#### An Overview of Survival Statistics in SEER\*Stat

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NCI Analytic Tools SEERies





#### Agenda

- 1. Overview of survival
- 2. Relative Survival Rates
  - Period Survival
  - Conditional Survival
- Demos of relative survival and the period method
- 4. Cause-specific Survival
- 5. Crude survival (Crude probabilities of death)
- 6. Demo 3



### Cause-specific survival

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### Challenges in Relative Survival

- Relative survival assumes life tables are representative of the cancer cohort's other causes mortality
- General population life tables may not represent well the 'other cause mortality' for:
  - Ethnic minorities,
  - Cancers affected by common risk factor affecting other diseases (e.g. lung cancer and smoking)
  - Screen-detected cancers (local stage breast and prostate cancers) relative survival may be higher than 100%
- Although relative survival is the default, SEER uses cause-specific survival to show survival by detailed race/ethnicity



## Examples of Relative survival being problematic (Table 4 Howlader et al JNCI 2010)

	White										
Selected cancer cohort	RS, % (95% CI)	CSS, % (95% CI)	Dif.,								
Breast											
In situ and <65 y	100.9†	99.7 (99.6 to 99.8)	1.2								
In situ and ≥65 y	107.5†	98.6 (98.4 to 98.8)	8.9								
Prostate											
Localized/ regional and <65 y	101.3†	98.3 (98.2 to 98.4)	3.0								
Localized/ regional and ≥65 y	104.5†	94.8 (94.6 to 94.9)	9.8								

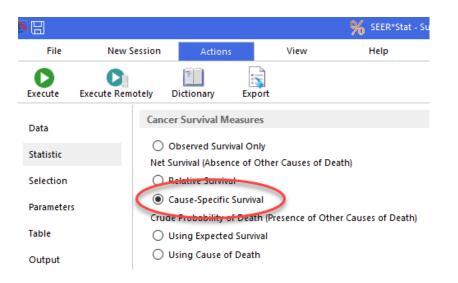


# Examples of Relative survival being problematic (Table 1 Forjaz et al CEBP 2019).

		RS		CSS	Abs. Dif.			RS		Abs. Dif.		
	N	5-y (95% CI)	N	5-y (95% CI)	(%)		N	5-y (95% CI)	N	5-y (95% CI)	(%)	
Esophagu	S					Breast						
20-49	3,329	19.7 (18.3-21.2)	3,299	21.8 (20.3-23.3)	-2.1	20-49	158,585	88.8 (88.6-88.9)	158,005	89.1 (88.9-89.3)	-0.3	
50-64	15,114	19.7 (19.0-20.4)	14,998	22.1 (21.4-22.9)	-2.4	50-64	243,843	89.9 (89.8-90.1)	242,910	89.6 (89.4-89.7)	0.3	
65-74	11,423	19.4 (18.6-20.3)	11,324	22.3 (21.4-23.2)	-2.9	65-74	131,276	90.9 (90.6-91.1)	130,592	89.3 (89.1-89.5)	1.6	
75-84	8,300	13.7 (12.7-14.7)	8,223	15.2 (14.3-16.1)	-1.5	75-84	88,889	88.2 (87.8-88.7)	88,190	83.9 (83.7-84.2)	4.3 <sup>b</sup>	
85+	2,789	5.8 (4.5-7.4)	2,770	6.5 (5.3-7.8)	-0.7	85+	30,515	80.3 (79.0-81.5)	30,261	69.9 (69.3-70.5)	10.4 <sup>b</sup>	
All	40,960	17.6 (17.2-18.1)	40,619	19.8 (19.4-20.3)	-2.2	All	653,181	89.2 (89.1-89.3)	650,031	87.8 (87.8-87.9)	1.4	
ages						ages						



### Cause-specific survival (Uses cause of death)



- Deaths associated with cancer
   →event of interest
- Deaths due to other causes → censoring event
  - Net survival measure (in the hypothetical world that patients do not die of other causes)



