Life Tables

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Section A

Clinical Life Tables, Part 1
A fundamental technique of survival analysis that deals with “time to event”
  - A basic example is “time to death”
It can answer the question of the chance of survival after being diagnosed with the disease or after beginning the treatment
The event can be any other health event—not just death
  - It can be relapse, receiving organ transplant, pregnancy (in a study of infertility), failure of treatment, recovery, etc.
It handles variable time of entry and (variable time of) withdrawal of individuals from the population
It calculates cumulative event-free probabilities and generates a survival curve
**Example**

- A group of 200 subjects were followed for three years
- Deaths (events) occurred throughout the three years
- What is the chance of surviving at the end of the three years?

<table>
<thead>
<tr>
<th>Time since beginning of follow-up (Year)</th>
<th>Number at beginning</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>200</td>
<td>20</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>30</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td>40</td>
</tr>
</tbody>
</table>
Following a Population

Patient

Begin follow-up

Death

Year since follow-up

0 1 2 3

1995 2000

Year
Clinical Life Table Notation

- $l_t = \text{number alive at the \textbf{beginning} of time } t$
- $d_t = \text{number of deaths \textbf{during} the time interval}$
Apply notation to the table in the example

<table>
<thead>
<tr>
<th>Time since beginning of follow-up (Year)</th>
<th>Number at beginning $l_t$</th>
<th>Deaths $d_t$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>200</td>
<td>20</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>30</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td>40</td>
</tr>
</tbody>
</table>
Fill in the “Number at Beginning” Column

- Fill in the missing cells

<table>
<thead>
<tr>
<th>Time since beginning of follow-up (Year)</th>
<th>Number at beginning $l_t$</th>
<th>Deaths $d_t$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>200</td>
<td>20</td>
</tr>
<tr>
<td>2</td>
<td>180</td>
<td>30</td>
</tr>
<tr>
<td>3</td>
<td>150</td>
<td>40</td>
</tr>
</tbody>
</table>

200 – 20 = 180

180 – 30 = 150
Clinical Life Table Notation

- \( I_t \) = number alive at the beginning of time \( t \)
- \( d_t \) = number of deaths during the time interval
- \( q_t = d_t / I_t \) = probability of dying during the time interval
- \( p_t = 1 - q_t \) = probability of surviving in the time interval
## Calculate Probabilities of Dying (q) and Surviving (p)

<table>
<thead>
<tr>
<th>Interval</th>
<th>$l_t$</th>
<th>$d_t$</th>
<th>$q_t$</th>
<th>$p_t$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>200</td>
<td>20</td>
<td>0.1</td>
<td>0.9</td>
</tr>
<tr>
<td>2</td>
<td>180</td>
<td>30</td>
<td>0.17</td>
<td>0.83</td>
</tr>
<tr>
<td>3</td>
<td>150</td>
<td>40</td>
<td>0.27</td>
<td>0.73</td>
</tr>
</tbody>
</table>

$20/200 = 0.1$

$30/180 = 0.17$

$1.0 - 0.1 = 0.9$

$30/180 = 0.17$

$1.0 - 0.17 = 0.83$
Clinical Life Table Notation

- \( l_t \) = number alive at the beginning of time \( t \)
- \( d_t \) = number of deaths during the time interval
- \( q_t = d_t / l_t \) = probability of dying during the time interval
- \( p_t = 1 - q_t \) = probability of surviving in the time interval
- \( P_t \) = cumulative probability of surviving at the beginning of the time interval
  = cumulative probability of surviving at the end of the previous interval

- At the beginning of the study (zero time), \( P(1) = 1.0 \)
- \( P(t+1) = p_t \, P_t \)
Clinical Life Table Notation

- \( l_t \) = number alive at the beginning of time \( t \)
- \( d_t \) = number of deaths during the time interval
- \( q_t = d_t / l_t \) = probability of dying during the time interval
- \( p_t = 1 - q_t \) = probability of surviving in the time interval
- \( P_t \) = cumulative probability of surviving at the beginning of the time interval
  = cumulative probability of surviving at the end of the previous interval
  - At the beginning of the study (zero time), \( P(1) = 1.0 \)
  - \( P(t+1) = p_t \cdot P_t \)
  - For example: \( P_1 = 1.0 \)
    
    \[
    P_2 = p_1 \cdot P_1 \\
    P_3 = p_2 \cdot P_2
    \]
Calculate the Cumulative Probabilities of Surviving (P)

\[ P_1 = 1.0 \]
\[ P_2 = p_1 \times P_1 \]
\[ P_3 = p_2 \times P_2 \]
\[ P_4 = p_3 \times P_3 \]

\[
\begin{array}{|c|c|c|c|c|c|}
\hline
\text{Interval} & l_t & d_t & q_t & p_t & P_t \\
\hline
1 & 200 & 20 & 0.1 & 0.9 & 1.0 \\
\hline
2 & 180 & 30 & 0.17 & 0.83 & 0.9 \\
\hline
3 & 150 & 40 & 0.27 & 0.73 & 0.747 \\
\hline
\end{array}
\]

