Swiss Re

Mortality studies

AAIM Webinar, June 2012

Ken Krause MD, MS, DBIM

Swiss Re

Goals

- Idea for this webinar grew out of Ross MacKenzie's JIM editorial calling for more mortality papers for JIM
- Brief overview of mortality (survival) analysis concepts and methods
- Review the Insurance Medicine approach for developing a mortality abstract from a clinical article

Swiss Re

Survival basics

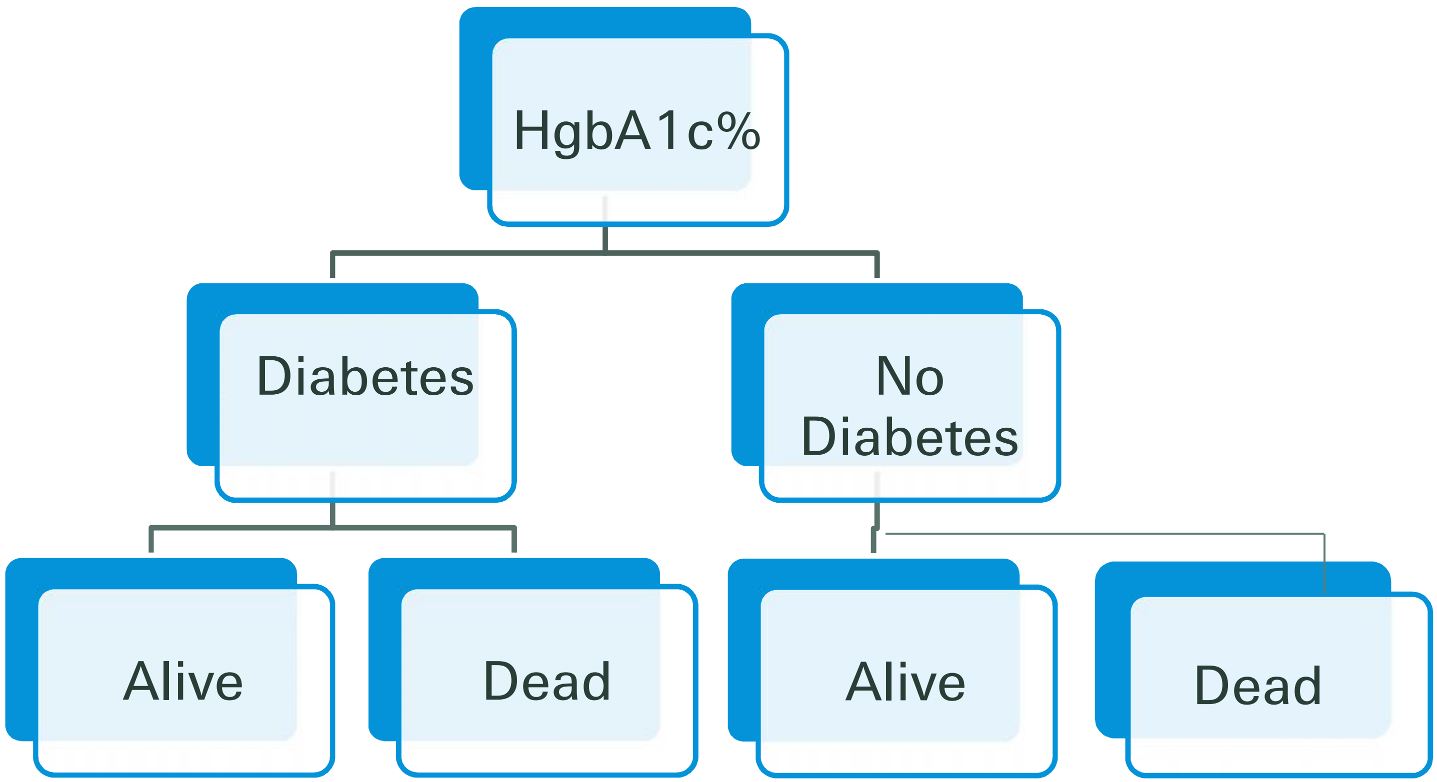
- The essence of survival analysis is measuring the probability of an event over some era, period or subdivision of time
  - Oncologists are interested in 5-year cancer-free survival after diagnosis and treatment
  - Cardiac surgeons are interested in the median time to re-operation following prosthetic valve surgery
  - Bioengineers are interested in the time to failure of an joint prosthesis
  - Demographers are interested in measuring the median life expectancy of individuals born in 1900
  - Actuaries, underwriters, and medical directors are interested in the survival of insurance applicants with diabetes over a 15-year term policy

Swiss Re

Survival analysis approaches

Approach	Expression	Considerations
Rate	Risk or case/control ratio	Count data
Logistic regression	Odds ratio	Considers time if observation is uniform, complete
Life table	Kaplan-Meier, actuarial methods	Considers non-uniform exposure time, censoring, comparison of groups
Regression analysis	Cox proportional hazards function	Considers exposure time, allows for multiple adjustment. No assumption for underlying survival function but, proportionality must be met
Regression analysis	Parametric survival function	Assumes an underlying survival function
Regression analysis	Poisson regression function	Permits use of grouped data, comparison to external reference

Rate ratio

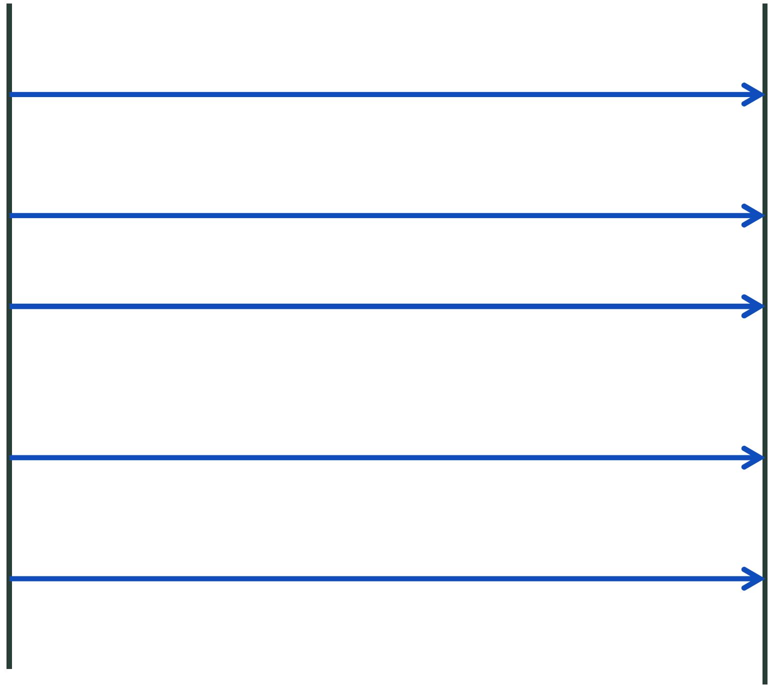


$$\text{Rate Ratio} = \frac{\Pr(\text{Dead} \mid \text{Diabetes})}{\Pr(\text{Dead} \mid \text{No Diabetes})}$$

Swiss Re

Logistic regression

- Result can reflect element of time if those monitored from same start to same finish are considered-others' data are lost.