### SEER Cause-Specific Death Classification Variable

- SEER algorithm to improve cause of death indicator:
  - For cases without a prior history of cancer (Howlader et al, JNCI 2010)
  - For cancer patients with a prior cancer (Forjaz et al, Cancer 2021)
- The algorithm takes into account COD in conjunction with
  - Site of original cancer diagnosis
  - Tumor sequence (the only cancer or the first of more than 1)
  - Diseases related to the cancer of diagnosis (e.g., HIV/AIDS)
- Cause of death was evaluated using respective International Classification of Disease Codes (ICD): ICD-8 (1973-1978), ICD-9 (1979-1998), ICD-10 (1999+)
- For more details: http://seer.cancer.gov/causespecific/index.html



# Cancer patient Survival with and without A Prior Cancer (Table 2 Forjaz et al Cancer 2021)

		Cause	-Specific Sur	rvival	Relative Survival								
Cancer Site	First E	Ever Primary <sup>b</sup>	Earliest M	latching Primary <sup>c</sup>		First E	Ever Primary <sup>b</sup>	Earliest M					
	No.	Survival (95% CI)	No.	Survival (95% CI)	Abs Dif (%)	No.	Survival (95% CI)	No.	Survival (95% CI)	Abs Dif (%)			
Esophagus	50,279	20.1 (19.7-20.5)	63,156	20.7 (20.3-21.0)	-0.6	50,694	18.0 (17.6-18.4)	63,638	17.7 (17.4-18.1)	0.3			
Stomach	86,541	31.4 (31.1-31.8)	105,812	32.2 (31.8-32.5)	-0.8	87,802	29.4 (29.0-29.7)	107,240	28.9 (28.6-29.3)	0.5			
Colon and rectum	515,015	65.0 (64.9-65.2)	614,816	65.3 (65.2-65.5)	-0.3	518,910	64.7 (64.5-64.9)	619,356	63.8 (63.7-64.0)	0.9			
Liver	86,350	19.7 (19.4-20.0)	98,638	20.5 (20.2-20.8)	-0.8	87,723	16.4 (16.1-16.7)	100,144	16.6 (16.3-16.9)	-0.2			
Pancreas	138,406	9.6 (9.4-9.8)	170,448	10.2 (10.0-10.4)	-0.6	139,684	9.0 (8.9-9.2)	171,936	9.3 (9.1-9.5)	-0.3			
Lung	645,286	20.6 (20.4-20.7)	819,066	22.4 (22.3-22.5)	-1.8	650,391	18.4 (18.3-18.6)	825,127	19.3 (19.2-19.4)	-0.9			
Melanoma	234,701	90.4 (90.3-90.6)	289,016	90.5 (90.4-90.6)	-0.1	235,592	92.0 (91.8-92.2)	290,146	91.2 (91.0-91.3)	0.8			
Breast	810,202	87.1 (87.0-87.1)	938,510	87.1 (87.0-87.2)	0.0	814,107	89.3 (89.1-89.4)	943,078	88.6 (88.4-88.7)	0.7			
Cervix uteri	54,407	65.4 (64.9-65.9)	58,422	65.4 (65.0-65.9)	0.0	54,877	62.5 (62.0-63.0)	58,928	61.9 (61.4-62.4)	0.6			
Ovary	82,001	40.9 (40.5-41.2)	96,245	41.7 (41.4-42.0)	-0.8	82,579	40.9 (40.5-41.3)	96,899	41.1 (40.7-41.5)	-0.2			
Prostate	846,398	92.2 (92.2-92.3)	931,249	92.2 (92.2-92.3)	0.0	852,351	97.4 (97.3-97.5)	937,752	96.2 (96.1-96.3)	1.2			
Brain	66,839	27.8 (27.5-28.1)	76,691	27.6 (27.3-27.9)	0.2	67,525	26.7 (26.4-27.0)	77,439	26.4 (26.1-26.7)	0.3			
Thyroid	150,593	94.5 (94.4-94.7)	171,238	94.7 (94.6-94.8)	-0.2	150,995	96.2 (96.0-96.5)	171,722	94.9 (94.6-95.1)	1.3			
Lymphoma	257,439	69.7 (69.5-69.9)	308,639	69.8 (69.6-70.0)	-0.1	259,222	68.6 (68.3-68.8)	310,735	67.6 (67.3-67.8)	1.0			
Leukemia	135,165	59.5 (59.2-59.8)	171,063	57.1 (56.9-57.4)	2.4	136,153	56.9 (56.6-57.2)	172,269	53.7 (53.4-54.0)	3.2 <sup>d</sup>			
All sites	5,350,148	65.0 (65.0-65.1)	5,928,693	65.0 (65.0-65.1)	0.0	5,387,992	64.6 (64.6-64.7)	5,970,181	64.0 (63.9-64.0)	0.6			



