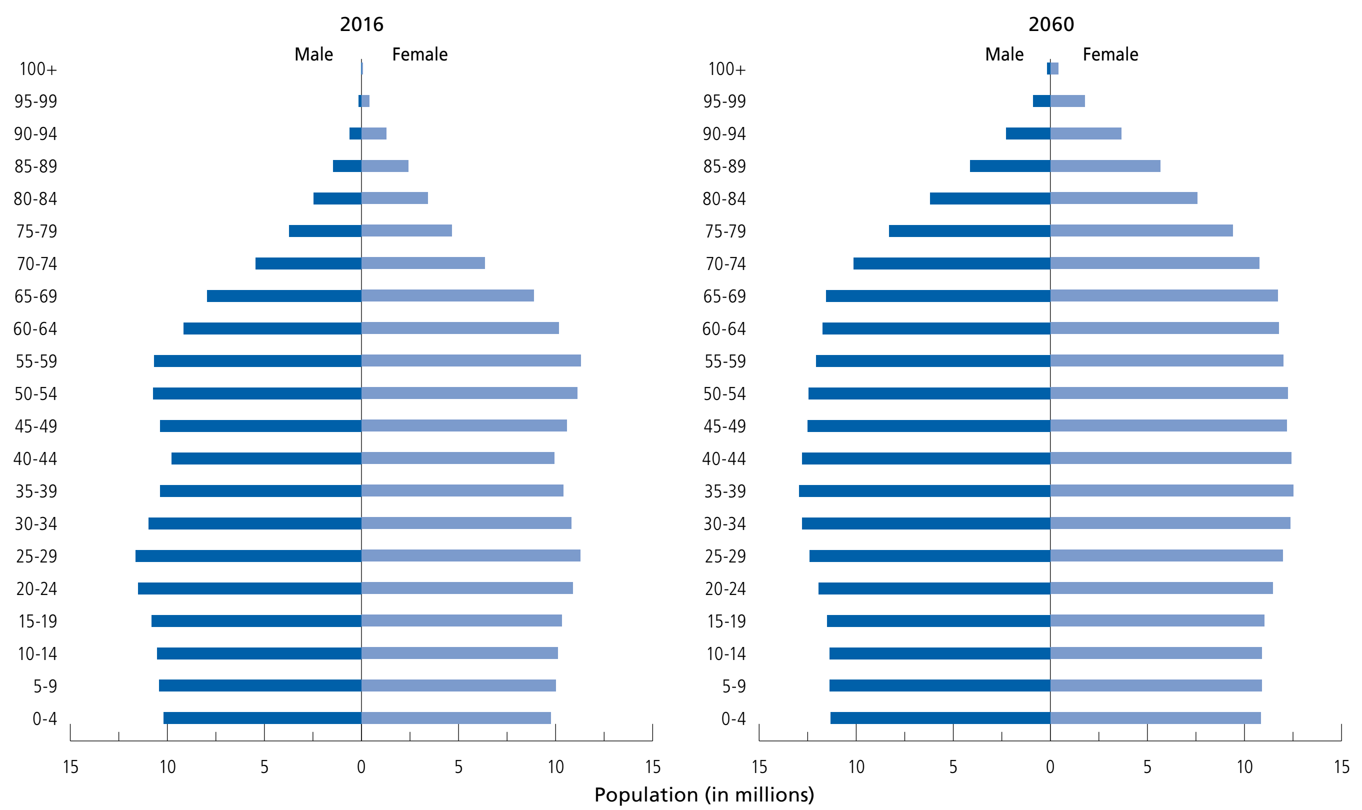
Special Section: Cancer in the Oldest Old

Introduction

Adults ages 85 and older are the fastest-growing population group in the US. Sometimes referred to as the "oldest old," the number of adults ages 85+ is expected to nearly triple from 6.4 million in 2016 to 19.0 million by 2060 (Figure S1).[1] The growth of the older population is primarily fueled by increasing life expectancy because of declines in all cause mortality due to less smoking and improvements in treatment. However, the obesity epidemic and persistent socioeconomic inequalities threaten to slow this progress.[2-4] In addition, the delay in smoking cessation among women is expected to narrow the current gender gap. For example, by 2030, remaining life expectancy at age 65 is projected to increase to 20 and 22 years in men and women, respectively, up from 18 and 21 years in 2010.[4] As a result of the longer life expectancy in women than men, women outnumber men in the oldest age group. In 2016, there were 4.2 million women compared to 2.2 million men ages 85 and older, or 186 women for every 100 men.

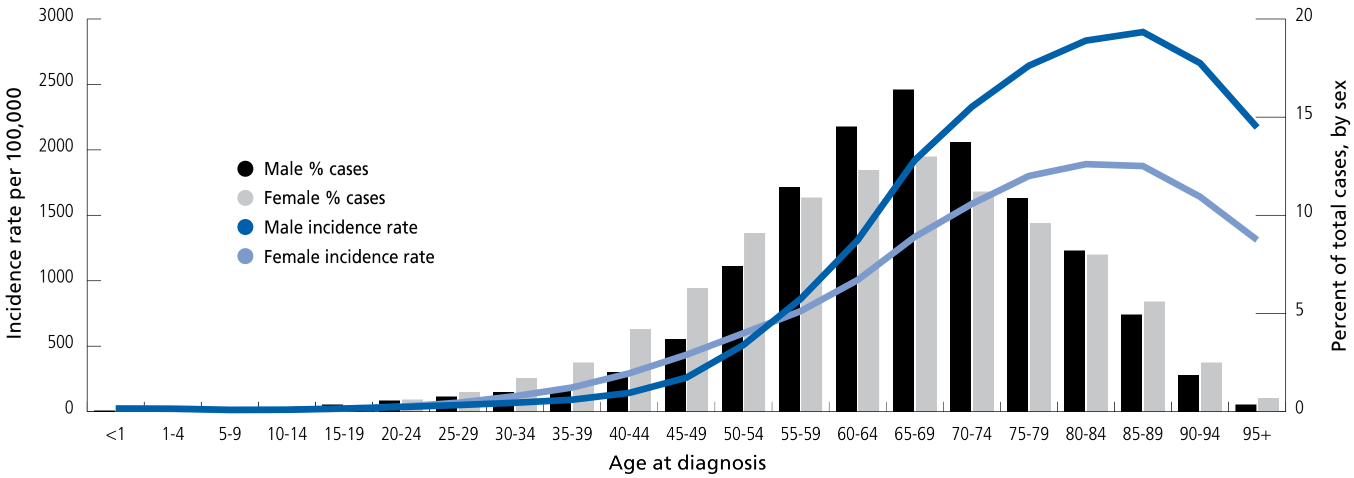
Cancer risk increases with age, peaking in men and women in their 80s (Figure S2). The rapidly growing older population will increase demand for cancer care in this population, which will have a substantial impact on health care resource allocation. Diagnosis and treatment of cancer at older ages are often complicated by preexisting medical conditions (comorbidities), cognitive impairment, frailty, and other factors.[5] Screening is not recommended because current evidence suggests that the harms outweigh the benefits for adults older than 75 years of age. As a result, cancers in this age group are often more advanced than those diagnosed at earlier ages. Relatively little is known about the complex health

Figure S1. Age Distribution of US Population in Millions: 2016 versus 2060



Source: US Census Bureau, Population Progections 2017-2060.[1]

Figure S2. Average Annual Incidence Rates and Case Distribution by Age, US, 2011-2015



Sources: Surveillance, Epidemiology, and End Results (SEER) program, 18 SEER registries, custom data (2000-2015).

care needs of older cancer patients due to the limited representation of this population in clinical research.[6,7] This special section profiles cancer in the oldest old in the US, including data on incidence, mortality, survival, and treatment, and discusses some of the unique challenges affecting these patients.