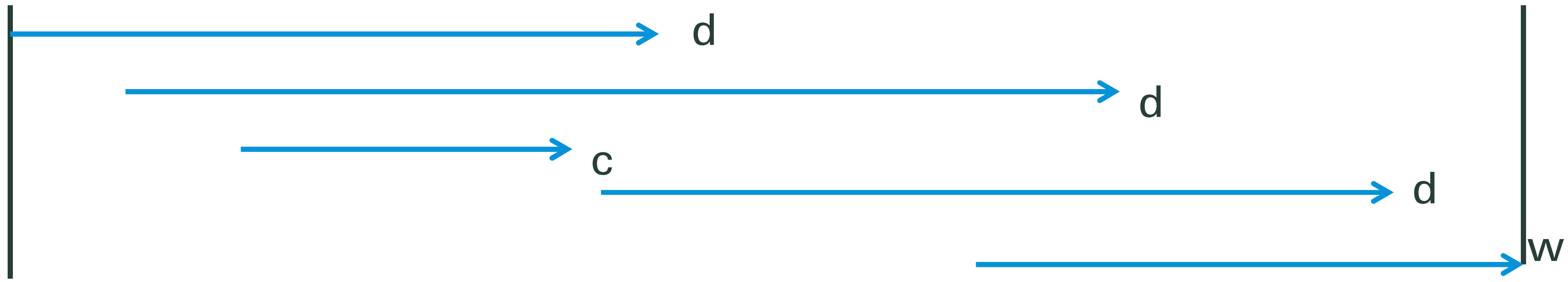
Odds ratio: for study period of defined duration that starts and ends same times for all.

Study opens or observation begins

Study closes or observation ends

Swiss Re

Life table analysis

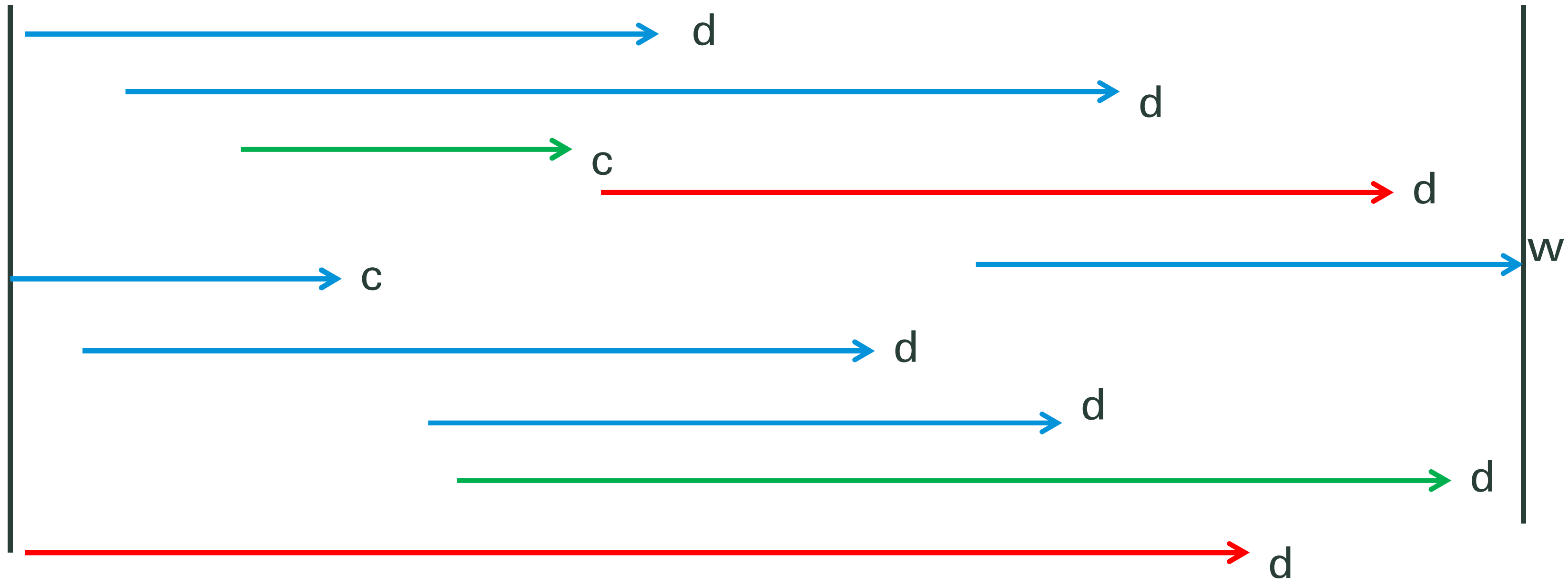


Calendar time: Individuals enter at any time and are followed until death, lost to follow up, or observation ends

d=dead
c=censored
w=withdrawn

Life table time: each individual contributes to analysis even though exact survival time is unknown for some.
Exposure is measured in person-years

Regression analysis



Different colors = different characteristics. Examples: smoking status, location, diagnosis, treatments, etc.

d=dead
c=censored
w=withdrawn

Regression analysis enables consideration of the effects of different subject characteristics simultaneously.

Swiss Re

Life table format

No. i	Interval Start-End t to $t+\Delta t$	OBSERVED RATES — Survival Data: Cumulative P	Interval p_i	Geo. Ave. Ann. $\check{p}$	Mortality Data: Cumulative Q	Interval q_i	Geo. Ave. Ann. $\check{q}$	EXPECTED RATES — Survival Data: Cumulative P'	Interval p'_i	Geo. Ave. Ann. $\check{p}'$	Mortality Data: Cumulative Q'	Interval $q_i'^*$	Geo. Ave. Ann. $\check{q}'$
1	0-1 yr.	0.955	0.955	—	0.045	0.045	—	0.9922	0.9922	—	0.0078	0.0078	—
2	1-2	0.915	0.958	—	0.085	0.042	—	0.9838	0.9915	—	0.0162	0.0085	—
3	2-3	0.875	0.956	—	0.125	0.044	—	0.9747	0.9908	—	0.0253	0.0092	—
4	3-4	0.855	0.977	—	0.145	0.023	—	0.9649	0.9899	—	0.0351	0.0101	—
5	4-5	0.840	0.982	—	0.160	0.018	—	0.9542	0.9889	—	0.0458	0.0111	—
1 and 2	0-2	0.915	0.915	0.957	0.085	0.085	0.043	0.9838	0.9838	0.9919	0.0162	0.0162	0.0081
3 to 5	2-5	0.840	0.918	0.972	0.160	0.082	0.028	0.9542	0.9699	0.9899	0.0458	0.0301	0.0101
1 to 5	0-5	0.840	0.840	0.966	0.160	0.160	0.034	0.9542	0.9542	0.9907	0.0458	0.0458	0.0093
6	5-10	0.735	0.875	0.974	0.265	0.125	0.026	0.8877	0.9303	0.9857	0.1123	0.0697	0.0143
7	10-15	0.655	0.891	0.977	0.345	0.109	0.023	0.7937	0.8941	0.9779	0.2063	0.1059	0.0221

*Basis of expected mortality: 1979-81 U.S. Life Tables For Total Males.

