Life Tables

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Based on slides by Craig Higgins

Learning Objectives

At the end of this lecture, participants should be able to:

1. review the **design features** of follow-up studies.
2. **calculate** the **risk**:
    - **Excluding** subjects with incomplete follow-up
    - **Adjusting** for subjects with incomplete follow-up
3. split follow-up into **time intervals**
4. calculate **survival probabilities** within each interval
5. construct **life tables** and **survival curves**
6. use the **Kaplan-Meier** method when exact censor time is known
7. compare survival curves.

Review of follow-up (cohort) studies (1)

- Individuals followed for period of time
- Occurrence of event (e.g. mortality) is measured
- Crude measure of effect is *risk* (D/N)
- **D** = no. of events during follow-up; **N** = no. of individuals
- But…

Review of follow-up (cohort) studies (2)

- Individuals followed for period of time
- Occurrence of event (e.g. mortality) is measured
- Crude measure of effect is *risk* (D/N)
- **D** = no. of events during follow-up; **N** = no. of individuals
- But… *no account taken of* ***when*** *events occurred.*

Review of follow-up (cohort) studies (3)

- Individuals followed for period of time
- Occurrence of event (e.g. mortality) is measured
- Crude measure of effect is *risk* (D/N)
- **D** = no. of events during follow-up; **N** = no. of individuals
- But… *no account taken of* ***when*** *events occurred.*
- Timing of event can influence estimate of risk.
- Taking account of time-until-event gives better estimate of risk.
- This can be done using **Life Tables.**

Review of follow-up (cohort) studies – Example context:

Example: 50 people diagnosed with melanoma, 1970-87

- Follow-up period defined as **first 5 years** following diagnosis.

- After 5-year follow-up patients either:
  - Dead (D) - of melanoma (M) or other cause (O)
  - Alive (A)

Review of follow-up (cohort) studies – Example data:

Example: 50 people diagnosed with melanoma, 1970-87

Data for first 10 patients:

Obs	Sex	Age	Entry	Exit	Status	Cause	FU
1	M	63	10/70	10/70	D	M	0
2	M	42	07/72	01/78	D	O	5
3	M	41	03/73	04/73	D	M	0
4	F	57	06/73	07/74	D	M	1
5	M	35	09/73	10/87	A	-	14
6	F	48	10/73	08/74	D	M	0
7	M	43	04/74	02/77	D	M	2
8	F	27	01/75	01/75	D	M	0
9	F	56	12/76	10/87	A	-	10
10	F	33	01/77	11/87	A	-	10

Review of follow-up (cohort) studies – Example analysis:

Example: 50 people diagnosed with melanoma, 1970-87

Crude analysis:

Restrict to those who die of melanoma or alive at 5-years

37 individuals:

20 died of melanoma and **17** were alive after 5 years

Probability of failure (i.e. risk of dying from melanoma)

= 20/37 = 0.541 or **54.1%**

But…

Review of follow-up (cohort) studies – Example constraints:

Example: 50 people diagnosed with melanoma, 1970-87

We ignored 13 subjects with < 5 years follow-up, they:

- died of other causes
- left the study (e.g. migrated out of country)
- entered study (diagnosed) too late (i.e. after 1982 if end is 1987)

These subjects were **at-risk** for some of the time.

Review of follow-up (cohort) studies – Example - censoring:

Example: 50 people diagnosed with melanoma, 1970-87

Obs 2, 5, 9 & 10 still alive after 5 years of follow-up

Obs 1,3,4,6,7 & 8 died of melanoma during follow-up

Obs 11 died of other cause

Obs 12 entered study too late

Obs	Sex	Age	Entry	Exit	Status	Cause	FU
1	M	63	10/70	10/70	D	M	0
2	M	42	07/72	01/78	D	O	5
3	M	41	03/73	04/73	D	M	0
4	F	57	06/73	07/74	D	M	1
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Obs	**Sex**	**Age**	**Entry**	**Exit**	**Status**	**Cause**	**FU**
11	F	43	01/76	10/78	D	O	2
12	M	31	05/85	12/87	A	-	2

Review of follow-up (cohort) studies – Example - adjusting:

Example: 50 people diagnosed with melanoma, 1970-87

But censored people are *at risk* for part of follow-up

They **did not** fail => need to adjust estimate of risk

Can assume at risk for **half** the follow-up period

<u>Notation</u>

N = no. of subjects in cohort

D = no. of observed failures

L = no. of censored subjects

Adjusted probability of failure = **D/(N-0.5L)**

Cohort reduced by **0.5L**

O.K provided L is **small** compared to N

Review of follow-up (cohort) studies – Example – probability of failure:

Example: 50 people diagnosed with melanoma, 1970-87

50 Patients entered study

- **20** died of melanoma
- **17** alive at end of study
- **13** < 5 years follow-up (assume 2.5y each)

Cohort reduced by 0.5x13 = **6.5 years**

Probability of failure = 20 / (50-6.5)

= **0.46 or 46%** **(previously 54.1%)**

Review of follow-up (cohort) studies – fixed follow up

Using fixed follow-up has disadvantages:

- only comparable with studies of same length
- timing of failure is ignored
- timing of censoring is ignored

Can divide follow-up into consecutive time intervals

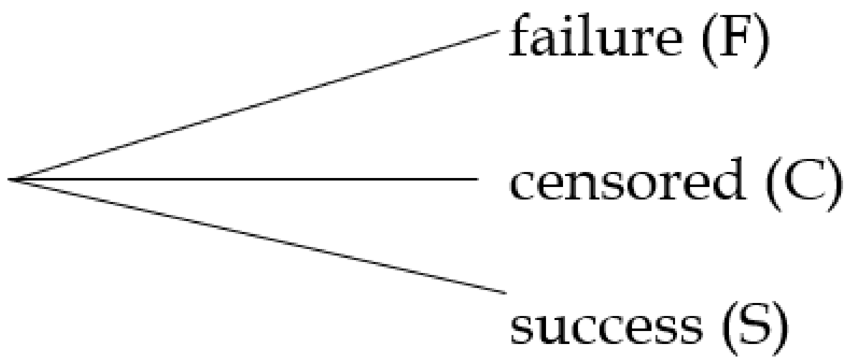
Estimate risk in each interval and pool to obtain overall estimate.....