### SEER\*Stat Cause- specific survival (Life page)

1-year Cause Specific Survival=67.0%

1-year Relative Survival=65.3%

Page:	Life							
		Alive at		Lost to	Cause-Sp	pecific	SE Cause-S	pecific
		Start	Died	Follow-up	Interval	Cum	Interval	Cum
1	< 1 mo	1,107,820	77,463	18,885	92.9%	92.9%	0.0%	0.0%
2	1-<2 mo	1,011,472	53,533	12,642	94.7%	88.0%	0.0%	0.0%
3	2-<3 mo	945,297	44,383	10,984	95.3%	83.8%	0.0%	0.0%
4	3-<4 mo	889,930	30,702	8,212	96.5%	80.9%	0.0%	0.0%
5	4-<5 mo	851,016	26,339	8,433	96.9%	78.4%	0.0%	0.0%
6	5-<6 mo	816,244	21,542	7,459	97.3%	76.3%	0.0%	0.0%
7	6-<7 mo	787,243	20,539	7,184	97.4%	74.3%	0.0%	0.0%
8	7-<8 mo	759,520	16,399	6,649	97.8%	72.7%	0.0%	0.0%
9	8-<9 mo	736,472	15,260	6,278	97.9%	71.2%	0.0%	0.0%
10	9-<10 mo	714,934	15,371	6,260	97.8%	69.7%	0.0%	0.0%
11	10-<11 mo	693,303	12,418	5,654	38.2%	66,4%	0.0%	0.0%
12	11-<12 mo	675,231	13,819	5,6(5	97.9%	67.0%	0.0%	0.0%
13	12-<13 mo	655,737	10,709	4,877	98.4%	65.9%	0.0%	0.0%
14	13-<14 mo	640,151	11,370	5,322	98.2%	64.7%	0.0%	0.0%
15	14-<15 mo	623,459	9,125	4,663	98.5%	63.8%	0.0%	0.0%
16	15-<16 mo	609,671	8,810	4,746	98.5%	62.9%	0.0%	0.0%
17	16-<17 mo	596,115	8,950	4,904	98.5%	61.9%	0.0%	0.0%
18	17-<18 mo	582,261	7,681	4,438	98.7%	61.1%	0.0%	0.0%
19	18-<19 mo	570,142	8,141	4,788	98.6%	60.2%	0.0%	0.0%
20	19-<20 mo	557,213	6,592	4,326	98.8%	59.5%	0.0%	0.0%
21	20-<21 mo	546,295	7,059	4,464	98.7%	58.7%	0.0%	0.0%
22	21-<22 mo	534,772	5,782	4,374	98.9%	58.1%	0.0%	0.0%
22	22 -22	ival time (inte						

Median survival time (interval = 1 month): Observed = 40.5635 intervals.

Confidence interval: Log(-Log()) Transformation. The level is 95%.

Actuarial method.





