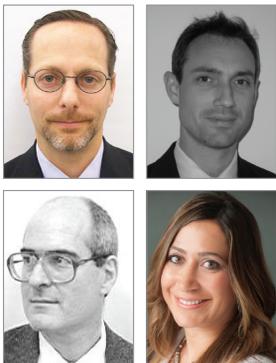




Long-Term Survival Prognosis After Stroke

A practical guide for clinicians.

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Evidence-Based Prognosis

As the Case Study demonstrates, discussion of survival after stroke can be challenging. Although prognosis was often part of medical training in the early 1900s, the ever-burgeoning body of clinical medical knowledge has slowly nudged this from most medical programs. Major advances in the past 50 years have focused more on

extending life, with quality/quantity of that remaining life often seen as lesser priorities.^{1,2}

In the modern context, prognosis plays a central role in oncology, and cancer survival papers are numerous. For each type of cancer there are substantial resources documenting the 1- and 5-year survival rates, often stratified by a person's age, sex, race, tumor stage, grade, histology, and treatment. As a result, physicians routinely quote survival and relapse rates to their patients with cancer. There are also numerous mortality risk indices for general use by clinicians in medical decision making for the geriatric population.³ Until recently nothing remotely similar existed for stroke, although it is the fifth leading cause of death in the US, second leading cause of death in the world, and the leading cause of disability.

Survival Prognosis After Stroke

A recent article⁴ on long-term survival after stroke provides life expectancies by age, sex, and severity of disability as measured by the modified Rankin Scale (mRS), the most widely used measure of long-term disability after stroke. The life-expectancy results in the article were based on a systematic review of the stroke literature including 11 key studies comprising more than 35,000 individuals

▶▶▶ Case Study. Mr. P's Prognosis

Clinical Presentation and History

Mr. P, who is age 70, and his family visit your clinic. He is a long-term cigarette smoker with a history of myocardial infarctions and had an ischemic stroke 2 years ago. Mr. P is now wheelchair bound, although he retains some ability to care for himself. His family is wondering how long they will have the energy to care for him at home or, alternatively, if they can afford placement in a skilled nursing facility. Both options depend in part on how long he is likely to live. What do you tell them?

Common Responses

- A. His prognosis is guarded.
- B. We physicians usually prefer not to prognosticate on such matters, knowing that if we give any prediction at all it will undoubtedly prove to be incorrect.
- C. He could live a long time or a short time. It depends on how well he is cared for, what complications arise, how quickly and properly they are treated, and his general health.
- D. The life expectancy of an average man age 70 is 14 more years (age 84). Because of Mr. P's past medical history and stroke with resulting disabilities, he will probably live less time than this, but I am not certain exactly how much less.

Discussion

Responses (A) and (B) are correct but decidedly unhelpful. Response (C) may also be correct, but could be said about any person with any medical condition. Response (D) at least provides some context, and is both sufficiently vague and properly worded to avoid the problems raised by (B). Yet none of these is truly helpful to Mr. P's family or him. Can clinicians be expected to do better than any of the above?



▶▶▶ **Box. Primer on Survival Analysis**

Life expectancy is, by definition, the average survival time in the defined group. Of course, most patients will live either longer or shorter, and very few will live exactly to the average. The statistical term for the inherent variability in actual survival times is dispersion, generally measured by what is referred to as the standard deviation. In this narrow context, survival times in a population might be reported as 20 years plus or minus 5 years, where 5 is the standard deviation. If the data are distributed normally (bell-shaped curve), roughly 95% of people would survive 10 to 30 years (Box Figure 1).

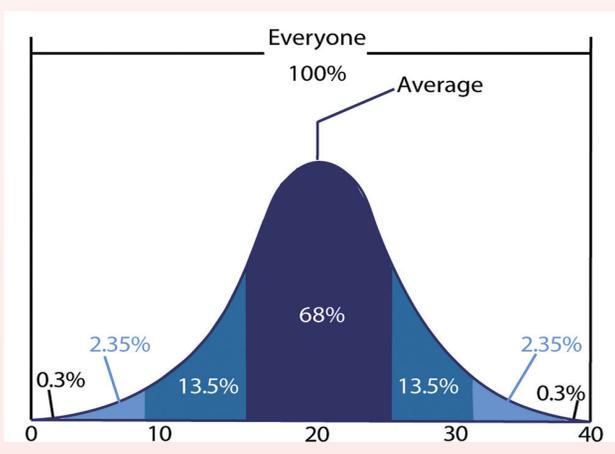
Life expectancy is an average of all the possible survival times, weighted by the likelihood of occurrences. The likelihoods are the annual survival probabilities, and these are given in any standard life table (Box Table).