How many new cases and deaths are expected to occur among persons 85 and older in 2019?

People ages 85 and older represent 8% of all new cancer diagnoses, translating to about 140,690 cases in 2019 (61,830 male and 78,860 female). Cancer is the second-leading cause of death, following heart disease, in this population, with about 103,250 cancer deaths expected in 2019 (49,040 male and 54,210 female), accounting for 17% of all cancer deaths.

How many cancer survivors are ages 85 and older?

As of January 1, 2019, an estimated 1,944,280 adults ages 85 and older were alive with a history of cancer, representing one-third of all men and one-fourth of all women in this age group in the United States.[8] The oldest old are the fastest-growing group of cancer survivors, with nearly 4.7 million cancer survivors ages 85 and older expected by 2040.[8]

What is the risk of developing or dying of cancer at age 85?

Among adults age 85 without a history of a cancer, the risk of a cancer diagnosis in their remaining lifetime is 16.4%, or 1-in-6, for men and 12.8%, or 1-in-8, for women. The remaining lifetime risk of cancer death for all adults age 85 is 14.4% (or 1-in-7) for men and 9.6% (or 1-in-10) for women.

Overall cancer risk increases with age until approximately ages 80-84 in women and 85-89 in men (Figure S2), reflecting lifetime accumulation of exposures (e.g., cigarette smoking, excess body weight, alcohol consumption) and genetic mutations.[9,10] Reasons for the subsequent decline in risk are unclear,[11-13] but may reflect lower genetic susceptibility or exposure to carcinogens, as well as consequences of the natural aging process that inhibit tumor growth.[14-17] For example, one theory suggests that cellular senescence, a stage associated with aging when cells (including cancer cells) lose their ability to divide, may protect against cancer formation.[10,14] Another theory is that the age-dependent reshaping of the immune system (increases in certain T-cells and natural killer cells) creates a hostile environment for cancer growth.[17] However, lower incidence rates in the oldest age groups may also be the result of undetected cancer related to less intensive use of screening and diagnostic testing,

Table S1. Leading Cancer Sites of New Cancer Cases and Deaths, Ages 85+, US

	Male	Estimated cases, 2019 N	%	Rate, 2011-2015	Female	Estimated cases, 2019 N	%	Rate, 2011-2015
Incidence	Lung & bronchus	9,800	16%	450.6	Breast	14,800	19%	332.8
	Prostate	7,960	13%	366.0	Colon & rectum	11,200	14%	252.0
	Urinary bladder	7,870	13%	361.7	Lung & bronchus	10,870	14%	244.4
	Colon & rectum	6,640	11%	305.2	Pancreas	4,150	5%	93.4
	Melanoma of the skin	4,000	6%	183.9	Non-Hodgkin lymphoma	3,710	5%	83.5
	Non-Hodgkin lymphoma	3,090	5%	142.1	Urinary bladder	3,360	4%	75.5
	Leukemia	2,740	4%	126.0	Leukemia	3,000	4%	67.6
	Pancreas	2,270	4%	104.1	Melanoma of the skin	2,510	3%	56.5
	Kidney & renal pelvis	1,730	3%	79.6	Uterine corpus	2,310	3%	51.9
	Stomach	1,390	2%	63.8	Ovary	1,900	2%	42.7
	All sites	**61,830**			**All sites**	**78,860**		

	Male	Estimated deaths, 2019 N	%	Rate, 2012-2016	Female	Estimated deaths, 2019 N	%	Rate, 2012-2016
Mortality	Prostate	9,860	20%	452.9	Lung & bronchus	10,200	19%	247.8
	Lung & bronchus	9,700	20%	445.6	Breast	7,150	13%	173.7
	Colon & rectum	4,380	9%	201.1	Colon & rectum	6,740	12%	163.7
	Urinary bladder	3,410	7%	156.9	Pancreas	4,210	8%	102.2
	Leukemia	2,590	5%	119.2	Leukemia	2,630	5%	63.8
	Pancreas	2,530	5%	116.4	Non-Hodgkin lymphoma	2,570	5%	62.4
	Non-Hodgkin lymphoma	2,160	4%	99.4	Ovary	2,060	4%	50.1
	Liver & intrahepatic bile duct	1,230	3%	56.6	Urinary bladder	1,680	3%	40.7
	Kidney & renal pelvis	1,200	2%	55.1	Liver & intrahepatic bile duct	1,380	3%	33.4
	Esophagus	1,120	2%	51.4	Uterine corpus	1,330	2%	32.4
	All sites	**49,040**			**All sites**	**54,210**		

Note: Estimated cases and deaths for 85+ are based on proportions of cases/deaths in that age group for each cancer in the NAACCR (2011-2015) and NCHS (2012-2016) data applied to the overall estimates for 2019.

Sources: Incidence rates - North American Association of Central Cancer Registries (NAACCR), 2018. Mortality rates - National Center for Health Statistics (NCHS), 2018.

given that autopsy studies often report undiagnosed cancer in this age group.[18] Nevertheless, for some cancers, including those of the colorectum, pancreas, stomach, and urinary bladder, as well as leukemia and skin melanoma, incidence rates continue to increase with age among adults in their 90s.[19, 20]

What kinds of cancers are most common among persons 85 and older?

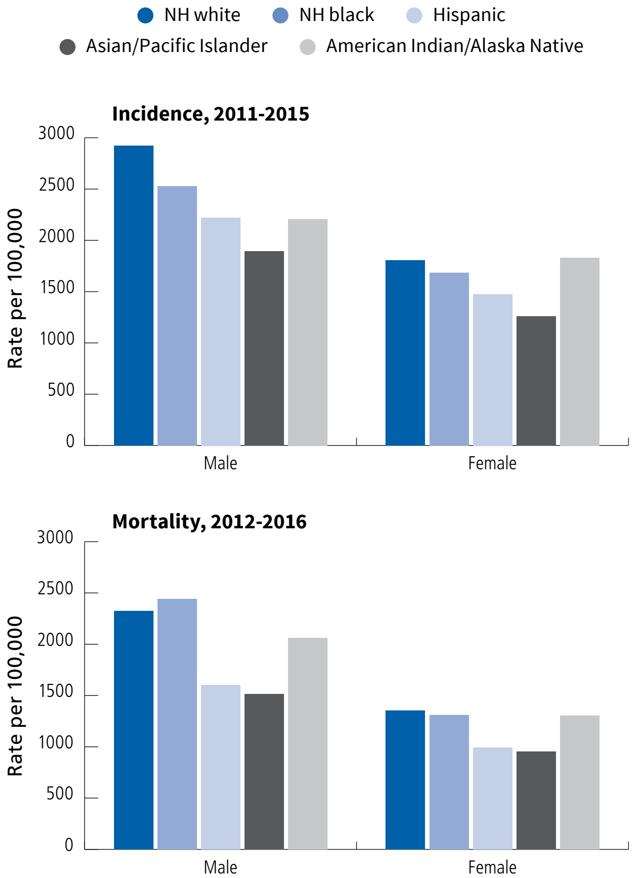
The most commonly diagnosed cancers are lung (16%), prostate (13%), and urinary bladder (13%) in older men and breast (19%), colorectal (14%), and lung (14%) in older women (Table S1). The top 10 cancers in older men and women are similar to those for all ages combined (Figure 3). The few exceptions include cancers of the stomach in men and urinary bladder and ovaries in women.