# Cause-specific survival vs. Relative survival summary

- Both methods involve assumptions specific to the approach
  - Cause-specific: Accurate classification of cause of death
  - Relative: Appropriate estimation of expected survival
- In most situations relative and cause-specific survival are similar (Howlader et al JNCI 2010, Forjaz et al CEBP 2019)
- Each study should be evaluated in terms of the more appropriate underlying assumptions
- Comparative population-based studies usually use relative survival because of difference in the quality of cause of death information



#### Crude survival or competing risk survival

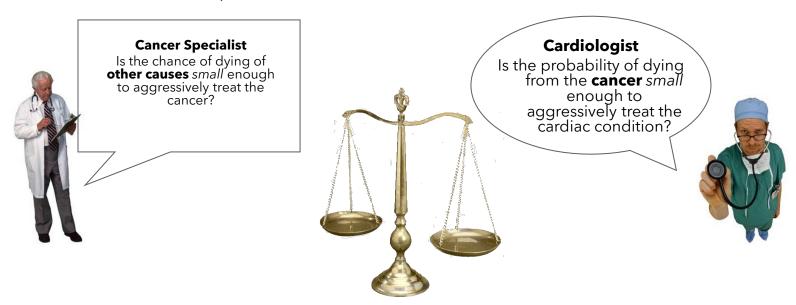
Probability of dying of cancer, dying of other causes and surviving





### Crude survival measure: patient prognosis

Example: Patient with cancer and cardiac conditions



Patients do not live in a hypothetical world: they can die of other causes

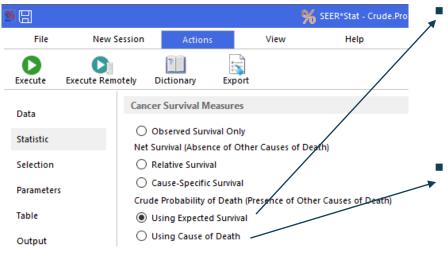


# Crude Probabilities of Death (survival under competing risks)

- Measure of the mortality patterns that are actually experienced in a cohort of cancer patients
- Better measure for treatment decisions since it includes risk of dying of other causes
- It is calculated and reported as:
  - Probability of surviving
  - Probability of dying of cancer
  - Probability of dying of other causes



### Methods for Calculating Crude Probability of Death in SEER\*Stat



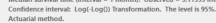
- Using expected survival
- Does not rely on cause of death information and uses life tables to estimate expected survival (Cronin & Feuer, 2000).
- Using cause of death information
- Similar to multiple decrement life tables (Marubini & Valsecchi, 1995; Schairer et al., 2004, Howlader et al, JNCI Monograph 2014)



### Crude probabilities of death using cause of death information

- Probability of surviving = 43.1%
- Probability of dying of cancer= 51.4%
- Probability of dying of other causes = 5.5%