The columns of the life table are standard, as defined in government, actuarial, and scientific sources. We restrict attention here to the basics. To begin, it is important to recognize that the life table is completely determined by the annual mortality rates (m) for each age x. These are the inputs to the table. The outputs are all other columns, including the remaining life expectancy at each age x, denoted by e(x). For example, e(70)=14.4. That is, the average survival time of a man age 70 in this population is about 14 additional years. Also of interest in the life table is the so-called survivorship function, column l(x), which shows the average number of people alive at each age x, following an initial group of 100,000 alive at age 70. For example, l(80)=69,580 indicating that roughly 70% of men age 70 will survive to age 80.

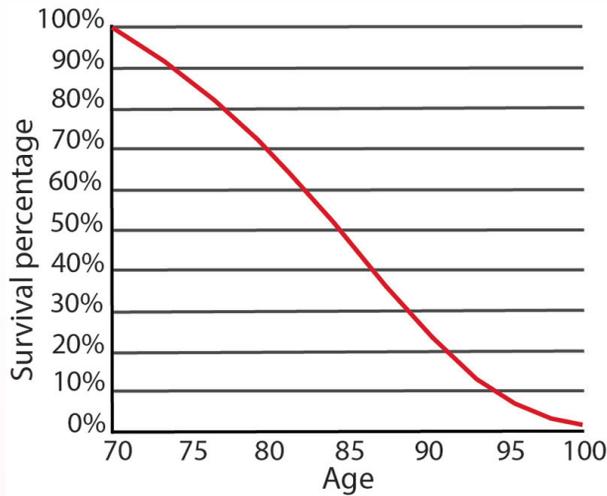
If we divide every entry in column l(x) by the initial number of 100,000, the new column will start at 1.00 (100%), and decrease with age. We can then plot this new column of values vs age. This resulting survival curve is shown in Box Figure 2.

As noted, a single individual's survival time cannot be predicted with any reasonable degree of precision. Consider, for example, a large group of men age 70. Obviously, any one of them could survive only a relatively short time, live a long time, or fall somewhere in between. Box Figure 3 shows the probabilities of these occurrences, grouped by 5-year age bins that show 13% of the group would not survive to age 75; as shown, they would survive to ages 70 to 74. This means that the average man age 70 has a 13% chance of passing away before reaching age 75. Similarly, there is a

BOX TABLE. LIFE TABLE							
age	l(x)	d(x)	q(x)	m(x)	L(x)	T(x)	e(x)
70	100000	2284	0.0228	0.0231	98858	1438960	14.4
71	97716	2441	0.0250	0.0253	96496	1340102	13.7
72	95275	2603	0.0273	0.0277	93974	1243606	13.1
73	92672	2775	0.0299	0.0304	91285	1149632	12.4
74	89898	2936	0.0327	0.0332	88430	1058347	11.8
75	86962	3092	0.0356	0.0362	85416	969918	11.2
76	83870	3272	0.0390	0.0398	82234	884501	10.5
77	80598	3477	0.0431	0.0441	78859	802268	10.0
78	77121	3673	0.0476	0.0488	75284	723408	9.4
79	73447	3868	0.0527	0.0541	71513	648124	8.8
80	69580	4059	0.0583	0.0601	67550	576611	8.3
81	65521	4234	0.0646	0.0668	63404	509061	7.8
82	61287	4377	0.0714	0.0741	59099	445657	7.3
83	56910	4496	0.0790	0.0823	54662	386558	6.8
84	52414	4607	0.0879	0.0920	50110	331896	6.3
85	47807	4731	0.0990	0.1042	45442	281786	5.9
86	43076	4745	0.1101	0.1167	40704	236344	5.5
87	38331	4690	0.1223	0.1305	35987	195640	5.1
88	33642	4558	0.1355	0.1456	31363	159654	4.7
89	29083	4357	0.1498	0.1623	26905	128291	4.4
90	24726	4081	0.1651	0.1804	22686	101386	4.1
91	20645	3744	0.1814	0.2001	18773	78701	3.8
92	16901	3357	0.1986	0.2214	15223	59928	3.5
93	13544	2936	0.2167	0.2443	12077	44705	3.3
94	10609	2501	0.2357	0.2688	9358	32628	3.1
95	8108	2071	0.2554	0.2949	7073	23270	2.9
96	6037	1664	0.2757	0.3225	5205	16197	2.7
97	4373	1296	0.2964	0.3516	3725	10992	2.5
98	3077	977	0.3174	0.3819	2588	7267	2.4
99	2100	711	0.3386	0.4134	1745	4679	2.2
100	1389	532	0.3827	0.4824	1123	2934	2.1