....Life Tables

Life Tables - basics

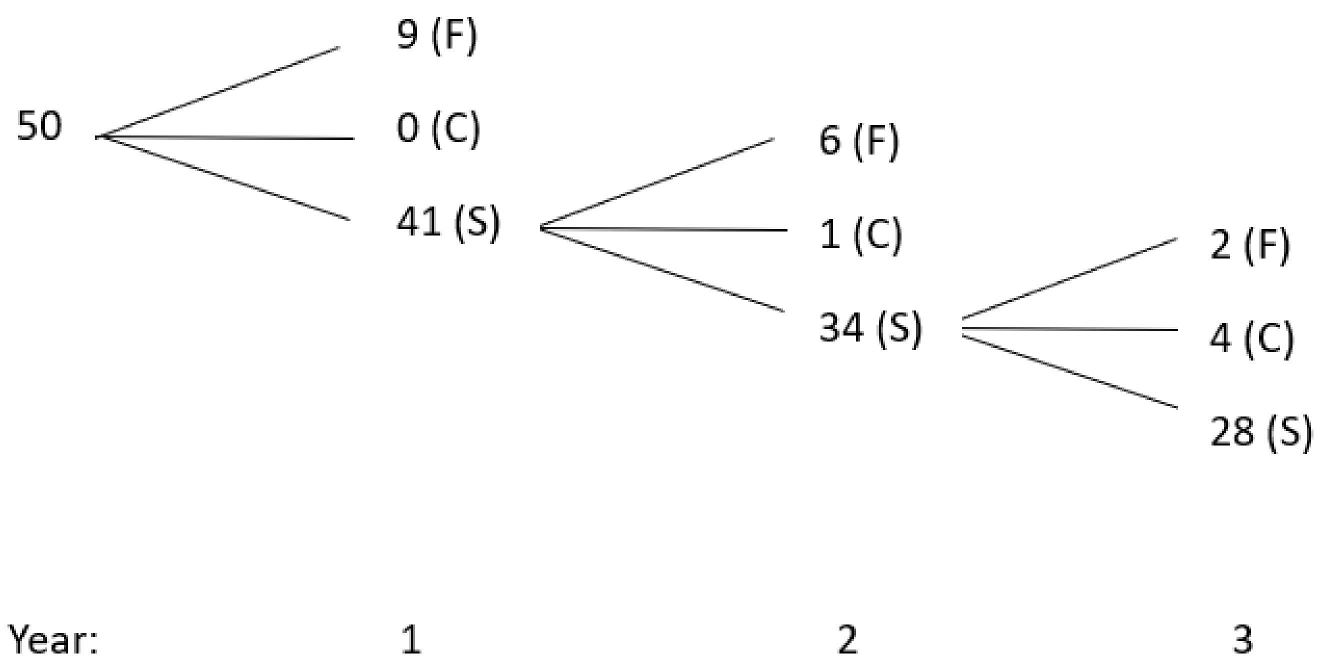
Within each time interval, individuals will either:

- *Fail*
- *Succeed (Survive)*
- *Become censored*



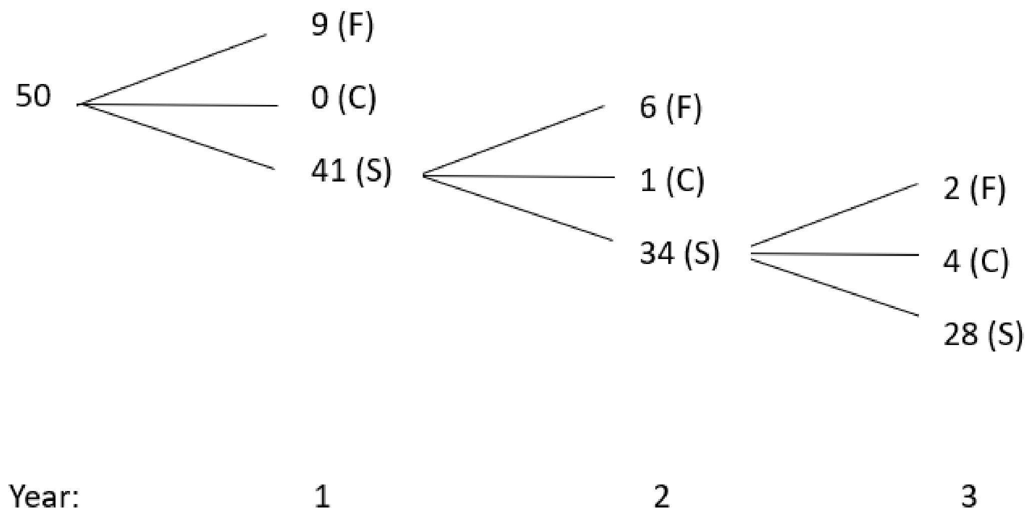
Life Tables: melanoma example

For the melanoma example, the first three years are:



Life Tables: melanoma example – Y1 probabilities (1)

For the melanoma example, the first three years are:

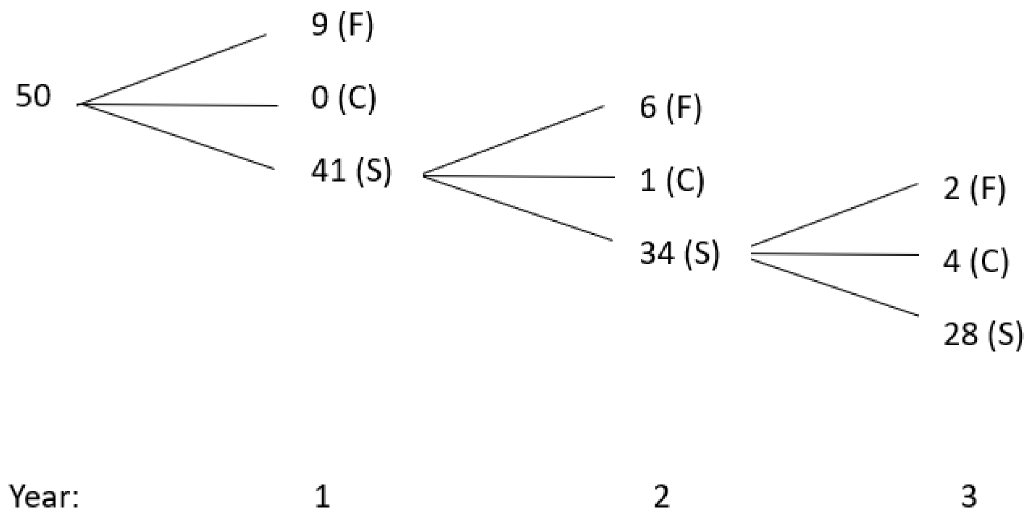


Probability of success = 1 - probability of failure

Year 1: prob of failure =
prob of success =

Life Tables: melanoma example – Y1 probabilities (2)