	Alive at	Died du	ie to	Lost to		Observed		SE Obs		Specified COD			Other CODs			SE Specified COD	
	Start	Specified COD	Other CODs	Follow-up	Interval	Cum	Interval	Cum	Cum	Interval	Uncond Int	Cum	Interval	Uncond Int	Cum	Interval	Uncond Int
< 1 mo	717,778	76,061	12,010	2,867	87.7%	87.7%	0.0%	0.0%	12.3%	10.6%	10.6%	10.6%	1.7%	1.7%	1.7%	0.0%	0.09
1-<2 mo	626,840	55,255	5,741	2,808	90.2%	79.2%	0.0%	0.0%	20.8%	8.8%	7.7%	18.4%	0.9%	0.8%	2.5%	0.0%	0.09
2-<3 mo	563,036	45,868	4,225	2,772	91.1%	72.1%	0.0%	0.1%	27.9%	8.2%	6.5%	24.8%	0.8%	0.6%	3.1%	0.0%	0.09
3-<4 mo	510,171	31,560	2,901	2,210	93.2%	67.2%	0.0%	0.1%	32.8%	6.2%	4.5%	29.3%	0.6%	0.4%	3.5%	0.0%	0.09
4-<5 mo	473,500	27,328	2,520	2,521	93.7%	63.0%	0.0%	0.1%	37.0%	5.8%	3.9%	33.2%	0.5%	0.4%	3.8%	0.0%	0.09
5-<6 mo	441,131	22,734	2,160	2,273	94.3%	59.4%	0.0%	0.1%	40.6%	5.2%	3,3%	36.4%	0.5%	0.3%	4.2%	0.0%	0.0
6-≺7 mo	413,964	22,218	1,981	2,158	94.1%	55.9%	0.0%	0.1%	44.1%	5.4%	3.2%	39.6%	0.5%	0.3%	4.4%	0.0%	0.0
7-<8 mo	387,607	18,448	1,668	2,028	94.8%	53.0%	0.0%	0.1%	47.0%	4.8%	2.7%	42.3%	0.4%	0.2%	4.7%	0.0%	0.0
8-<9 mo	365,463	17,035	1,550	2,020	94.9%	50.3%	0.0%	0.1%	49.7%	4.7%	2.5%	44.8%	0.4%	0.2%	4.9%	0.0%	0.0
9-<10 mo	344,858	16,930	1,493	1,859	94.6%	47.6%	0.0%	0.1%	52.4%	4.9%	2.5%	47.3%	0.4%	0.2%	5.1%	0.0%	0.0
10-<11 mo	324,576	13,560	1,220	1,748	95.4%	45.4%	0.0%	0.1%	54.6%	4.2%	2.0%	40.3%	0.4%	0.2%	5.3%	0.0%	0.0
11-<12 mo	308,048	14,380	1,344	1,680	94.9%	43.1%	0.0%	0.1%	56.9%	4.7%	2.1%	51.4%	0.4%	0.2%	5.5%	0.0%	0.0
12-<13 mo	290,644	10,839	1,062	1,464	95.9%	41.3%	0.0%	0.1%	58.7%	3.7%	1.6%	55.0%	0.4%	0.2%	3.7%	0.0%	0.0
13-<14 mo	277,279	11,265	1,175	1,566	95.5%	39.5%	0.0%	0.1%	60.5%	4.1%	1.7%	54.7%	0.4%	0.2%	5.8%	0.0%	0.0
14-<15 mo	263,273	8,729	930	1,463	96.3%	38.0%	0.0%	0.1%	62.0%	3.3%	1.3%	56.0%	0.4%	0.1%	6.0%	0.0%	0.0
15-<16 mo	252,151	8,283	919	1,358	96.3%	36.6%	0.0%	0.1%	63.4%	3.3%	1.3%	57.2%	0.4%	0.1%	6.1%	0.0%	0.0
16-<17 mo	241,591	7,894	880	1,485	96.4%	35.3%	0.0%	0.1%	64.7%	3.3%	1.2%	58.4%	0.4%	0.1%	6.3%	0.0%	0.0
17-<18 mo	231,332	6,799	813	1,319	96.7%	34.1%	0.0%	0.1%	65.9%	2.9%	1.0%	59.5%	0.4%	0.1%	6.4%	0.0%	0.0
18-<19 mo	222,401	6,641	882	1,411	96.6%	33.0%	0.0%	0.1%	67.0%	3.0%	1.0%	60.5%	0.4%	0.1%	6.5%	0.0%	0.0
19-<20 mo	213 467	5 605	727	1 336	97.0%	32.0%	0.0%	0.1%	68.0%	2.6%	0.9%	61.4%	0.3%	0.1%	6.6%	0.0%	0.0

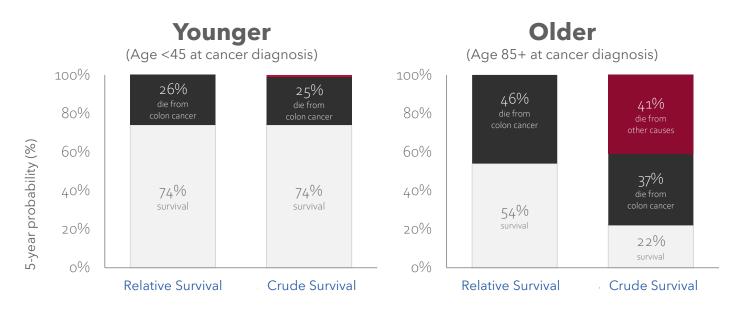




#### question

- 1- relative survival=Net probability of dying of cancer
- What do you expect to be bigger: (a)Net probability of dying of cancer or (b) crude probability of dying of cancer?

## Comparison of net and crude survival: colorectal cancer patients diagnosed with regional stage



J Natl Cancer Inst Monogr. 2014 Nov;2014(49):255-64. doi: 10.1093/jncimonographs/lgu022.