COMPARATIVE EXPERIENCE

No. i	Interval Start-End t to $t+\Delta t$	Mortality Ratios: Interval $100q_i/q'_i$	Geo. Ave. Ann. $100\check{q}/\check{q}'$	Cumulative $100Q/Q'$	Survival Ratios: Interval $100p_i/p'_i$	Geo. Ave. Ann. $100\check{p}/\check{p}'$	Cumulative $100P/P'$	Excess Death Rate: Interval $1000(q_i-q'_i)$	Geo. Ave. Ann. $1000(\check{q}-\check{q}')$
1	0-1 yr.	575	—	575	96.3	—	96.2	37	—
2	1-2	495	—	525	96.6	—	93.0	34	—
3	2-3	480	—	495	96.5	—	89.8	35	—
4	3-4	230	—	415	98.7	—	88.6	13	—
5	4-5	162	—	350	99.3	—	88.0	7	—
1 and 2	0-2	525	530	525	93.0	96.5	93.0	—	35
3 to 5	2-5	270	280	350	94.6	98.2	88.0	—	18
1 to 5	0-5	350	365	350	88.0	97.5	88.0	—	25
6	5-10	179	182	235	94.0	98.8	82.8	—	12
7	10-15	103	104	167	99.7	99.9	82.5	—	1

Based on: Pokorski RJ. J Insur Med 1988(4);20:20-45

Swiss Re

Survival basics: know your p's and q's!

- Survival probabilities denoted by:
  - p (for an interval, usually 1 year, but can be anything as long as specified)
  - P (cumulative, over a series of intervals such as 5 or 10 years)
  - p', P' (' usually denotes expected, or referent, often from an external source)
- Mortality (failure) probabilities denoted by:
  - q (for an interval, usually 1 year)
  - Q (cumulative, over a series of intervals such as 5 or 10 years)
  - q', Q' (' usually denotes expected, or referent, often from an external source)

Survival basics: + — × ÷ !!!!

- Basic math rules for probabilities
  - Survival probabilities can be multiplied (and divided) to compute survival for longer (or shorter) intervals
    - the probability of surviving year 1 x the probability of surviving year 2 = cumulative probability of surviving 2 years
    - the probability of dying year 1 x probability of dying year 2 = cumulative probability of dying in 2 years? NOT! WHY?
  - Mortality probabilities are the mathematical complement of survival probabilities
    - $q = 1 - p$ OR $Q = 1 - P$
    - Never: $q_1 \times q_2 \times q_3 = Q_3$
  - So the essentials are:
    - $p_1 \times p_2 \times p_3 = P_3$
    - $1 - P_3 = Q_3$

Survival basics: + — × ÷ !!!!

- One more essential:
  - Cumulative 3- year survival is:

$$p_1 \times p_2 \times p_3 = P_3$$

Divide both sides of equation by ($p_1 \times p_2$):

$$\frac{(p_1 \times p_2 \times p_3)}{(p_1 \times p_2)} = \frac{P_3}{(p_1 \times p_2)}$$

$$p_3 = \frac{P_3}{(p_1 \times p_2)}$$

Since $p_1 \times p_2 = P_2$:

$$p_3 = P_3/P_2$$

Swiss Re

The answer you seek is.....

- (Standardized) Mortality Ratios
  - Observed/Expected mortality for a single or cumulative interval expressed as a fraction, or more commonly in insurance medicine, as a percentage:

$$\frac{q}{q'} \text{ or } \frac{Q}{Q'} \quad (\times 100\%)$$

  - Which you now know is also:

$$\frac{(1-P)}{(1-P')} \quad (\times 100\%)$$

Swiss Re

Steps for your assessment of a clinical study

- Derive the probability of survival for the impairment of interest from the clinical study you have identified. This is the source for **observed** survival which you use to derive observed mortality.
- Identify a reasonable comparison group to use for **expected** mortality
- Conduct a comparison to compute a **standardized** result you can use for your case, guidelines, manual, etc.
- Use this study as an example ....

  Sachs GA et al. Cognitive impairment. An independent predictor of excess mortality. *Ann Intern Med.* 2011;155:300-6

Original Research | Annals of Internal Medicine

Cognitive Impairment: An Independent Predictor of Excess Mortality

A Cohort Study

Greg A. Sachs, MD; Ravan Carter, MA; Laura R. Holtz, BS, CCRP; Faye Smith, MA; Timothy E. Stump, MA; Wanzhu Tu, PhD; and Christopher M. Callahan, MD

Background: Dementia is a leading cause of death among older adults, but less is known about the mortality risk associated with milder forms of cognitive impairment.

Objective: To determine whether cognitive impairment is independently associated with increased long-term mortality in primary care patients aged 60 years and older.

Design: Linkage of electronic health records from a cohort recruited between January 1991 and May 1993 with data from the National Death Index through 31 December 2006.

Setting: A public safety-net hospital and its community health centers.

Patients: 3957 older adults aged 60 to 102 years who were screened at scheduled primary care appointments.

Measurements: At baseline, patients were screened for cognitive impairment by using the Short Portable Mental Status Questionnaire and were categorized into groups with no, mild, or moderate to severe cognitive impairment. Baseline data from comprehensive electronic health records were linked with vital status obtained from the National Death Index. Kaplan–Meier survival curves compared time to death for the groups with cognitive impairment. Cox proportional hazards models controlled for mortality risk factors.

Results: At baseline, 3157 patients had no cognitive impairment, 533 had mild impairment, and 267 had moderate to severe impairment. Overall, 2385 of the 3957 patients (60.3%) died during the observation period: 1812 (57.4%) patients with no cognitive impairment, 363 (68.1%) patients with mild impairment, and 210 (78.7%) patients with moderate to severe impairment. Both mild and moderate to severe cognitive impairment were associated with increased mortality hazard independent of other mortality risk factors (hazard ratio, 1.184 [95% CI, 1.051 to 1.334] and for mild impairment 1.447 [CI, 1.235 to 1.695] for moderate to severe impairment). Median survival for all 3957 participants was 129 months. Median survival for participants with no, mild, and moderate to severe cognitive impairment was 138, 106, and 63 months, respectively.

Limitations: Cognition was assessed only at enrollment by using a screening instrument. Participants were drawn from a single safety-net health system and had low educational and socioeconomic status, which limits generalizability to other populations. Changes in cognition, function, and comorbid conditions were not measured over time.