The leading causes of cancer death in the oldest old parallel those for all ages. Among men 85 and older, prostate and lung cancer are the most common causes of cancer death, together representing 40% of cancer deaths. Among women, lung cancer is the leading cause of cancer death (19%) followed by breast cancer (13%). For men and women, colorectal cancer is the third-leading cause of cancer death, representing 9% and 12% of cancer deaths, respectively.

How do cancer rates vary by race/ethnicity in persons ages 85 and older?

Among the oldest men, cancer incidence rates are highest in non-Hispanic (NH) whites and lowest among Asians/Pacific Islanders (APIs) (Figure S3). The overall cancer incidence rate is 16% higher in NH white men than in non-Hispanic black (black) men, largely driven by higher rates of urinary bladder cancer, melanoma, and non-

Figure S3. Cancer Incidence and Mortality Rates among Adults 85+ by Race/Ethnicity, US, 2011-2016



NH: Non-Hispanic. Asians/Pacific Islanders and American Indians/Alaska Natives exclude persons of Hispanic ethnicity. Rates for American Indians/Alaska Natives based on cases/deaths in Contract Health Service Delivery Area counties.

Sources: Incidence – NAACCR, 2018. Mortality – NCHS, 2018.

Hodgkin lymphoma. This is in contrast to younger men and men of all ages combined, among whom rates are higher in blacks than whites. For example, compared to NH white men, rates among black men are 30% higher in ages 50-64. Among the oldest women, American Indians/Alaska Natives (AIANs) have the highest cancer incidence rate, reflecting their high burden of lung and colorectal cancers.

Cancer mortality patterns differ from those for incidence, especially in men. Despite a lower incidence rate than white men, black men have a 5% higher cancer mortality rate (Figure S3). Recent studies have demonstrated that racial/ethnic disparities in stage at diagnosis and survival persist for older cancer patients.[21, 22] Although racial differences in stage at diagnosis are generally smaller than observed in the general population, survival differences are striking. For example, 5-year relative survival for both local- and regional-stage lung cancer patients ages 85 years and older was 3 times higher in whites compared to blacks.[22] This disparity may reflect inequalities in access to and receipt of quality health care, as well as differences in the burden of comorbidities.[23-25] Despite universal access to health care, some costs of cancer care are not fully covered by Medicare and can be burdensome for older cancer patients with limited, fixed income.[26] Importantly, racial/ethnic minority population growth will lead to increasing diversity in the 85 and older age group over the next several decades, with the proportion of NH whites declining from 84% in 2012 to 61% in 2060.[27, 28]

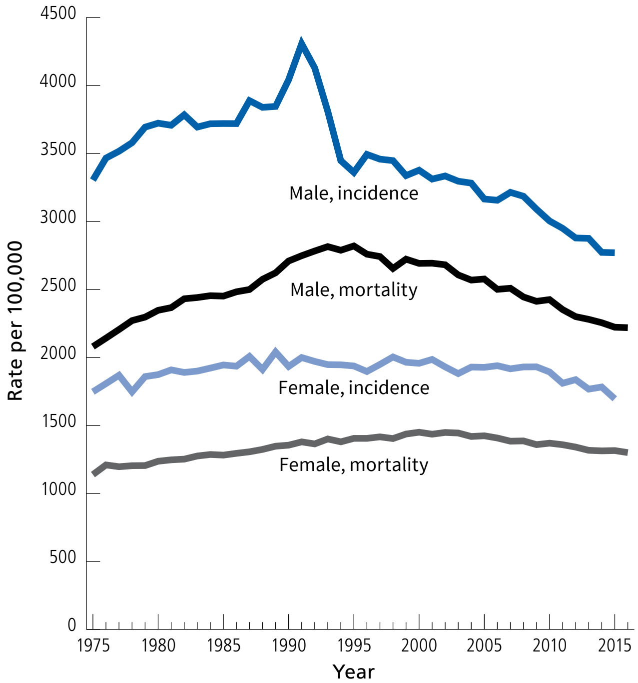
How has the occurrence of cancer in ages 85 and older varied over time?

Incidence trends

Overall cancer incidence rates have decreased in the oldest men since about 1990 (Figure S4), with an acceleration in the decline since 2007, largely reflecting the sharp declines in cancers of the prostate and colorectum, and more recently, lung (Figure S5, Table S2). The lung cancer pattern differs in older men compared to younger men; incidence rates peaked in the 2000s among men 85+ compared to a peak in the 1980s among men ages 65 to 84. The delayed decline in the oldest men reflects generational differences in smoking patterns. The generation of men born in 1920 (who entered the 85+ age group in 2005) had the highest smoking rate of any birth cohort, with peak smoking prevalence exceeding 70% during the 1950s.[29] As younger generations with lower smoking rates enter the oldest age group, lung cancer rates in this age group will continue to decline.

In contrast, the decline in prostate cancer incidence rates has been more rapid in men 85+ compared to younger men. Prior to 2009, prostate cancer was the most common cancer in men 85 and older, but rates are now similar to urinary bladder cancer, the third-leading cancer in this age group. This is because of rapid declines in prostate cancer incidence, likely reflecting a shift toward detection at earlier ages through PSA testing.

Figure S4. Trends in Cancer Incidence and Death Rates by Sex, Ages 85+, US, 1975 to 2016



Sources: Incidence – SEER 9 registries, 2018. Mortality – NCHS, 2018.

The decrease in colorectal cancer incidence rates since 2000 has been similar among men 65 to 84 years of age and those ages 85 and older. Melanoma incidence rates, on the other hand, have increased more rapidly over the past several decades in the oldest men (4.3% per year during 2002-2015), which is thought to be due to excessive sun exposure among children during the first half of the 20th century.[30] Melanoma is predicted to become the second most commonly diagnosed cancer among men 85 and older by 2030.[31]

Among women 85 and older, overall cancer incidence rates peaked around 1990 before subsequently decreasing (Figure S4), with an acceleration in the decline in 2009 largely reflecting declines in breast and colorectal cancers (Figure S5, Table S2). Although breast cancer rates have increased slightly among women ages 65 to 84 years since 2004, rates have continued to decline in the oldest age group (2.1% per year since 2009). Breast cancer surpassed colorectal cancer in 2005 as the most commonly diagnosed cancer in the oldest women due to faster declines in colorectal cancer rates. Lung cancer incidence rates increased more rapidly in older versus younger women from 1995 to the mid-2000s but are now declining at a similar pace in both groups. Although pancreatic cancer rates continue to increase in women ages 65 to 84, rates have leveled off in women 85+ since 2008. Similar to men, melanoma rates have increased rapidly (3.7% per year during 1995-2015) among the oldest women.

