EPI-210

CANCER IN THE ELDERLY

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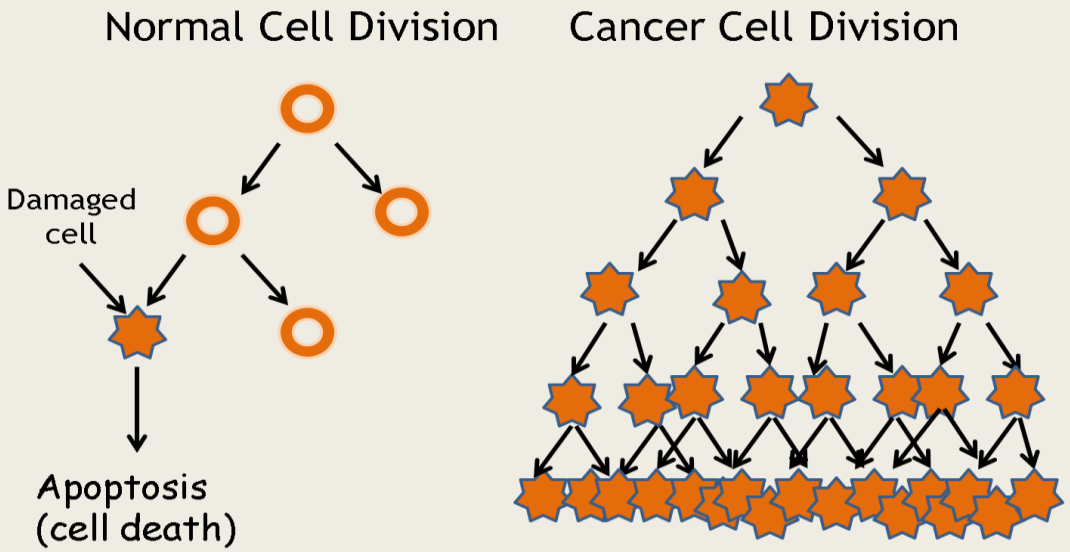
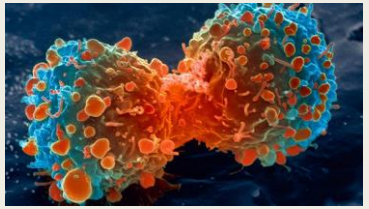
Cancer

- Group of related diseases (>100 types)
  - *Described by:*
    - Organ or tissue- lung, breast
    - Cell- epithelial, squamous
- In all types of cancer, cells begin to divide without stopping –uncontrollably-, ultimately forming a tumor.



- In US:
  - 2nd cause of death (CVD), all population
  - 1st cause of death, 65-84 years

Cancer cell dividing (Lung)



What Is Cancer? National Cancer Institute. https://www.cancer.gov/about-cancer/understanding/what-is-cancer.

Leading Causes for 2016. National Vital Statistics Reports; vol 67 no 6. Hyattsville, MD: National Center for Health Statistics. 2018.

“Nine hallmarks of aging have been proposed, including genomic instability and epigenetic alteration, which are also hallmarks of cancer.” White et al., 2014

Hallmarks of Cancer: The Next Generation

Hanahan and Weinberg, 2011

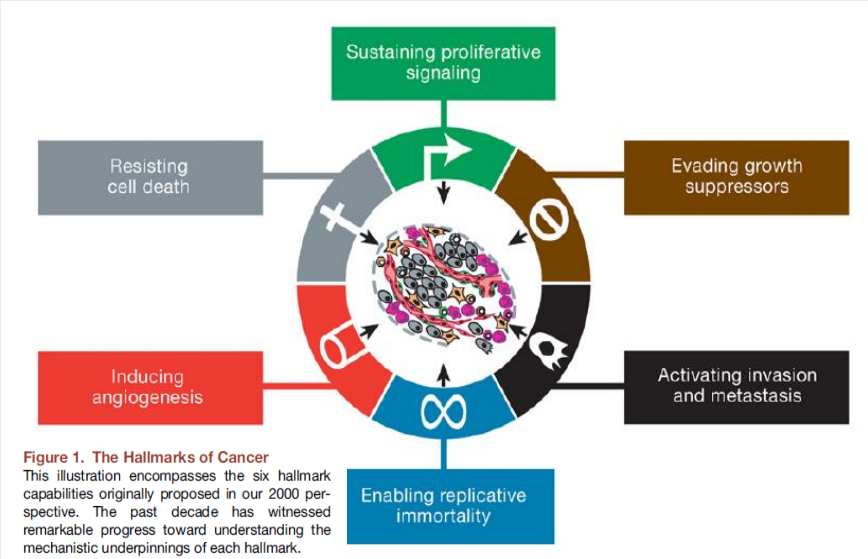


Figure 1. The Hallmarks of Cancer
This illustration encompasses the six hallmark capabilities originally proposed in our 2000 perspective. The past decade has witnessed remarkable progress toward understanding the mechanistic underpinnings of each hallmark.

