Instantaneous geometric rates via generalized linear models

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1 September 2017
Outline of this presentation

• Geometric rates
• Instantaneous geometric rates
• Models for the instantaneous geometric rates
• Instantaneous geometric rates via generalized linear models
• Example: survival in metastatic renal carcinoma
• Final remarks
Geometric rates
Geometric rates

- The geometric rate represents the average probability of the event of interest per unit of time over a specific time interval \((0, t)\)

\[
g(0, t) = 1 - S(t)^\frac{1}{t}
\]
Geometric rates

![Graph showing survival probability and geometric rate over follow-up time (years). The survival curve decreases sharply, while the geometric rate remains relatively constant.]
Geometric rates
Geometric rates

Follow-up time (years)

Survival probability

Survival

Geometric rate

Annual rate

0.0 0.2 0.4 0.6 0.8 1.0

0 1 2 3 4 5 6
The instantaneous geometric rate (IGR) represents the instantaneous probability of the event of interest per unit of time.
Instantaneous geometric rates

The limit of the geometric rate over shrinking time intervals \((t, t + \Delta t)\) gives the instantaneous geometric rate (Bottai, 2015)

\[
g(t) \equiv \lim_{\Delta t \to 0^+} g(t, t + \Delta t)
\]

\[
= \lim_{\Delta t \to 0^+} 1 - \left[ \frac{S(t + \Delta t)}{S(t)} \right]^{\frac{1}{\Delta t}}
\]

\[
= \lim_{\Delta t \to 0^+} 1 - \exp \left\{ \frac{\log S(t + \Delta t) - \log S(t)}{\Delta t} \right\}
\]

\[
= 1 - \exp \left\{ \frac{\partial \log S(t)}{\partial t} \right\}
\]

\[
= 1 - \exp \left\{ - \frac{f(t)}{S(t)} \right\}
\]

\[
= 1 - \exp \left\{ - h(t) \right\}
\]
Models for the instantaneous geometric rate

- Proportional instantaneous geometric rate model

\[ g_i(t|x_i) = g_0(t) \exp\{x_i^T \beta\} \] (2)

- Proportional instantaneous geometric odds model

\[ \frac{g_i(t|x_i)}{1 - g_i(t|x_i)} = \frac{g_0(t)}{1 - g_0(t)} \exp\{x_i^T \beta\} \] (3)

- These models can be estimated within the generalized linear model (GLM) framework by using two nonstandard link functions
Instantaneous geometric rates via GLM

Let’s focus on the proportional instantaneous geometric rate model

By taking the logarithm of both sides of (2) we get

$$\log[g_i(t|x_i)] = \log[g_0(t)] + x_i^T \beta$$

and by equation (1) we write

$$\log[1 - \exp\{-h_i(t)|x_i\}] = \log[g_0(t)] + x_i^T \beta$$

(4)

where $\log[g_0(t)]$ (baseline log-IGR) is modelled using for example polynomials or splines.
To model the baseline log-IGR, we split each individual’s follow-up time into very short intervals (\texttt{stssplit})

Given equation (4) we use the following link function

\[
\eta_{ij} \equiv k(\mu_{ij}) = \log \left[ 1 - \exp \left\{ -\frac{\mu_{ij}}{t_{ij}} \right\} \right]
\]

where:

- \( t_{ij} \) is the length of the \( j \)th interval relative to the \( i \)th subject
- \( \mu_{ij} \) is the expected value of \( d_{ij} \) (the event/censoring indicator), which is assumed to follow a distribution of the exponential family
Instantaneous geometric rates via GLM

- In model (2) the exponentiated coefficients $\exp\{\beta\}$ are interpreted as instantaneous geometric rate ratios, whereas in model (3) they are interpreted as instantaneous geometric odds ratios.
- If the instantaneous geometric rates are proportional across different populations, the instantaneous geometric odds are not, and vice-versa.
- Link functions for models (2) and (3) are implemented in two user-defined link programs: log_igr and logit_igr.
Example: survival in metastatic renal carcinoma

- Data from a clinical trial on 347 patients diagnosed with metastatic renal carcinoma
- The patients were randomly assigned to either interferon-\(\alpha\) (IFN) or oral medroxyprogesterone (MPA)
- A total of 322 patients died during follow-up