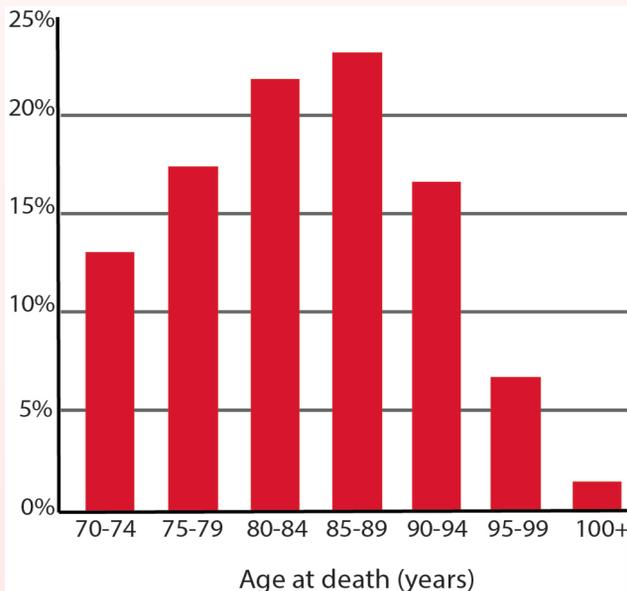


Box Figure 1. Normally distributed data exhibit the classic bell curve with 68% of data points lying within 1 standard deviation of the mean and an additional 27% within 2 standard deviations. This accounts for 95% of the data and is related to a 95% confidence interval.



Box Figure 2. Survival curve for men age 70 in the US.

roughly 17% chance that an average man would live to ages 75 to 79, 22% to ages 80 to 84, 23% to 85 to 89, 16% to 90- to 94, 7% to ages 95 to 99, and 2% to age 100 or more. Using these groupings, the best prediction of survival time would be to ages 85 to 89, yet only 23% of the men fall into this range. To capture more people, we would have to widen the range, for example to ages 75-89, where 62% reside. Even then, there would be 13% who live for a shorter time and 25% who live longer. In sum, we cannot predict actual survival times with any reasonable degree of precision.



Box Figure 3. Histogram (bar chart) of survival times for men age 70 in the general US population. This shows that even in the case where survival times are fairly limited (98% of people live shorter than 30 years), it is not possible to predict an individual's actual survival time very accurately, even using 5-year age ranges.

followed for at least 1 year. Prognosis was made from at least 3 months poststroke, following the acute period of increased mortality risk and after most structured rehabilitation programs. All types of strokes were considered, along with possible comorbid factors.

As indicated in the study, it is a matter of empiric observation that age and severity have the largest effects on long-term survival. For example, male individuals had an overall hazard ratio (HR) of approximately 1.2 compared with women, indicating 20% higher mortality risk; the risk approximately doubles (HR=2.0) with each decade of age; and the largest cohort study⁵ evaluating survival reported that the effects of diabetes, smoking, and atrial fibrillation each had an HR of approximately 1.4. By contrast, the very same studies show that those with mRS grade 4 have nearly 3 times the risk compared with mRS grade 0, and those with mRS 5 have 5 times the risk. If factors other than age, sex, and severity are ultimately deemed relevant, these too can be considered in the analysis.

We believe the complete set of results from the study, including the underlying survival probabilities, together with some practical instruction regarding prognosis, can effectively be used by clinicians to provide evidence-based guidance on long-term survival after stroke. To facilitate this, we provide a web-based survival tool for rapid and accurate calculations at <http://www.LifeExpectancy.org/asp/stroke/>.