For the melanoma example, the first three years are:

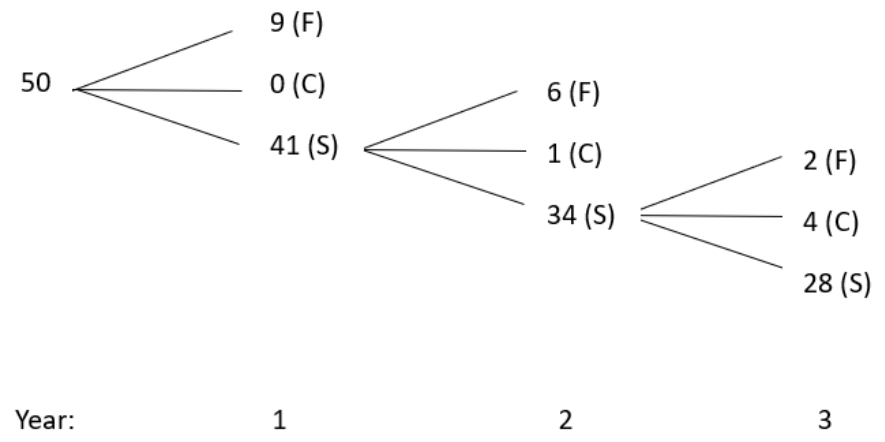


Probability of success = 1 - probability of failure

Year 1: prob of failure = 9/(50-0.5x0) = 0.18
prob of success = 1-0.18 = **0.82**

Life Tables: melanoma example – Y2 probabilities (1)

For the melanoma example, the first three years are:



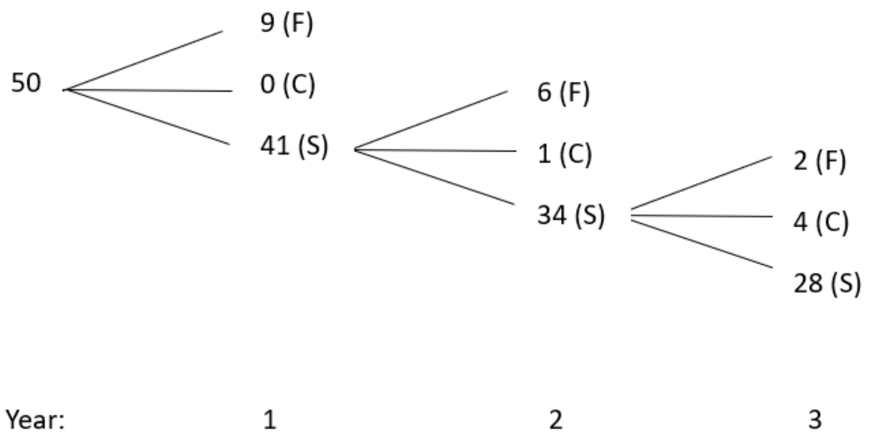
Probability of success = 1 - probability of failure

Year 1: prob of failure = 9/(50-0.5x0) = 0.18
prob of success = 1-0.18 = **0.82**

Year 2: prob of failure =
prob of success =

Life Tables: melanoma example – Y2 probabilities (2)

For the melanoma example, the first three years are:



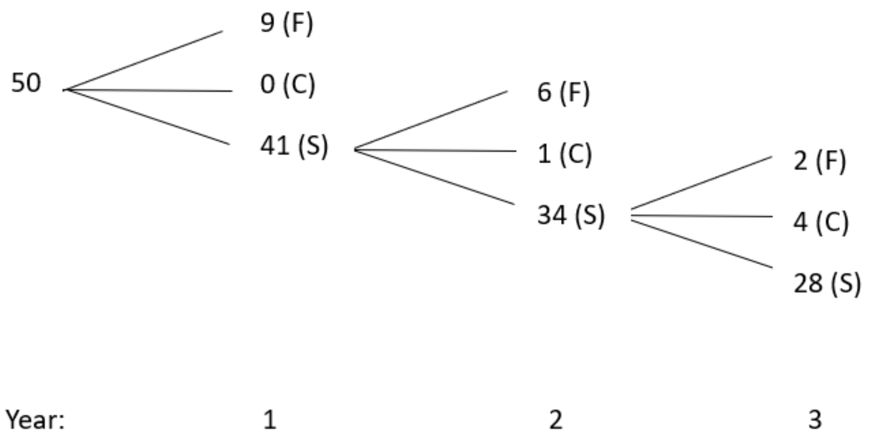
Probability of success = 1 - probability of failure

Year 1: prob of failure = 9/(50-0.5x0) = 0.18
prob of success = 1-0.18 = **0.82**

Year 2: prob of failure = 6/(41-0.5x1) = 0.148
prob of success = 1-0.148 = **0.852**

Life Tables: melanoma example – Y3 probabilities (1)

For the melanoma example, the first three years are:



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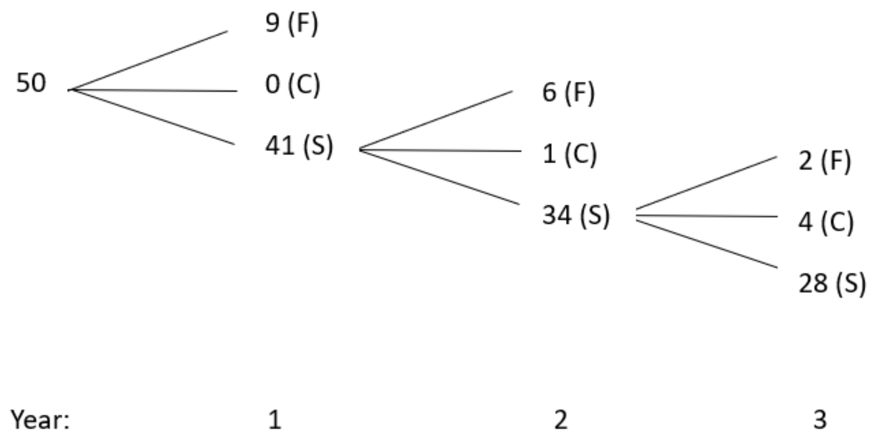
Year 1: prob of failure = 9/(50-0.5x0) = 0.18
prob of success = 1-0.18 = **0.82**

Year 2: prob of failure = 6/(41-0.5x1) = 0.148
prob of success = 1-0.148 = **0.852**

Year 3: prob of failure =
prob of success =

Life Tables: melanoma example – Y3 probabilities (2)

For the melanoma example, the first three years are:



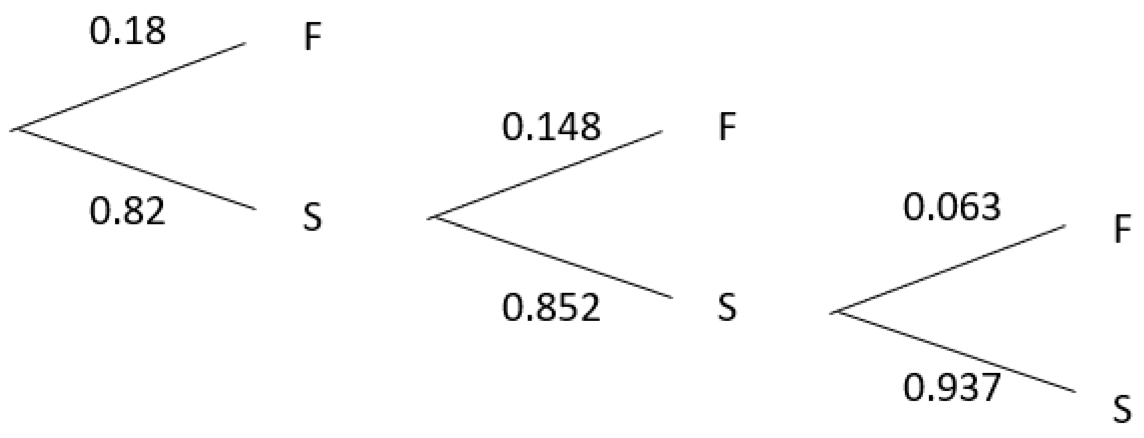
Probability of success = 1 - probability of failure

Year 1: prob of failure = 9/(50-0.5x0) = 0.18
prob of success = 1-0.18 = **0.82**

Year 2: prob of failure = 6/(41-0.5x1) = 0.148
prob of success = 1-0.148 = **0.852**

Year 3: prob of failure = 2/(34-0.5x4) = 0.063
prob of success = 1-0.063 = **0.937**

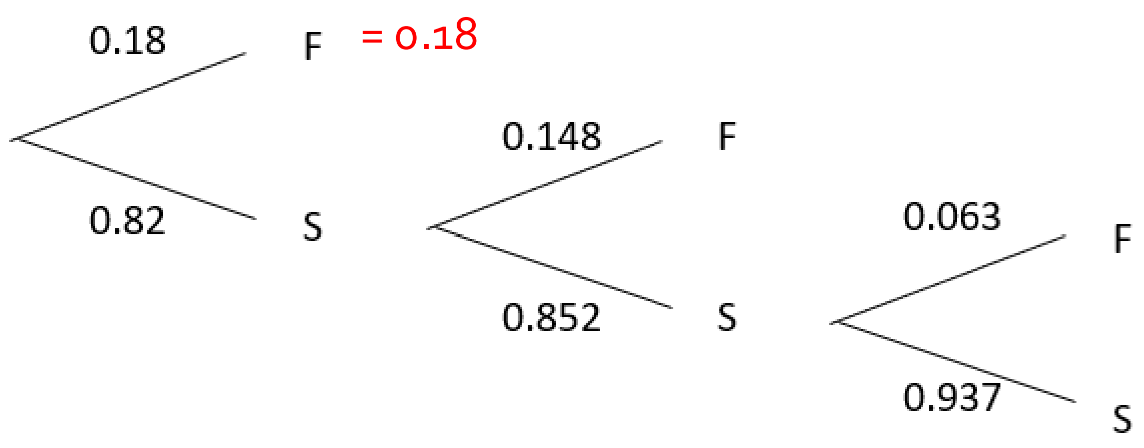
Life Tables: melanoma example - outcomes



Four possible outcomes (tips of trees) during study:

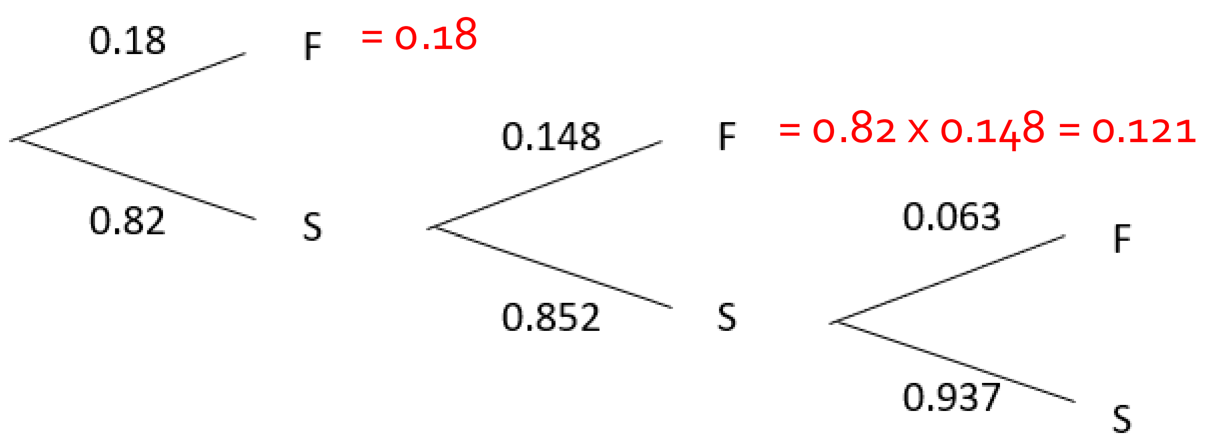
1. Fail during first year =

Life Tables: melanoma example – outcomes – Y1



Four possible outcomes (tips of trees) during study:
1. Fail during first year = **0.18**