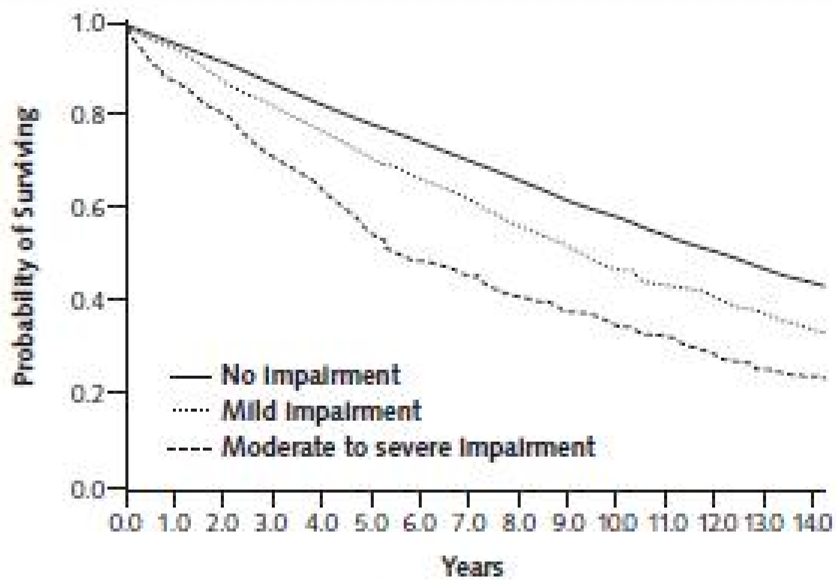
Conclusion: Both mild and moderate to severe cognitive impairment as identified by the Short Portable Mental Status Questionnaire are associated with an increased risk for mortality.

Primary Funding Source: Agency for Healthcare Research and Quality.

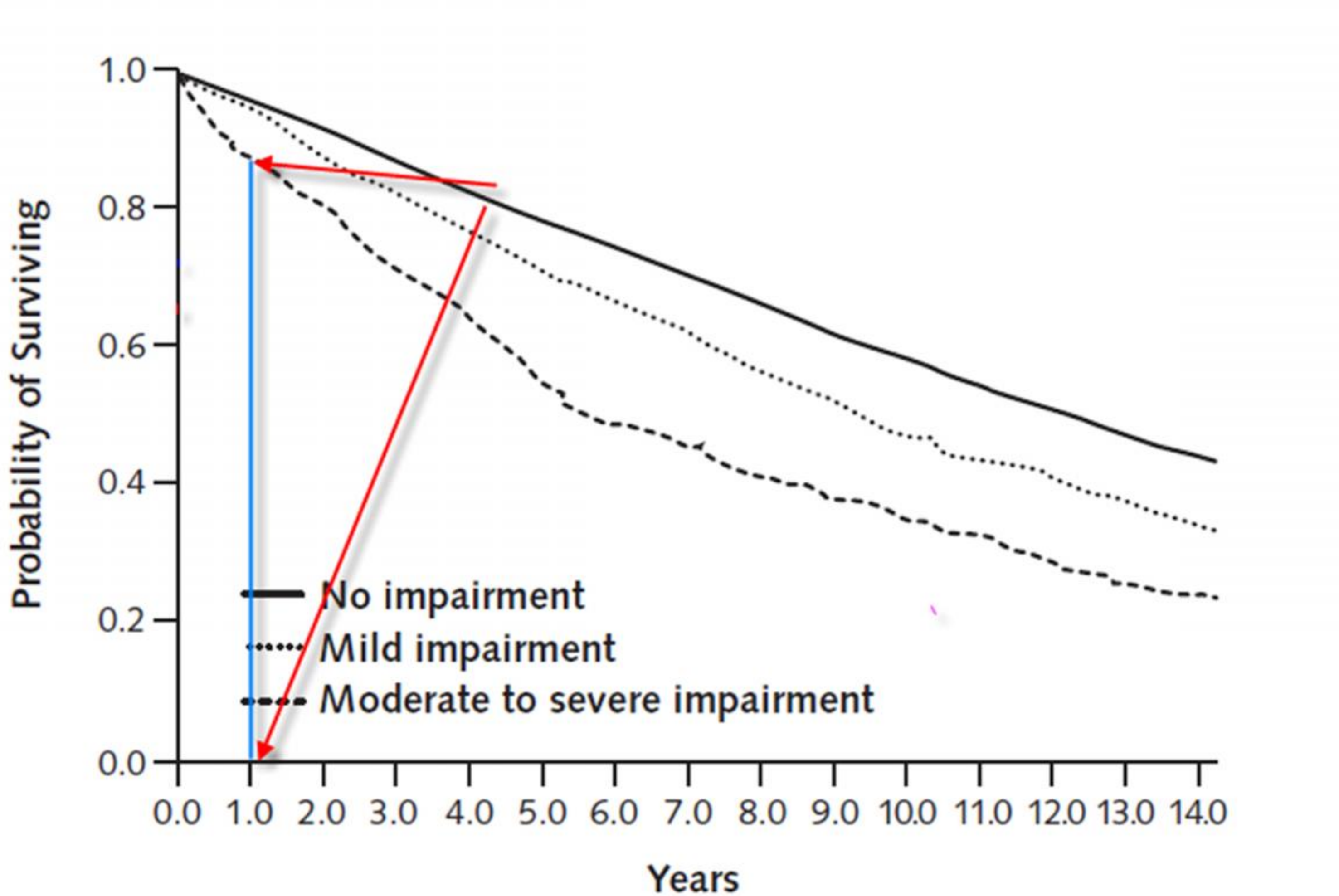
Ann Intern Med. 2011;155:300-308. www.annals.org
For author affiliations, see end of text.