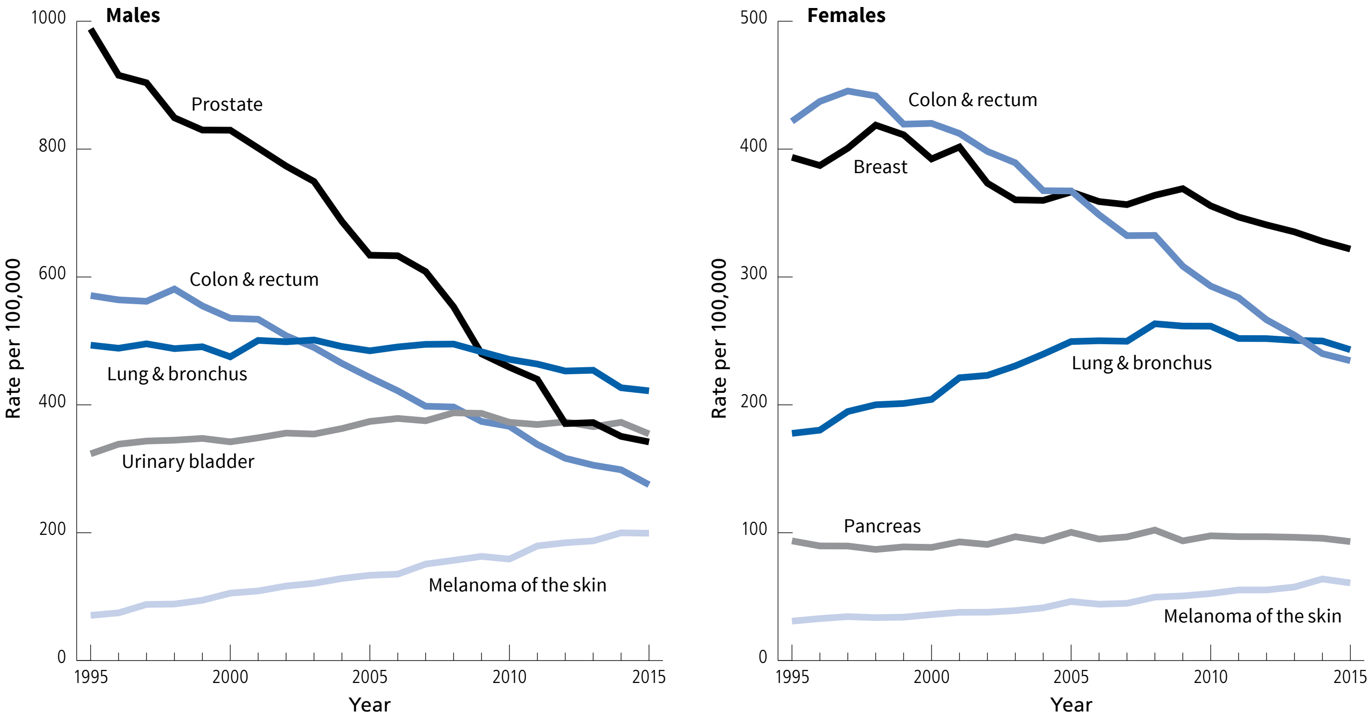
Mortality trends

Cancer death rates peaked in men 85+ in the mid-1990s and have declined by 1.4% per over the past decade (Figure S4). The spike and subsequent decline in overall mortality rates largely reflect trends in prostate cancer (Figure S6). The prostate cancer death rate in men increased sharply until 1993, then dropped precipitously until plateauing during 2014-2016 at a slightly lower rate than observed in 1975. Among men 65 to 84 years, the increase was much smaller, but the subsequent decline was larger, and as a result, rates are now much lower than they were in 1975. Reasons for the sharp increase in prostate cancer death rates in the oldest men are not known, but are thought to be due to mislabeling of deaths from other causes as prostate cancer on death certificates because of the rapid rise in disease prevalence following the introduction of widespread PSA testing.[32] The subsequent decline in rates may result from earlier detection and improvements in treatment for advanced disease, but it remains unclear why rates have recently plateaued.[33]

Declines in death rates for lung and colorectal cancers are similar to incidence patterns over the past 2 decades (Figure S5). Notably, urinary bladder cancer death rates have increased in the oldest men by 1% per year from 2000 to 2016, whereas rates have declined in men ages 65 to 84 since the late 1970s. Reasons for the divergent pattern are not known, but may reflect increasing incidence rates through 2008 that were limited to the oldest men. Death rates have also increased for pancreatic cancer (0.3% per year since 1975), while melanoma rates increased by 3.3% annually until stabilizing in 2009.

Among the oldest women, death rates increased until the early 2000s and have subsequently declined by 0.8% per year (Figure S4). The overall pattern reflects decreasing

Figure S5. Trends in Cancer Incidence Rates for Selected Sites, Ages 85+, US, 1995-2015



Note: Rates have been adjusted for reporting delays using delay ratios from the SEER 18 registries.
Sources: NAACCR, 2018.

death rates for cancers of the colorectum and breast that until the mid-2000s were offset by increasing death rates for lung cancer (Figure S6). Lung cancer death rates in the oldest women increased nearly 4-fold from 1975 to 2006 and stabilized thereafter. In contrast, among women ages 65 to 84, lung cancer death rates have decreased since the mid-2000s. Historically, colorectal cancer was the leading cause of cancer death in the oldest women. However, colorectal death rates dropped nearly 50% from a peak of 297 deaths per 100,000 in 1984 to 156 per 100,000 in 2016. As a result, colorectal cancer is now the third-leading cause of cancer death among women 85 and older. Breast cancer death rates have also declined by about 0.9% per year since their peak in the mid-1990s. In contrast, death rates increased for melanoma and pancreatic cancer, similar to the trends in older men.

Can cancer be detected early in older adults?

Cancer patients ages 85 and older are less likely to be diagnosed at an early stage than younger patients. For example, 57% of the oldest breast cancer patients and 41% of the oldest prostate cancer patients are diagnosed at a local stage, compared to 68% and 77% of patients ages 65-84, respectively (Figure S7). Later stage at diagnosis among the oldest cancer patients, in part, reflects less screening. Notably, the oldest cancer patients are two to

Joinpoint trends

Table S2 describes trends in incidence rates based on Joinpoint analyses. This method involves fitting a series of joined straight lines on a logarithmic scale to the trends in annual rates, with each junction or "joinpoint" of two lines denoting a statistically significant change in trend. The direction and magnitude of the resulting trends over the 1995-2015 period are described as the annual percent change (APC). If the program detects no change during the period, then only a single APC will be given. If the program detects multiple trends, then the magnitude, direction, and applicable years for each will be listed separately.