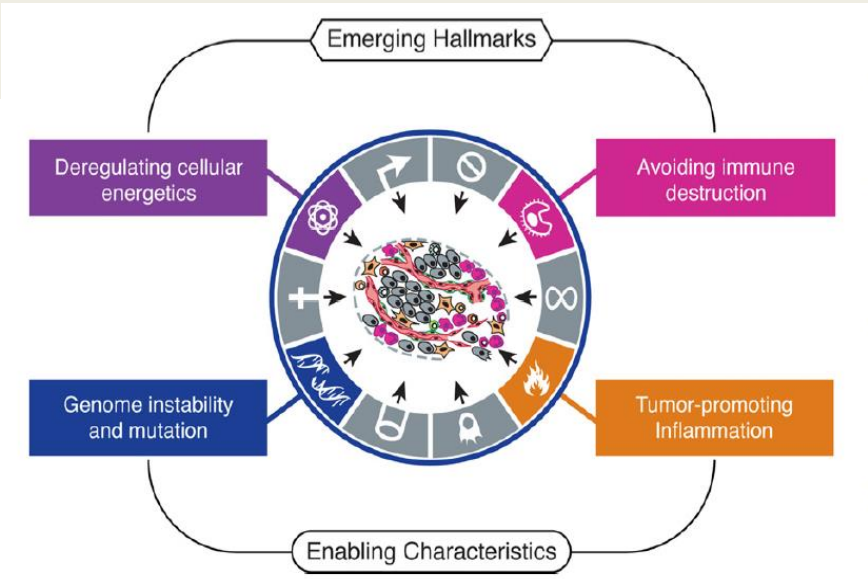


Figure 3. Emerging Hallmarks and Enabling Characteristics
An increasing body of research suggests that two additional hallmarks of cancer are involved in the pathogenesis of some and perhaps all cancers. One involves the capability to modify, or reprogram, cellular metabolism in order to most effectively support neoplastic proliferation. The second allows cancer cells to evade immunological destruction, in particular by T and B lymphocytes, macrophages, and natural killer cells. Because neither capability is yet generalized and fully validated, they are labeled as emerging hallmarks. Additionally, two consequential characteristics of neoplasia facilitate acquisition of both core and emerging hallmarks. Genomic instability and thus mutability endow cancer cells with genetic alterations that drive tumor progression. Inflammation by innate immune cells designed to fight infections and heal wounds can instead result in their inadvertent support of multiple hallmark capabilities, thereby manifesting the now widely appreciated tumor-promoting consequences of inflammatory responses.

The Hallmarks of Aging

López-Otín et al., 2013

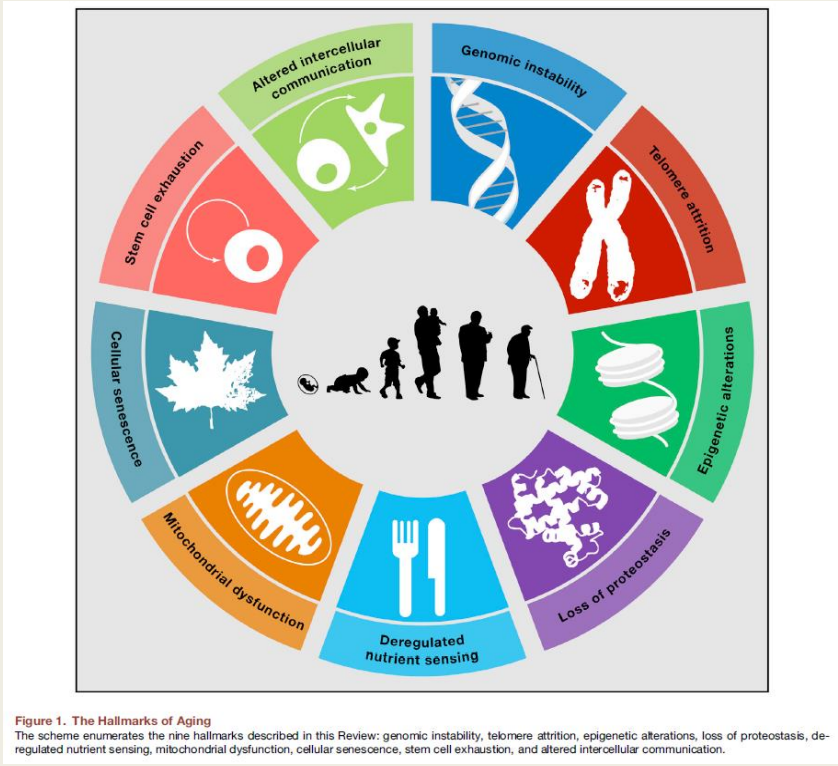


Figure 1. The Hallmarks of Aging
The scheme enumerates the nine hallmarks described in this Review: genomic instability, telomere attrition, epigenetic alterations, loss of proteostasis, deregulated nutrient sensing, mitochondrial dysfunction, cellular senescence, stem cell exhaustion, and altered intercellular communication.