- \( 0.9 \times 1.0 = 0.9 \)
- \( 0.83 \times 0.9 = 0.747 \)
Calculate the Cumulative Probabilities of Surviving (P)

\[ P_1 = 1.0 \]
\[ P_2 = p_1 \times P_1 \]
\[ P_3 = p_2 \times P_2 \]
\[ P_4 = p_3 \times P_3 \]

<table>
<thead>
<tr>
<th>Interval</th>
<th>( l_t )</th>
<th>( d_t )</th>
<th>( q_t )</th>
<th>( p_t )</th>
<th>( P_t )</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>200</td>
<td>20</td>
<td>0.1</td>
<td>0.9</td>
<td>1.0</td>
</tr>
<tr>
<td>2</td>
<td>180</td>
<td>30</td>
<td>0.17</td>
<td>0.83</td>
<td>0.9</td>
</tr>
<tr>
<td>3</td>
<td>150</td>
<td>40</td>
<td>0.27</td>
<td>0.73</td>
<td>0.747</td>
</tr>
</tbody>
</table>

\[ 0.73 \times 0.747 = 0.545 \]

\[ 0.73 \times 0.747 = 0.545 \]
Quick Check

- What is the (cumulative) probability of surviving at the beginning? (time 0) = 1.0
- What is the cumulative probability of surviving to the beginning of the second year? = 0.9
- What is the cumulative probability of surviving at the end of the first year? = 0.9
- What is the cumulative probability of surviving to the beginning of year 3? = 0.747
- What is the cumulative probability of surviving to the beginning of year 4 or end of year 3? = 0.545
Section B

Clinical Life Tables: Part 2
Another View of Cumulative Probabilities ($P$)

- $P_t = \text{cumulative probability of surviving at the beginning of the time interval}$

<table>
<thead>
<tr>
<th>Interval</th>
<th>$l_t$</th>
<th>$d_t$</th>
<th>$q_t$</th>
<th>$p_t$</th>
<th>$p_t$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>200</td>
<td>20</td>
<td>0.1</td>
<td>0.9</td>
<td>1.0</td>
</tr>
<tr>
<td>2</td>
<td>180</td>
<td>30</td>
<td>0.17</td>
<td>0.83</td>
<td>0.900</td>
</tr>
<tr>
<td>3</td>
<td>150</td>
<td>40</td>
<td>0.27</td>
<td>0.73</td>
<td>0.747</td>
</tr>
</tbody>
</table>

$0.545$
Censoring

- Observations are considered to be censored if:
  - Individuals withdraw from the study or are lost to follow-up
  - Individuals are not followed long enough to experience the event of interest
  - Individuals experience an event which precludes the event of interest
- Those who are censored during an interval are assumed to have been followed, on average, for half the interval
Clinical Life Table Notation

- $w_t = $ number withdrew ("censored") during the interval
- $l' = l_t - w_t / 2 = $ adjusted number at risk of the event in the interval
- $q_t = d_t / l'_t$
## Life Table with Censored Observations

<table>
<thead>
<tr>
<th>Interval</th>
<th>$l_t$</th>
<th>$d_t$</th>
<th>$w_t$</th>
<th>$l'_t$</th>
<th>$q_t$</th>
<th>$p_t$</th>
<th>$P_t$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>200</td>
<td>20</td>
<td>50</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>130</td>
<td>30</td>
<td>40</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>60</td>
<td>40</td>
<td>20</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Life Table with Censored Observations

<table>
<thead>
<tr>
<th>Interval</th>
<th>( l_t )</th>
<th>( d_t )</th>
<th>( w_t )</th>
<th>( l'_t )</th>
<th>( q_t )</th>
<th>( p_t )</th>
<th>( P_t )</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>200</td>
<td>20</td>
<td>50</td>
<td>175</td>
<td>0.114</td>
<td>0.886</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>130</td>
<td>30</td>
<td>40</td>
<td>110</td>
<td>0.273</td>
<td>0.727</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>60</td>
<td>40</td>
<td>20</td>
<td>50</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\( 200 - (50/2) = 200 - 25 = 175 \)