Table S2. Joinpoint Trends in Cancer Incidence Rates for Selected Sites in Two Age Groups, US, 1995-2015

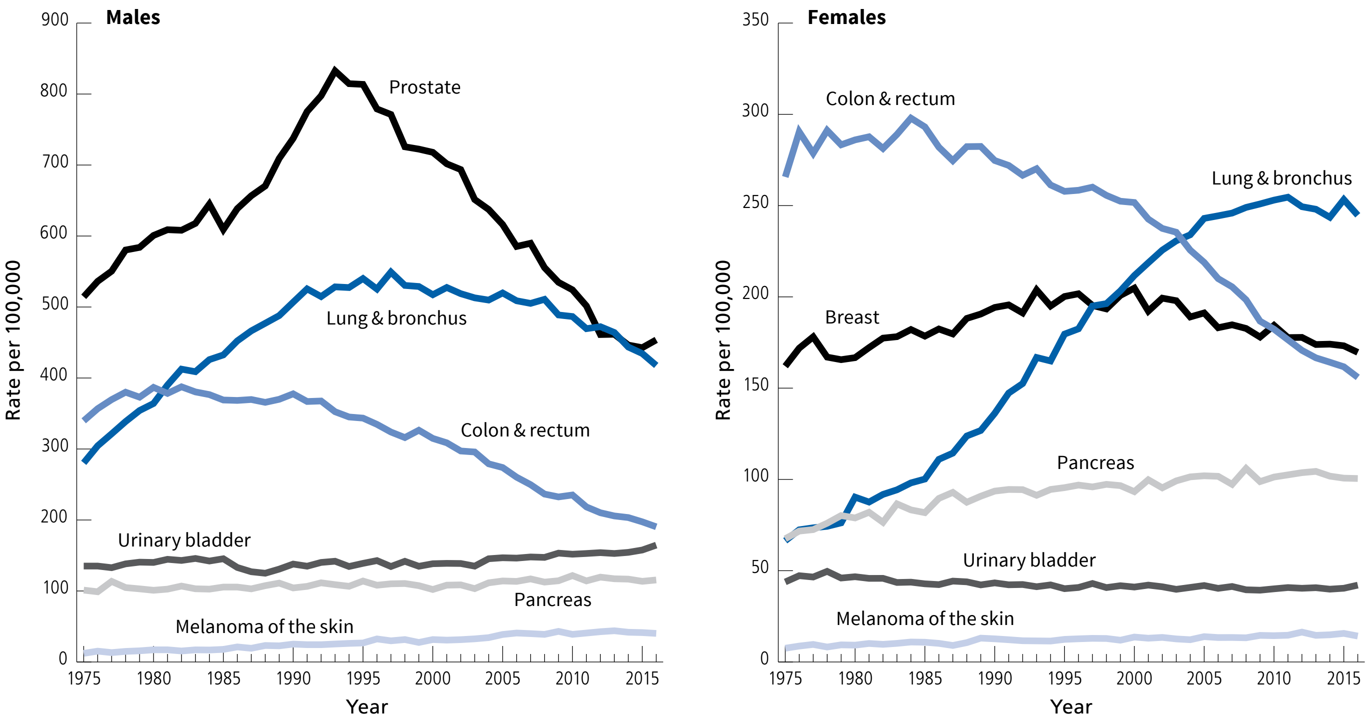
	Trend 1		Trend 2		Trend 3		Trend 4	
	Years	APC	Years	APC	Years	APC	Years	APC
MALES								
Colon & rectum								
65-84	1995-2000	0.0	2000-2015	-4.2*				
85+	1995-2000	-0.5	2000-2015	-4.4*				
Lung & bronchus								
65-84	1995-2008	-1.2*	2008-2015	-2.8*				
85+	1995-2008	0.0	2008-2015	-2.1*				
Melanoma of the skin								
65-84	1995-2000	5.5*	2000-2015	3.4*				
85+	1995-2002	7.4*	2002-2015	4.3*				
Prostate								
65-84	1995-2001	0.9	2001-2004	-5.7	2004-2007	2.0	2007-2015	-6.7*
85+	1995-2003	-3.0*	2003-2015	-6.7*				
Urinary bladder								
65-84	1995-1998	1.9*	1998-2005	0.2	2005-2013	-0.9*	2013-2015	-3.3*
85+	1995-2008	1.2*	2008-2015	-0.9*				
FEMALES								
Breast								
65-84	1995-1999	1.6*	1999-2004	-2.7*	2004-2015	0.8*		
85+	1995-1999	1.9*	1999-2003	-3.6*	2003-2009	0.1	2009-2015	-2.1*
Colon & rectum								
65-84	1995-1998	1.5*	1998-2005	-2.7*	2005-2015	-4.3*		
85+	1995-1998	1.7	1998-2008	-3.0*	2008-2015	-5.0*		
Lung & bronchus								
65-84	1995-1997	2.4*	1997-2007	1.1*	2007-2015	-1.2*		
85+	1995-2008	3.0*	2008-2015	-1.2*				
Melanoma of the skin								
65-84	1995-2000	5.1*	2000-2015	3.1*				
85+	1995-2015	3.7*						
Pancreas								
65-84	1995-2015	0.8*						
85+	1995-2008	0.8*	2008-2015	-0.7				

*Indicates trend is significantly different from zero, p<0.05. Note: Rates have been adjusted for reporting delays using delay ratios from the SEER 18 registries.
Source: NAACCR, 2018.

four times more likely to be diagnosed with unstaged cancer than patients ages 65-84 (Figure S7). This may be due to the inability or undesirability of some older patients to undergo complete diagnostic testing due to other health conditions. However, staging information is important for the provision of appropriate treatment.

Routine cancer screening is generally not recommended for those ages 85+ due to the higher prevalence of serious medical conditions, diminished life expectancy, and limited evidence of benefit, partly because this population has not been included in clinical trials evaluating screening. For most in this age group, the small potential benefit of extending life is likely to be outweighed by the possible harms of screening, which are more common with increasing age. Harms include the need for additional tests; emotional stress; overdiagnosis, which may lead to overtreatment; and procedure-related risks.[34, 35] Older adults are more likely to experience overdiagnosis due to higher rates of indolent tumors and competing mortality risks.[36] In addition, one study found that following a screening colonoscopy, adults 85+ were more than twice as likely to experience a serious gastrointestinal event, such as perforation or bleeding,

Figure S6. Trends in Cancer Death Rates for Selected Sites, Ages 85+, US, 1975-2016