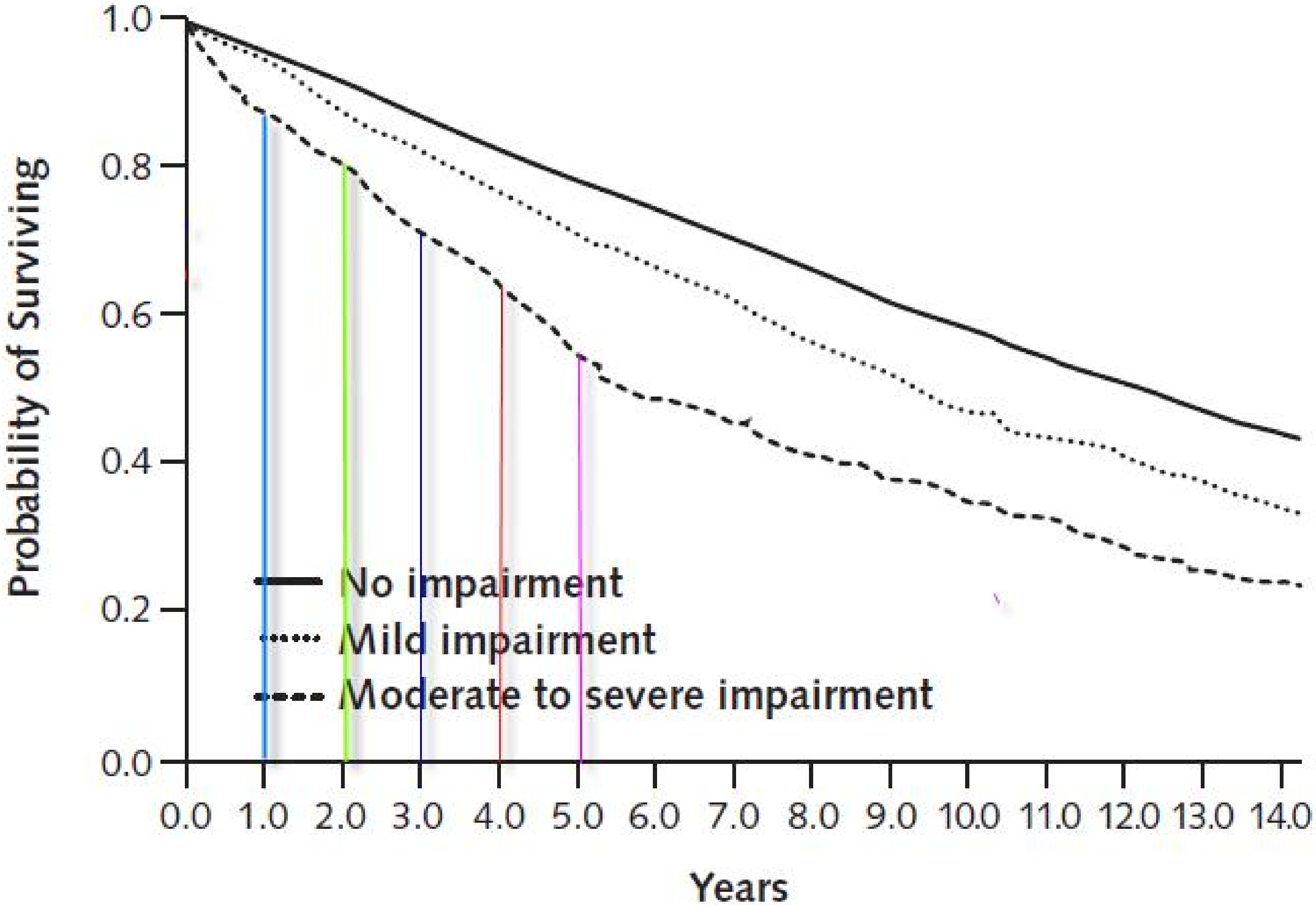
Swiss Re

Figure 2. **Kaplan–Meier survival curves comparing time to death for patients with no, mild, and moderate to severe cognitive impairment.**

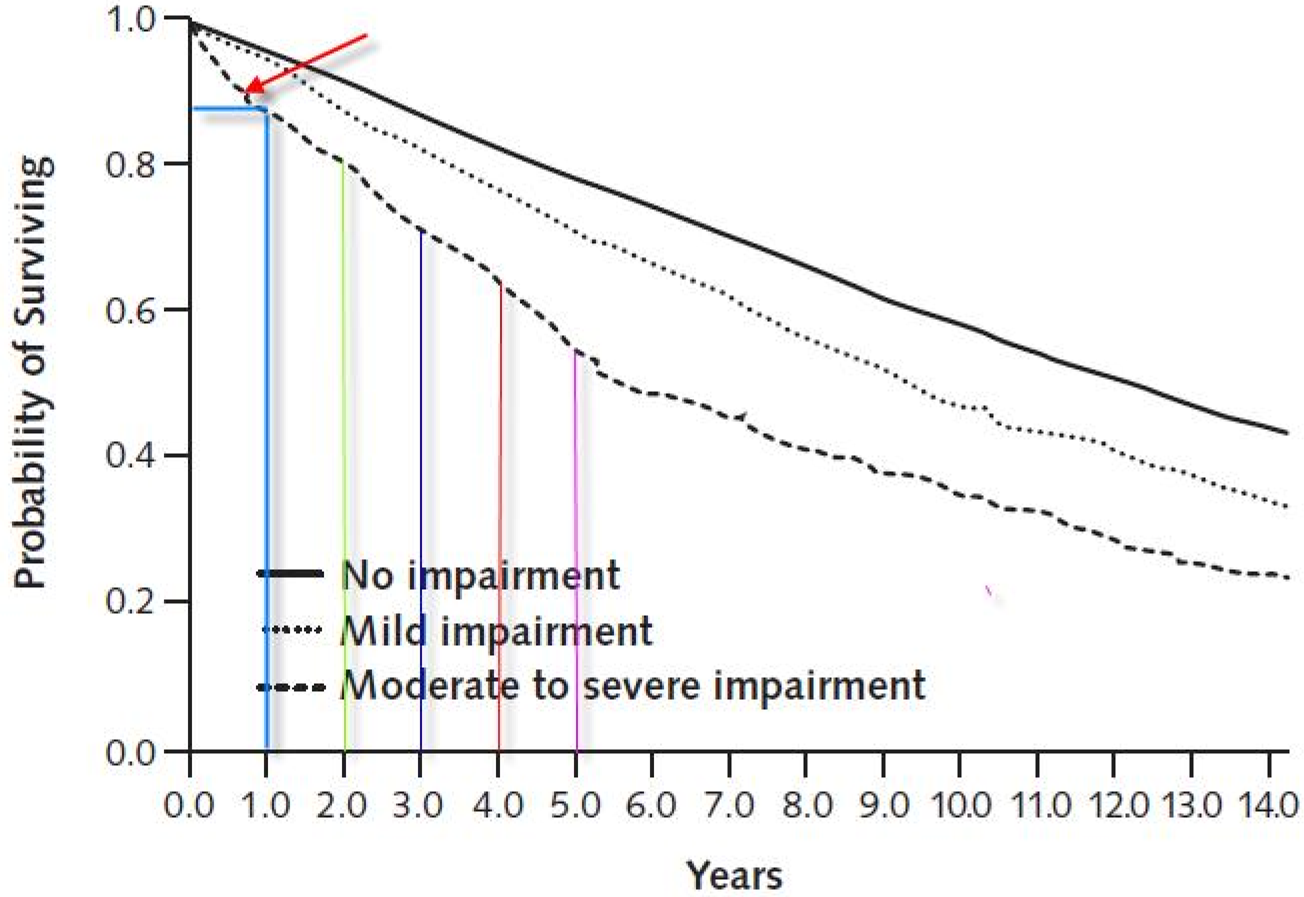


Number of Patients Remaining Alive	0 y	2 y	4 y	6 y	8 y	10 y	12 y	End of study
No impairment	3157	2887	2606	2326	2031	1765	1518	1345
Mild impairment	533	462	403	344	285	236	198	170
Moderate to severe impairment	267	212	165	125	103	84	66	57