Survival Prognoses In General

Life expectancy is a precise technical term referring to the average (arithmetic mean) survival time in a group of similar persons. Life expectancy is generally derived using a life table; see the Box for a refresher on this scientific tool.

While colloquially the term life expectancy may be used to express a summary view about a patient's prognosis, it is not meant to be a prediction about a given person's actual survival time. For example, the general population life expectancy of males age 70 is 14 years, but death much sooner or instead after twice as long is entirely possible. Similar patients can live very different lifespans. For example, 1 identical twin may outlive the other by 30 years. It is a truism that an individual patient's survival time cannot be predicted with any reasonable degree of precision. It is not merely difficult; it is impossible (Box Figure 3).

To give an opinion on an individual's likely prognosis requires 1) sufficient information to identify factors, features, or characteristics of the individual known to be related to survival and 2) identified groups (cohorts) of similarly situated persons' actual survival experience. Prognosis requires matching the person in question to the survival of similar persons. Medical doctors routinely perform this sort of comparison when making diagnoses, identifying treatment options, and deciding upon surgical techniques. In



the simplest life-expectancy context, we merely identify the appropriate patient groups for comparison, then report on their empiric survival.

In our experience, most medical doctors feel confident in providing survival prognoses only when a person is at the extremes of the survival spectrum—when the prognosis is poor, on the one hand, or very good on the other. When prognosis is poor and medical intervention is frequent and often invasive with long hospital stays, patients and family may already essentially know the prognosis, and it need not be quantified with any precision. In the latter case, the clinician may feel that the condition does not affect the person’s mortality risk and therefore does not affect life expectancy. In that case, mortality risk and life expectancy may be said to be normal, and general population figures can be cited, as appropriate, to support this statement. In the remaining intermediate cases, which are quite common in practice, the clinician may not have any known guideposts and, thus, may be reluctant to offer an opinion. For example, clinicians know that smoking reduces life expectancy, but few would know by how much, or how it depends on the number of pack-years. More difficult still are cases with multiple complex risk factors, such as heart disease, diabetes, and obesity.

A busy practicing clinician would not be expected to have or to develop the scientific expertise to make accurate calculations of life expectancy in every case, even in their own medical discipline. Furthermore, survival in some conditions

has changed much in the past 20 years, making knowledge gained in medical school less applicable. Such calculations are squarely in the realm of medical directors, life actuaries, underwriters, and medical researchers. Yet some medical doctors (especially oncologists) do routinely use specific literature from their given field of expertise to provide at least approximate survival figures. We believe that the same can be done for stroke cases.

Survival Prognoses After Stroke

The Table reproduces the summary life expectancy figures from the aforementioned article on long-term survival after stroke.⁴ For a man age 70, such as the person described in the opening Case Study, whose disabilities are consistent with Rankin grade 4, the stated life expectancy is 6 additional years. That is, amongst a group of similarly situated men, the arithmetic mean, or average, survival time is 6 years.

The fact that the life expectancy for this group is less than the corresponding general population figure of 14 years indicates that Mr. P’s life expectancy is not normal. But this single life expectancy figure does not specify with certainty exactly how long he will live.

In the present context, we are concerned with giving an accurate and helpful description of survival that is tailored to the case at hand. Broad statements such as those offered in the Case Study, although correct, are not entirely helpful. More precise statements are usually needed, although

TABLE. LIFE EXPECTANCY (YEARS) BY AGE, SEX, AND GRADE ON THE MODIFIED RANKIN SCALE

Age*	Modified Rankin Scale Grade						
Male	GP	0	1	2	3	4	5
50	30	28	27	22	17	13	9
60	22	20	19	16	13	9	7
70	14	13	13	11	8	6	5
80	8	7	7	6	5	4	3
Female							
50	33	32	30	25	19	14	9
60	25	24	22	18	14	10	7
70	17	16	15	12	9	7	5
80	10	9	9	7	6	4	3

*Age Age at follow-up, rather than at stroke onset

GP General population

Grade Description

0 No symptoms or disabilities due to stroke

1 No significant disability following stroke, despite symptoms: Able to carry out all usual duties and activities

2 Slight disability: Unable to carry out all previous activities but able to look after own affairs without assistance

3 Moderate disability: Requiring some help with daily activities, but is able to walk without assistance

4 Moderately severe disability: Unable to walk without assistance, and unable to attend to own bodily needs

5 Severe disability: Bedridden, incontinent, and requires constant nursing care and attention



presenting the average for the group may not be sufficient. Indeed a single figure cannot provide a complete description of a person’s prognosis for survival. What is required are all the details concerning survival. These are embodied in the probabilities of surviving for 1, 2, or more years, which are, in fact, given in the commonly known survival curves, frequently presented in the medical literature (Box).