“Aging is characterized by a progressive loss of physiological integrity, leading to impaired function and increased vulnerability to death. This deterioration is the primary risk factor for major human pathologies, including cancer…”

Risk Factors

Common types of cancer

US (IR-MR)

(1-2) **Breast-** older age, family history, personal history of breast cancer or benign (noncancer) breast disease, dense breasts, exposure of breast tissue to estrogen made in the body, taking hormone therapy for symptoms of menopause, radiation therapy to the breast or chest, obesity, drinking alcohol

(2-3) **Prostate-** older age, family history, race, hormones, vitamin E, folic acid, dairy and calcium

(3-1) **Lung-** older age, cigarette, cigar, and pipe smoking, secondhand smoke, family history, HIV infection, environmental risk factors, beta carotene supplements in heavy smokers

(4-4) **Colorectal-** older age, family history, excessive alcohol use, obesity, being physically inactive, cigarette smoking, diet, history of inflammatory bowel disease, inherited conditions (Lynch syndrome and familial adenomatous polyposis)

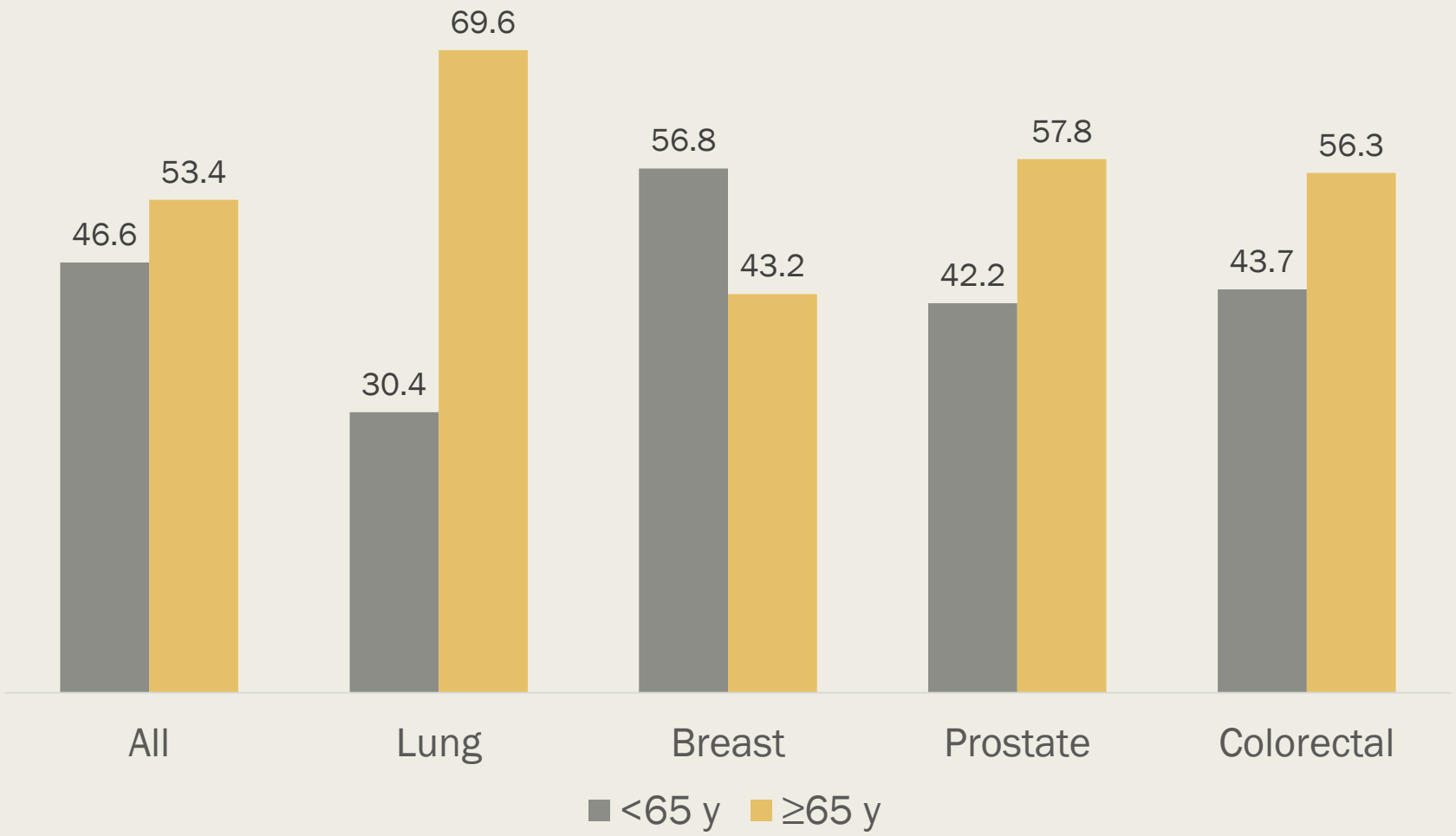
"Age is a well-recognized risk factor for cancer development. In fact, you could say aging is the major carcinogen."

-Dr. Norman E. Sharpless, NCI Director (2018)

Cancer Types. National Cancer Institute. https://www.cancer.gov/types.