- Stata code to reproduce the worked-out example is available at: www.imm.ki.se/biostatistics
Example: survival in metastatic renal carcinoma

```
. qui use http://www.imm.ki.se/biostatistics/data/kidney, clear
. qui stset survtime, failure(cens) id(pid) scale(365.24)
. qui stsplit click, every(`=1/52')
. qui generate risktime = _t - _t0
. qui rcsgen _t, df(3) if2(_d == 1) gen(_rcs)

. glm _d i.trt c._rcs?, family(poisson) link(log_igr risktime) vce(robust) ///
   > nolog search eform baselevel noheader
initial: log pseudolikelihood = -<inf> (could not be evaluated)
feasible: log pseudolikelihood = -4804.4455
rescale: log pseudolikelihood = -1959.6083

|     _d | exp(b) Std. Err.  z    P>|z|    [95% Conf. Interval] |
|-------|-----------------|-----------------|--------|------------------------|
|   trt |                 |                |        |                        |
|    MPA| 1.00 (base)    |                |        |                        |
|   IFN | 0.84           | 0.06           | -2.62  | 0.009                  |
|   IFN | 0.96           | 0.29           | -0.13  | 0.894                  |
|   IFN | 0.90           | 0.24           | -0.39  | 0.693                  |
|   IFN | 0.72           | 0.06           | -3.63  | 0.000                  |
```

- IGRR comparing IFN versus MPA patients: 0.84 (0.73–0.96)
Example: survival in metastatic renal carcinoma
Example: survival in metastatic renal carcinoma

```stata
.glm _d i.trt##c._rcs?, family(poisson) link(log_igr risktime) vce(robust) ///
   nolog search baselevel noheader
initial: log pseudolikelihood = -<inf> (could not be evaluated)
feasible: log pseudolikelihood = -4804.4455
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|      | Robust Coef. | Std. Err. | z    | P>|z| | [95% Conf. Interval] |
|------|--------------|-----------|------|-----|---------------------|
| _d   |              |           |      |     |                     |
| trt  |              |           |      |     |                     |
| MPA  | 0.00 (base)  |           |      |     |                     |
| IFN  | -0.37        | 0.19      | -1.92| 0.054| -0.74               |
|      |              |           |      |     |                     |
| _rcs1| -0.31        | 0.36      | -0.86| 0.389| -1.02               |
|      |              |           |      |     |                     |
| _rcs2| -0.29        | 0.82      | -0.36| 0.722| -1.91               |
|      |              |           |      |     |                     |
| _rcs3| 0.12         | 0.33      | 0.35 | 0.727| -0.54               |
|      |              |           |      |     |                     |
| trt#c._rcs1|    |           |      |     |                     |
| IFN  | 0.78         | 0.66      | 1.18 | 0.238| -0.52               |
|      |              |           |      |     |                     |
| trt#c._rcs2|    |           |      |     |                     |
| IFN  | 1.57         | 1.38      | 1.14 | 0.256| -1.14               |
|      |              |           |      |     |                     |
| trt#c._rcs3|    |           |      |     |                     |
| IFN  | -0.62        | 0.55      | -1.11| 0.267| -1.70               |
|      |              |           |      |     |                     |
| _cons| -0.26        | 0.09      | -3.02| 0.003| -0.44               |
```
Example: survival in metastatic renal carcinoma

![Graph showing survival rates over years from randomization]

- **Instantaneous geometric rate ratio**
- **Years from randomization**: 0, 1, 2, 3, 4, 5, 6
- **MPA**
- **IFN**

<table>
<thead>
<tr>
<th>Years from randomization</th>
<th>Instantaneous geometric rate ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0.70</td>
</tr>
<tr>
<td>1</td>
<td>0.84</td>
</tr>
<tr>
<td>2</td>
<td>1.00</td>
</tr>
</tbody>
</table>
Final remarks

- Instantaneous geometric rates are easy to interpret
- Instantaneous geometric rates \( \neq \) hazard rates

- Proportional instantaneous geometric rate/odds models for the effect of covariates on the IGR
- These models can be estimated within the GLM framework by using nonstandard link functions
References