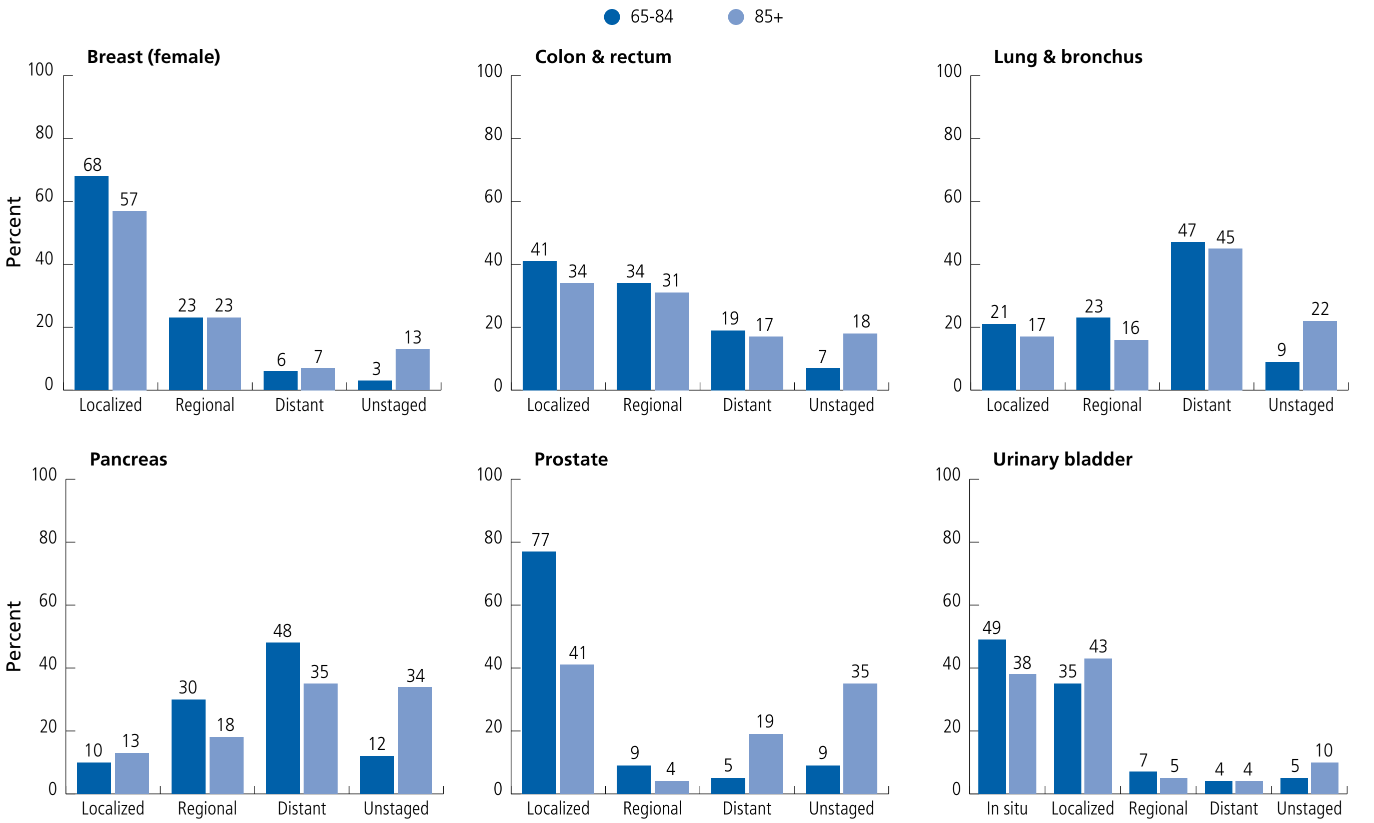
Sources: NCHS, 2018.

compared to adults ages 66-69 (12 versus 5 events per 1,000 colonoscopies, respectively).[37] Moreover, the benefits of screening are accrued over time. It is estimated that there is a 10-year delay to save 1 life per 1,000 people screened for breast or colorectal cancer, and an even greater delay for prostate cancer.[34, 38] As a result, the benefit of screening is substantially reduced in those with limited life expectancy.

While most guidelines generally recommend against cancer screening in those with less than a 10-year life expectancy, differences across organizations can complicate decisions for patients and their providers. For breast cancer screening, the American Cancer Society recommends mammography for all women with a life expectancy of at least 10 years.[39] The US Preventive Services Task Force (USPSTF) also endorses individualized breast cancer screening decisions, but highlights the lack of evidence for screening in women over 75.[40, 41] Both of these organizations recommend against screening for colorectal cancer after age 75.[39, 42] While the American Cancer Society guidelines recommend an informed decision-making process to guide prostate cancer testing in men with at least a 10-year life expectancy, the USPSTF recommends against PSA testing in men 70 and older.[43] Cervical cancer screening is not recommended after age 65 in women who have adequate prior screening, and the upper age limit for lung cancer screening among heavy and former longtime smokers is age 80.[44, 45] The American Geriatrics Society, on the other hand, has a general recommendation to consider life expectancy and the risks of testing, overdiagnosis, and overtreatment in screening decisions of older patients.[46] In addition, Medicare generally covers cancer screenings without an upper age limit or other restrictions.

Although research has shown that the benefit of screening is dependent on sufficient life expectancy, accurately assessing life expectancy and communicating this information to patients can be challenging. Mortality indexes that incorporate comorbid conditions and functional status along with age can help clinicians estimate life expectancy.[47] However, a recent study of adults ages 65 and older reported that although older

Figure S7. Stage Distribution (%) for Selected Cancers in Two Age Groups, US, 2008-2014



Note: Cases reported through autopsy only were excluded.
Source: NAACCR, 2018.

adults were amenable to using age and health status in the context of discussing screening cessation, there were concerns with discussions focused on life expectancy.[48] Another study found that patients prefer clinicians to frame the decision to stop screening in terms of prioritizing other health issues.[49]

Nevertheless, data from the National Health Interview Survey indicate unexpectedly high rates of screening in adults ages 85 and older (Table S3). In 2015, more than one-third of women 85 and older reported receiving a mammogram in the previous two years and 18% reported receiving recent cervical cancer screening tests. More than half of adults ages 85+ reported receiving either a stool screening test in the past year or a sigmoidoscopy or colonoscopy in the past five or 10 years, respectively. Nearly 30% of men in this age group reported receiving a PSA test in the past year.

What percentage of people ages 85 and older survive cancer?

Cancer survival rates decline with age, and patients 85 and older have the lowest relative survival of any age group.[50] Relative survival is the proportion of people who are alive for a designated time after a cancer diagnosis divided by the proportion of people of similar age, race, etc. expected to be alive in the absence of cancer based on normal life expectancy. Five-year relative survival rates for the top five cancers in men and women ages 85+ and 65-84 are shown in Figure S8. In both age groups, relative survival approaches 100% for early-stage breast and prostate cancers, and is 95% for in situ urinary bladder cancer. However survival is 35% lower (in absolute terms) in adults 85+ than in ages 65-84 for regional-stage prostate cancer and 20-23% lower for local-stage lung and bladder cancers. For breast and colorectal cancers, age-related disparities are largest for

Table S3. Screening Prevalence (%) among Adults 85+, US, 2015

Breast	Mammography in the past 2 years	34
Cervix	Pap test within the past 3 years	18
Colon & rectum	Stool test or endoscopy*	52
	Men	60
	Women	47
Prostate	PSA test† in the past 1 year	29

Note: Estimates do not distinguish between examinations for screening and diagnosis. PSA: prostate-specific antigen test. *Either a fecal occult blood test or fecal immunochemical test within the past year, sigmoidoscopy within the past five years, or a colonoscopy within the past 10 years. †Among those with no reported prior diagnosis of prostate cancer.