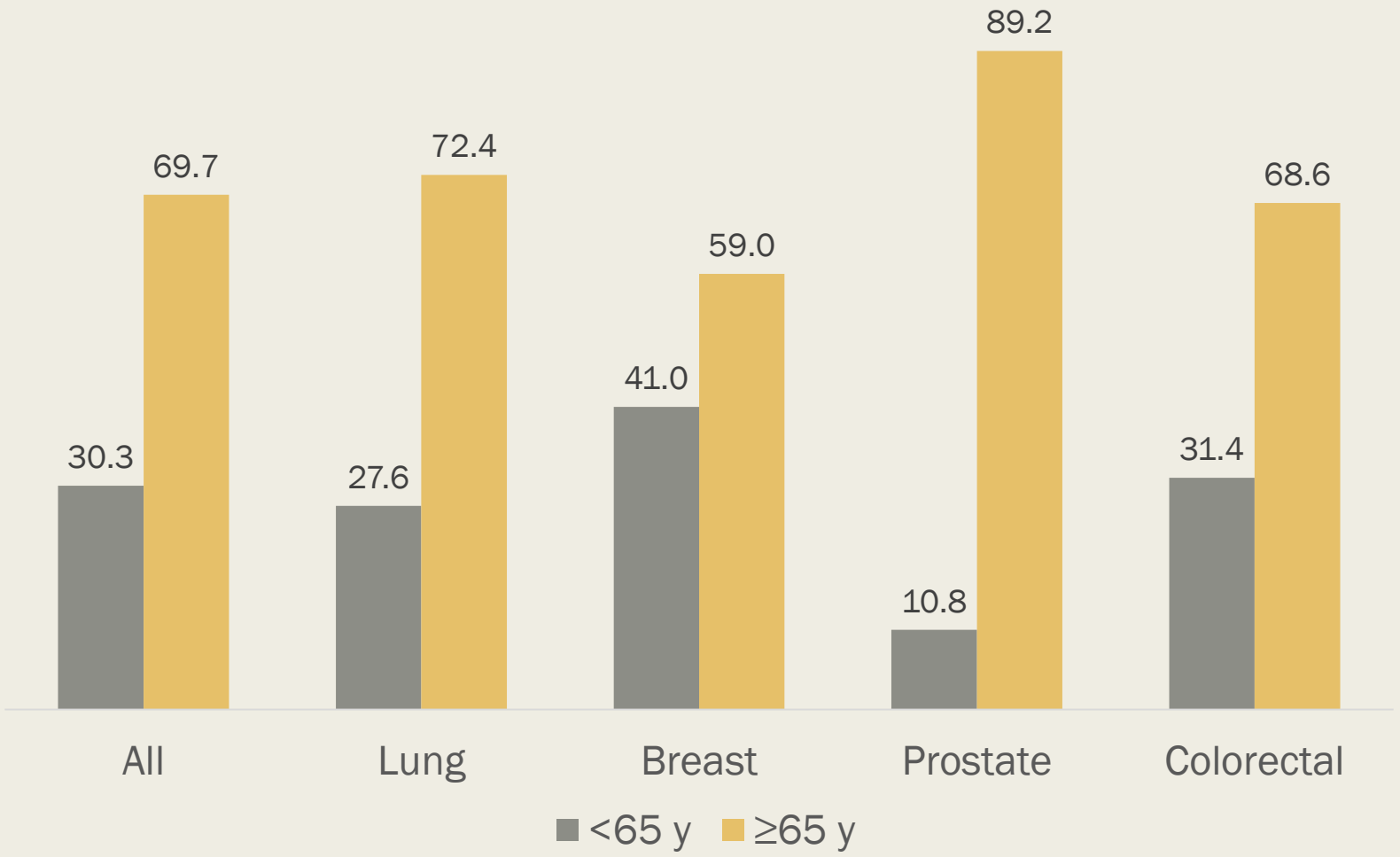
The Challenging Landscape of Cancer and Aging. National Cancer Institute. https://www.cancer.gov/news-events/cancer-currents-blog/2018/sharpless-aging-cancer-research.