1.0
0.8
0.6
0.4
0.2
0.0
Probability of Surviving
No impairment
Mild impairment
Moderate to severe impairment
0.0 1.0 2.0 3.0 4.0 5.0 6.0 7.0 8.0 9.0 10.0 11.0 12.0 13.0 14.0
Years

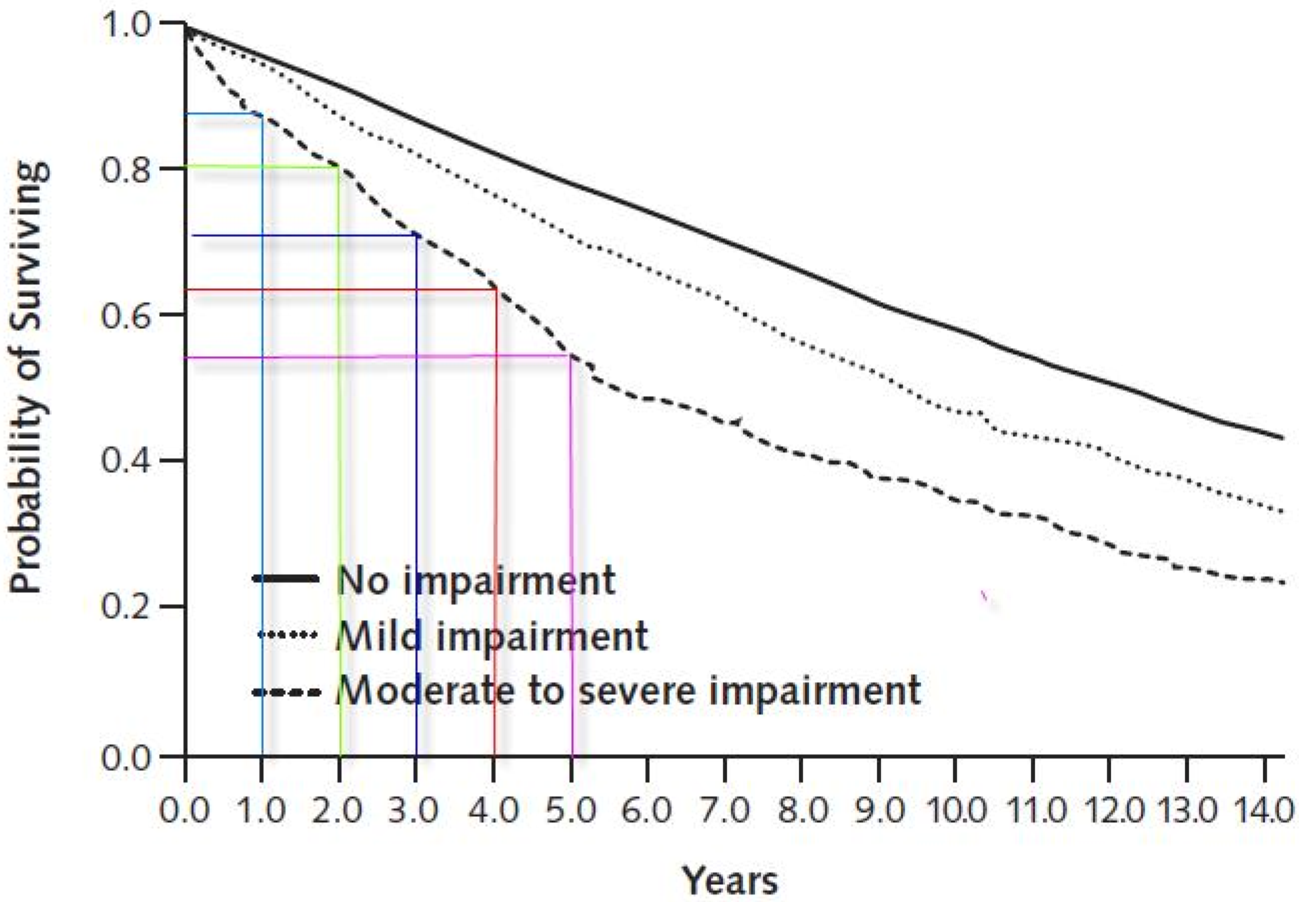

Probability of Surviving
1.0
0.8
0.6
0.4
0.2
0.0
0.0 1.0 2.0 3.0 4.0 5.0 6.0 7.0 8.0 9.0 10.0 11.0 12.0 13.0 14.0
Years
No impairment
Mild impairment
Moderate to severe impairment

Swiss Re



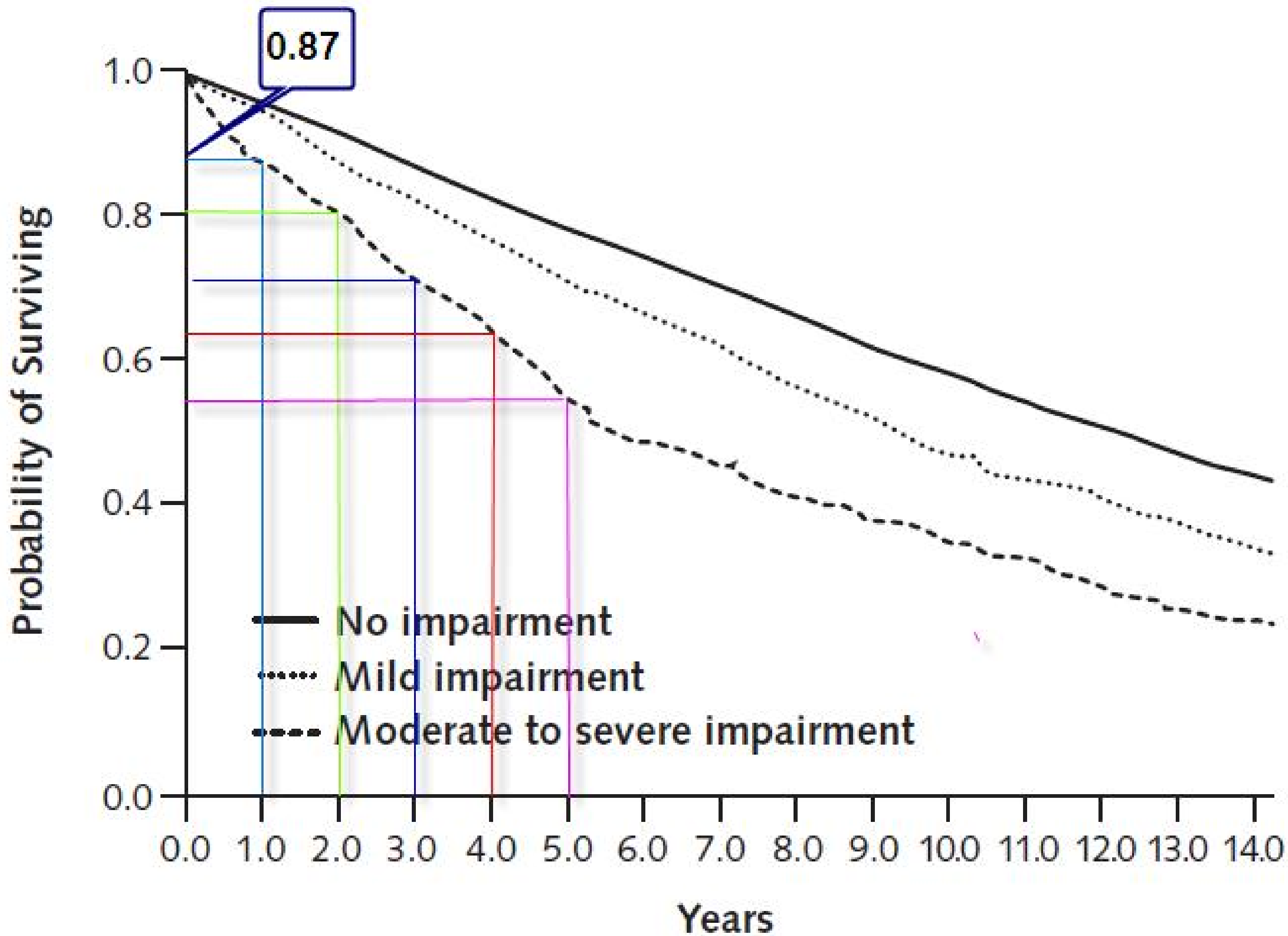
1.0
0.8
0.6
0.4
0.2
0.0
Probability of Surviving
No impairment
Mild impairment
Moderate to severe impairment
0.0 1.0 2.0 3.0 4.0 5.0 6.0 7.0 8.0 9.0 10.0 11.0 12.0 13.0 14.0
Years