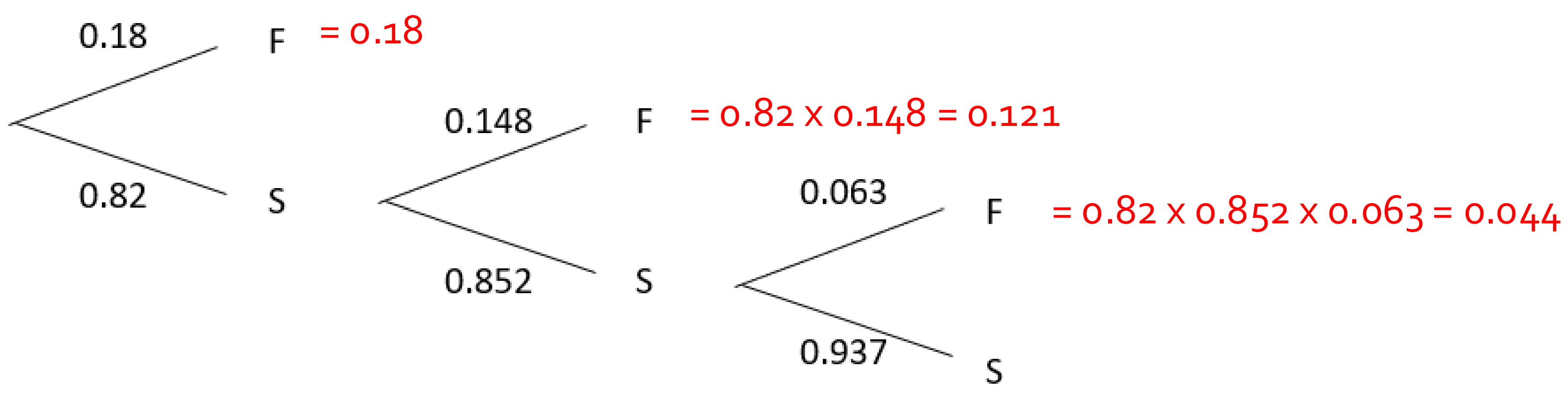
Life Tables: melanoma example – outcomes – Y2



Four possible outcomes (tips of trees) during study:

1. Fail during first year = **0.18**
2. Fail during second year = 0.82 x 0.148 = **0.121**

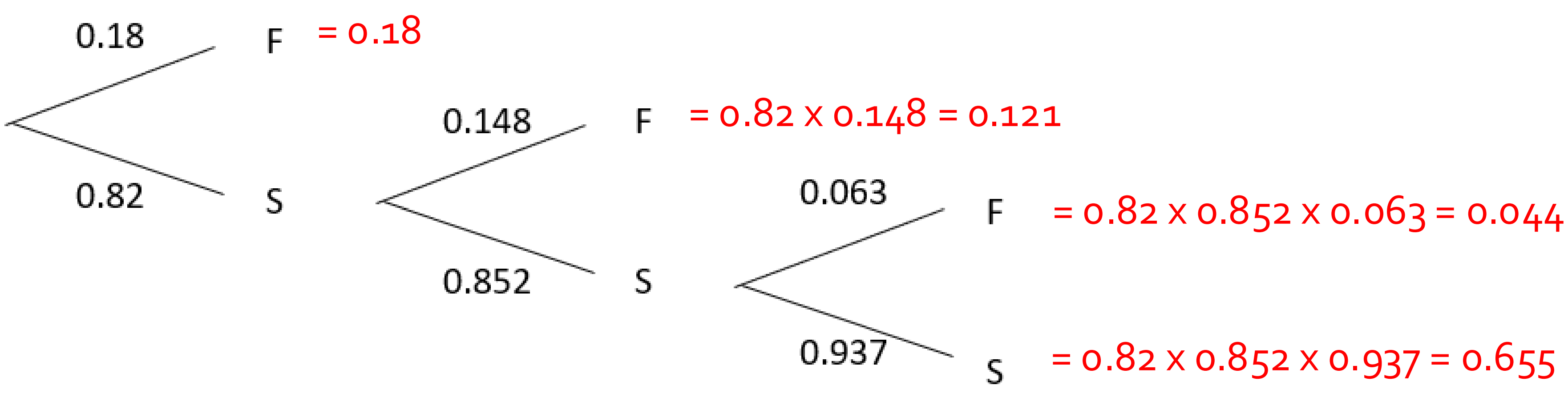
Life Tables: melanoma example – outcomes – Y3



Four possible outcomes (tips of trees) during study:

1. Fail during first year = **0.18**
2. Fail during second year = 0.82 x 0.148 = **0.121**
3. Fail during third year = 0.82 x 0.852 x 0.063 = **0.044**