Percent of *new cancer cases* in US by age group , 2011-2015



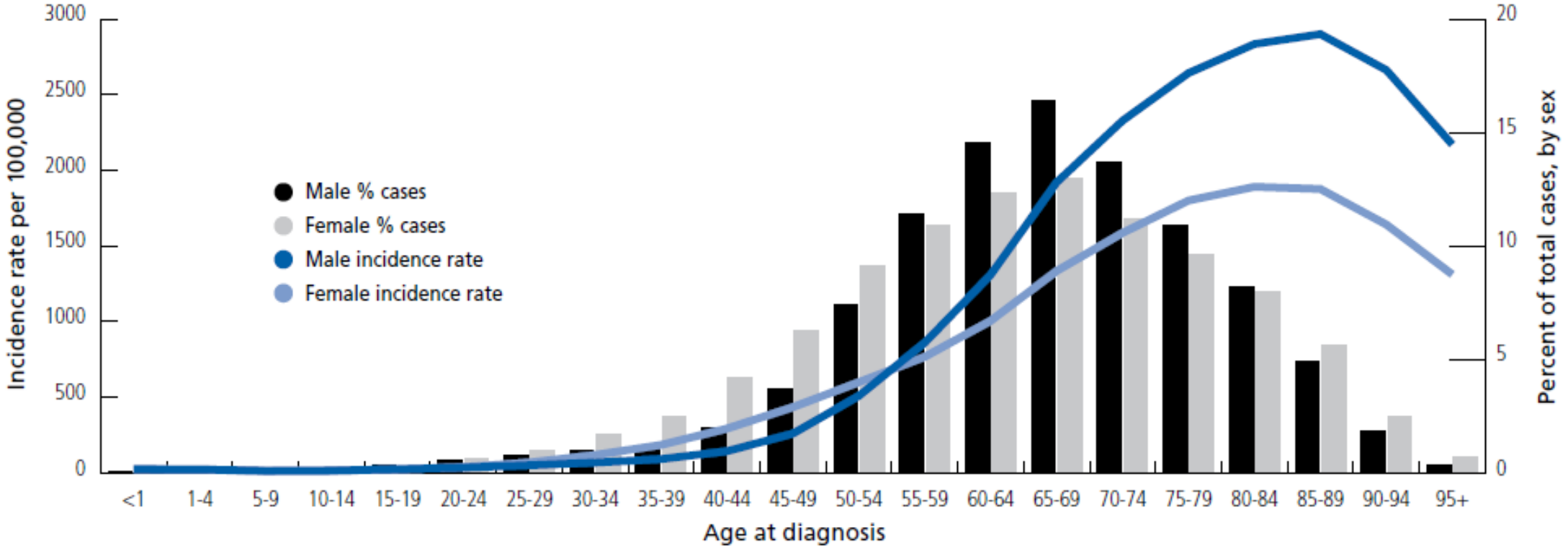
Cancer Stat Facts. SEER. https://seer.cancer.gov/statfacts

Percent of *cancer deaths* in US by age group, 2011-2015



Cancer Stat Facts. SEER. https://seer.cancer.gov/statfacts

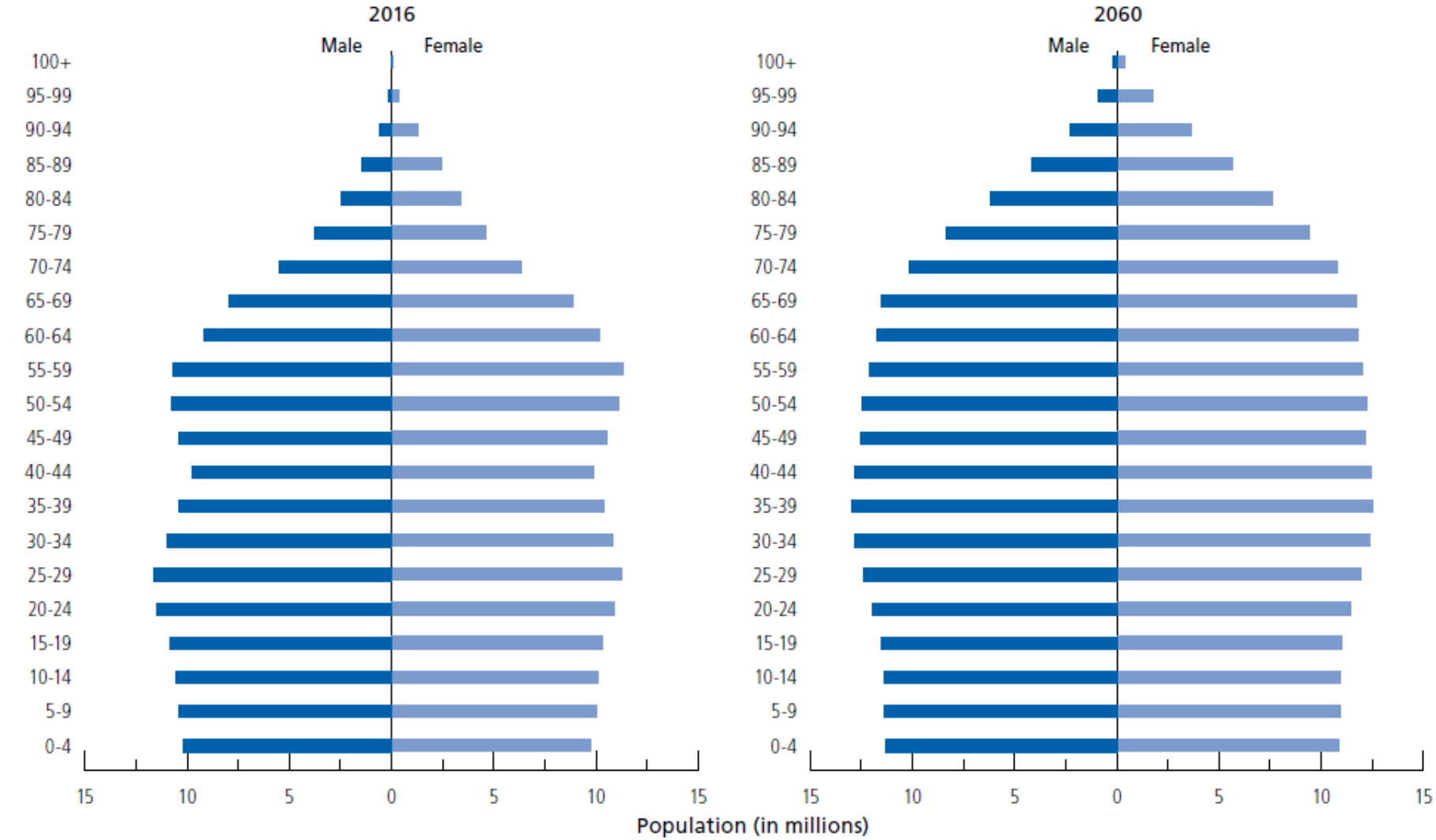
Figure S2. Average Annual Incidence Rates and Case Distribution by Age, US, 2011-2015