Swiss Re

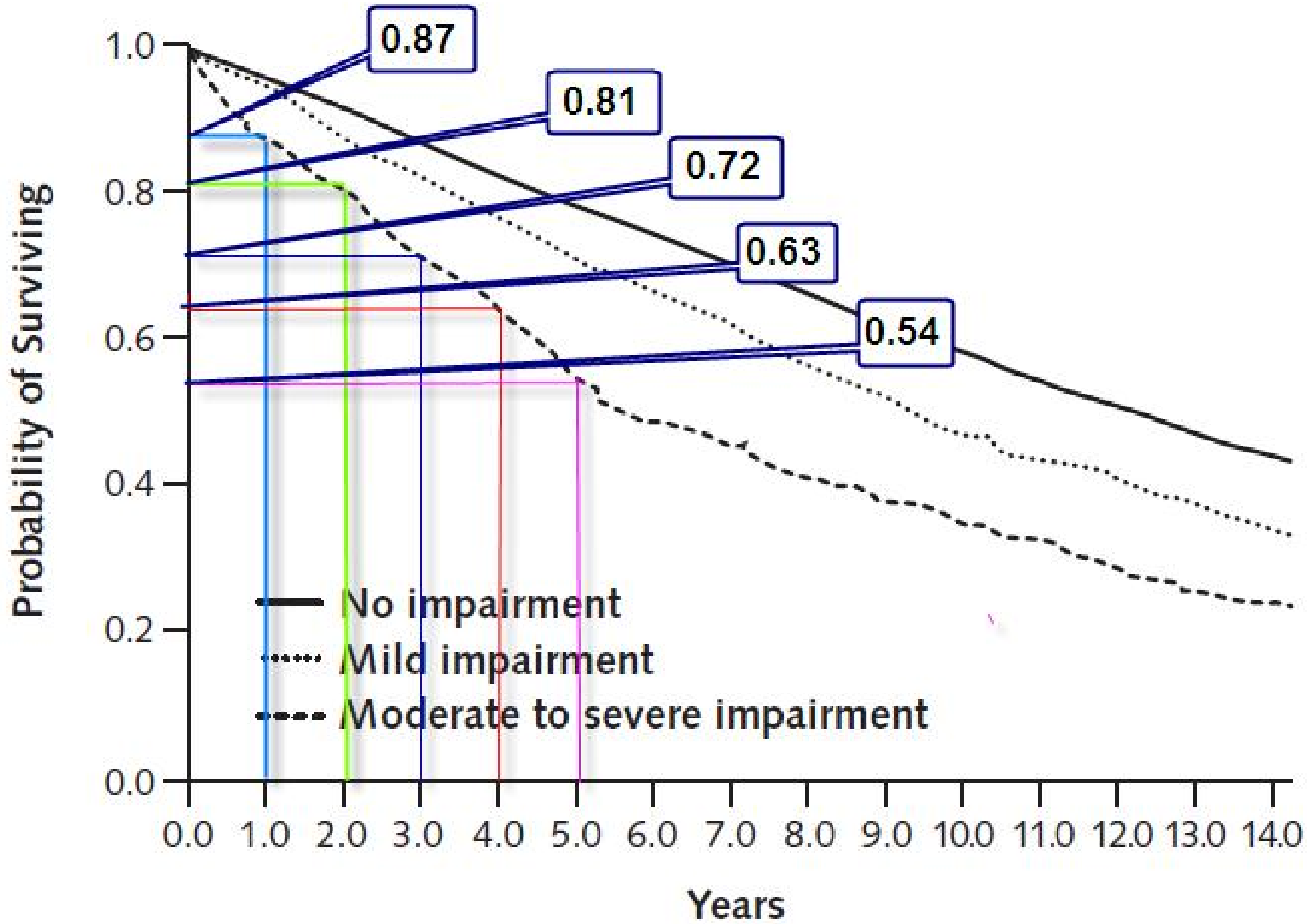


Probability of Surviving
1.0
0.8
0.6
0.4
0.2
0.0
No impairment
Mild impairment
Moderate to severe impairment
0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
9.0
10.0
11.0
12.0
13.0
14.0
Years

Swiss Re



0.87
1.0
0.8
0.6
0.4
0.2
0.0
Probability of Surviving
0.0 1.0 2.0 3.0 4.0 5.0 6.0 7.0 8.0 9.0 10.0 11.0 12.0 13.0 14.0
Years
No impairment
Mild impairment
Moderate to severe impairment


1.0
0.8
0.6
0.4
0.2
0.0
Probability of Surviving
0.87
0.81
0.72
0.63
0.54
No impairment
Mild impairment
Moderate to severe impairment
0.0 1.0 2.0 3.0 4.0 5.0 6.0 7.0 8.0 9.0 10.0 11.0 12.0 13.0 14.0
Years

Swiss Re

Building (reverse engineering) a life table

Interval	d, w, l	P	p	q	Q
0 to 1		0.87			
1 to 2		0.81			
2 to 3		0.72	**0.72/0.81 = 0.89**		
3 to 4		0.63			
4 to 5		0.54			

Remember the math?