Source: NCHS, National Health Interview Survey, 2015.

local- and regional-stage disease. Poorer survival in the oldest cancer patients in part reflects the numerous treatment challenges (discussed in the next section). In addition, research suggests that older adults may be less willing to sacrifice quality of life and tolerate treatment toxicities to extend survival.[51] Studies suggest that older patients have benefited less than younger patients from recent advances in cancer treatment.[52] One recent study found smaller improvements in survival for older cancer patients from 1990 to 2009 for six leading cancers has resulted in widening age-related disparities.[52]

How is cancer treated in adults 85 and older?

The oldest old cancer patients are less likely to receive surgical treatment than patients ages 65-84 for each of the most common cancers (Figure S9). The most striking difference is observed for breast cancer; 89% of patients 65-84 years of age receive surgery, compared to just 65% of those 85+. Other studies have found that older breast cancer patients are less likely to receive guideline concordant care, even after accounting for patient comorbidities.[53, 54]

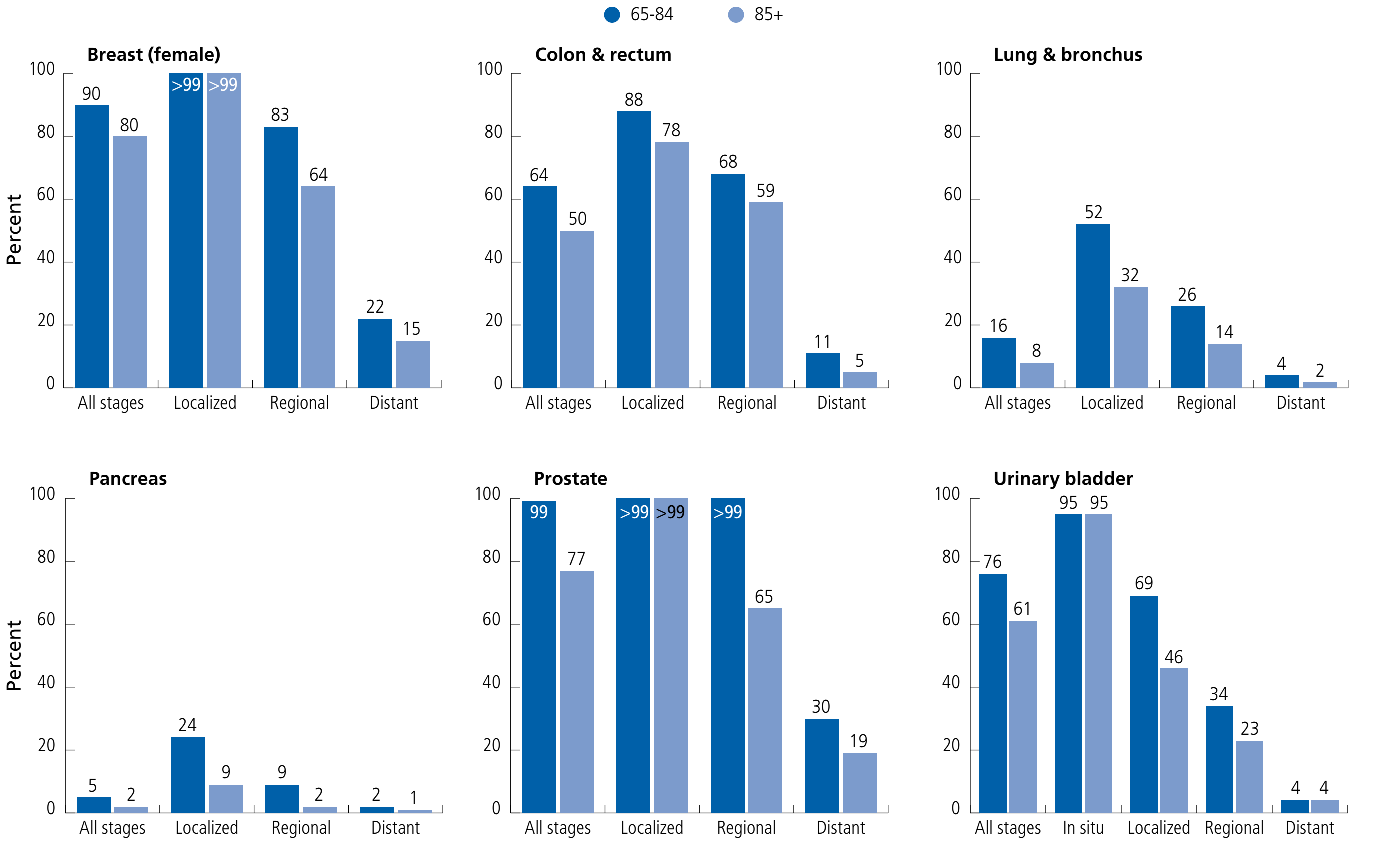
Although National Comprehensive Cancer Network guidelines do not recommend less intensive therapy for any patient with potentially curable cancer, studies have shown that older patients often receive little or no treatment.[36, 55, 56] This is partly because cancer-directed therapy is not appropriate for some older patients because the benefit of prolonged survival does not outweigh potential adverse effects and impact on quality of life. In addition, for many older patients, death may be more likely to occur from other causes.[57, 58]

Age alone does not predict life expectancy, physical function, or the ability to tolerate treatment. A large body of research is currently focused on developing tools that will enable clinicians to evaluate the functional age of patients as part of the treatment decision-making process. The Geriatric Assessment (GA) is a multidimensional, multidisciplinary tool that can be used to evaluate medical, psychosocial, and functional capabilities in older adults. Studies have shown that the GA can identify previously unknown health problems and predict treatment toxicities and overall survival in cancer patients.[59] Although the GA can help guide appropriate treatment, it requires significant time and resources to implement.[60, 61] A panel of geriatric oncology experts recommended the use of the GA in cancer patients 75 years of age and older, and more recently, the American Society of Clinical Oncology recommended use of the GA in patients 65 and older who are receiving chemotherapy.[62, 63] Nevertheless, additional research is needed to determine effectiveness and best practices for the use of the GA in older cancer patients.[60]

Biomarkers, including markers of chronic inflammation (e.g. C-reactive protein and plasma interleukin 6 levels) and coagulation (e.g. d-dimer, sVCAM), as well as commonly measured laboratory blood values (hemoglobin and albumin) are being investigated for their potential to aid in the assessment of functional age and frailty, and their ability to predict mortality.[61, 64, 65] Although these markers are easily obtained through routine bloodwork, they require careful interpretation because they can be produced by cancer itself and thus may be most useful in patients who have had their tumor surgically removed. Potential age-related biomarkers under investigation that are not produced by tumors, including telomere length and p16 levels, are associated with cellular senescence (when cells stop dividing) and require more specialized analysis.[64]

Treating cancer patients ages 85+ is complex due to the higher likelihood of other health conditions, declines in health associated with aging, and the dearth of data

Figure S8. Five-year Relative Survival for Selected Cancers in Two Age Groups, US, 2008-2014