Calculating Survival Curves After Stroke

The Figure shows survival curves for 70 year-old males from an online calculator (<http://www.LifeExpectancy.org/asp/stroke/>) based on the same published research shown in the Table. The calculator produces survival curves based on any combination of age, sex, and disability. As noted, age and severity of disability are the 2 factors with the largest effect on survival after stroke. Sex is also included because doing so is standard in most survival analysis, and indeed being female is a modestly positive factor amongst persons with mild or no disabilities following stroke.

In the Figure, there are 7 curves, one for each of Rankin grades 0 to 5 and the general population (GP). Notice that each curve starts at time 0 (age 70) with 100% of persons alive and then decreases with the passage of time. Also notice that the curves for more severe disability are uniformly lower than those for less severe disability, reflecting the lower survival at each age and time.

The red curve (second from the bottom) is for Rankin grade 4, which applies to Mr. P and provides exact survival values, detailed in the table below the graph. For example, 79% of people survive 2 years, 61% survive 3 years, ..., 5% survive 16 years, and only 1% survive 20 years.

In the highlighted row, for Rankin grade 4, observe that 100%–79%=21% will live 0 to 2 more years, 18% will live 2 to 4 years, 16% will live 4 to 6 years, 13% will live 6 to 8 years, 10% will live 8 to 10 years, 8% will live 10 to 12 years, 6% will live 12 to 14 years, and 8% will live 12 or more years. The sum of these 8 probabilities is 100%, as appropriate.

Notice that the 2-year time interval that captures the most likely survival time is 0 to 2 years; yet only 18% (less than one-fifth) of the group falls into this bin. To capture more of the survival times, years 0 to 4 could be used, but this would contain only 39% of the observed values.

The median survival time—also known as the more likely than not survival time—is the time after which exactly 50% of the initial group are still alive. By interpolation from the data in the Figure, this is 5.4 years. That is, 50% of similar patients will survive at least 5.4 additional years, and the other 50% will have passed away prior to this time point.

Practical Application

What then should be said to Mr. P and his family? Of course, such discussions are both art and science. Much has