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

American Cancer Society. Cancer Facts & Figures 2019. Atlanta: American Cancer Society; 2019.

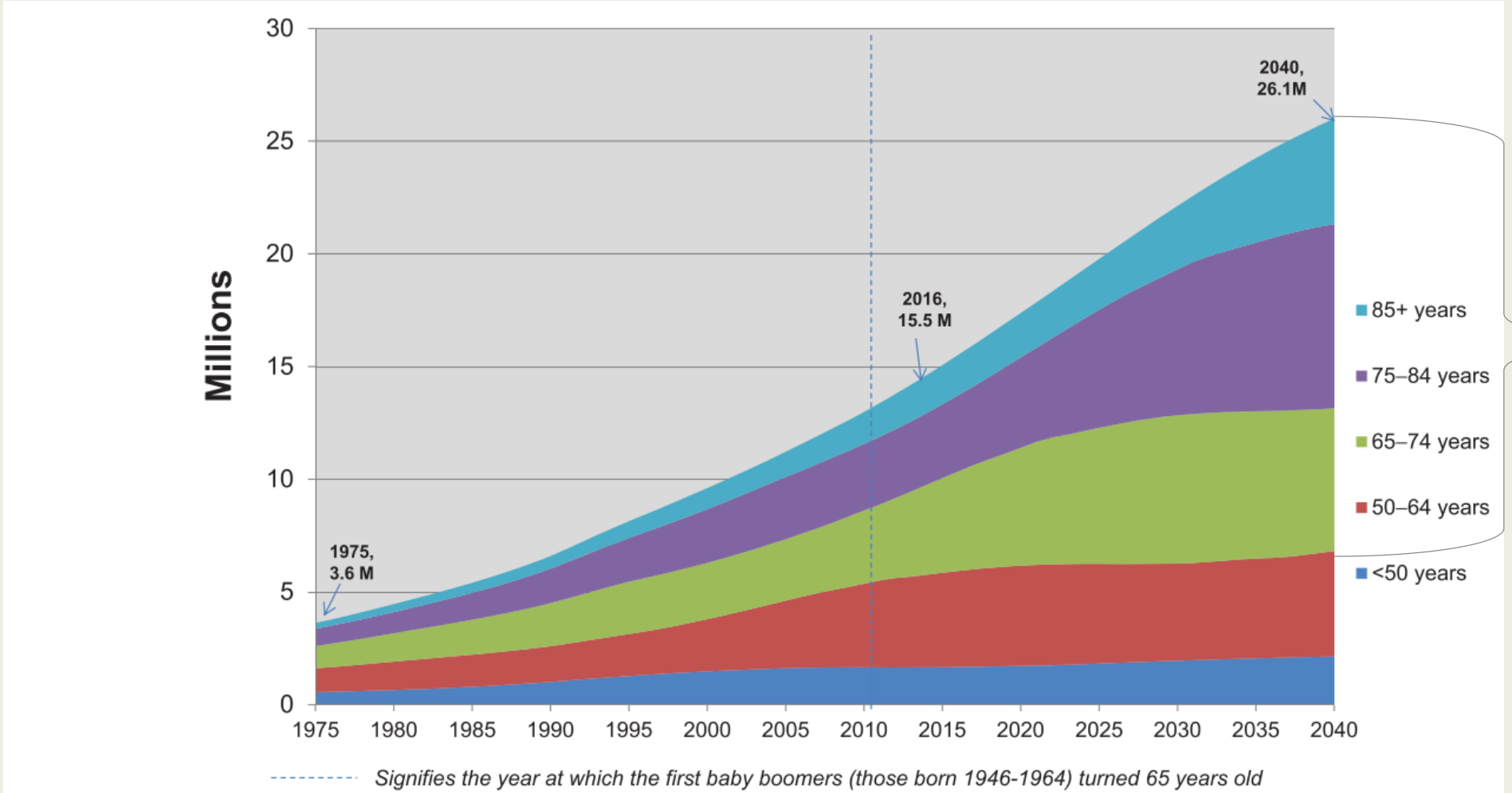
Figure S1. Age Distribution of US Population in Millions: 2016 versus 2060



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

American Cancer Society. Cancer Facts & Figures 2019. Atlanta: American Cancer Society; 2019.