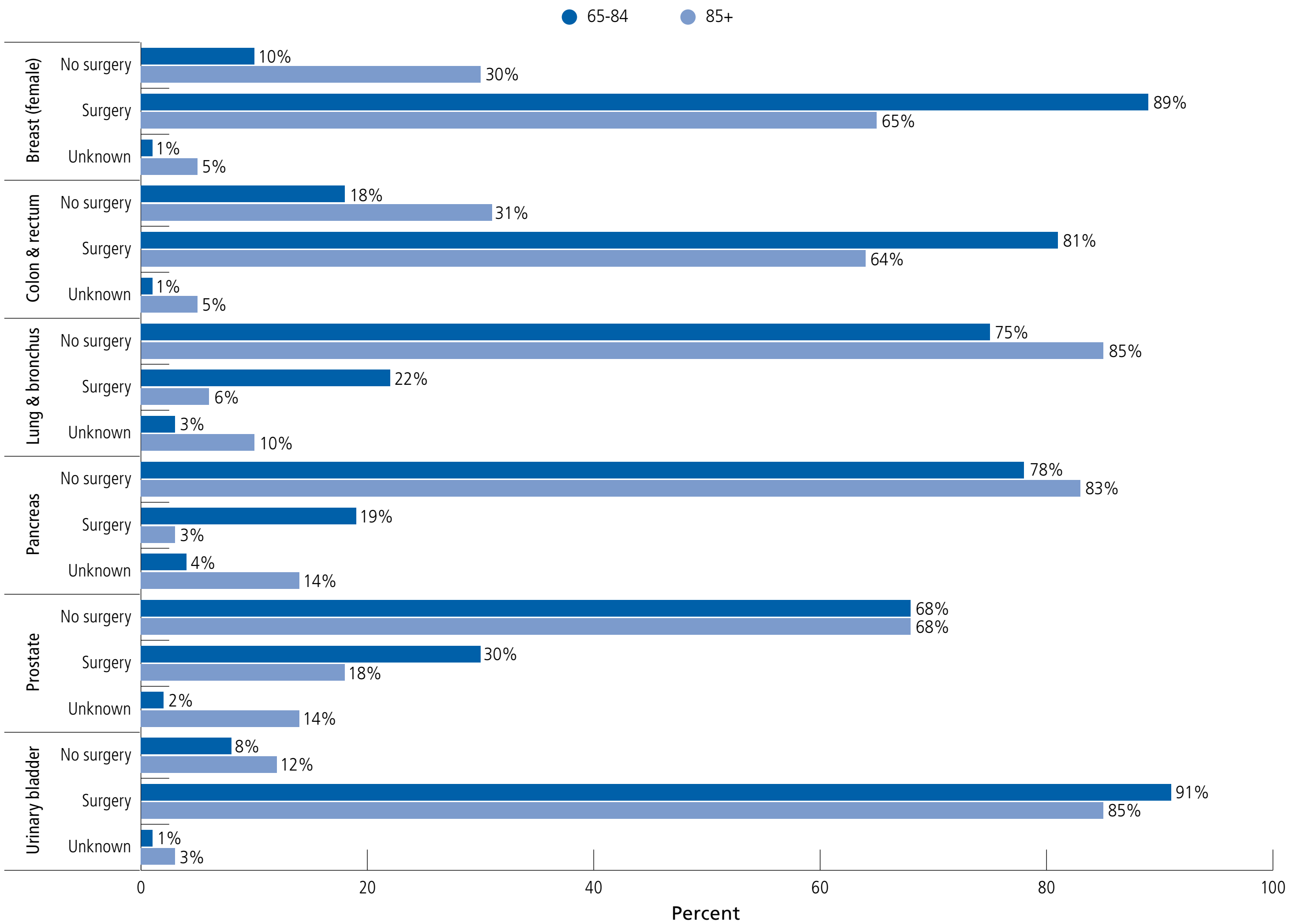
Source: SEER 18 registries, 2018.

about cancer treatment in this age group. Nearly half (47%) of cancer patients 85 and older have serious medical conditions that would require adjustment of cancer treatment.[8] Most studies have found that cancer patients with comorbidities are less likely to receive curative treatment.[66] This in part reflects concerns about increased risks of death from these other health issues as well as treatment side effects, including exacerbating coexisting conditions and drug interactions. One study found that 39% of cancer patients over 80 were taking five or more medications including their cancer drugs.[67] In addition, age-associated physiologic changes, such as declines in liver and kidney function, can affect drug metabolism and influence therapeutic benefit and risk of adverse effects.[68, 69] Much remains unknown about the intersection of side effects of cancer therapies and age-related declines, such as cognitive impairment, in older patients.[70, 71] Finally, clinicians have inadequate evidence on which to base treatment decisions in older cancer patients because of extremely limited representation in clinical trials.[72, 73] As a result, it is difficult to predict tolerance and response to therapies, as well as their influence on other health conditions or medications.[7] The Institute of Medicine report, *Delivering High-Quality Cancer Care: Charting a New Course for a System in Crisis*, highlighted the critical need of improving the evidence-base for treating older adults with cancer.[74] Although several recent trials focusing on older patients have been successful, accrual rates remain low.

What unique challenges do older people with cancer face?

Although research on the cancer survivor experience in the oldest old population is limited, some studies suggest higher rates of depression, distress, and anxiety.[75, 76] Furthermore, cancer and its treatment often accelerate the aging process by further reducing physical

Figure S9. Receipt of Surgical Treatment for Selected Cancers in Two Age Groups, US, 2011-2015



Source: SEER 18 registries, 2018.

functioning, especially among older survivors with multiple additional chronic conditions.[77] Nevertheless, some survivors in this age group remain resilient. Physical activity, maintaining a healthy weight, and subjective happiness serve as protective factors against physical functioning decline among older cancer survivors.[77] Recommendations for physical activity in the oldest old should be individualized to optimize participation, safety, and efficacy. Older cancer survivors can also benefit from programs that encourage smoking cessation, weight management, and social support.[78]

Resources

American Federation for Aging Research
www.afar.org

The mission of this national nonprofit organization is to support and advance healthy aging through biomedical research.

American Society of Clinical Oncology (ASCO)
www.asco.org/practice-guidelines/cancer-care-initiatives/geriatric-oncology

ASCO has compiled the most practice-changing, cutting-edge research and clinical guidelines in geriatric oncology, along with effective tools, assessments, and other resources for clinicians, patients, and caregivers.

Cancer and Resource Aging Group
www.mycarg.org

The Cancer and Aging Research Group aims to improve the care of older adults with cancer through research collaborations and clinical trials. Their website also provides a wealth of information and resources for older adults including guidance on nutrition, safety, and emotional support.

International Society of Geriatric Oncology
www.siog.org

The International Society of Geriatric Oncology is a multidisciplinary team of oncology and geriatrics physicians, along with allied health professionals, collaborating to address the rising public health challenges related to aging and cancer to foster the development of health professionals in the field of geriatric oncology and optimize treatment for older adults with cancer worldwide.

National Institute on Aging (NIA)
www.nia.nih.gov

As one of the 27 institutes and centers of the National Institutes of Health, the National Institute on Aging leads the federal government in conducting and supporting research on aging and the health and well-being of older people by seeking to understand the nature of aging and the aging process, and diseases and conditions associated with growing older, in order to extend healthy, active years of life.

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