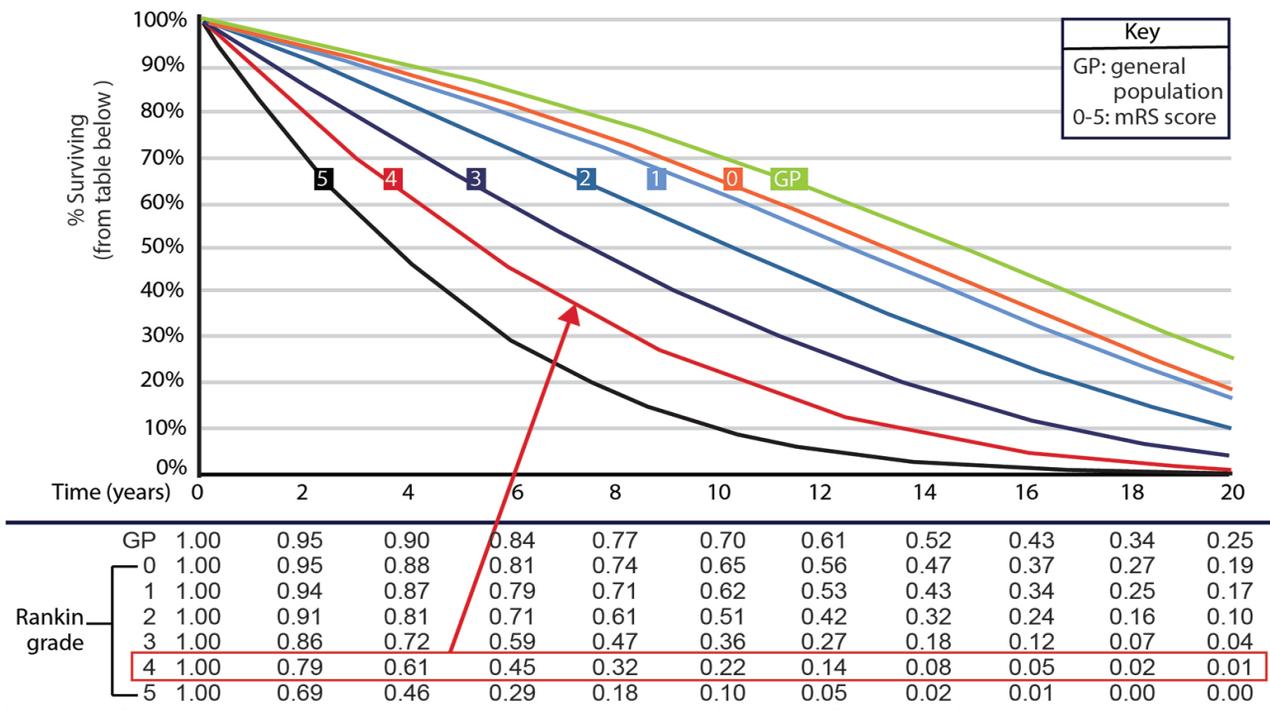


Figure. Survival Curves By Rankin Grade: 70 Year-Old Men



been written about the former; we concentrate here on the latter: what can be said, rather than on how to do so.

1. Identify the appropriate Rankin Group. For Mr. P it is grade 4, because he cannot walk but retains some ability in self care.
2. Observe that median survival time for males age 70 in this group is 5.4 years. That is, Mr. P has a 50% chance to survive roughly 5 more years.
3. Note that amongst men like him, the average survival time (ie, the life expectancy) is 6 years.
4. Explain that Mr. P has an 8% chance of surviving at least 14 years, which is the average survival time for men his age in the general population. Because he does not have a normal life expectancy, it is not surprising that he has a reduced chance of living what would be the normal amount of time.
5. Convey what is known about the entire survival distribution for men like him— all of the survival possibilities and probabilities—if that is of interest. For example, the family may have a strong desire to care for the patient at home, although understanding that the burden of doing so may not be sustainable for more than 2 years. Their understanding that the patient is quite likely (79%) to live more than 2 years may well affect their decision-making.

It may be, of course, that a person has additional risk factors that make prognosis worse than average amongst the Rankin grade 4 group, or perhaps conversely, no other risk factors, making prognosis more favorable for the individual. In such cases the calculated figures would be either somewhat pessimistic or optimistic. Nonetheless, they provide a rational starting point from which further scientific adjustments could be made.

Limitations and Conclusions

As can be seen, there are limitations inherent in the science. Most obviously, no specific survival time, even if rounded to the nearest integer, or even any narrow range of such figures, will occur in 100% of cases. As noted, it is impossible to predict accurately an individual person's exact survival time except in the most unusual of circumstances. Also, in the case of stroke and other neurologic injuries it may be prudent to postpone discussions of long-term prognosis until after functional recovery has plateaued, as a proportion of persons with even exceptionally severe acute strokes may actually return to baseline.

Further, there are limitations in the practitioners. As documented by Nicholas Christakis, MD, PhD, in *Death Foretold*, predictions of survival by medical doctors are known to be systematically optimistic, and more so the better the doctor knows the patient.⁶ By contrast, as explored more than 50 years ago by Paul Meehl, evidence-

based predictions have been documented to be generally superior to clinical ones.⁷⁻⁹

At the same time, a clinician can often identify factors, features, or characteristics of a given person that make them better or worse than average amongst an otherwise similar group, suggesting that the nominal figures may require some adjustment. In economic circles this is known as tailoring. In such cases the empirical evidence regarding the effect of known factors is considered before accounting for other factors.

The solution for the practitioner, then, is to rely on the scientific evidence as possible, despite its inherent limitations, in order to convey to the patient what is known about the survival of similarly situated persons. The figures and tables here, together with the online calculator, can provide clinicians with the best currently available evidence on the prognosis of their stroke patients.

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