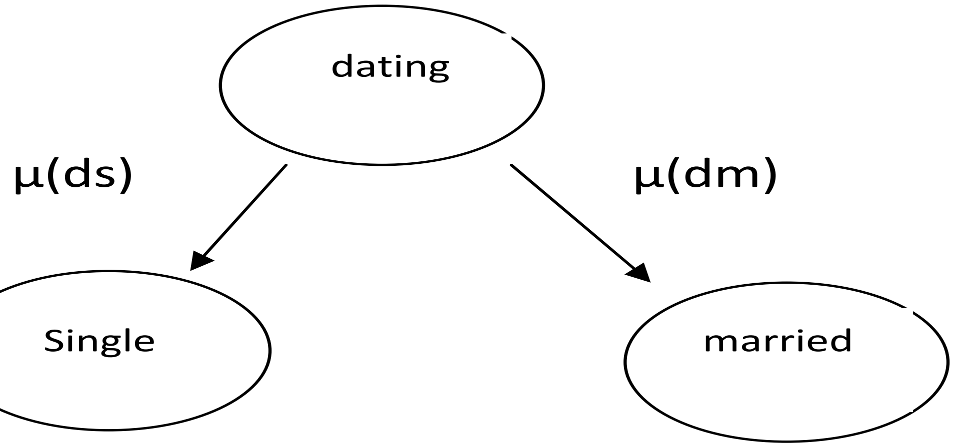
# Survival Models: Week 8

# Markov models - Multi-state Example




What is the probability of transferring from the dating state to the married state?

## Markov models - Multi-state Example

Using the Kolmogorov equations we have:

$$\begin{aligned}\frac{d}{dt}{}_tp_x^{dm} &= {}_tp_x^{ds}\mu^{sm} - {}_tp_x^{dm}\mu^{ms} + {}_tp_x^{dd}\mu^{dm} - {}_tp_x^{dm}\mu^{md} \\ &= {}_tp_x^{dd}\mu^{dm}\end{aligned}$$

For this model we have that ${}_tp_x^{dd} = \exp[-t(\mu^{ds} + \mu^{dm})]$ giving:

$$\frac{d}{dt}{}_tp_x^{dm} = \exp[-t(\mu^{ds} + \mu^{dm})]\mu^{dm}$$

This last relationship implies that:

$${}_tp_x^{dm} = \frac{-\mu^{dm}}{\mu^{ds} + \mu^{dm}} \exp[-t(\mu^{ds} + \mu^{dm})] + C$$

To find the value of the constant $C$ we use the fact that ${}_0p_x^{dm} = 0$ and solve:

$$ {}_0p_x^{dm} = \frac{-\mu^{dm}}{\mu^{ds} + \mu^{dm}} \exp[-0(\mu^{ds} + \mu^{dm})] + C. $$

Putting this together we have that:

the prob of moving out of state d after time t

$$ {}_tp_x^{dm} = \frac{\mu^{dm}}{\mu^{ds} + \mu^{dm}} (1 - \exp[-t(\mu^{ds} + \mu^{dm})]). $$

What is the intuition for this result?

# The Binomial Model

The binomial model is an alternative means of modelling survival times.

- In the material on multi-state modelling we estimated the hazard $\mu_x$. The hazard was then used to estimate probabilities of interest.
- In the binomial model we estimate $q_x$, the probability an individual aged $x$ dies before reaching age $x+1$.

major difference: Quantity of interest is different

## The Binomial Model - Data

We observe the following data for each of $N$ individuals aged $[x, x+1)$:

- $x + a_i$ is the age that individual $i$ comes under observation.
- $x + b_i$ is the age that individual $i$ stops being observed or is censored.
- $\delta_i$ is an indicator variable taking the value 1 if individual $i$ is observed to die.

To estimate $q_x$ we need to write the likelihood for $\delta_i$. The likelihood is:

$$L = \prod_{i=1}^{N} {}_{b_i - a_i}q_{x+a_i}^{\delta_i} (1 - {}_{b_i - a_i}q_{x+a_i})^{1-\delta_i}.$$

## The Binomial Model - Estimation

To work with this likelihood we need to make assumptions about ${}_tq_x$ over the year of age $[x, x+1)$. Three common assumptions are:

- Uniform distribution of deaths (UDD): ${}_tq_x = t\,q_x$, where $(0 \le t \le 1)$.
- Constant hazard: ${}_tq_x = 1 - \exp\{-\mu t\}$, where $(0 \le t \le 1)$.