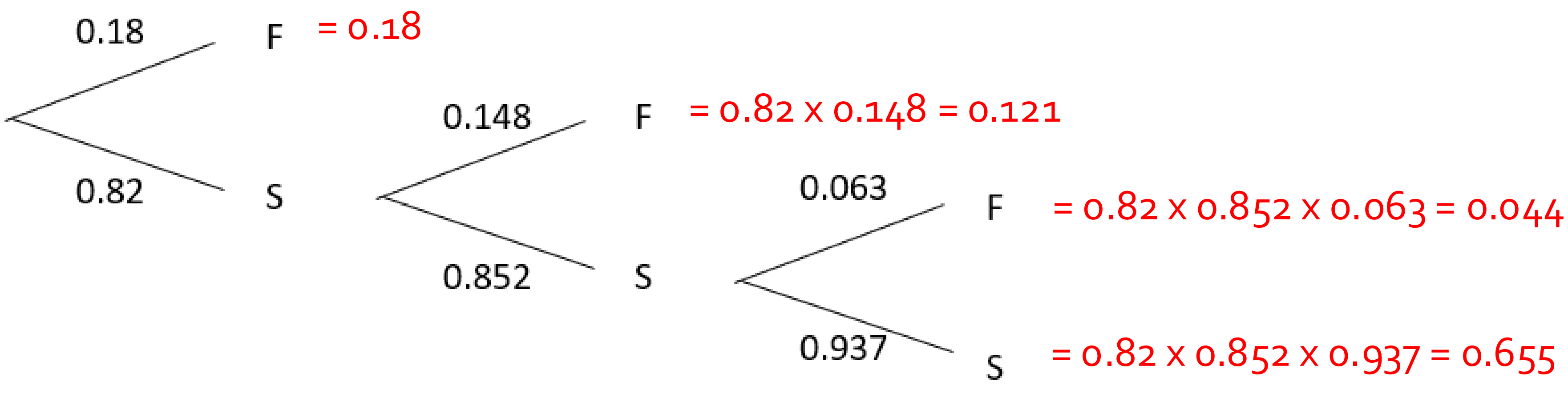
Life Tables: melanoma example – outcomes - survival



Four possible outcomes (tips of trees) during study:

1. Fail during first year = **0.18**
2. Fail during second year = 0.82 x 0.148 = **0.121**
3. Fail during third year = 0.82 x 0.852 x 0.063 = **0.044**
4. Alive after three years = 0.82 x 0.852 x 0.937 = **0.655**

Life Tables: melanoma example – outcomes – cumulative survival probability

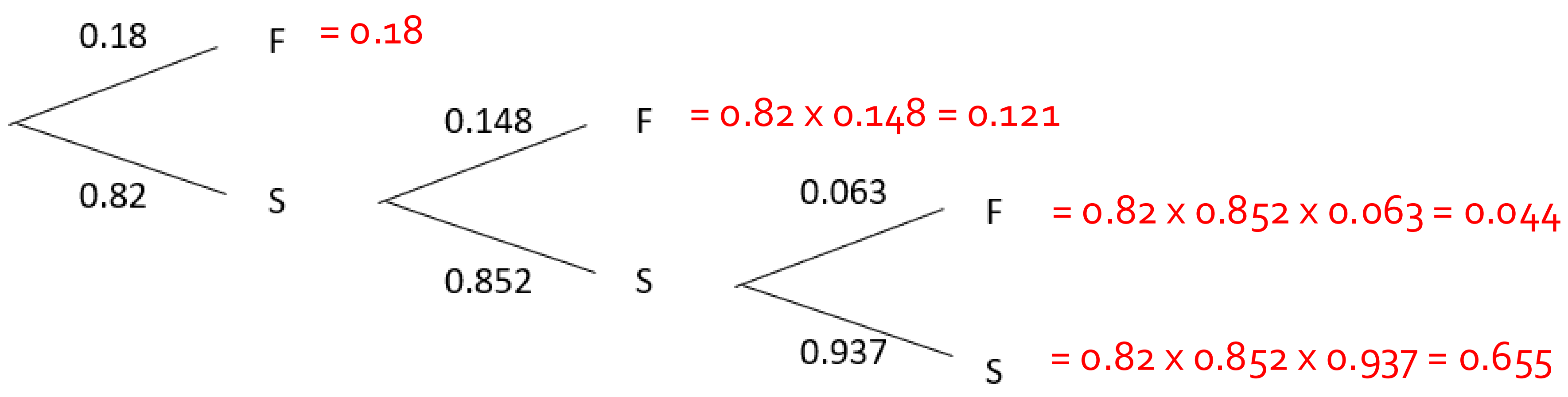


Four possible outcomes (tips of trees) during study:

1. Fail during first year = **0.18**
2. Fail during second year = 0.82 x 0.148 = **0.121**
3. Fail during third year = 0.82 x 0.852 x 0.063 = **0.044**
4. Alive after three years = 0.82 x 0.852 x 0.937 = **0.655**

No. 4 = cumulative survival probability

Life Tables: melanoma example – failure calculation



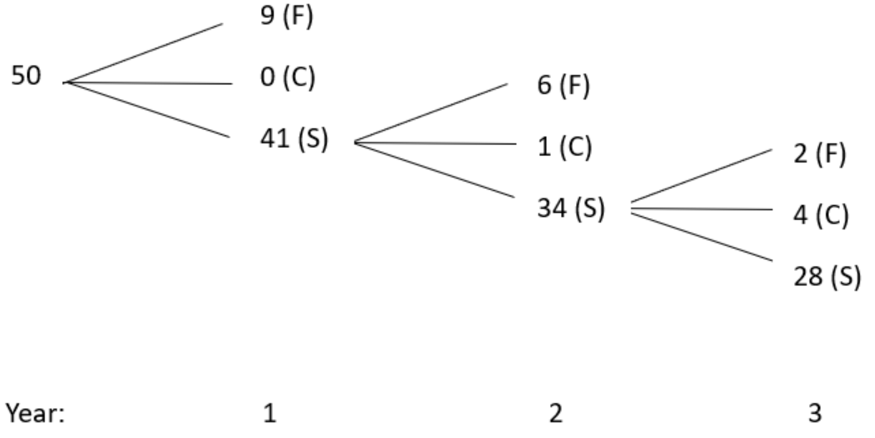
Probability of failing at some point during three years =

Sum of failure probability in each year = 0.18 + 0.121 + 0.044 = **0.345**

Or

1 – probability of surviving 3 years = 1 – 0.655 = **0.345**

Life Tables: using probabilities



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prob of success = 1-0.148 = **0.852**

Year 3: prob of failure = 2/(34-0.5x4) = 0.063
prob of success = 1-0.063 = **0.937**

Use these probabilities to construct **life table.**

Constructing a life table

Year	N	D	L	(1)	(2)	(3)	(4)
1	50	9	0	50.0	0.18	0.82	0.82
2	41	6	1	40.5	0.148	0.852	0.699
3	34	2	4	32.0	0.063	0.937	0.655