Cancer Survivors in US, 1975-2040



73% Older adults (≥65 y)

Figure 1.
Estimated cancer prevalence by age in the U.S. population from 1975 (216 M) to 2040 (380 M).

Bluethmann et al., 2016

Cancer Survivors in US, 2016

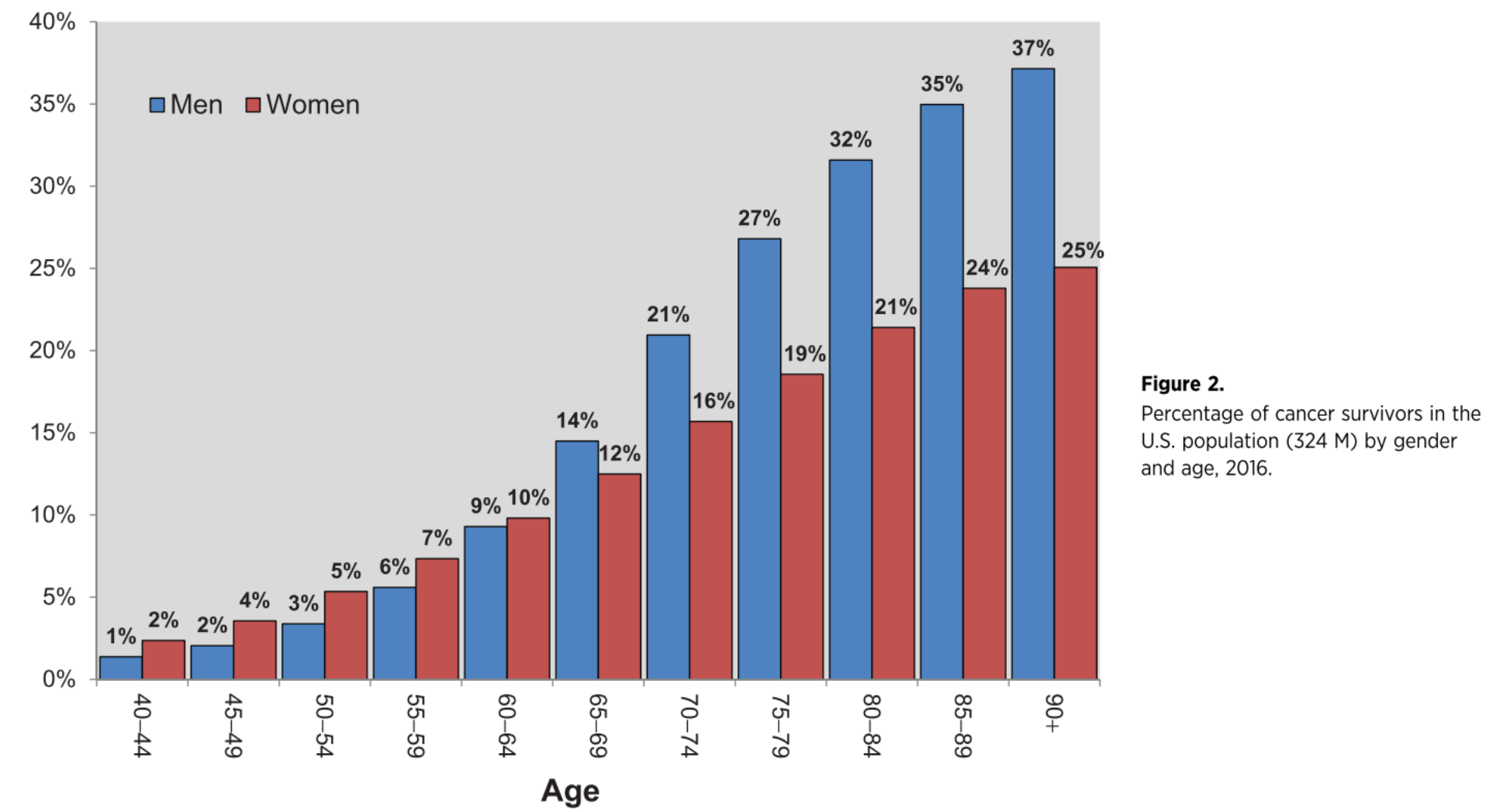


Figure 2.
Percentage of cancer survivors in the U.S. population (324 M) by gender and age, 2016.