# Example - UDD

Behavior between $x$ and $x+1$:

$$\begin{aligned}
\mu_x(t) &= \frac{d}{dt} - \log S(x+t) \\
&= \frac{d}{dt} - \log({}_t p_x) \\
&= \frac{d}{dt} - \log(1 - {}_t q_x) \\
&= \frac{d}{dt} - \log(1 - t q_x) \\
&= \frac{q_x}{1 - t q_x}
\end{aligned}$$

## Example - O'Neill notes

Suppose all individuals start observation exactly aged $x$ and that all censoring takes place at age $x + 0.5$. This means $a_i = 0$ for all individuals and that $b_i = 1$ or $b_i = 0.5$ for uncensored and censored individuals, respectively. We will let $w$ denote the number of censored individuals. If we use the constant hazard assumption we have:

$$
\begin{aligned}
1 -_{0.5} q_x &= 1 - (1 - \exp(-0.5\mu)) \\
&= \exp(-0.5\mu) \\
&= (1 - q_x)^{0.5}
\end{aligned}
$$

Using this fact we can write the likelihood as:

$$
q_x^{\delta}(1 - q_x)^{N-w-\delta}(1 - q_x)^{0.5w},
$$

where, $\delta$ is the total number of observed deaths. Maximising the likelihood gives: $\hat{q}_x = \frac{\delta}{N-0.5w}$

$$L = q_x^{\delta}(1-q_x)^{N-w-\delta} \cdot (1-q_x)^{0.5w}$$

$$= q_x^{\delta}(1-q_x)^{N-0.5w-\delta}$$

under constant hazard assumption

$$l = \delta \log(q_x) + (N-0.5w-\delta)\log(1-q_x)$$

$$\frac{\partial l}{\partial q_x} = \frac{\delta}{q_x} + \frac{N-0.5w-\delta}{1-q_x}\cdot(-1) = 0$$

$$\Rightarrow \frac{\delta}{q_x} - \frac{N-0.5w-\delta}{1-q_x} = 0$$

$$\delta(1-q_x) = (N-0.5w-\delta)q_x$$

$$\delta = (N-0.5w)q_x$$

$$\hat{q}_{x_{MLE}} = \frac{\delta}{N-0.5w}$$

# The Poisson Model

Another method for estimation is the Poisson model. The Poisson distribution can be used to model the number of events that occur over a given period of time. A random variable $X$ follows the Poisson distribution if:

$$P[X = x] = \frac{e^{-\lambda}\lambda^x}{x!},$$

for $x = 0, 1, 2, \ldots$.

For the Poisson distribution $E(X) = Var(X) = \lambda$.

## The Poisson Model

To use the Poisson model we need to observe the total number of deaths that occur $\delta$ and the total waiting time. The total waiting time is the quantity denoted $v$ in last week's lecture notes. The total waiting can also be denoted $E_x^c$, the central exposed to risk. Define the total number of deaths as $X$, the Poisson model assumes that $X$ is Poisson with mean $\mu E_x^c$.

$$P[X = j] = \frac{e^{-\mu E_x^c}(\mu E_x^c)^j}{j!},$$

so the MLE of $\mu$ is $\hat{\mu} = \frac{\delta}{E_x^c}$. Note: For the Poisson distribution we know that $\lambda$ can be estimated by the observed number of deaths so that $\hat{\lambda} = \delta$. This fact and the fact that $\lambda = \mu E_x^c$ give the desired result.

For Poisson distribution

$$P(X=x) = \frac{e^{-\lambda}\lambda^{x}}{x!}$$

~~$E(X)=\lambda$ $\quad \hat{\lambda}_{MLE} = \sum_{i=1}^{n} x_i = \boxed{\delta}$ total # of death~~

but we define $\lambda$ differently $\boxed{\lambda = \mu \cdot E_x^c}$

$$\hat{\mu}_{MLE} = \frac{\hat{\lambda}_{MLE}}{E_x^c} = \frac{\delta}{E_x^c}$$

According to slides

$$P(\delta = j) = \frac{e^{-\lambda}\lambda^{j}}{j!}$$ total # of deaths ~ Poisson

In this case $\hat{\lambda} = E[\delta] = \delta$

## Poisson Model - Example

At a particular university the hazard of a student dropping out is 0.01 in year 2010. Additionally, during the year 2010 there were 2950 years of study observed (i.e. $E_x^c = 2950$). What is the probability there were more than 60 students dropping out during 2010?