\( 20/175 = 0.114 \)
Life Table with Censored Observations

<table>
<thead>
<tr>
<th>Interval</th>
<th>( l_t )</th>
<th>( d_t )</th>
<th>( w_t )</th>
<th>( l'_t )</th>
<th>( q_t )</th>
<th>( p_t )</th>
<th>( P_t )</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>200</td>
<td>20</td>
<td>50</td>
<td>175</td>
<td>0.114</td>
<td>0.886</td>
<td>1.000</td>
</tr>
<tr>
<td>2</td>
<td>130</td>
<td>30</td>
<td>40</td>
<td>110</td>
<td>0.273</td>
<td>0.727</td>
<td>0.886</td>
</tr>
<tr>
<td>3</td>
<td>60</td>
<td>40</td>
<td>20</td>
<td>50</td>
<td>0.800</td>
<td>0.200</td>
<td>0.644</td>
</tr>
</tbody>
</table>

\[ 200 - \frac{50}{2} = 200 - 25 = 175 \]

\[ \frac{20}{175} = 0.114 \]
**Clinical Life Table: Assumptions**

1. There are no changes in survivorship over calendar time
2. The experience of individuals who are lost to follow-up is the same as the experience of those who are followed
Clinical Life Table: Assumptions

1. There are no changes in survivorship over calendar time
2. The experience of individuals who are lost to follow-up is the same as the experience of those who are followed
3. Withdrawal occurs uniformly within the interval
4. Event occurs uniformly within the interval
Example 1: Clinical Life Table—No Withdrawal/No Loss

- 21 patients with leukemia were followed after treatment over time
- Time from treatment to relapse was observed for all patients
- The remission times (months) were: 6, 6, 6, 6, 7, 8, 10, 10, 11, 13, 16, 17, 19, 20, 22, 23, 25, 32, 32, 34, 35
Example 1: Clinical Life Table—No Withdrawal/No Loss

<table>
<thead>
<tr>
<th>Time</th>
<th>$l_t$</th>
<th>$d_t$</th>
<th>$q_t = d_t/l_t$</th>
<th>$p_t$</th>
<th>$P_t$</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–&lt;6</td>
<td>21</td>
<td>0</td>
<td>0.0000</td>
<td>1.0000</td>
<td>1.0000</td>
</tr>
<tr>
<td>6–&lt;12</td>
<td>21</td>
<td>9</td>
<td>0.4286</td>
<td>0.5714</td>
<td>1.0000</td>
</tr>
<tr>
<td>12–&lt;18</td>
<td>12</td>
<td>3</td>
<td>0.2500</td>
<td>0.7500</td>
<td>0.5714</td>
</tr>
<tr>
<td>18–&lt;24</td>
<td>9</td>
<td>4</td>
<td>0.4444</td>
<td>0.5556</td>
<td>0.4286</td>
</tr>
<tr>
<td>24–&lt;30</td>
<td>5</td>
<td>1</td>
<td>0.2000</td>
<td>0.8000</td>
<td>0.2381</td>
</tr>
<tr>
<td>30–&lt;36</td>
<td>4</td>
<td>4</td>
<td>1.0000</td>
<td>0.0000</td>
<td>0.1905</td>
</tr>
</tbody>
</table>
Example 1: Plot of Time to Relapse $P_t$
Example 1: Clinical Life Table—No Withdrawal/No Loss

- $P_t$ = the cumulative probability in remission at time $t$
  - At the beginning of the time interval
- The cumulative probability still in remission at 24 months is:
  - 0.2381 or 24%
- The probability of relapse between 24 and 30 months is:
  - $q_{30} = 0.20$ or 20%
Example 2

- 50 patients with skin melanoma were treated in one hospital during the time period October, 1952–June, 1967
- Patients were followed annually
- The study was closed to patient follow-up on December 31, 1969
- 20 deaths occurred
- 30 observations were censored due to withdrawal or lack of follow-up
- What are the **two-year and five-year survival rates?**
### Example 2: Clinical Life Table

<table>
<thead>
<tr>
<th>Interval</th>
<th>I</th>
<th>d</th>
<th>w</th>
<th>I′</th>
<th>q</th>
<th>p</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–1</td>
<td>50</td>
<td>9</td>
<td>0</td>
<td>50.0</td>
<td>0.180</td>
<td>0.820</td>
<td>1.000</td>
</tr>
<tr>
<td>1–2</td>
<td>41</td>
<td>6</td>
<td>1</td>
<td>40.5</td>
<td>0.148</td>
<td>0.852</td>
<td>0.820</td>
</tr>
<tr>
<td>2–3</td>
<td>34</td>
<td>2</td>
<td>4</td>
<td>32.0</td>
<td>0.063</td>
<td>0.937</td>
<td><strong>0.699</strong></td>
</tr>
<tr>
<td>3–4</td>
<td>28</td>
<td>1</td>
<td>5</td>
<td>25.5</td>
<td>0.039</td>
<td>0.961</td>
<td>0.655</td>
</tr>
<tr>
<td>4–5</td>
<td>22</td>
<td>2</td>
<td>3</td>
<td>20.5</td>
<td>0.098</td>
<td>0.902</td>
<td>0.629</td>
</tr>
<tr>
<td>5–6</td>
<td>17</td>
<td>0</td>
<td>17</td>
<td>8.5</td>
<td>0</td>
<td>1.000</td>
<td><strong>0.567</strong></td>
</tr>
</tbody>
</table>

**P = 0.567**
Example 2: Cumulative Probability of Survival

- $P$ is the cumulative probability of surviving at the beginning of the time interval or at the end of the previous interval.
- Two-year survival (rate) is the probability of surviving at the end of two years or at the beginning of year 3.
- The two-year survival (rate) is 0.699, or 69.9%.
- The five-year survival (rate) is 0.567, or 56.7%.

<table>
<thead>
<tr>
<th>Interval</th>
<th>l</th>
<th>d</th>
<th>w</th>
<th>l'</th>
<th>q</th>
<th>p</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–1</td>
<td>50</td>
<td>9</td>
<td>0</td>
<td>50.0</td>
<td>0.180</td>
<td>0.820</td>
<td>1.000</td>
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</tr>
<tr>
<td>5–6</td>
<td>17</td>
<td>0</td>
<td>17</td>
<td>8.5</td>
<td>0</td>
<td>1.000</td>
<td>0.567</td>
</tr>
</tbody>
</table>

The table shows the cumulative probabilities at different intervals.
Section C

The Kaplan-Meier Method
Kaplan-Meier Method

- **Kaplan-Meier** is also a survival analysis method
  - It is very similar to the clinical life table method
- It uses the exact times that events occurred—rather than the intervals of follow-up
- The probability of the event is equal to the number of events at that time divided by the number at risk at that point in time (including those who had the events)
- If there are withdrawals before the time of event, they are subtracted from the number at risk
Example: Kaplan-Meier Method

- From *Gordis* textbook
- 6 patients
  - 4 died
  - 2 lost to follow-up
- Deaths occurred at 4, 10, 14, and 24 months
- Lost occurred before 10 months and before 24 months
Example: Kaplan-Meier Table and Kaplan-Meier Plot

- The table is similar to the clinical life table
  - Instead of intervals, it uses the exact time of events
- In this example, the events occurred at 4, 10, 14, and 24 months (so there will be 4 rows in the table)
- All other calculations (q, p, and P) are the same
- The calculated cumulative probability of surviving is for that time point
- Up to that time point, the cumulative probability of surviving takes on the value of the previous time point, thus leading to a step function (see K-M plot)
- When there is no event, the survival curve in a K-M plot will be drawn out horizontally over time and only drop (vertically) down at the time of events (e.g., deaths) to the calculated cumulative probability of surviving
One died at 4 months, and one was lost to follow-up before 10 months; therefore, 4 were known to be alive at 10 months.

Kaplan-Meier Survival Table

<table>
<thead>
<tr>
<th>Time to deaths</th>
<th>Number alive</th>
<th>$d_t$</th>
<th>$q_t$</th>
<th>$p_t$</th>
<th>$P_t$</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>6</td>
<td>1</td>
<td>0.167</td>
<td>0.833</td>
<td>0.833</td>
</tr>
<tr>
<td>10</td>
<td>4</td>
<td>1</td>
<td>0.250</td>
<td>0.750</td>
<td>0.625</td>
</tr>
<tr>
<td>14</td>
<td>3</td>
<td>1</td>
<td>0.333</td>
<td>0.667</td>
<td>0.417</td>
</tr>
<tr>
<td>24</td>
<td>1</td>
<td>1</td>
<td>1.000</td>
<td>0.000</td>
<td>0.000</td>
</tr>
</tbody>
</table>

Another “lost” occurred here before 24 months.
Kaplan-Meier Plot of Survival Study

Probability of surviving

Months after enrollment

0 4 10 14 24
Use of Kaplan-Meier Method

- K-M method takes advantage of all information available in the calculation and is useful for small sample size studies.
- Clinical studies use K-M plots to display prognosis over time.
- K-M estimates can be used for comparison purpose in clinical trials when groups are similar and adjustment is not needed.
Review

- What is the difference between \( I \) and \( I' \)?
- What is the difference between \( p \) and \( P \)?
- What are the assumptions in a clinical life table?