Bluethmann et al., 2016

Comorbidities

Table 1. Comorbidity burden[a] by age and cancer site

	Noncancer	All sites	Bladder	CRC	Female breast	Leukemia	Lung	Oral	Prostate
Total	100,000	457,659	26,045	48,138	52,179	12,447	76,365	8,043	80,087
66–69 y	20,180	92,362	4,036	7,361	11,407	1,893	14,558	1,918	22,196
None	66%	56%	52%	56%	65%	56%	39%	56%	66%
Moderate	17%	18%	20%	20%	17%	19%	12%	16%	18%
Severe	16%	26%	28%	24%	17%	24%	48%	27%	16%
70–74 y	24,699	113,029	5,740	10,036	12,870	2,512	18,982	1,998	25,315
None	61%	50%	47%	51%	59%	51%	34%	52%	61%
Moderate	19%	19%	21%	20%	20%	20%	13%	16%	19%
Severe	20%	31%	32%	29%	21%	30%	52%	32%	19%
75–79 y	21,555	98,644	5,848	10,077	10,951	2,623	17,781	1,592	17,185
None	54%	45%	43%	46%	54%	45%	32%	46%	55%
Moderate	19%	19%	20%	19%	20%	20%	13%	18%	20%
Severe	26%	36%	37%	35%	26%	35%	55%	35%	24%
80–84 y	17,409	79,676	5,339	9,630	8,824	2,528	14,180	1,241	9,362
None	48%	40%	38%	42%	49%	42%	30%	43%	49%
Moderate	18%	18%	19%	19%	21%	17%	14%	17%	19%
Severe	33%	41%	42%	40%	30%	41%	56%	40%	32%
85+ y	16,157	73,948	5,082	11,034	8,127	2,891	10,864	1,294	6,029
None	42%	37%	36%	37%	44%	36%	29%	39%	43%
Moderate	17%	17%	17%	17%	19%	15%	13%	17%	16%
Severe	42%	47%	47%	46%	37%	49%	57%	44%	41%

[a]Categories included comorbidities described in the Charlson Index and weighted for effect on noncancer mortality. None implies a "0" score for comorbidities, though this may not reflect common conditions that are not currently included in the Index. Moderate comorbidity included conditions that usually do not require physicians to adjust cancer treatment. Severe comorbidity burden refers to severe illnesses that frequently lead to organ failure or systemic dysfunction and always require adjustment of cancer treatment for survivors. See Materials and Methods for more detail.

Bluethmann et al., 2016

Methods Concern

Table 1. Common biases in studies of postdiagnosis exposures and outcomes among persons with a history of cancer

Type of bias	Cause of bias	Approaches to reducing bias
Reverse causation (sometimes called protopathic bias)	Undiagnosed occurrence of the outcome leads to changes in the exposure or measurement of the exposure	Restrict to persons recurrence-free at exposure (Design) Lag exposure (Analysis)
Confounding		
Confounding by disease progression	Undetected progression or recurrence alters subsequent exposure, causing bias in studies of cancer-related mortality	Restrict to persons recurrence-free at exposure (Design) Use marginal structural models (Analysis) Lag exposure (Analysis)
Confounding by precancer exposures	Exposure before cancer diagnosis affects risk of recurrence/mortality and is also associated with exposure after cancer	Restrict to persons unexposed before cancer diagnosis (Design) Adjust for precancer exposures (Analysis)
Selection bias		
Self-selection (sometimes called volunteer bias, nonresponse bias)	People who choose to participate in a study may have different risk factors and a different risk of the outcome than those who do not.	Select a study population that is a random sample of target population (Design) Weight individuals based on probability of responding (Analysis)
Failure to account for left truncation (sometimes called length bias, survival bias)	Only those persons who remain event-free until a later time point are included in the study, but they contribute person-time starting earlier.	Observe all participants starting at cancer diagnosis (Design) Participants enter into the analysis when they begin being followed for the outcome and not before (Analysis)
Differential loss to follow-up	Being censored is an effect of both the exposure and the outcome	Ascertain the presence or absence of the outcome in a way that is unlikely to be affected by whether the outcome has occurred (Design) Design surveys, study visits, etc. to maximize response rate (Design) Inverse probability of treatment weighting using variables related to loss-to-follow-up (Analysis)

Chubak et al., 2013

Selection Bias

- Differential loss to follow-up (associated with exposure and outcome)
- Example: Study in Breast Cancer Survivors, DM -> Recurrence
  - *DM+ are more likely to drop out than those DM- because of complications of their disease.*
  - *BC survivors with a recurrence are more likely to drop out than those without a recurrence before the event is diagnosed or recorded.*
  - *A woman with a recurrence who stays is less likely to have DM than a person without a recurrence.*

    Overrepresentation of DM- and Recurrence +
  - *Result: False association between DM+ and a reduced risk of recurrence.*

Discussion

Implications (aging population, increased survivorship, more people with cancer, comorbidities)

- Patients care
  - *Needs- physical, cognitive, psychological, social*
  - *Healthcare- multiple providers (fragmented care), polypharmacy*
  - *Approach- age ("bias", chronological vs physiological), comprehensive geriatric assessment*
  - *Evidence based best practices- research, inclusion of older adults in studies, RCTs*
- Cancer care costs
  - *US- $158 B in 2010, $173 B in 2020 (estimated)- Mariotto et al., 2011*
  - *Patients and family*
    - Among survivors (<65 y) with more than 1-year postdiagnosis, annual healthcare expenditures were double that in the general population. - Short et al., 2011