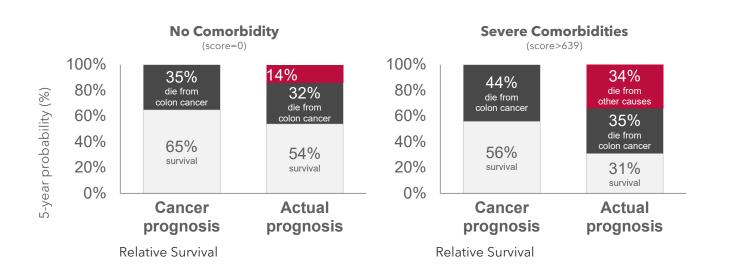
Providing clinicians and patients with actual prognosis: cancer in the context of competing causes of death.

Howlader N<sup>1</sup>, Mariotto AB<sup>2</sup>, Woloshin S<sup>2</sup>, Schwartz LM<sup>2</sup>.





# Comparison of Cancer and Actual prognosis: colorectal cancer patients diagnosed with regional stage age 66+ Comorbidity information only available for ages 66+



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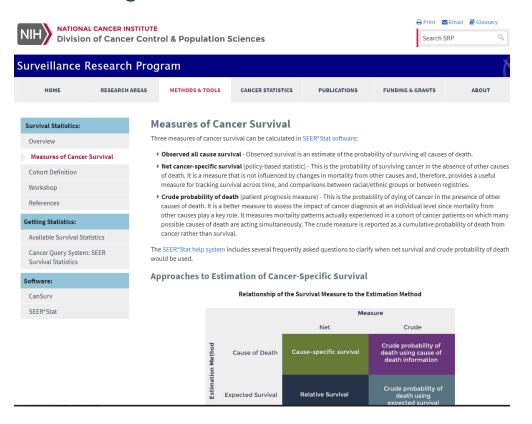
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## Summary of Methods and Measures

#### https://surveillance.cancer.gov/survival/measures.html







#### Net Vs crude

Net	CRUDE
Survival measure not affected by changes in other-cause mortality	Survival including the risk of dying of other causes (competing risks)
Measures how quickly progress in clinical research is transferred into clinical practice	Measure mortality pattern actually observed in cancer patients
Cancer progress- Policy measure	Prognosis survival measures

Both can be calculated in the relative or cause-specific methods

## Different Types of Questions >> different survival statistics

- Patient 1: I have just been diagnosed with ovarian cancer. What are my chances of surviving this cancer?
- Patient 2: I have cardiovascular disease and have been diagnosed with localized breast cancer, what are my chances of dying of breast cancer in the next 5 years?
- Science Writer: How has survival of prostate cancer changed over time? How do you expect it to change in the future?
- Congressperson: What is the most recent estimate of 5-year survival for breast cancer? How does it differ by race/ethnicity?
- Cancer Survivor: I have survived five years after diagnosis with colorectal cancer. What is the possibility that I am cured? What are my chances of not dying of cancer in the next 5 years?
- Researcher: Do cancer patients have higher risks of death for other causes (in the absence of cancer death) compared to the general population?



## Different Types of Questions >> different survival statistics

- Patient 1: I have just been diagnosed with ovarian cancer. What are my chances of surviving this cancer?
- Crude (or Net)
- Patient 2: I have cardiovascular disease and have been diagnosed with localized breast cancer, what are my chances of dying of breast cancer in the next 5 years?
- ----- Crude
- Science Writer: How has survival of prostate cancer changed over time? How do you expect it to change in the future?
  - → Net (Relative survival)
- Congressperson: What is the most recent estimate of 5-year survival for breast cancer? How does it differ by race/ethnicity?
- Net (Relative Survival)
- Cancer Survivor: I have survived five years after diagnosis with colorectal cancer. What is the possibility that I am cured? What are my chances of not dying of cancer in the next 5 years?
- Crude (or Net)
- Researcher: Do cancer patients have higher risks of death for other causes (in the absence of cancer death) compared to the general population?







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