The Poisson mean is $\mu * E = .01(2950) = 29.50$ drop outs per year.

Solution:

$$P(X > 60) \approx P(Z > [60 - 29.50]/\sqrt{29.50}).$$

Note: For multistate, even if $\mu=0$, prob could be non-zero.

## R Example

The package msm in R can fit multi-state markov models. The dataset "cav" contains information from heart transplant patients. the dataset contains information on 614 individuals. There are four states that a patient can be in: "1": no cav; "2": mild cav: "3": severe CAV; "4": death. An example of the data is provided below:

| | PTNUM | age | years | dage | sex | pdiag | cumrej | state | firstobs |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 100002 | 52.49589 | 0.000000 | 21 | 0 | IHD | 0 | 1 | 1 |
| 2 | 100002 | 53.49863 | 1.002740 | 21 | 0 | IHD | 2 | 1 | 0 |
| 3 | 100002 | 54.49863 | 2.002740 | 21 | 0 | IHD | 2 | 2 | 0 |
| 4 | 100002 | 55.58904 | 3.093151 | 21 | 0 | IHD | 2 | 2 | 0 |
| 5 | 100002 | 56.49589 | 4.000000 | 21 | 0 | IHD | 3 | 2 | 0 |
| 6 | 100002 | 57.49315 | 4.997260 | 21 | 0 | IHD | 3 | 3 | 0 |
| 7 | 100002 | 58.35068 | 5.854795 | 21 | 0 | IHD | 3 | 4 | 0 |

The variable year is the time since the transplant.

```
#obtaining transition intensities and prob transitioning in 1 year.
#code taken from http://www.jstatsoft.org/v38/i08/ by C Jackson 2011.

library(msm)
data("cav")
cav<-cav[!is.na(cav$pdiag),]

statetable.msm(state, PTNUM, data = cav)
> statetable.msm(state, PTNUM, data = cav)
    to
from    1    2    3    4
   1 1348  203   44  147
   2   46  134   54   47
   3    4   13  107   55

twoway4.q <- rbind(c(0, 0.25, 0, 0.25), c(0.166, 0, 0.166, 0.166),c(0, 0.25, 0, 0.25), c(0, 0, 0, 0))
rownames(twoway4.q) <- colnames(twoway4.q) <- c("Well", "Mild","Severe", "Death")
cav.msm <- msm(state ~ years, subject = PTNUM, data = cav,qmatrix = twoway4.q, death = 4)
cav.msm
Call:
msm(formula = state ~ years, subject = PTNUM, data = cav, qmatrix = twoway4.q,     death = 4)

Maximum likelihood estimates:
Transition intensity matrix

       Well                     Mild
```

```
Well   -0.1682 (-0.188,-0.1505) 0.1276 (0.111,0.1467)
Mild   0.2264 (0.1692,0.303)    -0.618 (-0.7195,-0.5309)
Severe 0                        0.1226 (0.07308,0.2056)
Death  0                        0
       Severe                    Death
Well   0                         0.04057 (0.03227,0.051)
Mild   0.3375 (0.2713,0.4199)    0.05405 (0.02233,0.1308)
Severe -0.4144 (-0.5245,-0.3275) 0.2919 (0.2274,0.3746)
Death  0                         0

-2 * log-likelihood:  3945.363



pmatrix.msm(cav.msm, t = 1, ci = "normal")
> pmatrix.msm(cav.msm, t = 1, ci = "normal")
       Well                        Mild
Well   0.8558 (0.8426,0.8685)      0.08785 (0.07751,0.09805)
Mild   0.1559 (0.1189,0.1965)      0.5602 (0.5061,0.6017)
Severe 0.009393 (0.005577,0.01616) 0.07416 (0.04564,0.1183)
Death  0                           0
       Severe                   Death
Well   0.01458 (0.0116,0.01792) 0.04175 (0.03462,0.05111)
Mild   0.2042 (0.1672,0.2402)   0.07974 (0.05931,0.1291)
Severe 0.6736 (0.6028,0.7264)   0.2429 (0.1965,0.3023)
Death  0                        1 (1,1)
```