


Module 7: Markov Models & Time

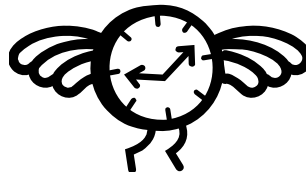


1. Time Dependence & Tables 

2. Time-In-State & Tunnels 

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Time Dependence & Tables



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Time Dependence & Tables

- In Module 6, the Markov model transition probabilities and rewards were fixed
- Some probabilities/rewards may be...
 - **Time-dependent** $y = f(_stage)$
 - **Age-dependent** $y = f(_stage + startAge)$
 - Time-in-state dependent (next section)
 - ...

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Time Dependence & Tables

- Time-dependent transition probabilities
 - If only 2 or 3 possible values, use If() or Choose()...

```
Prob = IF(_stage<10; 0; .1)
Prob = Choose(whichVal; Val1; Val2; Val3)
```
 - Otherwise, use tables
- Tables allow you to enter a list of values that can be retrieved by an index
 - Retrieve by `_stage` to use different table value for each cycle

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Time Dependence & Tables

- Tables in TreeAge Pro:
 - Table properties control behavior
 - Table data organized by rows & columns
 - Index column is required
 - Multiple value columns allowed
 - Values are retrieved by index and value column

TableName[index; valueColumn]

TableName[2; 2] = 2000

TableName[3] = 300

- If value column not provided, first column is assumed

- Note the square brackets in table lookups

- Can rename value columns, but not “Index” column

Index	Value	Value 2
1	100	1000
2	200	2000
3	300	3000
4	400	4000
5	500	5000

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Time Dependence & Tables

- We will now incorporate tables and time-dependent probabilities into our Cancer model
- Example 9:
 - Start with Example8-MarkovCancer.tre
 - Save as new document
 - Add transition before disease-related progression and/or death to account for background mortality
 - Use new mortality tables for probabilities of death from background mortality
 - Assume cohort starts at age 50

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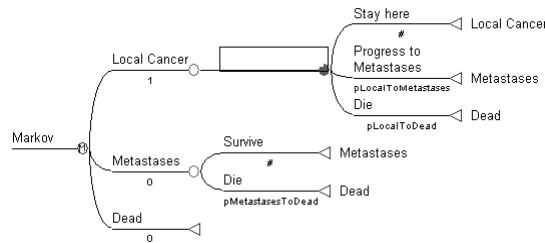
Time Dependence & Tables



• Example 9:

– Before starting on tables, we need to change the structure of the model

- Select Local Cancer node
- Menu: Options > Insert Branch > To Right



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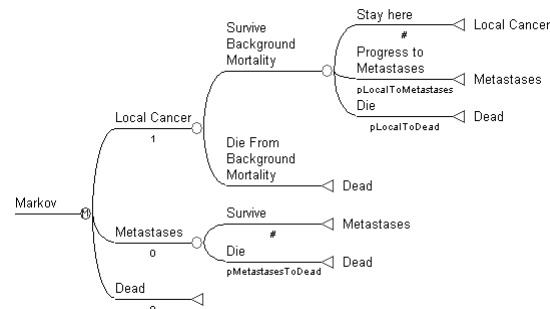
Time Dependence & Tables



• Example 9:

– Add branch for background mortality

- Select new node
- Menu: Options > Insert Branch > Below
- Label: Die From Background Mortality
- Change type to Terminal; jump to Death



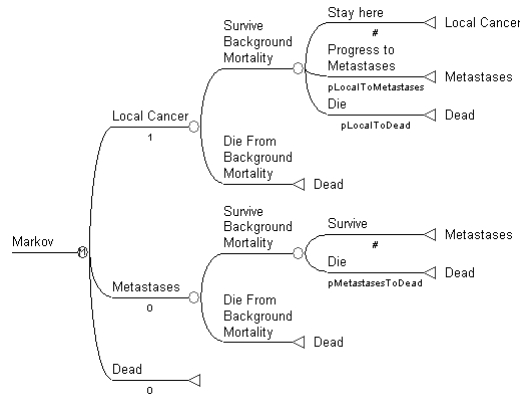
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Time Dependence & Tables



- Example 9:
 - Repeat for Metastases state



– Now we are ready for the background mortality table MK 53
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Time Dependence & Tables



- To add the table to our model, we will need to...
 1. Create table
 2. Set table properties
 3. Enter table data
 4. Incorporate table into tree

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Time Dependence & