Cervical Cancer^a (N = 59) 2007 - 2015

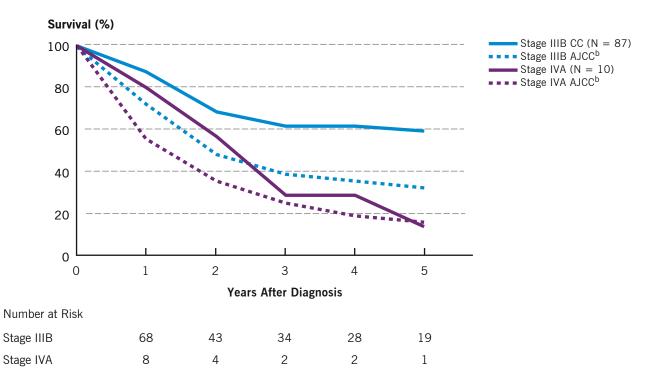


AJCC = American Joint Committee on Cancer, CC = Cleveland Clinic

^aIncludes patients treated at main campus and Fairview Hospital, a Cleveland Clinic hospital

^bComparison group data from the National Cancer Data Base (Commission on Cancer of the American College of Surgeons and the American Cancer Society) 2000–2002, as reported in: Edge SB, Byrd DR, Compton CC, Fritz AG, Greene FL, Trotti A. *AJCC Cancer Staging Manual*. 7th ed. New York, NY: Springer Science & Business Media; 2010.

Five-Year Overall Survival of Patients With Stage IIIB and IVA Cervical Cancer a (N = 97) 2007 - 2015



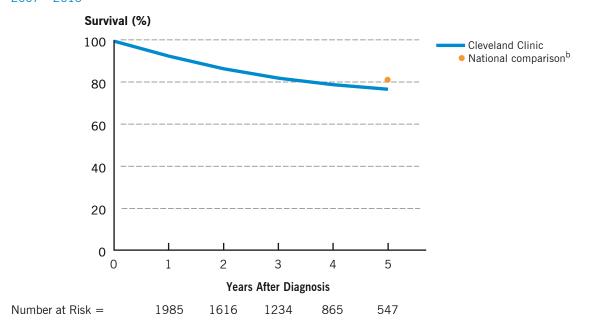
AJCC = American Joint Committee on Cancer, CC = Cleveland Clinic

^aIncludes patients treated at main campus and Fairview Hospital, a Cleveland Clinic hospital

^bComparison group data from the National Cancer Data Base (Commission on Cancer of the American College of Surgeons and the American Cancer Society) 2000–2002, as reported in: Edge SB, Byrd DR, Compton CC, Fritz AG, Greene FL, Trotti A. *AJCC Cancer Staging Manual*. 7th ed. New York, NY: Springer Science & Business Media; 2010.

Endometrial Cancer

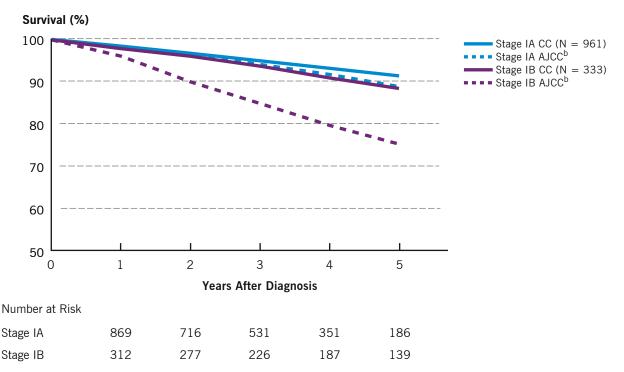
Five-Year Overall Survival of Patients With Endometrial Cancer^a (N = 2269) 2007 - 2015



^aIncludes patients treated at main campus and Fairview Hospital, a Cleveland Clinic hospital

^bNational comparison represents relative survival after diagnosis from Fast Stats: An interactive tool for access to Surveillance, Epidemiology, and End Results (SEER) cancer statistics. Surveillance Research Program, National Cancer Institute. http://seer.cancer.gov/statfacts/html/corp.html. Accessed on Mar. 30, 2017.

Five-Year Overall Survival of Patients With Stage IA and IB Endometrial Cancer^a (N = 1294) 2007 - 2015



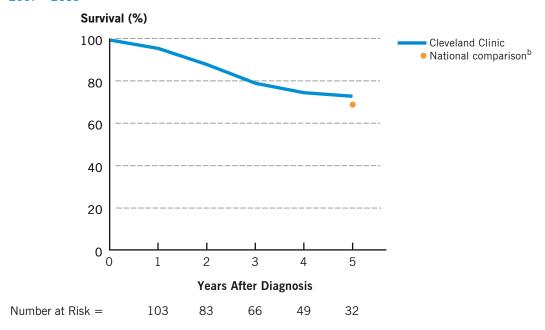
AJCC = American Joint Committee on Cancer, CC = Cleveland Clinic

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^aIncludes patients treated at main campus and Fairview Hospital, a Cleveland Clinic hospital

^bComparison group data from the National Cancer Data Base (Commission on Cancer of the American College of Surgeons and the American Cancer Society) 2000–2002, as reported in: Edge SB, Byrd DR, Compton CC, Fritz AG, Greene FL, Trotti A. *AJCC Cancer Staging Manual*. 7th ed. New York, NY: Springer Science & Business Media; 2010.

Five-Year Overall Survival of Patients With Stage II Endometrial Cancer a (N = 116) 2007 - 2015

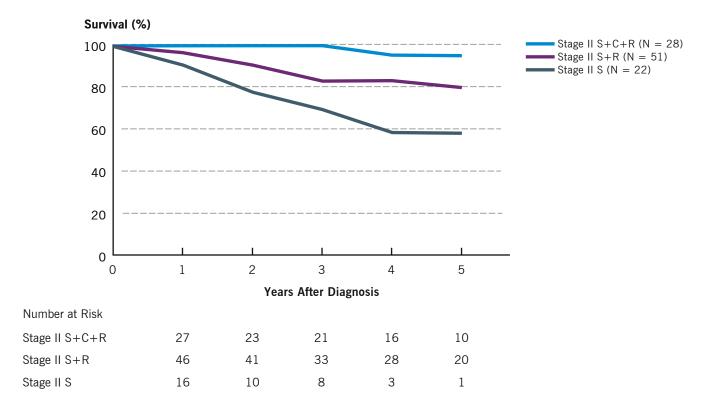


^aIncludes patients treated at main campus and Fairview Hospital, a Cleveland Clinic hospital

^bNational comparison represents relative survival after diagnosis from Fast Stats: An interactive tool for access to Surveillance, Epidemiology, and End Results (SEER) cancer statistics. Surveillance Research Program, National Cancer Institute. http://seer.cancer.gov/statfacts/html/corp.html. Accessed on Mar. 30, 2017.

Solid Tumor Oncology | Gynecologic Cancer

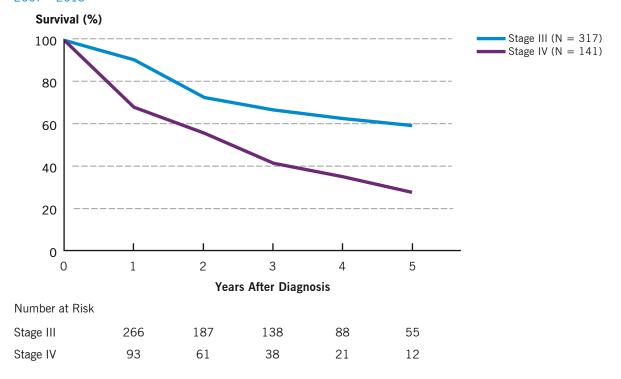
Five-Year Overall Survival of Patients With Stage II Endometrial Cancer by Treatment Modality a (N = 101) $^{2007-2015}$



C = chemotherapy, R = radiation, S = surgery

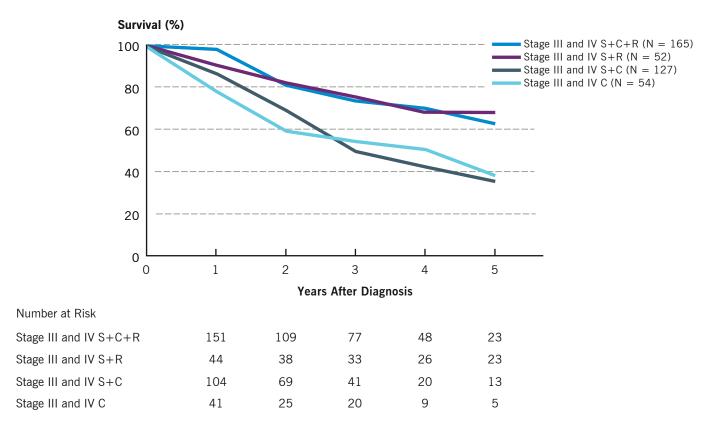
^aIncludes patients treated at main campus and Fairview Hospital, a Cleveland Clinic hospital

Five-Year Overall Survival of Patients With Stage III and IV Endometrial Cancer a (N = 458) 2007 - 2015



^aIncludes patients treated at main campus and Fairview Hospital, a Cleveland Clinic hospital

Five-Year Overall Survival of Patients With Stage III and IV Endometrial Cancer by Treatment Modality a (N = 398) 2007 – 2015



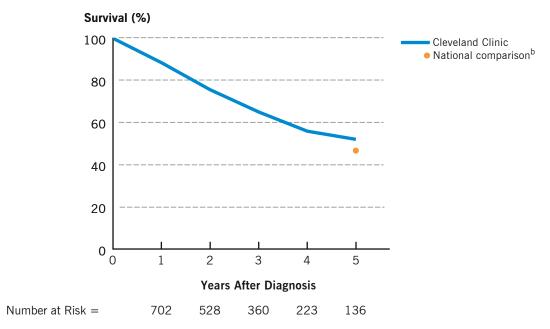
C = chemotherapy, R = radiation, S = surgery

^aIncludes patients treated at main campus and Fairview Hospital, a Cleveland Clinic hospital

Ovarian Cancer

Five-Year Overall Survival of Patients With Ovarian Cancer a (N = 847)

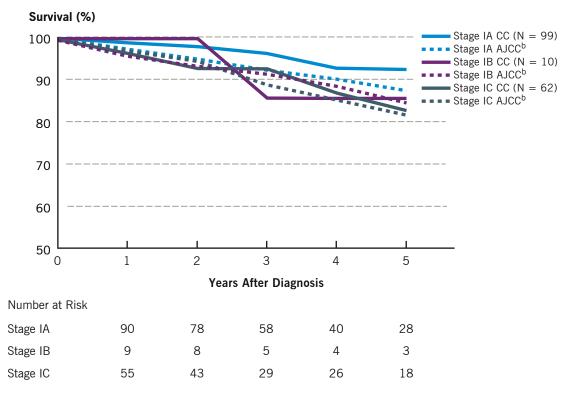
2007 - 2015



^aIncludes patients treated at main campus and Fairview Hospital, a Cleveland Clinic hospital

^bNational comparison represents relative survival after diagnosis from Fast Stats: An interactive tool for access to Surveillance, Epidemiology, and End Results (SEER) cancer statistics. Surveillance Research Program, National Cancer Institute. http://seer.cancer.gov/statfacts/html/ovary.html. Accessed on Mar. 30, 2017.

Five-Year Overall Survival of Patients With Stage IA, IB, and IC Ovarian Cancer^a (N=171) 2007-2015

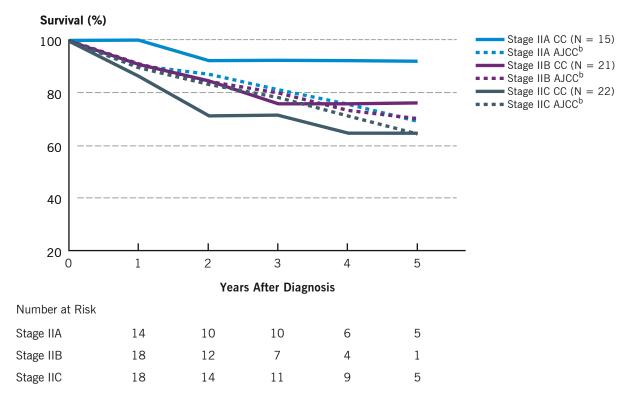


AJCC = American Joint Committee on Cancer, CC = Cleveland Clinic

^aIncludes patients treated at main campus and Fairview Hospital, a Cleveland Clinic hospital

^bNational comparison group data from the National Cancer Data Base (Commission on Cancer of the American College of Surgeons and the American Cancer Society) 2000–2002, as reported in: Edge SB, Byrd DR, Compton CC, Fritz AG, Greene FL, Trotti A. *AJCC Cancer Staging Manual*. 7th ed. New York, NY: Springer Science & Business Media; 2010.

Five-Year Overall Survival of Patients With Stage IIA, IIB, and IIC Ovarian Cancer^a (N = 58) 2007 - 2015

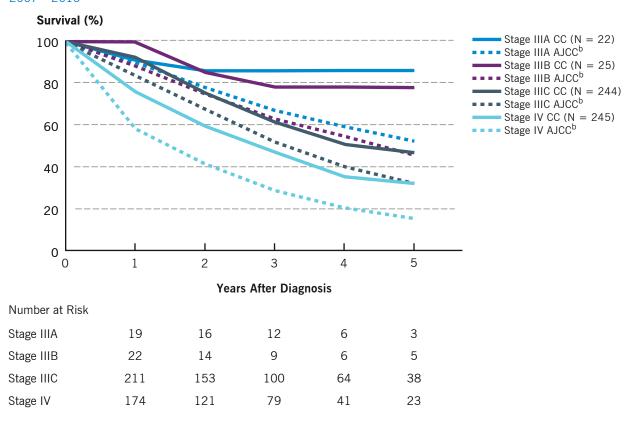


AJCC = American Joint Committee on Cancer, CC = Cleveland Clinic

^aIncludes patients treated at main campus and Fairview Hospital, a Cleveland Clinic hospital

^bNational comparison group data from the National Cancer Data Base (Commission on Cancer of the American College of Surgeons and the American Cancer Society) 2000–2002, as reported in: Edge SB, Byrd DR, Compton CC, Fritz AG, Greene FL, Trotti A. *AJCC Cancer Staging Manual*. 7th ed. New York, NY: Springer Science & Business Media; 2010.

Five-Year Overall Survival of Patients With Stage III and IV Ovarian Cancer^a (N = 536) 2007 - 2015

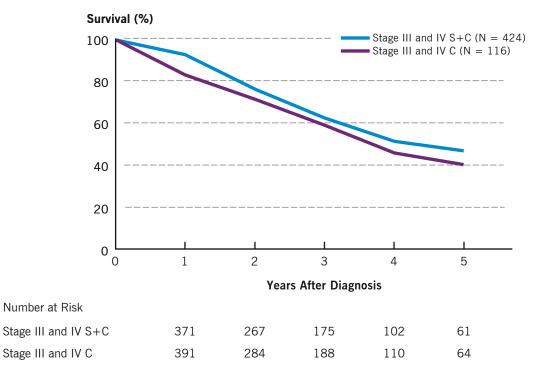


AJCC = American Joint Committee on Cancer, CC = Cleveland Clinic

^aIncludes patients treated at main campus and Fairview Hospital, a Cleveland Clinic hospital

^bNational comparison group data from the National Cancer Data Base (Commission on Cancer of the American College of Surgeons and the American Cancer Society) 2000–2002, as reported in: Edge SB, Byrd DR, Compton CC, Fritz AG, Greene FL, Trotti A. *AJCC Cancer Staging Manual*. 7th ed. New York, NY: Springer Science & Business Media; 2010.

Five-Year Overall Survival of Patients With Stage III and IV Ovarian Cancer by Treatment Modality^a (N = 540) 2007 - 2015



C = chemotherapy, S = surgery

^aIncludes patients treated at main campus and Fairview Hospital, a Cleveland Clinic hospital

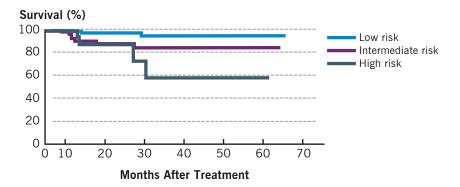
Solid Tumor Oncology | Head and Neck Cancer

At Cleveland Clinic, patients with head and neck cancer benefit from multidisciplinary care involving a complete assessment by surgical, medical, and radiation oncologists. Individualized treatment plans for patients with these malignancies are developed through the collaborative efforts of all specialists. For patients with localized disease, surgery or radiation therapy is the mainstay of their care plan. The head and neck cancer care team is actively involved in cooperative group research studies and also conducts in-house clinical trials to maximize value and to ensure that patients receive quality care that increases survival and improves quality of life.

Oropharynx Cancer

Overall Survival in Oropharyngeal Squamous Cell Carcinoma After Risk Stratification Based on Human Papillomavirus Status, Tobacco Use, T-Stage, and N-Stage a (N = 150)

2009 - 2014

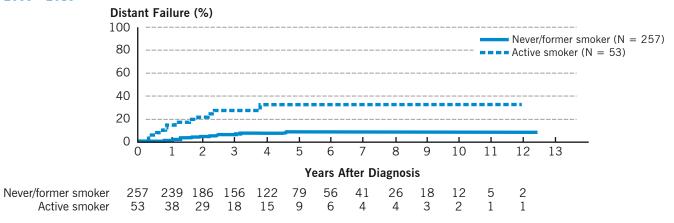


At a median follow-up of 26.5 months (range 5.4-65.5 months), the projected 3-year overall survival for the low-risk, intermediate-risk, and high-risk oropharyngeal cancer groups are 94.7%, 84.2%, and 57.8%, respectively (P = 0.012).

^aGreskovich JF, Woody NM, Joshi NP, Burkey B, Scharpf J, Lorenz R, Lamarre E, Nwizu T, Houston N, Harr B, Bodmann J, Ives D, Rahe M, Adelstein DJ, Koyfman SA. Single institution results of high quality, narrow-margin IMRT with concurrent CDDP-based chemotherapy for stage III-IVB, risk stratified oropharyngeal squamous cell cancer. Poster presented at: American Head and Neck Society 9th International Conference on Head and Neck Cancer: July 16-20, 2016: Seattle, WA.

Rates of Distant Metastases in Patients With Human Papillomavirus-Positive Oropharyngeal Cancer by Smoking Status a (N = 310)

2003 – 2013



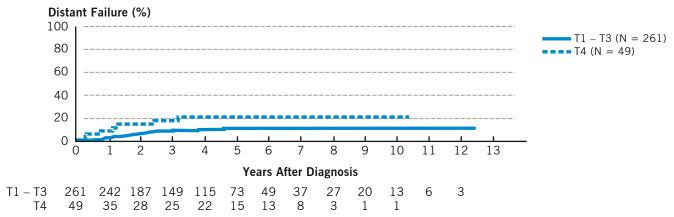
^aWeller MA, Ward MC, Berriochoa C, Reddy CA, Trosman S, Koyfman S. Cetuximab-based bioradiation therapy is associated with higher rates of distant metastases than platinum-based chemoradiation therapy in human papillomavirus-positive oropharyngeal cancer. *Int J Radiat Oncol Biol Phys.* 2015;93(3):S76.

At follow-up, rates of distant metastases were significantly increased among patients who were active smokers at diagnosis compared to those who were never or former smokers (32% vs 9% at 5 years, P < 0.001).

Solid Tumor Oncology | Head and Neck Cancer

Rates of Distant Metastases in Patients With Human Papillomavirus-Positive Oropharyngeal Cancer by T-Stage^a (N = 310)





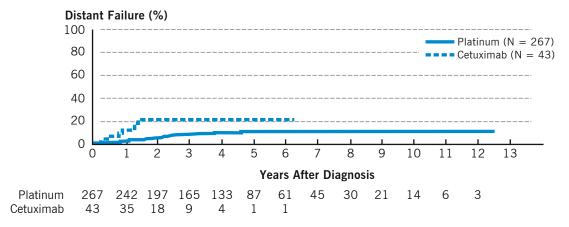
^aWeller MA, Ward MC, Berriochoa C, Reddy CA, Trosman S, Koyfman S. Cetuximab-based bioradiation therapy is associated with higher rates of distant metastases than platinum-based chemoradiation therapy in human papillomavirus-positive oropharyngeal cancer. *Int J Radiat Oncol Biol Phys.* 2015;93(3):S76.

At follow-up, rates of distant metastases were significantly higher for those patients with T4 status compared to patients with T1-3 status (21 vs 11% at 5 years, P = 0.045).

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Rates of Distant Metastases in Patients With Human Papillomavirus-Positive Oropharyngeal Cancer by Type of Systemic Therapy a (N = 310)

2003 – 2013



^aWeller MA, Ward MC, Berriochoa C, Reddy CA, Trosman S, Koyfman S. Cetuximab-based bioradiation therapy is associated with higher rates of distant metastases than platinum-based chemoradiation therapy in human papillomavirus-positive oropharyngeal cancer. *Int J Radiat Oncol Biol Phys.* 2015;93(3):S76.

Rates of distant metastases were significantly higher among those patients receiving cetuximab-based bioradiation therapy compared to those receiving cisplatin-based chemoradiation (23% vs 11% at 5 years, P < 0.004).

Solid Tumor Oncology | Head and Neck Cancer

Feeding Tube Use in Patients With Human Papillomavirus-Positive Oropharyngeal Cancer a (N = 421)



HPV = Human Papillomavirus

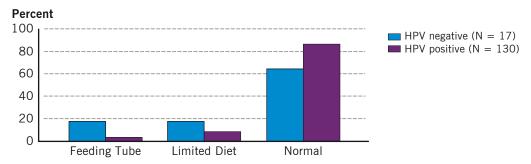
2007 - 2014

^aKoyfman S, Ward MC, Houston N, Joshi NP, Harr B, Nwizu T, Adelstein DJ, Xia P, Greskovich JF. Dramatic reduction in the need for feeding tube use in human papillomavirus-positive oropharyngeal cancer in the intensity modulated radiation therapy era. *Int J Radiat Oncol Biol Phys.* 2016;96(2S):E359.

Feeding tube use in patients with human papillomavirus-positive oropharyngeal cancer has become the exception rather than the rule at Cleveland Clinic.

Impact of Human Papillomavirus Status on Diet in Patients With Oropharyngeal Squamous Cell Carcinoma Following Definitive Chemoradiation Therapy a (N = 147)

2002 - 2010

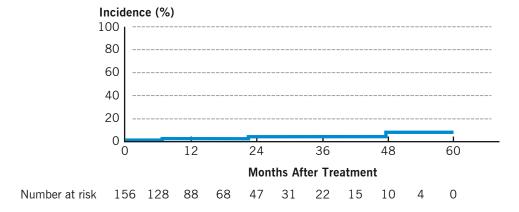


Research conducted with patients receiving exclusively conventional 3-field radiotherapy with chemotherapy at Cleveland Clinic indicates that better swallowing outcomes are not only the result of intensity-modulated radiation therapy (IMRT). Patients with human papillomavirus-related oropharynx squamous cell carcinoma had better swallowing outcomes following definitive chemoradiotherapy, in this case demonstrated by the percentage of patients who had returned to normal diets at follow-up.

^aNaik M, Ward MC, Bledsoe TJ, Kumar AM, Rybicki LA, Saxton JP, Burkey BB, Greskovich JF, Adelstein DJ, Koyfman SA. It is not just IMRT: Human papillomavirus related oropharynx squamous cell carcinoma is associated with better swallowing outcomes after definitive chemoradiotherapy. *Oral Oncol*. 2015 Aug;51(8):800-804.

Long-term survival rates for oropharyngeal cancer have improved, mainly due to the rapidly increasing incidence of good-prognosis human papillomavirus (HPV)-induced disease. With cure rates over 90% among nonsmoking patients with newly diagnosed, locoregionally advanced HPV-related oropharynx cancer, research has begun to focus more on severe late toxic effects (ie, dysphagia, radionecrosis, or xerostomia).

Cumulative Incidence of Severe Late Toxic Effects After Modern Definitive Image-Guided Intensity-Modulated Radiation Therapy in Patients With Human Papillomavirus-Associated Oropharyngeal Cancer (N = 156) 2009 – 2015



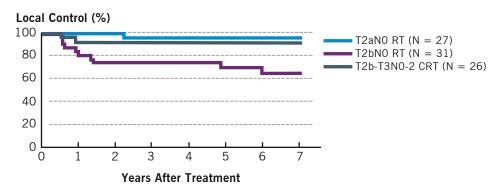
Cleveland Clinic uses modern definitive image-guided IMRT for such cancers, with or without cisplatin-based chemotherapy. Compared with conventional radiation techniques, IMRT delivers better dose distribution to the target while limiting the dose to nearby critical structures, thereby markedly reducing severe late toxicity.

Reference

¹Ward MC, Ross RB, Koyfman SA, Lorenz R, Lamarre ED, Scharpf J, Burkey BB, Joshi NP, Woody NM, Prendes B, Houston N, Reddy CA, Greskovich JF, Adelstein DJ. Modern image-guided intensity-modulated radiotherapy for oropharynx cancer and severe late effect toxicities: implications for clinical trial design. *JAMA Otolaryngol Head Neck Surg.* 2016 Dec;142(12):1164-1170.

Larynx Cancer

Local Control for Patients With Squamous Cell Carcinoma of the True Glottis Treated With Radiation^a (N = 84) 1986 - 2013

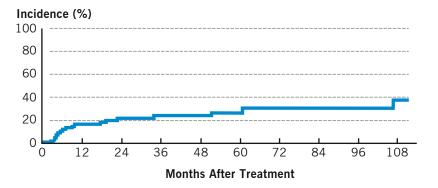


CRT = concurrent chemoradiotherapy, RT = radiotherapy

^aBhateja P, Ward MC, Hunter GH, Greskovich JF, Reddy CA, Nwizu TI, Lamarre E, Burkey BB, Adelstein DJ, Koyfman SA. Impaired vocal cord mobility in T2N0 glottic carcinoma: suboptimal local control with radiation alone. *Head Neck*. 2016 Dec;38(12):1832-1836.

Radiation therapy alone provides suboptimal local control. Cleveland Clinic considers concurrent chemoradiotherapy for patients with T2b disease.

Cumulative Incidence of Severe Late Dysphagia in Patients With Larynx Cancer a (N = 84) 1993 - 2003

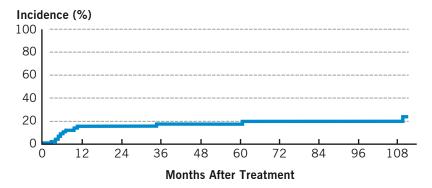


^aWard MC, Adelstein DJ, Bhateja P, Nwizu TI, Scharpf J, Houston N, Lamarre ED, Lorenz R, Burkey BB, Greskovich JF, Koyfman SA. Severe late dysphagia and cause of death after concurrent chemoradiation for larynx cancer in patients eligible for RTOG 91-11. *Oral Oncol.* 2016 Jun;57:21-26.

Unlike the results seen in patients with HPV-associated oropharyngeal cancer, severe late dysphagia remains a significant concern after definitive nonoperative treatment. This is consistent with cooperative group experience.

64

Cumulative Incidence of Stricture Dilations in Patients With Larynx Cancer^a (N = 84) 1993 - 2003

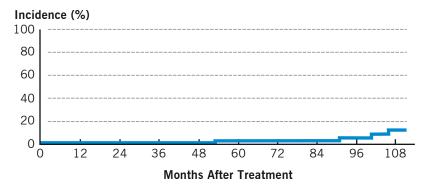


^aWard MC, Adelstein DJ, Bhateja P, Nwizu TI, Scharpf J, Houston N, Lamarre ED, Lorenz R, Burkey BB, Greskovich JF, Koyfman SA. Severe late dysphagia and cause of death after concurrent chemoradiation for larynx cancer in patients eligible for RTOG 91-11. *Oral Oncol.* 2016 Jun;57:21-26.

The cumulative incidence of stricture dilation at 5 years was 17.2% (95% CI, 8.9-25.6%).

Cumulative Incidence of Hospital Admission From Aspiration Pneumonia in Patients With Larynx Cancer a (N = 84)

1993 – 2003

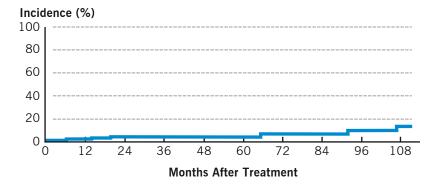


^aWard MC, Adelstein DJ, Bhateja P, Nwizu TI, Scharpf J, Houston N, Lamarre ED, Lorenz R, Burkey BB, Greskovich JF, Koyfman SA. Severe late dysphagia and cause of death after concurrent chemoradiation for larynx cancer in patients eligible for RTOG 91-11. *Oral Oncol*. 2016 Jun;57:21-26.

The cumulative incidence of hospital admission from aspiration pneumonia at 5 years was 2.8% (95% CI, 0-6.9%).

66

Cumulative Incidence of Feeding Tube Insertions in Patients With Larynx Cancer a (N = 84) 1993 - 2003



^aWard MC, Adelstein DJ, Bhateja P, Nwizu TI, Scharpf J, Houston N, Lamarre ED, Lorenz R, Burkey BB, Greskovich JF, Koyfman SA. Severe late dysphagia and cause of death after concurrent chemoradiation for larynx cancer in patients eligible for RTOG 91-11. *Oral Oncol.* 2016 Jun;57:21-26.

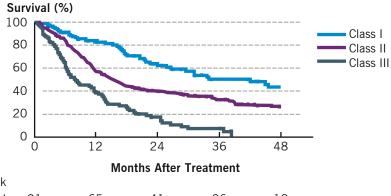
The cumulative incidence of feeding tube dependency at 5 years was 1.8% (95% CI, 0.2-11.2%).

Risk of severe late dysphagia was the highest within the first 2 years, and the risk remained for years to come. Patients treated for head and neck cancer should be closely followed by dedicated head and neck caregivers for their lifetime.

Reirradiation

Overall Survival of Patients Following Second Course of Radiation in Recurrent Disease by Prognostic Class^a (N = 412)

1998 – 2015



Number at Risk					
Class I	91	65	41	26	18
Class II	240	123	68	48	24
Class III	81	29	10	4	0

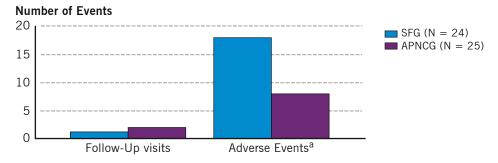
^aWard MC, Riaz N, Caudell JJ, Dunlap NE, Isrow D, Zakem SJ, Dault J, Awan MJ, Vargo J, Heron DE, Higgins KA, Beitler JJ, Yao M, Machtay M, Siddiqui F, Trotti A, Lee N, Koyfman S. Multi-institution analysis of intensity-modulated radiation therapy-based reirradiation for head and neck cancer: prognostic factors and recursive partitioning analysis for overall survival. *Int J Rad Onc Bio Phys.* 2016;96(2):S115.

Based on the results of a Cleveland Clinic-led 8-institution analysis, patients with recurrent or second primary (RSP) squamous cell carcinomas are separated into 3 prognostic groups: those > 2 years from initial course of radiotherapy with resectable tumors (Class I); those > 2 years with unresectable tumors or those ≤ 2 years and without organ dysfunction (Class II); and those ≤ 2 years with organ dysfunction (Class III). These prognostic subgroups help identify the best candidates for protracted courses of reirradiation.

Advanced Practice Nurse Follow-Up Clinic Reduces Emergency Room Visits and Hospital Admissions in High-Risk Patients After Radiotherapy for Head and Neck Cancer

In the months immediately following definitive therapy for head and neck cancer, patients are at increased risk for emergency department visits and hospital admissions. In 2014, Taussig Cancer Institute initiated an advanced practice nurse (APN)-led clinic to focus on the acute rehabilitation of patients considered at high risk. High-risk patients were seen in the APN follow-up clinic beginning 2–4 weeks after radiotherapy, then every 2–4 weeks until symptoms stabilized. This compares with the prior standard follow-up, in which patients were seen 4–6 weeks after radiotherapy and then at 3 months.

Impact of Follow-Up on High-Risk Patients in an Advanced Practice Clinic vs Prior Standard (N = 46) 2012 – 2015



APNCG = advanced practice nurse clinic group; SFG = standard follow-up group

Patients in the advanced practice nurse group were seen nearly twice as often as those in the standard follow-up group and experienced 55% fewer adverse events. As a result of these findings, high-risk patients who receive definitive treatment for head and neck cancer at Cleveland Clinic now receive follow-up care in the advanced practice nurse follow-up clinic as a standard practice.

^aEmergency department visits and hospital admissions constitute adverse events.

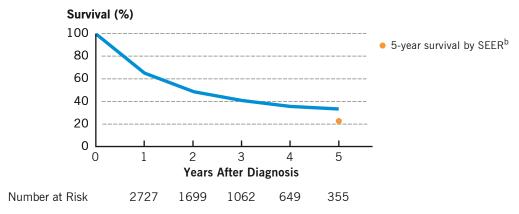
Solid Tumor Oncology | Lung Cancer

Taussig Cancer Institute's Thoracic Oncology Program offers patients with thoracic malignancies leading-edge, multidisciplinary care. In consultation with patients, collaborative teams of surgical, medical, and radiation oncologists tailor treatment plans to the needs of each patient. An active clinical research program provides patients with additional treatment options.

The Department of Radiation Oncology actively participates in Cleveland Clinic in-house protocols and is a full member of the NRG Oncology research organization. The department is among the leading institutions nationally for accrual of patients to multiple NRG Oncology clinical trials.

Lung Cancer

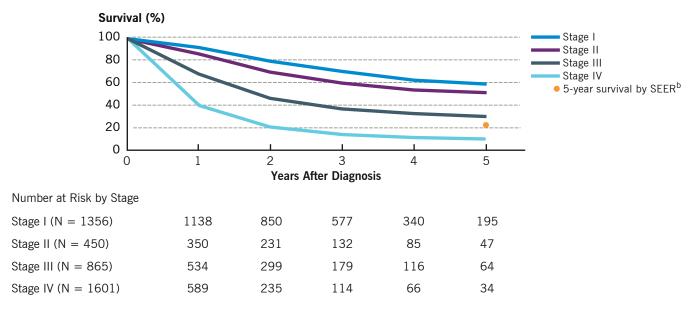
Five-Year Overall Survival of Patients With All Stages^a of Non-Small Cell Lung Cancer (N = 4471) 2007 - 2015



^aAmerican Joint Committee on Cancer (AJCC) stage I-IV non-small cell lung cancer

bHowlader N, Noone AM, Krapcho M, Miller D, Bishop K, Altekruse SF, Kosary CL, Yu M, Ruhl J, Tatalovich Z, Mariotto A, Lewis DR, Chen HS, Feuer EJ, Cronin KA (eds). SEER Cancer Statistics Review, 1975-2013, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975 2013/, based on November 2015 SEER data submission, posted to the SEER website, April 2016.

Five-Year Overall Survival of Patients With Non-Small Cell Lung Cancer by Stage^a (N = 4272) 2007 - 2015

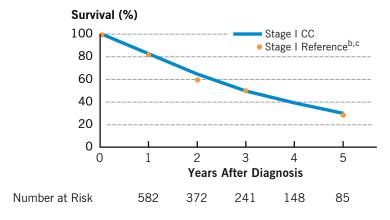


^aAJCC stage I-IV non-small cell lung cancer

bHowlader N, Noone AM, Krapcho M, Miller D, Bishop K, Altekruse SF, Kosary CL, Yu M, Ruhl J, Tatalovich Z, Mariotto A, Lewis DR, Chen HS, Feuer EJ, Cronin KA (eds). SEER Cancer Statistics Review, 1975-2013, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2013/, based on November 2015 SEER data submission, posted to the SEER website, April 2016.

Overall Survival of Patients With Medically Inoperable Stage I^a Non-Small Cell Lung Cancer Treated With Stereotactic Body Radiation Therapy (N = 771)

2006 – 2015



CC = Cleveland Clinic

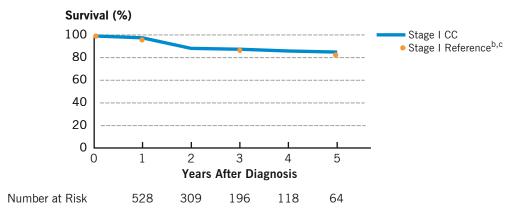
^cZheng X, Schipper M, Kidwell K, Lin J, Reddy R, Ren Y, Chang A, Lv F, Orringer M, Spring Kong FM. Survival outcome after stereotactic body radiation therapy and surgery for stage I non-small cell lung cancer: a meta-analysis. *Int J Radiat Oncol Biol Phys.* 2014 Nov 1;90(3):603-611.

^aAmerican Joint Committee on Cancer (AJCC) stage I non-small cell lung cancer

^bThere is no reference value for year 4.

Local Control for Patients With Medically Inoperable Stage I^a Lung Cancer Treated With Stereotactic Body Radiation Therapy (N = 771)

2006 - 2015



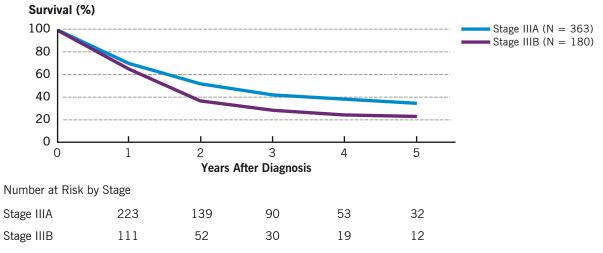
CC = Cleveland Clinic

^cZheng X, Schipper M, Kidwell K, Lin J, Reddy R, Ren Y, Chang A, Lv F, Orringer M, Spring Kong FM. Survival outcome after stereotactic body radiation therapy and surgery for stage I non-small cell lung cancer: a meta-analysis. *Int J Radiat Oncol Biol Phys.* 2014 Nov 1;90(3):603-611.

^aAJCC stage I non-small cell lung cancer

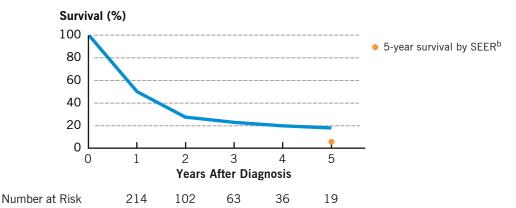
^bThere is no reference value for years 2 and 4.

Five-Year Overall Survival of Patients With Stage III^a Non-Small Cell Lung Cancer Treated With Radiation (N=543) 2007-2015



^aAJCC stage III non-small cell lung cancer

Five-Year Overall Survival of Patients With All Stages a of Small Cell Lung Cancer (N = 475) 2007 - 2015

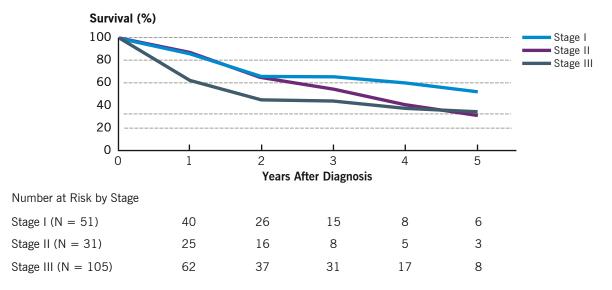


^aAJCC stage I-IV small cell lung cancer

74

^bHowlader N, Noone AM, Krapcho M, Miller D, Bishop K, Altekruse SF, Kosary CL, Yu M, Ruhl J, Tatalovich Z, Mariotto A, Lewis DR, Chen HS, Feuer EJ, Cronin KA (eds). SEER Cancer Statistics Review, 1975-2013, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975 2013/, based on November 2015 SEER data submission, posted to the SEER website, April 2016.

Five-Year Overall Survival of Patients With Early Stage^a Small Cell Lung Cancer (N = 187) 2007 - 2015

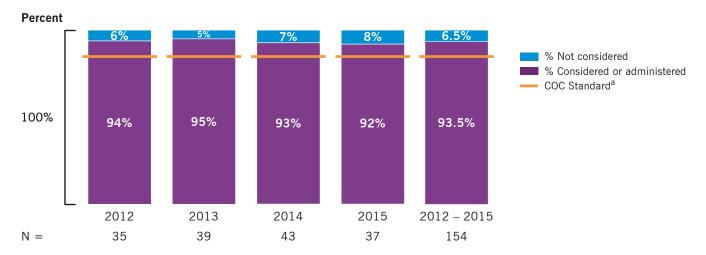


^aAJCC stage I-III small cell lung cancer

Quality Measures

Systemic Chemotherapy Administered 4 Months to 1 Day Preoperatively or Day of Surgery to 6 Months Postoperatively, or Considered for Surgically Resected Cases With Pathologic Lymph Node-Positive (pN1 or pN2) for Patients With Non-Small Cell Lung Cancer (N=154)

2012 - 2015



^aAmerican College of Surgeons. Commission on Cancer Quality of Care Measures. National Cancer Database Web site. https://www.facs.org/quality-programs/cancer/ncdb/qualitymeasures. Accessed March 2, 2017.

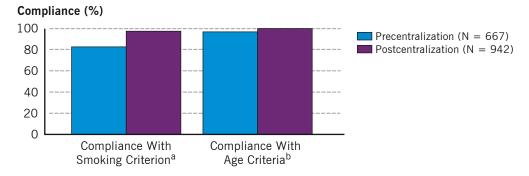
Cleveland Clinic's performance was 92% (34 of 37 patients) in 2015 for this Commission on Cancer quality improvement measure.

Lung Cancer Screening

The primary goal of low dose computed tomography (LDCT) lung cancer screening is to detect lung cancer at curable stages while minimizing harm to those without lung cancer. In the past 5 years, Cleveland Clinic's lung cancer screening program has screened > 1600 patients, diagnosing 14 lung cancers while performing only 4 procedures on patients with benign lung nodules.

Prior to 2015, the provider ordering LDCT was responsible for managing the screening results. Management of the LDCT screening program was centralized to lung cancer specialists in April 2015. Rather than ordering the screening themselves, providers instead order a consult to the screening program, which then decides whether the patient is eligible.

Improvement in Compliance With Screening Guidelines Following Centralization (N = 1609) 2012 - 2016

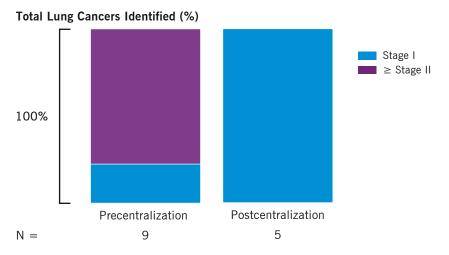


^aEligible smoking criterion is tobacco smoking history of at least 30 pack years

Following centralization, compliance with the criteria set forth by the Centers for Medicare & Medicaid Services increased.

^bEligible age range for LDCT screening is 55-77 for current smokers or those who have quit smoking within the past 15 years

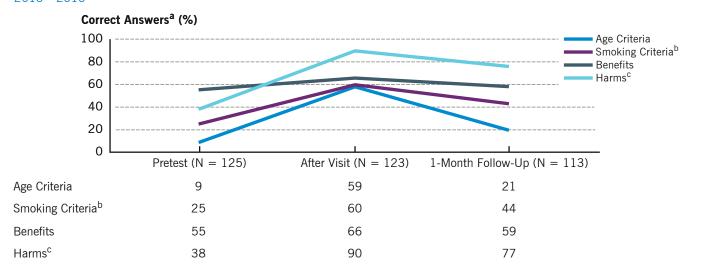
Early Stage Cancers Diagnosed as a Percentage of Total Lung Cancers Identified (N = 14) 2012 - 2016



Following centralization, the percentage of stage I cancers discovered increased to 100%.

An important aspect of Cleveland Clinic's lung cancer screening program is its centralized counseling and shared decision making visit, which includes patient education about screening eligibility criteria related to age and smoking status, and the benefits and harms of lung cancer screening. Surveys were administered before the shared decision making visit, immediately following the visit, and after 1 month to evaluate the amount of information retained. ¹

Change in Knowledge of Lung Cancer Screening Following Shared Decision Making Visit 2015 – 2016



^aPercentages rounded to the nearest whole number

These results indicate a substantial increase in knowledge about lung cancer screening eligibility and the knowledge of benefits and harms. Knowledge levels waned at the 1-month follow-up survey; however, they remained significantly higher than at the initial visit.

Reference

^bPercentage of those surveyed who gave partially correct or correct answers

^cPercentage of those surveyed who were able to identify at least 1 potential harm of lung cancer screening

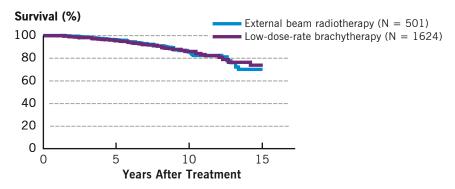
¹Mazzone PJ, Tenenbaum A, Seeley M, Petersen H, Lyon C, Han X, Wang XF. Impact of a lung cancer screening counseling and shared decision-making visit. *Chest*. 2017 Mar;151(3):572-578.

Genitourinary Oncology Program

Taussig Cancer Institute's Genitourinary Oncology Program has made advancements in the treatment of adrenal, bladder, renal, testicular, and prostate cancer through research and innovation. The program's multidisciplinary approach offers exceptional clinical care using surgery, chemotherapy, radiation therapy, and innovative clinical treatments for patients in all stages of disease.

Prostate Cancer

Biochemical Relapse Free Survival of Patients With Low-Risk Prostate Cancer by Treatment Type^a (N = 2125) 1996 - 2016

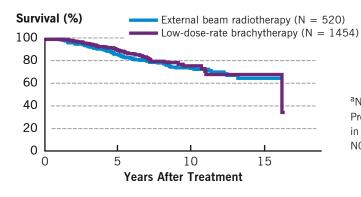


Number at Risk

External beam radiotherapy	330	130	14
Low-dose-rate brachytherapy	778	143	12

^aNational Comprehensive Cancer Network (NCCN). Prostate Cancer. NCCN Clinical Practice Guidelines in Oncology. V.2.2007. Fort Washington, PA: NCCN; 2007.

Biochemical Relapse Free Survival of Patients With Intermediate-Risk Prostate Cancer by Treatment Type^a (N = 1974) 1996 – 2016



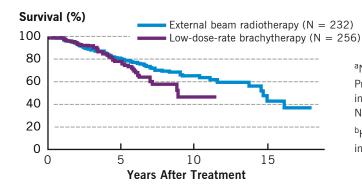
^aNational Comprehensive Cancer Network (NCCN). Prostate Cancer. NCCN Clinical Practice Guidelines in Oncology. V.2.2007. Fort Washington, PA: NCCN; 2007.

Number at Risk

External beam radiotherapy	273	109	5
Low-dose-rate brachytherapy	451	44	4

Biochemical Relapse Free Survival of Patients With High-Intermediate Risk Prostate Cancer by Treatment Type a,b (N = 488)

1996 – 2016



^aNational Comprehensive Cancer Network (NCCN). Prostate Cancer. NCCN Clinical Practice Guidelines in Oncology. V.2.2007. Fort Washington, PA: NCCN; 2007.

^bHigh-intermediate risk is defined as having ≥2 intermediate risk factors.

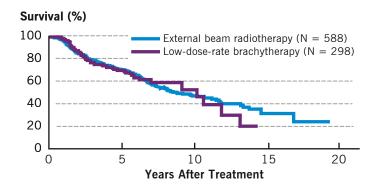
Number at Risk

External beam radiotherapy	131	48	10
Low-dose-rate brachytherapy	69	5	0

Solid Tumor Oncology | Genitourinary Cancer

Biochemical Relapse Free Survival of Patients With High-Risk Prostate Cancer by Treatment $Type^{a}$ (N = 886)

1996 – 2016



Number at Risk

External beam radiotherapy	261	28	8
Low-dose-rate brachytherapy	73	8	0

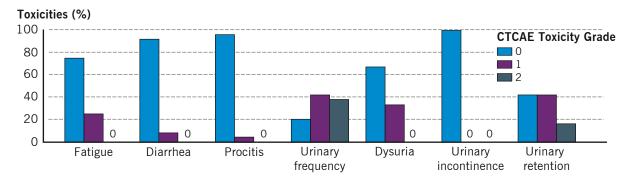
^aNational Comprehensive Cancer Network (NCCN). Prostate Cancer. NCCN Clinical Practice Guidelines in Oncology. V.2.2007. Fort Washington, PA: NCCN; 2007.

Dose-Escalated Stereotactic Body Radiation Therapy for Patients With Intermediate- and High-Risk Prostate Cancer

Patients with intermediate- and high-risk prostate cancer were treated to a minimum dose of 36.25 Gy in 5 fractions, with a simultaneous dose escalation to a dose of 50 Gy to the target volume away from a high-dose avoidance zone. Acute and late onset genitourinary and gastrointestinal toxicity outcomes were measured according to the 5-point (0-4) National Cancer Institute Common Terminology Criteria for Adverse Events toxicity scale, version 4.1

Acute Treatment-Related Adverse Events by Toxicity Type and Grade (N = 24)

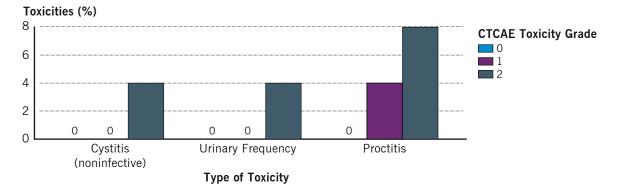
2011 - 2014



CTCAE = National Cancer Institute common terminology criteria for adverse events toxicity scale, version 4.

Late-Onset Treatment-Related Adverse Events by Toxicity Grade (N = 24)

2011 - 2014



CTCAE = National Cancer Institute common terminology criteria for adverse events toxicity scale, version 4.

Acceptably low rates of acute (< 90 days after treatment) and long-term (> 90 days after treatment) genitourinary and gastrointestinal toxicity can be achieved in patients with intermediate and high-risk prostate cancer treated without sacrificing biochemical control with stereotactic body radiation therapy.

Reference

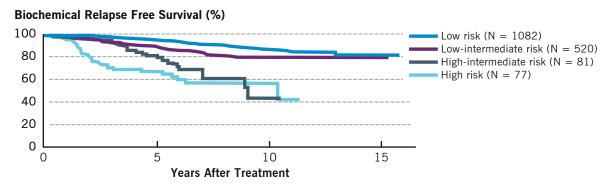
¹Kotcha R, Djemil T, Tendulark Rd, Reddy CA, Thousand RA, Vassil A, Stovsky M, Berglund RK, Klein EA, Stephans KL. Dose-escalated stereotactic body radiation therapy for patients with intermediate- and high-risk prostate cancer: initial dosimetry analysis and patient outcomes. *Int J Radiat Oncol Biol Phys.* 2016 Jul 1;95(3):960-964.

Long-Term Efficacy and Toxicity of Low-Dose-Rate ¹²⁵I Prostate Brachytherapy as Monotherapy in Prostate Cancer

A large cohort of prostate brachytherapy patients were followed up prospectively since the beginning of brachytherapy treatment at Taussig Cancer Institute. Patients were treated with ¹²⁵I brachytherapy as monotherapy up to 144 Gy.

Biochemical Relapse Free Survival in Prostate Cancer Patients Treated With Low-Dose-Rate 125 I Prostate Brachytherapy by Risk Group (N = 1760)

1996 - 2007



	5-	5-Year		10-Year	
Patients (N)	Patients at Risk (N)	Survival (%) [95% CI]	Patients at Risk (N)	Survival (%) [95% CI]	
All (1760)	1092	91.9 [90.5-93.3]	169	81.5 [78.8-84.3]	
Low risk (1082)	700	95.3 [94.0-96.7]	125	86.7 [83.5-89.9]	
Low-intermediate risk (520)	315	90.0 [87.3-92.8]	39	79.3 [74.1-84.4]	
High-intermediate risk (81)	45	80.9 [71.5-90.3]	-	-	
High risk (77)	32	67.5 [56.4-78.5]	-	-	

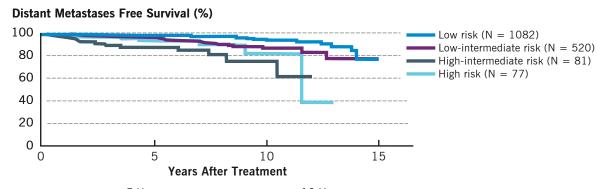
CI = confidence interval

Reference

¹Kittel JA, Reddy CA, Smith KL, Stephans KL, Tendulkar RD, Ulchaker J, Angermeier K, Campbell K, Stephenson A, Klein EA, Wilkinson DA, Ciezki JP. Long-term efficacy and toxicity of low-dose-rate ¹²⁵I prostate brachytherapy as monotherapy in low-, intermediate-, and high risk prostate cancer. *Int J Radiat Oncol Biol Phys.* 2015 Jul 15;92(4):884-893.

Distant Metastases-Free Survival in Prostate Cancer Patients Treated With Low-Dose-Rate ¹²⁵I Prostate Brachytherapy by Risk Group (N = 1760)

1996 – 2007

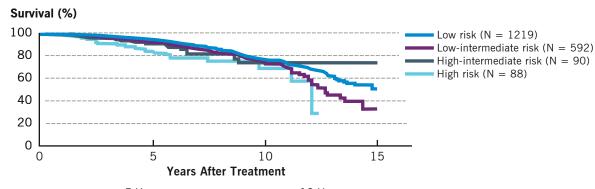


	5-	Year	10-Year	
Patients (N)	Patients at Risk (N)	Survival (%) [95% CI]	Patients at Risk (N)	Survival (%) [95% CI]
All (1760)	1160	97.8 [97.0-98.5]	206	91.5 [89.1-93.8]
Low risk (1082)	725	99.0 [98.4-99.7]	144	94.6 [92.0-97.2]
Low-intermediate risk (520)	339	96.9 [95.3-98.5]	50	88.0 [83.0-92.9]
High-intermediate risk (81)	51	94.2 [88.7-99.8]	-	-
High risk (77)	45	88.8 [81.5-96.1]	-	-

CI = confidence interval

Overall Survival in Prostate Cancer Patients Treated With Low-Dose-Rate 125 I Prostate Brachytherapy by Risk Group (N = 1989)

1996 – 2007

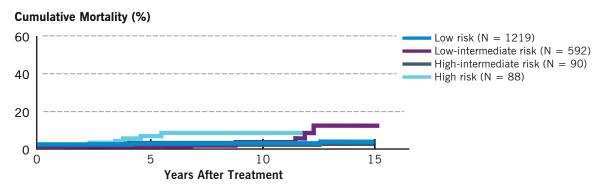


	5-	5-Year		O-Year
Patients (N)	Patients at Risk (N)	Survival (%) [95% CI]	Patients at Risk (N)	Survival (%) [95% CI]
All (1989)	1443	93.7 [92.6-94.9]	356	76.1 [73.4-78.9]
Low risk (1219)	896	95.0 [93.7-96.3]	248	77.6 [74.2-80.9]
Low-intermediate risk (592)	425	92.8 [90.6-95.0]	87	74.1 [68.6-79.7]
High-intermediate risk (90)	65	91.1 [84.7-97.4]	11	75.4 [63.0-87.8]
High risk (88)	57	84.5 [76.5-92.6]	10	70.6 [56.7-84.4]

CI = confidence interval

Cumulative Incidence of Prostate Cancer-Specific Mortality in Patients Treated With Low-Dose-Rate 125 I Prostate Brachytherapy by Risk Group (N = 1989)

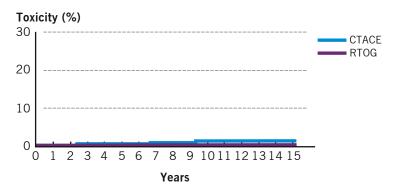
1996 – 2007



	5-	5-Year		10-Year	
Patients (N)	Patients at Risk (N)	Survival (%) [95% CI]	Patients at Risk (N)	Survival (%) [95% CI]	
All (1989)	1443	0.71 [0.32-1.10]	356	2.53 [1.53-3.53]	
Low risk (1219)	896	0.29 [0.00-0.63]	248	2.07 [0.88-3.26]	
Low-intermediate risk (592)	425	0.40 [0.00-0.96]	87	2.57 [0.69-4.45]	
High-intermediate risk (90)	65	2.63 [0.00-6.23]	11	2.63 [0.00-6.23]	
High risk (88)	57	6.51 [0.98-12.03]	10	8.05 [1.84-14.25]	

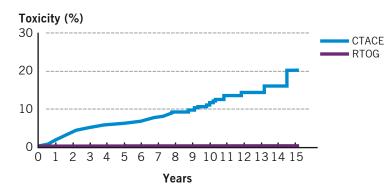
CI = confidence interval

Late Grade ≥3 Gastrointestinal Toxicity in Patients Treated With Low-Dose-Rate ¹²⁵I Prostate Brachytherapy (N = 1989) 1996 – 2007



CTACE = National Cancer Institute common terminology criteria for adverse events toxicity scale, version 4 RTOG = Radiation Therapy Oncology Group

Late Grade ≥3 Genitourinary Toxicity in Patients Treated With Low-Dose-Rate ¹²⁵I Prostate Brachytherapy (N = 1989) 1996 – 2007

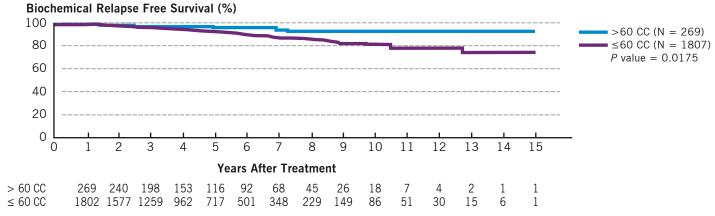


CTACE = National Cancer Institute common terminology criteria for adverse events toxicity scale, version 4 RTOG = Radiation Therapy Oncology Group

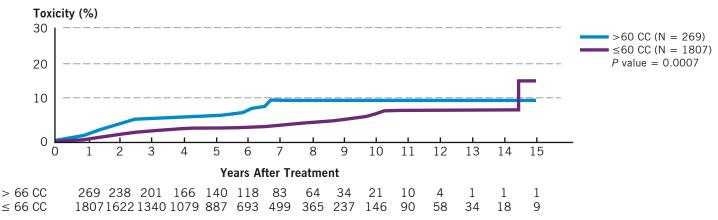
Overall, results show that prostate brachytherapy is effective and has low rates of late toxicity when performed as monotherapy.

A large cohort of patients with stage T1-T2Nx M0 low- and intermediate-risk prostate cancer who underwent low-dose-rate permanent prostate brachytherapy (PPB) with ¹²⁵I was followed up prospectively in a registry to determine the efficacy and toxicity of PPB based on prostate size.¹

Biochemical Relapse Free Survival in Patients With Stage T1a-T2Nx M0 Low- and Intermediate-Risk Prostate Cancer Treated with Permanent Prostate Brachytherapy Alone Without Androgen Deprivation Therapy by Gland Volume (N = 2076) 1996 – 2012



Late Grade ≥3 Genitourinary Toxicity in Patients With Stage T1a-T2Nx M0 Low- and Intermediate-Risk Prostate Cancer Treated with Permanent Prostate Brachytherapy Alone Without Androgen Deprivation Therapy by Gland Volume (N = 2076) 1996 – 2012



Long-term data indicate PPB implantation of large prostates > 60 cc results in favorable bRFS outcomes and is associated with increased, but acceptable, rates of Grade 3 and higher late genitourinary toxicities.

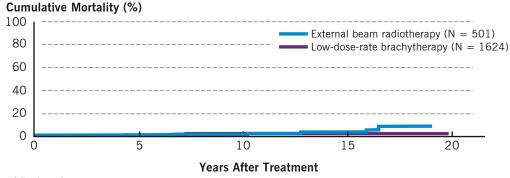
Reference

90

¹Pham YD, Kittel JA, Reddy CA, Ciezki JP, Klein EA, Stephans KL, Tendulkar RD. Outcomes for prostate glands > 60 cc treated with low-dose-rate brachytherapy. *Brachytherapy*. 2016 Mar-Apr;15(2):163-168.

Cumulative Mortality Due to Prostate Cancer of Patients With Low-Risk Prostate Cancer by Treatment $Type^{a}$ (N = 2125)

1996 – 2016

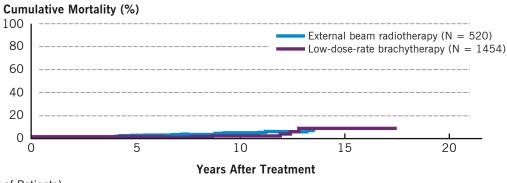


Mortality Rates (Number of Patients)

External beam radiotherapy 0.9 (381) 1.7 (208) 3.1 (36) Low-dose-rate brachytherapy 0.3 (918) 2.1 (223) 2.4 (27)

Cumulative Mortality Due to Prostate Cancer of Patients With Intermediate-Risk Prostate Cancer by Treatment Type a (N = 1974)

1996 – 2016



Mortality Rates (Number of Patients)

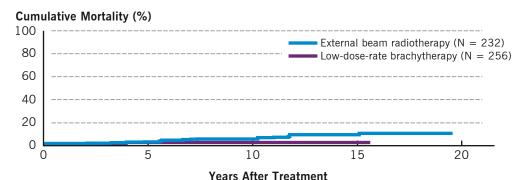
External beam radiotherapy 2.0 (359) 5.0 (181) 8.5 (19) Low-dose-rate brachytherapy 0.2 (550) 2.5 (86) 8.2 (5)

^aNational Comprehensive Cancer Network (NCCN). Prostate Cancer. NCCN Clinical Practice Guidelines in Oncology. V.2.2007. Fort Washington, PA: NCCN; 2007.

^aNational Comprehensive Cancer Network (NCCN). Prostate Cancer. NCCN Clinical Practice Guidelines in Oncology. V.2.2007. Fort Washington, PA: NCCN; 2007.

Cumulative Mortality Due to Prostate Cancer of Patients With High-Intermediate Risk Prostate Cancer by Treatment Type a,b (N = 488)

1996 – 2016



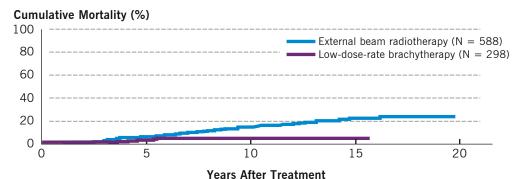
Mortality Rates (Number of Patients)

External beam radiotherapy	2.9 (178)	5.1 (96)	9.7 (31)
Low-dose-rate brachytherapy	2.1 (103)	2.1 (21)	2.1 (2)

^aNational Comprehensive Cancer Network (NCCN). Prostate Cancer. NCCN Clinical Practice Guidelines in Oncology. V.2.2007. Fort Washington, PA: NCCN; 2007.

Cumulative Mortality Due to Prostate Cancer of Patients with High Risk Prostate Cancer by Treatment $Type^{a}$ (N = 886)

1996 - 2016



Mortality Rates (Number of Patients)

External beam radiotherapy	6.2 (409)	14.6 (207)	21.8 (44)
Low-dose-rate brachytherapy	3.8 (126)	5.3 (22)	5.3 (1)

^aNational Comprehensive Cancer Network (NCCN). Prostate Cancer. NCCN Clinical Practice Guidelines in Oncology. V.2.2007. Fort Washington, PA: NCCN; 2007.

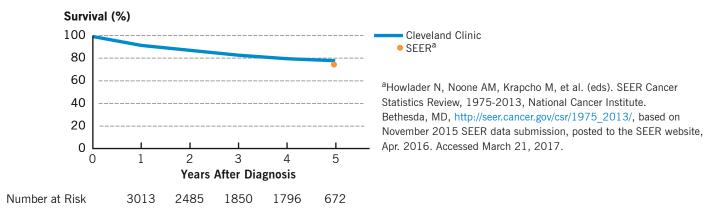
92

^bHigh-intermediate risk is defined as having ≥2 intermediate risk factors.

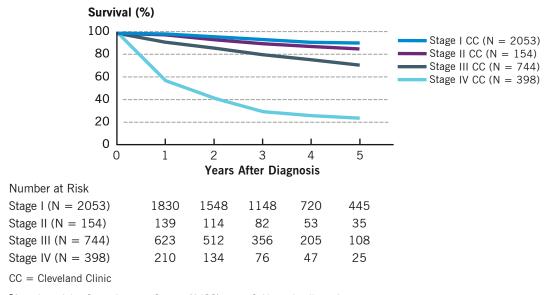
Renal Cancer

Five-Year Overall Survival of Patients With All Stages of Renal Cell Cancer (N = 3593)

2007 - 2015



Five-Year Overall Survival of Patients With Renal Cell Cancer by Stage a at Diagnosis (N = 3349) 2007 - 2015

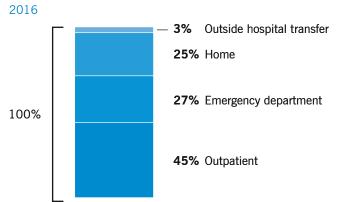


^aAmerican Joint Committee on Cancer (AJCC) stage 0-V renal cell carcinoma

Palliative Medicine

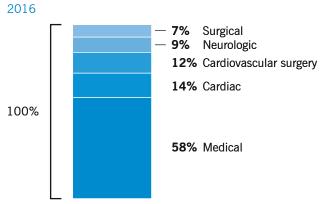
Patients with a complex, life-threatening, cancer-related illness often have unrelieved symptoms and significant physical difficulties. The Harry R. Horvitz Center for Palliative Medicine, part of Taussig Cancer Institute, is one of only a few comprehensive and integrated palliative cancer care programs in the country. The program is recognized as a European Society for Medical Oncology Designated Centre of Integrated Oncology and Palliative Care, and is also a World Health Organization demonstration project for palliative care.

Source of Admission to the Palliative Medicine Inpatient Unit (N = 472)



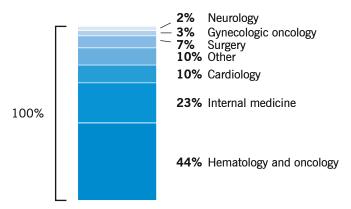
Of 472 patients admitted to the palliative medicine unit, 97% were patients with a cancer diagnosis.

Source of Intensive Care Unit Referrals to Palliative Medicine (N=498)



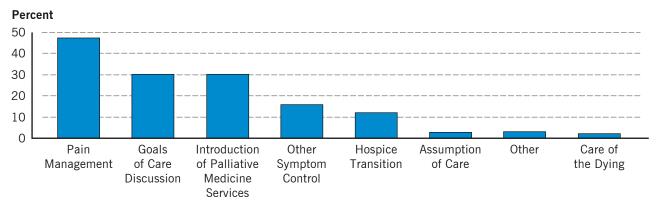
Source of Inpatient Referrals to Palliative Medicine (N = 1682)

2016



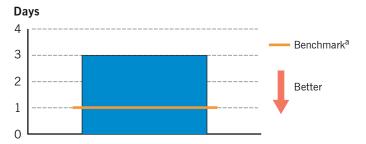
Reasons for Inpatient Palliative Medicine Consultation (N=1682)

2016



Palliative Medicine

Median Time to Palliative Medicine Consult (N = 1184) 2016

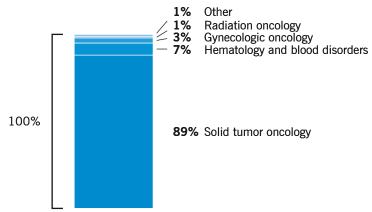


The median number of days from referral to palliative medicine consult was 3, compared with a median of 1 day as published in a multi-institution study. Studies indicate that early palliative care is associated with improved outcomes and reduced cost of care.

Reference

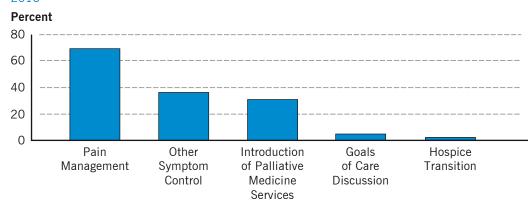
^aMay P, Garrido MM, Cassel JB, Kelley AS, Meier DE, Normand C, Smith TJ, Stefanis L, Morrison RS. Prospective cohort study of hospital palliative care teams for inpatients with advanced cancer: earlier consultation is associated with larger cost-saving effect. *J Clin Oncol.* 2015 Sep 1;33(25):2745-2752.

Source of Outpatient Referrals to Palliative Medicine (N = 568)2016



Reasons for Outpatient Palliative Medicine Consultation (N = 568)

2016



Advance care planning is the process of establishing a patient's goals and preferences for future care. Admission to and discharge from Taussig Cancer Institute's palliative medicine service are critical opportunities to discuss advance directives with patients.

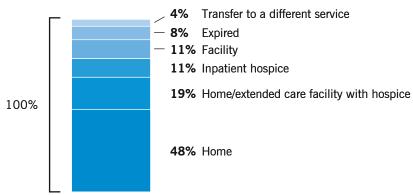
Advance Directives Discussed With Patient (N = 1275)





Discharge Disposition of Palliative Medicine Patients a (N = 598)



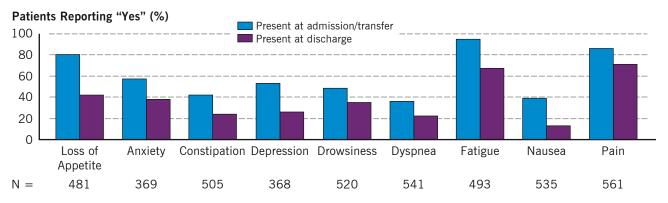


^aIncludes transfers and carryovers from previous year

Palliative Medicine

Symptoms Present at Admission and Discharge (N = 617)

2016

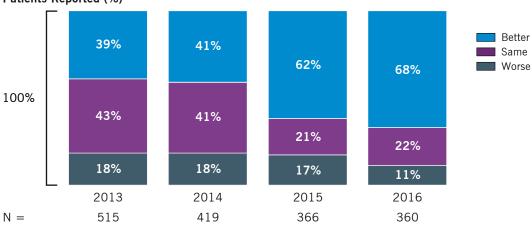


Symptoms were assessed and reported for 617 inpatients in 2016, including symptoms data for expired patients up to the time of death.

Loss of Appetite Status at Discharge

2013 - 2016

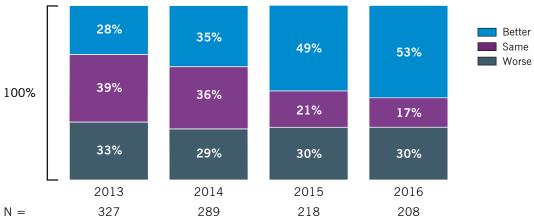




Anxiety Status at Discharge

2013 – 2016

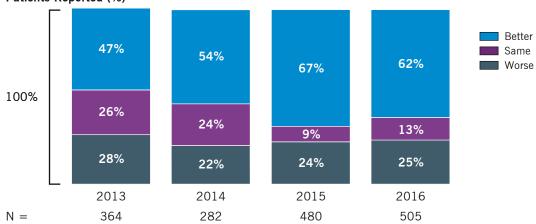
Patients Reported (%)



Constipation Status at Discharge

2013 – 2016

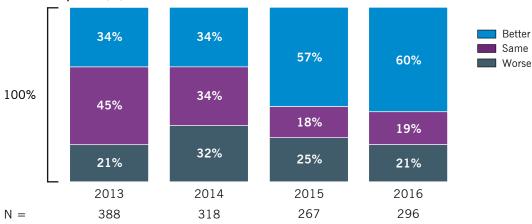
Patients Reported (%)



Palliative Medicine

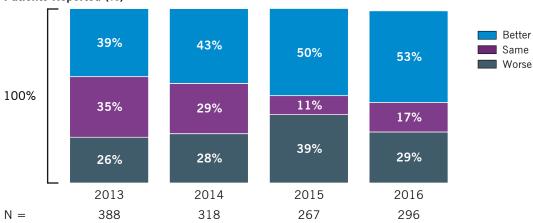
Depression Status at Discharge 2013 – 2016





Drowsiness Status at Discharge 2013 – 2016

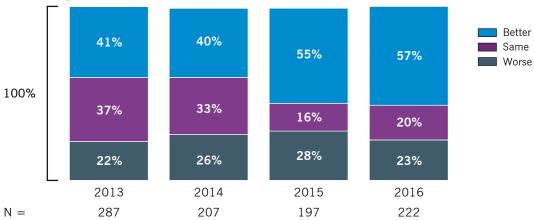
Patients Reported (%)



Dyspnea Status at Discharge

2013 – 2016

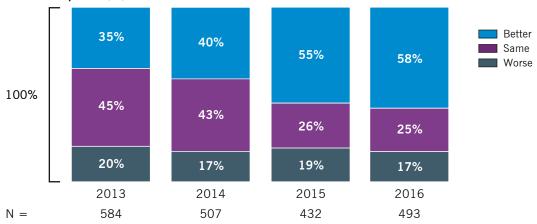
Patients Reported (%)



Fatigue Status at Discharge

2013 - 2016

Patients Reported (%)

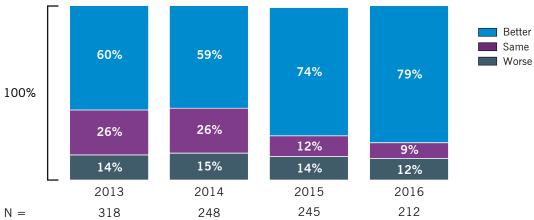


Palliative Medicine

Nausea Status at Discharge

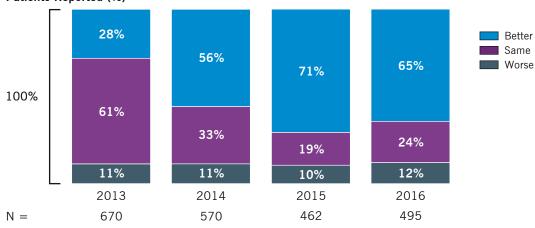
2013 - 2016





Pain Status at Discharge 2013 – 2016

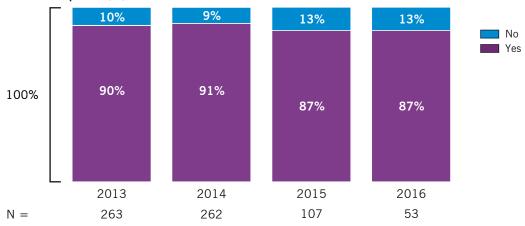
Patients Reported (%)



Comfortable End-of-Life Care

2013 - 2016

Patients Reported (%)



In this case, comfort is reported by caregivers for patients receiving comfort measures prior to death in the hospital or while awaiting discharge planning/placement.

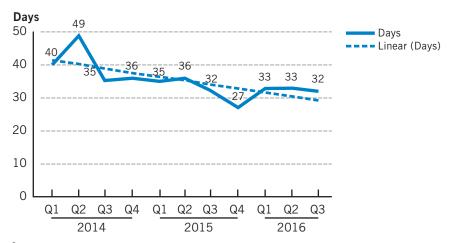
Institute Quality Improvement

Cleveland Clinic strives to deliver the best possible care to patients with cancer and empower employees to actively evaluate and improve the patient experience. Efforts to improve the quality of care and patient experience include soliciting direct feedback from our patients, regular monitoring of patient ratings of their care and patient outcomes, continuous improvement processes, reorganization of the delivery of care, and resource management. Below are examples of 2016 quality initiatives.

Time to Treatment

An initial diagnosis of cancer is a time when patients are often desperate for answers. Reducing this stress and anxiety by ensuring patients begin treatment as quickly as possible is a Taussig Cancer Institute imperative. Using the institute's Cancer Tumor Registry and proprietary Cancer Data Warehouse, the difference between the date of first positive biopsy and the first day the patient received any cancer-related treatment is measured quarterly for all patients diagnosed with or treated for cancer at Cleveland Clinic's main campus or family health centers.

Median Days to First Treatment by Quarter (N = 12,180) $2014 - 2016^a$



^aData are not yet available for 4Q 2016.

After median days to first treatment is calculated for all disease groups, the multidisciplinary teams work to increase access and improve efficiency to reduce the time to treatment. These intensive efforts to identify and solve institutional causes for treatment delays have reduced the median time to treatment initiation from 40 days to 32 days.

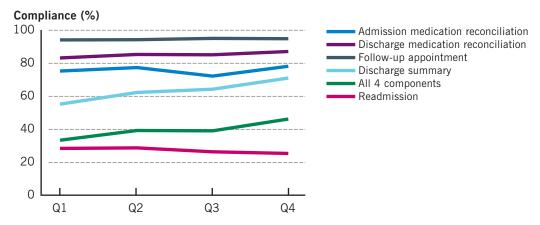
1. Bolwell BJ, Khorana AA. Enhancing value for patients with cancer: Time to treatment as a surrogate for integrated cancer care. *J Natl Compr Canc Netw.* 2016 Jan;14(1):115-116.

Focus on "Core 4" Reduces Unplanned Hospital Readmissions

Many factors that lead to readmission of cancer patients are nonmodifiable or treatment related. ¹⁻² Taussig Cancer Institute used Epic's Discharge Readiness Tool to better understand the role discharge planning and follow-up plays in unplanned readmissions. Efforts were focused on the "Core 4" issues linked to readmission:

- · Admission medication reconciliation completed and signed within 24 hours of admission
- Discharge medication reconciliation completed and signed by provider
- Follow-up appointment ordered or any appointment within 45 days
- Discharge summary signed within 48 hours of discharge

Compliance With "Core 4" Discharge Issues Compared With Readmission Rates 2016



Increased compliance in these 4 core areas moderately reduced readmissions. Results indicate that enhanced communication within care teams and well-coordinated transitions of care have a moderate impact on the number of unplanned readmissions.

- 1. Brown EG, Burgess D, Li CS, et al. Hospital readmissions: necessary evil or preventable target for quality improvement. *Ann Surg.* 2014 Oct;260(4):583-591.
- 2. Donzé JD, Lipsitz S, Schnipper JL. Risk factors and patterns of potentially avoidable readmission in patients with cancer. *J Oncol Pract*. 2017 Jan;13(1):e68-e76.

Patient Experience — Taussig Cancer Institute

Keeping patients at the center of all that Cleveland Clinic does is critical. Patients First is the guiding principle at Cleveland Clinic. Patients First is safe care, high-quality care, in the context of patient satisfaction, and high value. Ultimately, caregivers have the power to impact every touchpoint of a patient's journey, including their clinical, physical, and emotional experience.

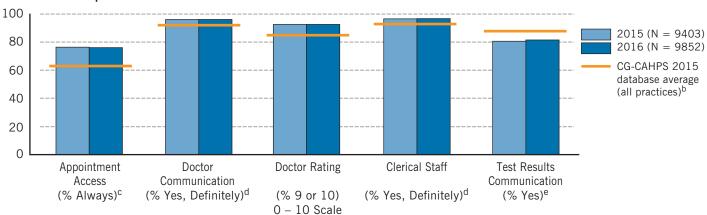
Cleveland Clinic recognizes that patient experience goes well beyond patient satisfaction surveys. Nonetheless, sharing the survey results with caregivers and the public affords opportunities to improve how Cleveland Clinic delivers exceptional care.

Outpatient Office Visit Survey — Taussig Cancer Institute

CG-CAHPS Assessment^a

2015 - 2016

Percent Best Response



^aIn 2013, Cleveland Clinic began administering the Clinician and Group Practice Consumer Assessment of Healthcare Providers and Systems surveys (CG-CAHPS), standardized instruments developed by the Agency for Healthcare Research and Quality (AHRQ) and supported by the Centers for Medicare & Medicaid Services for use in the physician office setting to measure patients' perspectives of outpatient care.

Source: Press Ganey, a national hospital survey vendor

^bBased on results submitted to the AHRQ CG-CAHPS database from 2829 practices in 2015

^cResponse options: Always, Usually, Sometimes, Never

dResponse options: Yes, definitely; Yes, somewhat; No

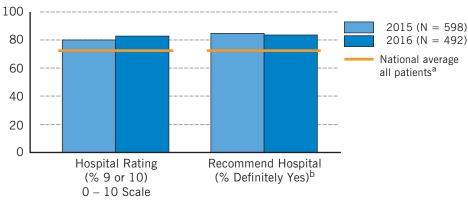
^eResponse options: Yes, No

Inpatient Survey — Taussig Cancer Institute

HCAHPS Overall Assessment

2015 - 2016

Best Response (%)



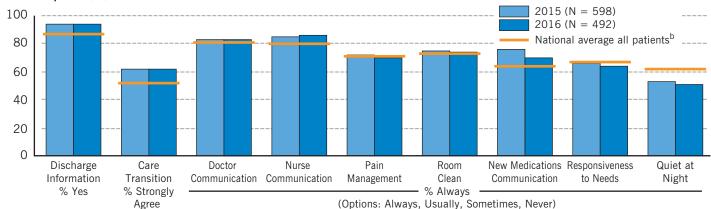
^aBased on national survey results of discharged patients, January 2015 – December 2015, from 4172 US hospitals. medicare.gov/hospitalcompare

The Centers for Medicare & Medicaid Services requires United States hospitals that treat Medicare patients to participate in the national Hospital Consumer Assessment of Healthcare Providers and Systems (HCAHPS) survey, a standardized tool that measures patients' perspectives of hospital care. Results collected for public reporting are available at medicare.gov/ hospitalcompare.

HCAHPS Domains of Care^a

2015 - 2016

Best Response (%)



^aExcept for "Room Clean" and "Quiet at Night," each bar represents a composite score based on responses to multiple survey questions.

^bBased on national survey results of discharged patients, January 2015 – December 2015, from 4172 US hospitals. medicare.gov/hospitalcompare

Source: Press Ganey, a national hospital survey vendor, 2016

^bResponse options: Definitely yes, Probably yes, Probably no, Definitely no

Cleveland Clinic — Implementing Value-Based Care

Overview

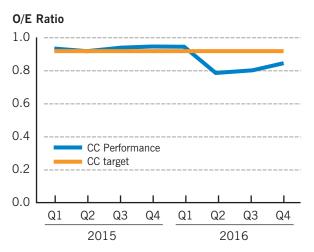
Cleveland Clinic health system uses a systematic approach to performance improvement while simultaneously pursuing 3 goals: improving the patient experience of care (including quality and satisfaction), improving population health, and reducing the cost of healthcare. The following measures are examples of 2016 focus areas in pursuit of this 3-part aim. Throughout this section, "Cleveland Clinic" refers to the academic medical center or "main campus," and those results are shown.

Real-time data are leveraged in each Cleveland Clinic location to drive performance improvement. Although not an exact match to publicly reported data, more timely internal data create transparency at all organizational levels and support improved care in all clinical locations.

Improve the Patient Experience of Care

Cleveland Clinic Overall Mortality Ratio

2015 - 2016



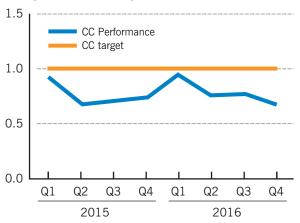
Source: Data from the Vizient Clinical Data Base/Resource ManagerTM used by permission of Vizient, All rights reserved.

Cleveland Clinic's observed/expected (O/E) mortality ratio outperformed its internal target derived from the Vizient 2016 risk model. Ratios less than 1.0 indicate mortality performance "better than expected" in Vizient's risk adjustment model.

Cleveland Clinic Central Line-Associated Bloodstream Infection, reported as Standardized Infection Ratio (SIR)

2015 - 2016

Rate per 1000 Line Days

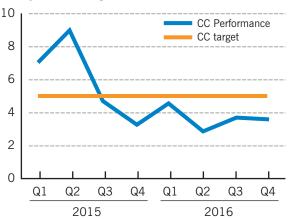


Cleveland Clinic has implemented several strategies to reduce central line-associated bloodstream infections (CLABSIs), including a central-line bundle of insertion, maintenance, and removal best practices. Focused reviews of every CLABSI occurrence support reductions in CLABSI rates in the high-risk critical care population.

Cleveland Clinic Postoperative Respiratory Failure Risk-Adjusted Rate

2015 - 2016

Rate per 1000 Eligible Patients

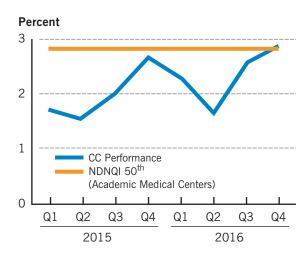


Source: Data from the Vizient Clinical Data Base/Resource ManagerTM used by permission of Vizient. All rights reserved.

Efforts continue toward reducing intubation time, assessing readiness for extubation, and preventing the need for reintubation. Cleveland Clinic has leveraged the technology within the electronic medical record to support ongoing improvement efforts in reducing postoperative respiratory failure (AHRQ Patient Safety Indicator 11). Prevention of respiratory failure remains a safety priority for Cleveland Clinic.

Cleveland Clinic Hospital-Acquired Pressure Ulcer Prevalence (Adult)

2015 - 2016



Source: Data reported from the National Database for Nursing Quality Indicators[®] (NDNQI[®]) with permission from Press Ganey.

A pressure ulcer is an injury to the skin that can be caused by pressure, moisture, or friction. These sometimes occur when patients have difficulty changing position on their own. Cleveland Clinic caregivers have been trained to provide appropriate skin care and regular repositioning while taking advantage of special devices and mattresses to reduce pressure for high-risk patients. In addition, they actively look for hospital-acquired pressure ulcers and treat them quickly if they occur.

Cleveland Clinic strategies to mitigate the risk of these pressure injuries include routine rounding to accurately stage pressure injuries, monthly multidisciplinary wound care meetings, and ongoing nursing education, both in the classroom and at the bedside.

Cleveland Clinic — Implementing Value-Based Care

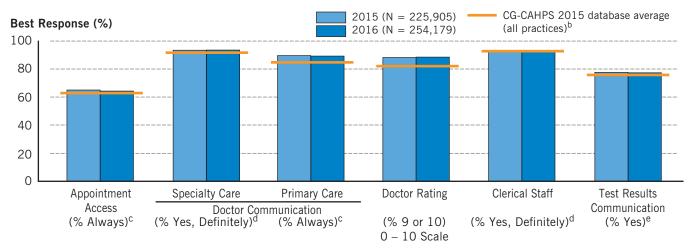
Keeping patients at the center of all that we do is critical. Patients First is the guiding principle at Cleveland Clinic. Patients First is safe care, high-quality care, in the context of patient satisfaction, and high value. Ultimately, our caregivers have the power to impact every touch point of a patient's journey, including their clinical, physical, and emotional experience.

We know that patient experience goes well beyond patient satisfaction surveys. Nonetheless, by sharing the survey results with our caregivers and the public, we constantly identify opportunities to improve how we deliver exceptional care.

Outpatient Office Visit Survey — Cleveland Clinic

CG-CAHPS Assessment^a

2015 - 2016



^aIn 2013, Cleveland Clinic began administering the Clinician and Group Practice Consumer Assessment of Healthcare Providers and Systems surveys (CG-CAHPS), standardized instruments developed by the Agency for Healthcare Research and Quality (AHRQ) and supported by the Centers for Medicare & Medicaid Services for use in the physician office setting to measure patients' perspectives of outpatient care.

Source: Press Ganey, a national hospital survey vendor

^bBased on results submitted to the AHRQ CG-CAHPS database from 2829 practices in 2015

^cResponse options: Always, Usually, Sometimes, Never

^dResponse options: Yes, definitely; Yes, somewhat; No

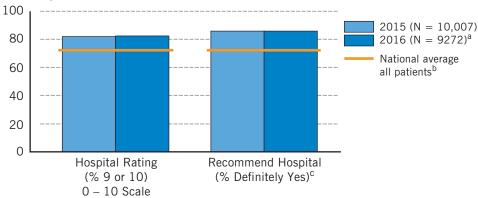
^eResponse options: Yes, No

Inpatient Survey — Cleveland Clinic

HCAHPS Overall Assessment

2015 - 2016

Best Response (%)



^aAt the time of publication, 2016 ratings have not been reported by the Centers for Medicare & Medicaid Services and ratings are not adjusted for patient mix.

^bBased on national survey results of discharged patients, January 2015 – December 2015, from 4172 US hospitals. medicare.gov/hospitalcompare

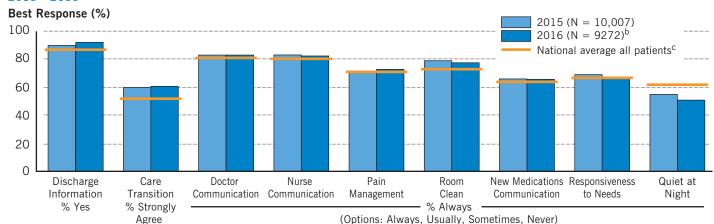
^cResponse options: Definitely yes, Probably yes, Probably no, Definitely no

& Medicaid Services requires United States hospitals that treat Medicare patients to participate in the national Hospital Consumer Assessment of Healthcare Providers and Systems (HCAHPS) survey, a standardized tool that measures patients' perspectives of hospital care. Results collected for public reporting are available at medicare.gov/hospitalcompare.

The Centers for Medicare

HCAHPS Domains of Care^a

2015 - 2016



^aExcept for "Room Clean" and "Quiet at Night," each bar represents a composite score based on responses to multiple survey questions.

^bAt the time of publication, 2016 ratings have not been reported by the Centers for Medicare & Medicaid Services and ratings are not adjusted for patient mix.

Source: Centers for Medicare & Medicaid Services, 2015: Press Ganey, a national hospital survey vendor, 2016

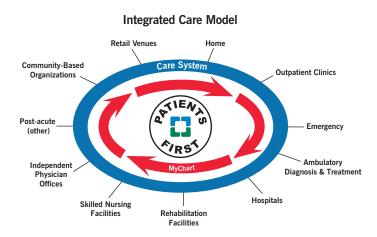
^cBased on national survey results of discharged patients, January 2015 – December 2015, from 4172 US hospitals. medicare.gov/hospitalcompare

Cleveland Clinic — Implementing Value-Based Care

Focus on Value

Cleveland Clinic has developed and implemented new models of care that focus on "Patients First" and aim to deliver on the Institute of Medicine goal of Safe, Timely, Effective, Efficient, Equitable, Patient-centered care. Creating new models of Value-Based Care is a strategic priority for Cleveland Clinic. As care delivery shifts from fee-for-service to a population health and bundled payment delivery system, Cleveland Clinic is focused on concurrently improving patient safety, outcomes, and experience.

What does this new model of care look like?



The Cleveland Clinic Integrated Care Model (CCICM) is a value-based model of care, designed to improve outcomes while reducing cost. It is designed to deliver value in both population health and specialty care.

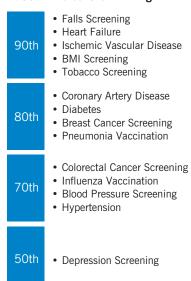
- The patient remains at the heart of the CCICM.
- The blue band represents the care system, which is a seamless pathway that patients move along as they receive care in different settings. The care system represents integration of care across the continuum.
- Critical competencies are required to build this new care system. Cleveland Clinic is creating disease- and
 condition-specific care paths for a variety of procedures and chronic diseases. Another facet is implementing
 comprehensive care coordination for high-risk patients to prevent unnecessary hospitalizations and emergency
 department visits. Efforts include managing transitions in care, optimizing access and flow for patients through the
 CCICM, and developing novel tactics to engage patients and caregivers in this work.
- Measuring performance around quality, safety, utilization, cost, appropriateness of care, and patient and caregiver experience is an essential component of this work.

Improve Population Health

Cleveland Clinic Accountable Care Organization Measure Performance

2016

National Percentile Ranking



Higher percentiles are better

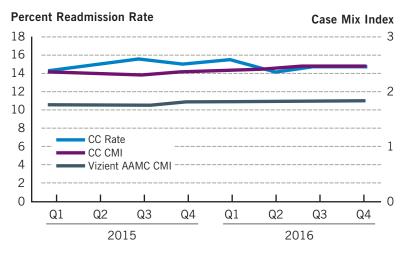
As part of Cleveland Clinic's commitment to population health and in support of its Accountable Care Organization (ACO), these ACO measures have been prioritized for monitoring and improvement. Cleveland Clinic is improving performance in these measures by enhancing care coordination, optimizing technology and information systems, and engaging primary care specialty teams directly in the improvement work. These pursuits are part of Cleveland Clinic's overall strategy to transform care in order to improve health and make care more affordable.

Cleveland Clinic — Implementing Value-Based Care

Reduce the Cost of Care

Cleveland Clinic All-Cause 30-Day Readmission Rate to Any Cleveland Clinic Hospital

2015 - 2016

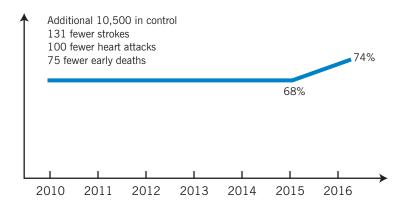


CMI = case mix index

Source: Data from the Vizient Clinical Data Base/Resource ManagerTM used by permission of Vizient. All rights reserved.

Cleveland Clinic monitors 30-day readmission rates for any reason to any of its system hospitals. Unplanned readmissions are actively reviewed for improvement opportunities. Comprehensive care coordination and care management for high-risk patients has been initiated in an effort to prevent unnecessary hospitalizations and emergency department visits. Sicker, more complex patients are more susceptible to readmission. Case mix index (CMI) reflects patient severity of illness and resource utilization. Cleveland Clinic's CMI remains one of the highest among American academic medical centers.

Accountable Care Organization (ACO) Improving Outcomes and Reducing Costs



Cleveland Clinic was one of the top performing new ACOs in the United States (for 2015 performance as determined in 2016) due to efficiency, cost reduction, and improvements in effectiveness of chronic disease management such as treating hypertension, reducing preventable hospitalizations through care coordination, and optimizing the care at skilled nursing facilities through its Connected Care program.

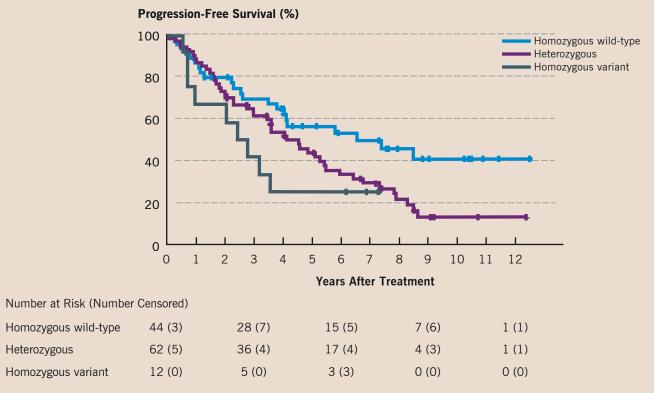
For example, a system-wide effort to improve the control of blood pressure for patients hypertension was begun in 2016 and resulted in an additional 10,500 patients with blood pressure controlled. This will translate to many fewer strokes, heart attacks, and preventable deaths.

Innovations

Androgen-Enhancing Gene Mutation Reduces Prostate Cancer Survival

A multicohort study determined prostate cancer patients with the inherited gene variant *HSD3B1* (1245C), which enhances androgen synthesis, are likely to develop tumors with more rapid resistance to androgen deprivation therapy (ADT). Cleveland Clinic researchers analyzed the outcomes of 443 prostate cancer patients based on genotype, and found the variant *HSD3B1* (1245C) allele was a strong predictor of which patients developed more rapid resistance to ADT. The investigators speculate that this genotyping could help personalize treatments by identifying which patients might benefit from early escalated therapy with androgen axis inhibiting drugs. Cleveland Clinic Cancer Center has begun a clinical trial to test whether escalated therapy in patients with this variant reverses the adverse biology.

Progression-Free Survival According to *HSD3B1* Genotype (N = 118) 1996 – 2009

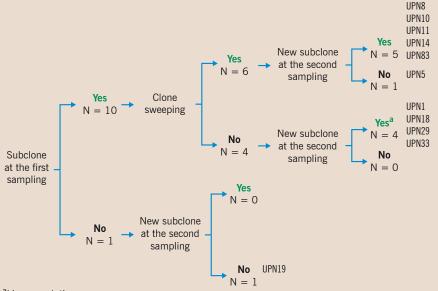


¹Hearn JW, AbuAli G, Reichard CA, Reddy CA, Magi-Galluzzi C, Chang KH, Carlson R, Rangel L, Reagan K, Davis BJ, Karnes RJ, Kohli M, Tindall D, Klein EA, Sharifi N. *HSD3B1* and resistance to androgen-deprivation therapy in prostate cancer: a retrospective, multicohort study. *Lancet Oncol*. 2016 Oct;17(10):1435-1444.

Dynamics of Clonal Evolution in Myelodysplastic Syndromes

To better understand the progression of myelodysplastic syndromes (MDS), in terms of gene mutations and their clonal architecture dynamics, Cleveland Clinic researchers, led by Jaroslaw P. Maciejewski, MD, PhD, analyzed the results of whole-exome sequencing and/or targeted deep sequencing from the largest set of MDS samples ever assembled. Results of the molecular analysis parallel the risk classification of MDS, showing that progression steps defined by pathologic criteria are accompanied or mediated by distinct molecular changes. The driver genes can be classified into molecular subtypes differentially associated with lower-risk MDS, higher-risk MDS, or secondary acute myeloid leukemia. This new categorization provides insights into clonal dynamics and allows the use of subclonal events as MDS progression biomarkers.

Summary of Longitudinally Collected Samples Analyzed by Whole-Exome Sequencing



^aLinear evolution

Radium 223 Dichloride for Osteoblastic Osteosarcoma and Other Bone Metastases

The osteoblastic activity of osteosarcoma makes it ideally suited for treatment with radium 223 dichloride (²²³RaCl₂), a bone-seeking pharmaceutical that emits high-energy alpha particles that cause difficultto-repair double strand breaks with low toxicity. The US Food and Drug Administration approved the use of ²²³RaCl₂ to treat prostate cancer with osteoblastic metastases. In November 2016, the National Comprehensive Cancer Network altered its bone tumor guidelines to include ²²³RaCl₂ as a level 2A recommendation for second and subsequent relapsed osteosarcoma. Research conducted by Taussig Cancer Institute's Peter Anderson, MD, was key in bringing about this change. This should ease the prior authorization process, making the treatment more widely available to patients.

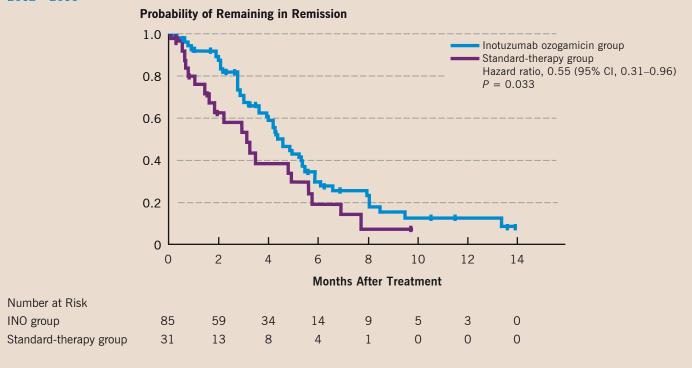
¹Makishima H, Yoshizato T, Yoshida K, Sekeres MA, Radivoyevitch T, Suzuki H, Przychodzen B, Nagata Y, Meggendorfer M, Sanada M, Okuno Y, Hirsch C, Kuzmanovic T, Sato Y, Sato-Otsubo A, LaFramboise T, Hosono N, Shiraishi Y, Chiba K, Haferlach C, Kern W, Tanaka H, Shiozawa Y, Gomez-Segui I, Husseinzadeh HD, Thota S, Guinta KM, Dienes B, Nakamaki T, Miyawaki S, Saunthararajah Y, Chiba S, Miyano S, Shih LY, Haferlach T, Ogawa S, Maciejewski JP. Dynamics of clonal evolution in myelodysplastic syndromes. *Nat Genet*. 2017 Feb;49(2):204-212.

Innovations

Novel Agent Holds Promise for Refractory/Relapsed Acute Lymphoblastic Leukemia

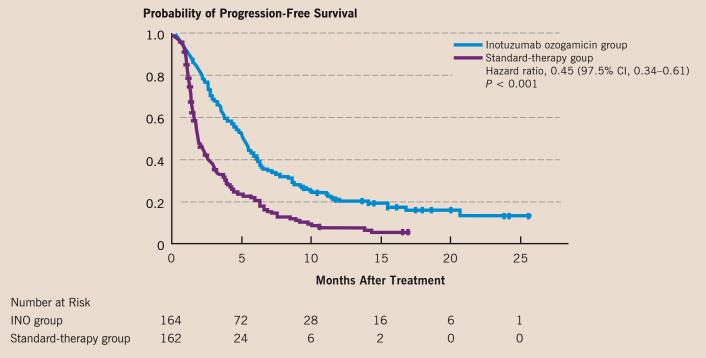
Through an international phase 3 clinical trial co-led by Anjali S. Advani, MD, researchers compared the outcomes of inotuzumab ozogamicin vs standard therapy in patients with relapsed or refractory acute lymphoblastic leukemia (ALL). Inotuzumab ozogamicin, an antibody-drug conjugate, produces significantly better results than standard chemotherapy, with a higher complete remission rate, less residual disease, and longer progression-free and overall survival. The findings are welcome news, since many ALL patients relapse after first-line therapy, and salvage therapies are often unsuccessful in producing complete remission, which is typically a prerequisite for allogeneic hematopoietic stem cell transplantation.

Probability of Remaining in Remission Among Patients Treated With Inotuzumab Ozogamicin vs Standard Therapy (N = 218)



INO = inotuzumab ozogamicin

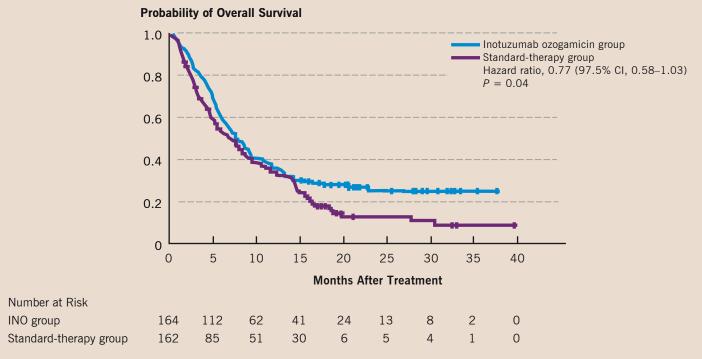
Probability of Progression-Free Survival in Patients Treated With Inotuzumab Ozogamicin vs Standard Therapy (N = 326) 2012 - 2016



INO = inotuzumab ozogamicin

Innovations

Probability of Overall Survival in Patients Treated With Inotuzumab Ozogamicin vs Standard Therapy (N = 326) 2012 - 2016



INO = inotuzumab ozogamicin

¹Kantarjian HM, DeAngelo DJ, Stelljes M, Martinelli G, Liedtke M, Stock W, Gökbuget N, O'Brien S, Wang K, Wang T, Paccagnella ML, Sleight B, Vandendries E, Advani AS. Inotuzumab ozogamicin versus standard therapy for acute lymphoblastic leukemia. *N Engl J Med*. 2016 Aug 25;375(8):740-753.

Genetic Basis for Cancer Cells' Vulnerability to DNA Damage Identified

Mohamed Abazeed, MD, PhD, co-led a multi-institutional team of researchers that identified genetic determinants that enable cancer cells to survive radiation exposure. Researchers collected 553 genetically profiled human tumor-derived cell lines and found that overall and individual somatic copy number alterations, gene mutations, and the expression of individual genes and gene sets correlated with cancer cells' ability to survive radiation exposure. Characterizing genetic factors that dictate cellular response to radiation is a first step toward personalized, genetically targeted cancer therapies.

Survival d(dose) IC P value **FDR** TPR^b -0.188 3.08x10⁻⁵ 0 **Nuclear architecture** -0.199 3.08x10⁻⁵ FLNA^b 0 Cvtoskeleton -0.173 3.08e⁻⁰⁵ 0.0167 **FLNC** p53-binding protein TP53BP1b -0.193 3.08x10⁻⁵ 0 -0.191 3.08x10⁻⁵ **Telomere maintenance** RIF1b 0 -0.176 3.08e⁻⁰⁵ **МСМЗАР** 0.0167 mRNA nuclear export -0.199 3.08x10⁻⁵ Nonsense-mediated decay SMG1b -0.183 3.08x10⁻⁵ 0 RANBP9b Alternative splicing -0.172 3.08e⁻⁰⁵ 0.0167 SMARCA4b Chromatin remodeling –0.175 3.08e⁻⁰⁵ 0.0167 STAG3b Chromatid cohesion -0.179 3.08x10⁻⁵ **Oxidative stress** SHC1 -0.192 3.08x10⁻⁵ Lipid metabolism LRP1 -0.177 3.08e⁻⁰⁵ 0.0167 MLLT4 Cell-cell adhesion -0.194 3.08x10⁻⁵ SULF1 0 -0.185 3.08x10⁻⁵ 0 CIC -0.181 3.08x10⁻⁵ 0 Signaling CNTN1 -0.184 3.08x10⁻⁵ 0 PIK3CA -0.182 3.08x10⁻⁵ 0 PIK3CD E3 ubiquitin ligase -0.189 3.08x10⁻⁵ HECW1

The Top 19 Genes That, When Mutated, Are Associated With Radiation Sensitivity

^aRed represents samples with a mutation

^bImplicated in DNA damage response

FDR = false discovery rate. IC = information coefficient

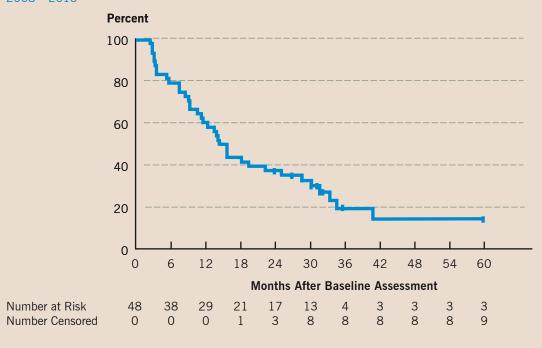
¹Yard BD, Adams DJ, Chie EK, Tamayo P, Battaglia JS, Gopal P, Rogacki K, Pearson BE, Phillips J, Raymond DP, Pennell NA, Almeida F, Cheah JH, Clemons PA, Shamji A, Peacock CD, Schreiber SL, Hammerman PS, Abazeed ME. A genetic basis for the variation in the vulnerability of cancer to DNA damage. *Nat Commun*. 2016 Apr 25;7:11428.

Innovations

Study Shows Active Surveillance Is Safe and Viable in Some Metastatic Renal Cell Carcinoma Patients

A prospective, phase 2 study led by Cleveland Clinic found active surveillance to be a viable initial strategy for select patients with metastatic renal cell carcinoma (mRCC). mRCC patients from 5 different hospitals underwent baseline and regular computerized tomography scans, close clinical monitoring, and quality of life assessments to determine changes in disease burden, time to progression, and mood. Median time on surveillance was 14.9 months. Median time to progression was 9.4 months. Estimated median overall survival from the start of surveillance was 44.5 months. Results indicate that certain patients can be managed through active surveillance, avoiding treatment burdens for months or several years before disease progression.

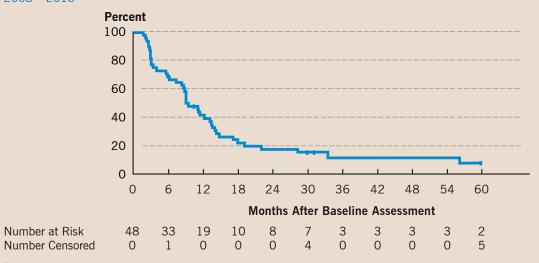
Time on Active Surveillance Among Study Participants (N = 48) 2008 – 2013



Overall Survival Among Study Participants (N = 48) 2008 – 2013



Progression-Free Survival Among Study Participants (N = 48) 2008 – 2013



¹Rini BI, Dorff TB, Elson P, Rodriguez CS, Shepard D, Wood L, Humbert J, Pyle L, Wong YN, Finke JH, Rayman PA, Larkin JM, Garcia JA, Plimack ER. Active surveillance in metastatic renal-cell carcinoma: a prospective, phase 2 trial. *Lancet Oncol*. 2016 Sep;17(9):1317-1324.

Contact Information

Taussig Cancer Institute Appointments/Referrals 216.444.7923 or 866.223.8100

Blood and Marrow Transplant Program Appointments/Referrals

This internationally recognized program offers autologous, allogeneic, reduced-intensity, related and unrelated transplants. Cell sources include bone marrow, peripheral stem cell, and umbilical cord blood transplants for treating patients with leukemias, lymphomas, and other hematological malignancies and bone marrow failure states.

216.445.5600 or 800.223.2273, ext. 55600

Bone Marrow Failure Clinic Appointments/Referrals

This subspecialty clinic offers expertise in aplastic anemia, myelodysplasia, single-lineage cytopenias, paroxysmal nocturnal hemoglobinuria, large granular lymphocytic leukemia, and other immune-mediated hematologic diseases.

216.444.6833 or 800.223.2273, ext. 46833

Radiation Oncology Appointments/Referrals 216.444.5571 or 800.223.2273, ext. 45571

Cancer Answer Line

Get the cancer information you need from the Cancer Answer Line. Two oncology advanced practice nurses and their staff provide information and answer questions.

Toll-free 866.223.8100 Monday–Friday, 8 a.m.–4:30 p.m.

Helen Meyers McLoraine Patient Resource Center

The Helen Meyers McLoraine Patient Resource Center provides brochures, a lending library, Internet access, and information on support groups, patient-related events, wigs, transportation, and lodging. It's located on the first floor of Taussig Cancer Center.

Monday-Friday, 7:30 a.m.-4:00 p.m. 216.444.0611

On the Web at clevelandclinic.org/cancer

Staff Listing

For a complete listing of Cleveland Clinic's Taussig Cancer Institute staff, please visit clevelandclinic.org/staff.

Publications

Taussig Cancer Institute staff authored **273** publications in 2016 as indexed within Web of Science.

Locations

For a complete listing of Cleveland Clinic's Cancer Care locations, please visit clevelandclinic.org/cancer.

Additional Contact Information

General Patient Referral

24/7 hospital transfers or physician consults

800.553.5056

General Information

216.444.2200

Hospital Patient Information

216.444.2000

General Patient Appointments

216.444.2273 or 800.223.2273

Referring Physician Center and Hotline

855.REFER.123 (855.733.3712)

Or email refdr@ccf.org or visit clevelandclinic.org/refer123

Request for Medical Records

216.444.2640 or 800.223.2273, ext. 42640

Same-Day Appointments

216.444.CARE (2273)

Global Patient Services/ International Center

Complimentary assistance for international patients and families

001.216.444.8184 or visit clevelandclinic.org/gps

Medical Concierge

Complimentary assistance for out-of-state patients and families

800.223.2273, ext. 55580, or email medicalconcierge@ccf.org

Cleveland Clinic Abu Dhabi

clevelandclinicabudhabi.ae

Cleveland Clinic Canada

888.507.6885

Cleveland Clinic Florida

866.293.7866

Cleveland Clinic Nevada

702.483.6000

For address corrections or changes,

please call

800.890.2467

About Cleveland Clinic

Overview

Cleveland Clinic is an academic medical center offering patient care services supported by research and education in a nonprofit group practice setting. More than 3500 Cleveland Clinic staff physicians and scientists in 140 medical specialties and subspecialties care for more than 7.1 million patients across the system annually, performing nearly 208,000 surgeries and conducting more than 652,000 emergency department visits. Patients come to Cleveland Clinic from all 50 states and 185 nations. Cleveland Clinic's CMS case-mix index is the second-highest in the nation.

Cleveland Clinic is an integrated healthcare delivery system with local, national, and international reach. The main campus in midtown Cleveland, Ohio, has a 1400-bed hospital, outpatient clinic, specialty institutes, labs, classrooms, and research facilities in 44 buildings on 167 acres. Cleveland Clinic has more than 150 northern Ohio outpatient locations, including 10 regional hospitals, 18 full-service family health centers, 3 health and wellness centers, an affiliate hospital, and a rehabilitation hospital for children. Cleveland Clinic also includes Cleveland Clinic Florida: Cleveland Clinic Nevada; Cleveland Clinic Canada; Cleveland Clinic Abu Dhabi, UAE: Sheikh Khalifa Medical City (management contract), UAE; and Cleveland Clinic London (opening in 2020). Cleveland Clinic is the largest employer in Ohio, with more than 51,000 employees. It generates \$12.6 billion of economic activity a year.

Cleveland Clinic supports physician education, training, consulting, and patient services around the world through representatives in the Dominican Republic, Guatemala, India, Panama, Peru, Saudi Arabia, and the United Arab Emirates. Dedicated Global Patient Services offices are located at Cleveland Clinic's main campus, Cleveland Clinic Abu Dhabi, Cleveland Clinic Canada, and Cleveland Clinic Florida.

The Cleveland Clinic Model

Cleveland Clinic was founded in 1921 by 4 physicians who had served in World War I and hoped to replicate the organizational efficiency of military medicine. The organization has grown through the years by adhering to the nonprofit, multispecialty group practice they established. All Cleveland Clinic staff physicians receive a straight salary with no bonuses or other financial incentives. The hospital and physicians share a financial interest in controlling costs, and profits are reinvested in research and education.

Cleveland Clinic Florida was established in 1987. Cleveland Clinic began opening family health centers in surrounding communities in the 1990s. Marymount Hospital joined Cleveland Clinic in 1995, followed by regional hospitals including Euclid Hospital, Fairview Hospital, Hillcrest Hospital, Lutheran Hospital, Medina Hospital, South Pointe Hospital, and affiliate Ashtabula County Medical Center. In 2015, the Akron General Health System joined the Cleveland Clinic health system.

Internally, Cleveland Clinic services are organized into patient-centered integrated practice units called institutes, each institute combining medical and surgical care for a specific disease or body system. Cleveland Clinic was among the first academic medical centers to establish an Office of Patient Experience, to promote comfort, courtesy, and empathy across all patient care services.

A Clinically Integrated Network

Cleveland Clinic is committed to providing value-based care, and it has grown the Cleveland Clinic Quality Alliance into the nation's second-largest, and northeast Ohio's largest, clinically integrated network. The network comprises more than 6300 physician members, including both Cleveland Clinic staff and independent physicians from the community. Led by its physician members, the Quality Alliance strives to improve quality and consistency of care; reduce costs and increase efficiency; and provide access to expertise, data, and experience.

Taussig Cancer Institute

Cleveland Clinic Lerner College of Medicine

Lerner College of Medicine is known for its small class sizes, unique curriculum, and full-tuition scholarships for all students. Each new class accepts 32 students who are preparing to be physician investigators. In 2015, Cleveland Clinic broke ground on a 477,000-square-foot multidisciplinary Health Education Campus. The campus, which will open in July 2019, will serve as the new home of the Case Western Reserve University (CWRU) School of Medicine and Cleveland Clinic's Lerner College of Medicine, as well as the CWRU School of Dental Medicine, the Frances Payne Bolton School of Nursing, and physician assistant and allied health training programs.

Graduate Medical Education

In 2016, nearly 2000 residents and fellows trained at Cleveland Clinic and Cleveland Clinic Florida in our continually growing programs.

U.S. News & World Report Ranking

Cleveland Clinic is ranked the No. 2 hospital in America by *U.S. News & World Report* (2016). It has ranked No. 1 in heart care and heart surgery since 1995. In 2016, 3 of its programs were ranked No. 2 in the nation: gastroenterology and GI surgery, nephrology, and urology. Ranked among the nation's top five were gynecology, orthopaedics, rheumatology, pulmonology, and diabetes and endocrinology.

Cleveland Clinic Physician Ratings

Cleveland Clinic believes in transparency and in the positive influence of the physician-patient relationship on healthcare outcomes. To continue to meet the highest standards of patient satisfaction, Cleveland Clinic physician ratings, based on nationally recognized Press Ganey patient satisfaction surveys, are published online at clevelandclinic.org/staff.

Resources

Referring Physician Center and Hotline

Call us 24/7 for access to medical services or to schedule patient appointments at 855.REFER.123 (855.733.3712), email refdr@ccf.org, or go to clevelandclinic.org/Refer123. The free Cleveland Clinic Physician Referral App, available for mobile devices, gives you 1-click access. Available in the App Store or Google Play.

Remote Consults

Anybody anywhere can get an online second opinion from a Cleveland Clinic specialist through our MyConsult service. For more information, go to clevelandclinic.org/myconsult, email myconsult@ccf.org, or call 800.223.2273, ext. 43223.

Request Medical Records

216.444.2640 or 800.223.2273, ext. 42640

Track Your Patients' Care Online

Cleveland Clinic offers an array of secure online services that allow referring physicians to monitor their patients' treatment while under Cleveland Clinic care and gives them access to test results, medications, and treatment plans. my.clevelandclinic.org/online-services

Dr**Connect** (online access to patients' treatment progress while under referred care): call 877.224.7367, email drconnect@ccf.org, or visit clevelandclinic.org/drconnect.

MyPractice Community (affordable electronic medical records system for physicians in private practice): 216.448.4617.

eRadiology (teleradiology consultation provided nationwide by board-certified radiologists with specialty training, within 24 hours or stat): call 216.986.2915 or email starimaging@ccf.org.

Medical Records Online

Patients can view portions of their medical record, receive diagnostic images and test results, make appointments, and renew prescriptions through MyChart, a secure online portal. All new Cleveland Clinic patients are automatically registered for MyChart. clevelandclinic.org/mychart

Access

Cleveland Clinic is committed to convenient access, offering virtual visits, shared medical appointments, and walk-in urgent care for your patients. clevelandclinic.org/access

Critical Care Transport Worldwide

Cleveland Clinic's fleet of ground and air transport vehicles is ready to transfer patients at any level of acuity anywhere on Earth. Specially trained crews provide Cleveland Clinic care protocols from first contact. To arrange a transfer for STEMI (ST-elevation myocardial infarction), acute stroke, ICH (intracerebral hemorrhage), SAH (subarachnoid hemorrhage), or aortic syndrome, call 877.379.CODE (2633). For all other critical care transfers, call 216.444.8302 or 800.553.5056.

CME Opportunities: Live and Online

Cleveland Clinic's Center for Continuing Education operates the largest CME program in the country. Live courses are offered in Cleveland and cities around the nation and the world. The center's website (ccfcme.org) is an educational resource for healthcare providers and the public. It has a calendar of upcoming courses, online programs on topics in 30 areas, and the award-winning virtual textbook of medicine, The Disease Management Project.

Clinical Trials

Cleveland Clinic is running more than 2200 clinical trials at any given time for conditions including breast and liver cancer, coronary artery disease, heart failure, epilepsy, Parkinson disease, chronic obstructive pulmonary disease, asthma, high blood pressure, diabetes, depression, and eating disorders. Cancer Clinical Trials is a mobile app that provides information on the more than 200 active clinical trials available to cancer patients at Cleveland Clinic. clevelandclinic.org/cancertrialapp

Healthcare Executive Education

Cleveland Clinic has programs to share its expertise in operating a successful major medical center. The Executive Visitors' Program is an intensive, 3-day behind-the-scenes view of the Cleveland Clinic organization for the busy executive. The Samson Global Leadership Academy is a 2-week immersion in challenges of leadership, management, and innovation taught by Cleveland Clinic leaders, administrators, and clinicians. Curriculum includes coaching and a personalized 3-year leadership development plan.

clevelandclinic.org/executiveeducation

Consult QD Physician Blog

A website from Cleveland Clinic for physicians and healthcare professionals. Discover the latest research insights, innovations, treatment trends, and more for all specialties. consultqd.clevelandclinic.org

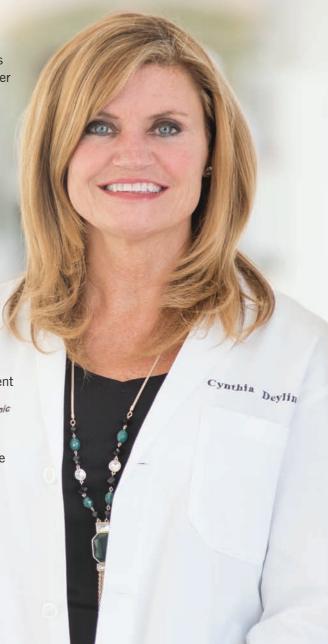
Social Media

Cleveland Clinic uses social media to help caregivers everywhere provide better patient care. Millions of people currently like, friend, or link to Cleveland Clinic social media — including leaders in medicine.

Facebook for Medical Professionals facebook.com/CMEclevelandclinic

Follow us on Twitter
@cleclinicMD

Connect with us on LinkedIn clevelandclinic.org/MDlinkedin



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Every life deserves world class care.

This project would not have been possible without the commitment and expertise of a team led by Mikkael Sekeres, MD, Kate Tullio, MPH, and Jen Lonzer, MA.

Graphic design and photography were provided by Cleveland Clinic's Center for Medical Art and Photography.



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