Column (1): adjusted size of cohort = (N-0.5L)
Column (2): probability of death during year = D/(N-0.5L)
Column (3): probability of surviving year = 1-D/(N-0.5L)
Column (4): cumulative survival probability = (current year survival probability x all previous years)

After 3 years = 0.82 x 0.852 x 0.937 = **0.655 (probability of surviving 3 years)**

Life table inferences

From a life table, we can examine:

- **Period-specific** failure (& success) probability
- Whether failure (& success) probability **changes** over time
- **Overall** failure (& success) probability

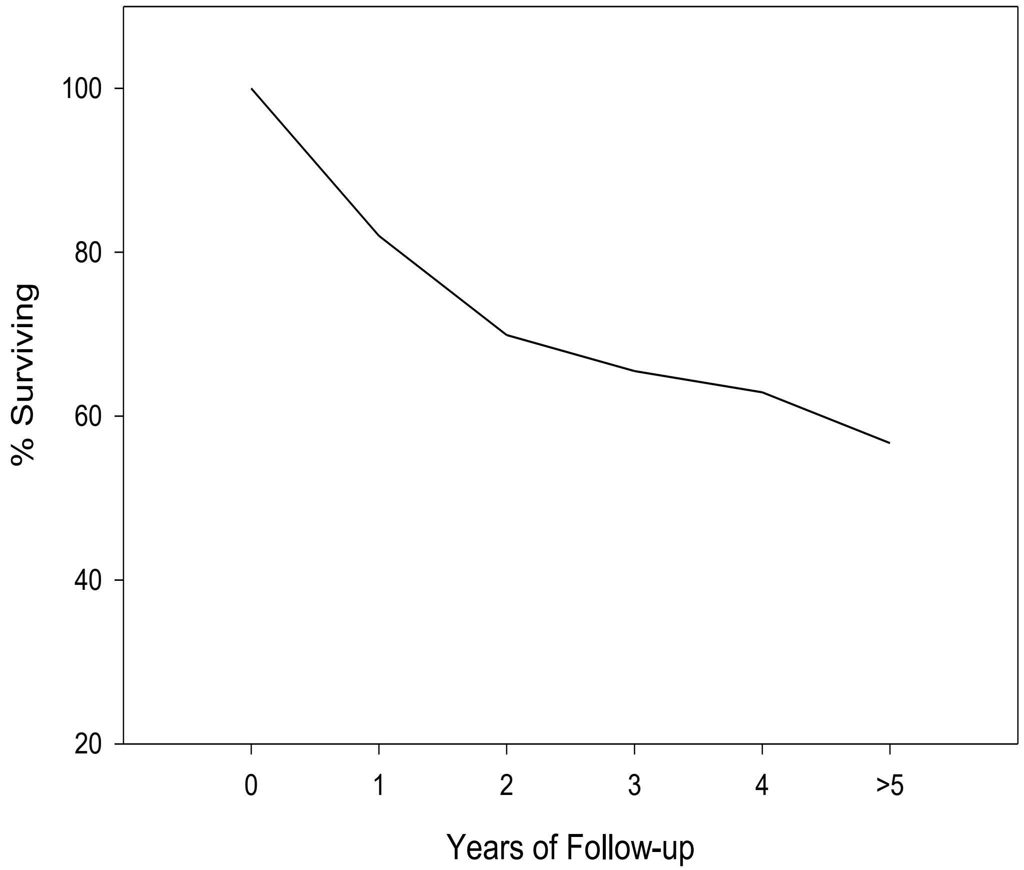
Survival curve:

- Plot cumulative survival prob at each time point
- y-axis starts at 1.0 (100%) since zero failure at start
- **Steepness** of line indicates failure rate

Survival curve

A **survival curve** is a plot of the cumulative survival probabilities.

Figure 1



Survival curve – Kaplan-Meier method

D/(N-0.5L) for censoring is not the best method

It is better to use exact time of censoring and exit

Re-calculate risk each time failure occurs. Known as:

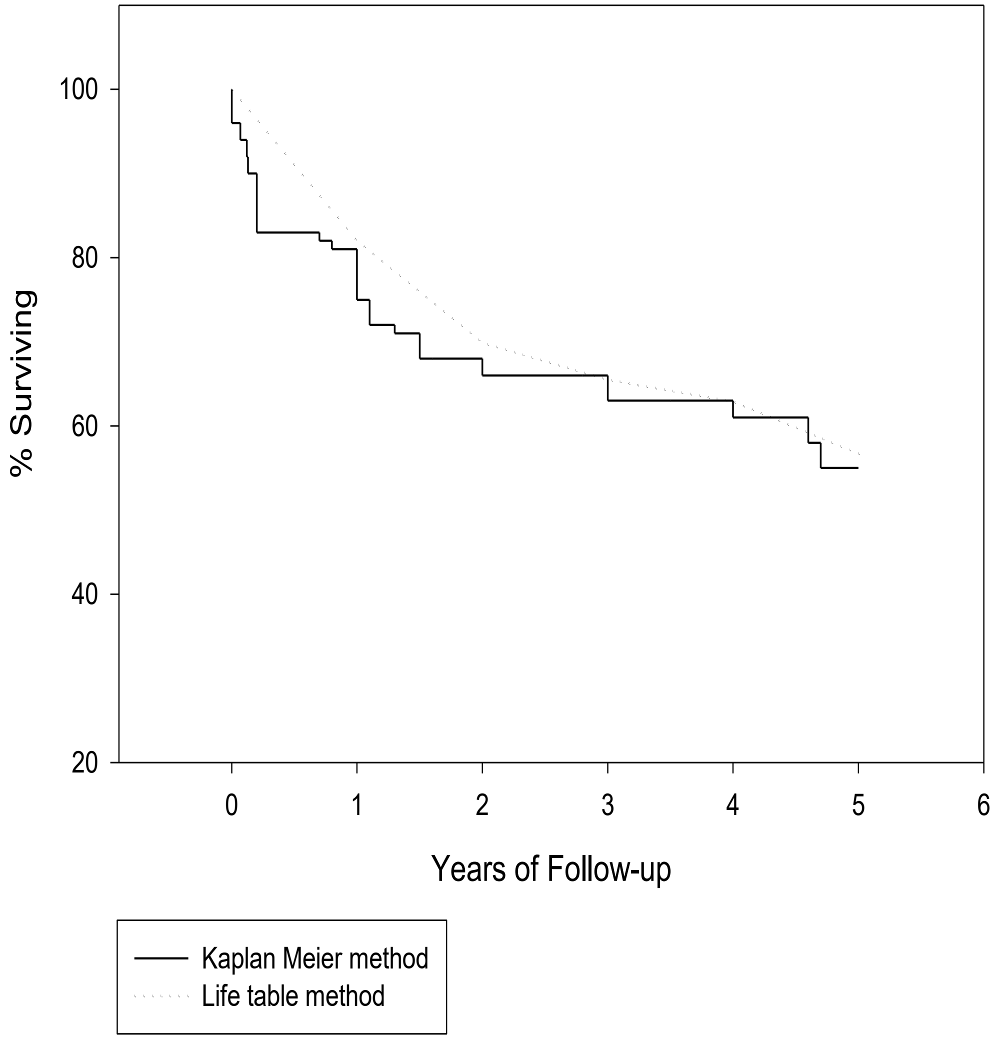
…Kaplan-Meier method

Line becomes more “stepped”

Gives more precise estimates of risk over time

Survival curve – Kaplan-Meier graph

Figure 2



Survival curve – comparing groups

Survival curves are also useful for comparing groups of people.

Produce a life table for each group and plot on the same axis…

Survival curve – comparing groups on graph

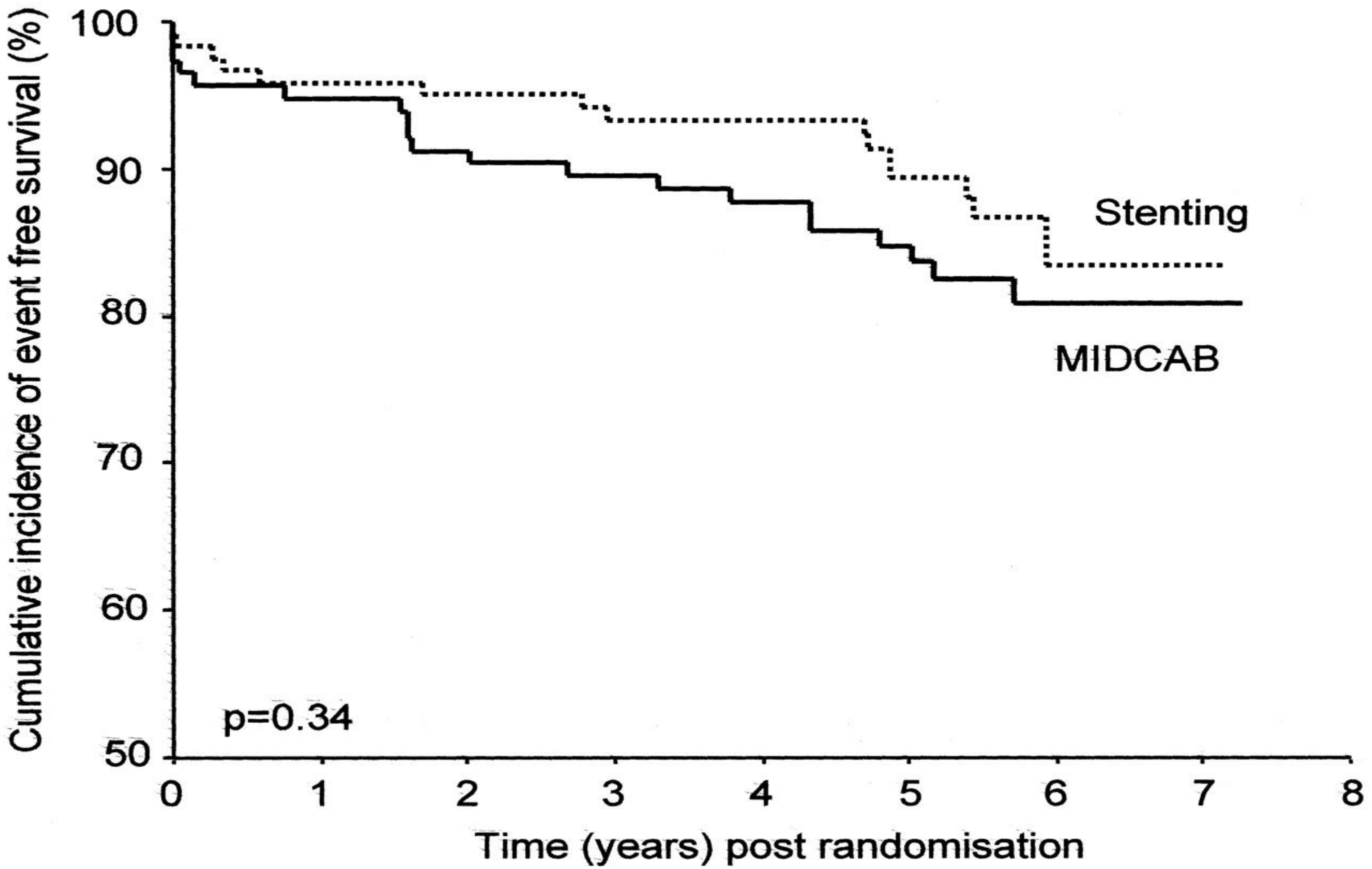


Figure 4. Kaplan-Meier curve showing freedom from death and myocardial infarction. Patients assigned to stenting are indicated by a dotted line and those assigned to minimally invasive direct coronary artery bypass surgery (MIDCAB) by a solid line.

Formal comparison methods

Also, formal methods of comparison exist.

E.g. **Log Rank** test, **Cox** regression

Lecture Summary

What we have learnt:

1. Ignoring censored individuals gives **incorrect estimate of risk**

2. Assuming censored individuals are at risk for **half the time** is ok if **L is small** and N is large

3. Better to divide study period into **consecutive time intervals**

4. You can use probabilities in each interval to construct ***life table***

5. Draw ***Kaplan-Meier*** survival curves can be helpful
   - **Compare** curves between different groups and carry out formal **significance tests**

Thank you