$p_1 \text{ x } p_2 \text{ x } p_3 = P_3$

$(p_1 \text{ x } p_2 \text{ x } p_3)/(p_1 \text{ x } p_2) = P_3/(p_1 \text{ x } p_2)$

$p_3 = P_3/(p_1 \text{ x } p_2) = P_3/P_2$

Swiss Re

Building a life table

Interval	d, w, l	P	p	q	Q
0 to 1		0.87	0.87		
1 to 2		0.81	0.81/0.87		
2 to 3		0.72	0.89	**1-0.89=0.11**	
3 to 4		0.63	0.63/0.72	0.13	
4 to 5		0.54	0.54/0.63	0.14	**1-0.54=0.46**

Remember the math?

$q = 1 - p$ OR $Q = 1 - P$

Never: $q_1 \times q_2 \times q_3 = Q_3$

Swiss Re

Building a life table

Interval	d, w, l	P	p	q	Q	
0 to 1		0.87	0.87	0.13	0.13	
1 to 2		0.81	0.93	0.07	0.19	
2 to 3		0.72	0.89	0.11	0.28	
3 to 4		0.63	0.87	0.13	0.37	
4 to 5		0.54	0.86	0.14	**0.46**	

Remember the math?
Q/Q' x 100% = MR%

Where does Q' (or q') come from?

Where does Q' (or q') come from?

- This assessment and choice of expected standard is the "art" of insurance mortality analysis
- Go to Methods section of the study to look for characteristics of the individuals included in the study
  - From what population or group are they taken?
    - General population?
    - A group selected because of location, affinity group, medical intervention, insurance status, etc. ?
  - What are their ages?
  - What is the gender distribution?

Swiss Re

Where does Q' (or q') come from?

- In this study the study subject characteristics are:
  - 68.8% women, mean age 68.1 ± 7.4 years
  - Drawn from general medicine practice of a mid-west university medical center where all adults age 60 and over were screened for cognitive impairment
    - "Public safety net hospital and its community health centers"
  - Authors present detailed accounting of co-morbid conditions
- Options for expected mortality could include:
  - US population life tables
  - Social security life table
  - Others may also be valid options

Swiss Re

Social Security, period life table 2007

Age	Males –death probability (q')	Females- death probability (q')
68	0.021468	0.014103
69	0.023387	0.015526
70	0.025579	0.017163
71	0.028032	0.018987
72	0.030665	0.020922
73	0.033467	0.022951
74	0.036519	0.025147
75	0.040010	0.022951

http://www.ssa.gov/oact/STATS/table4c6.html#ss

Now what?

- Use math rules to derive p' and q' that match the observed from the study
- Tables list separate mortality probability q for males and females
- You can create a weighted q' that reflects the proportion of males and females in the study
  - 69% women, so 31% men, mean age 68
  - $q_{study} = 0.31 * q_{SSmales} + 0.69 * q_{SSfemales}$
  - $q_{68} = 0.31 * (0.021468) + 0.69 * (0.014103) = 0.016386$
- Use this to solve for the expected p', cumulative P' and Q'

Swiss Re

Weighted q', p', P', and Q' calculated.....

Age	Weighted death probability (q')	p' = 1 - q'	Cumulative P' $=p_a p_b p_c$...	Cumulative Q' = 1 − P'
68	0.016386	0.983614	0.983614	0.016386
69	0.017963	0.982037	0.965945	0.034055
70	0.019772	0.980228	0.946847	0.053153
71	0.021791	0.978209	0.926214	0.073786
72	0.023942	0.976058	0.904038	0.095962
73	0.026211	0.973789	0.880343	0.119657
74	0.028672	0.971328	0.855101	0.144899
75	0.028239	0.971761	0.828146	0.171854

Swiss Re

Corresponding to time covered by study observations....

Study year	Weighted death probability (q')	p' = 1 - q'	Cumulative P' $=p_a p_b p_c$...	Cumulative Q' = 1 − P'
0 to 1	0.016386	0.983614	0.983614	0.016386
1 to 2	0.017963	0.982037	0.965945	0.034055
2 to 3	0.019772	0.980228	0.946847	0.053153
3 to 4	0.021791	0.978209	0.926214	0.073786
4 to 5	0.023942	0.976058	0.904038	0.095962

From slide 25 the 5-year cumulative Observed mortality Q= 0.46

From table above the 5-year Expected mortality Q'= 0.096

Mortality ratio(%) = Observed/Expected = 0.46/0.096 (x 100%) =**479%**

Swiss Re

A different standardized mortality ratio...

- You could also use the "no impairment" group from the study as the expected mortality for the comparison
- 5-year cumulative P from Figure 2 is 0.83
  - So Q' is 0.17 (=1 − 0.83)
  - Observed Q/ expected Q' is 0.46/0.17 , so this SMR is 270%
- An additional comparison:
  - How does "no impairment" group compare to an external expected mortality (Social Security)?
  - For this comparison: Q/Q' = 0.17/0.096, so SMR is 177%
  - What could you conclude about the patients attending this medical clinic?

Swiss Re

Regression analysis results

- This paper also included Cox regression analysis
  - These days regression analysis is more common analytic approach
  - Paper includes very detailed factor by factor analysis
- Cox regression results reported in this study:
  - Increased risk of death with moderate to severe cognitive impairment compared to no cognitive impairment
    - Expressed as a hazard ratio: 1.447 (95% CI, 1.235-1.695)
- How do you interpret this result?
  - Does it compare an observed/expected?
  - How does HR compare to MR%
  - Can you use the result in day to day underwriting?
  - Adjustment by other or multiple patient characteristics?

Swiss Re

Summary

- Things to remember when considering a mortality abstract:
  - Choose a study that includes life table analysis
  - The "art" of choosing the appropriate expected
  - Caution generalizing results from a medical study to insurance applicants
- Reasons for preparing an insurance mortality abstract
  - For your own use to assist case review or guideline development
  - For publication using the classic methods described in JIM and Mortality methodology courses
- Next steps
  - Review Basic Mortality materials
  - Find an article you want to use to try to develop a table on your own
  - Express interest in workshop or course to work and discuss examples, or possibly develop forum on AAIM website?

Swiss Re

References

- Pokorski RJ. Mortality methodology and analysis seminar. J Insur Med 1988(4);20:20-45.
  - Enhanced version reproduced in: Singer RB et al, Medical Risks 1991 Compend of Mortality and Morbidity, Praeger 1994
  - http://aaimedicine.org/members/jim_articles/020-04-0020.pdf
- Social Security Life table:

  http://www.ssa.gov/oact/STATS/table4c6.html#ss
- United States Life tables, 2006:

  http://www.cdc.gov/nchs/data/nvsr/nvsr58/nvsr58_21.pdf

Swiss Re

Thank you

Swiss Re

Legal notice

Although all the information used was taken from reliable sources, Swiss Re does not accept any responsibility for the accuracy or comprehensiveness of the details given. All liability for the accuracy and completeness thereof or for any damage resulting from the use of the information contained in this presentation is expressly excluded. Under no circumstances shall Swiss Re or its Group companies be liable for any financial and/or consequential loss relating to this presentation.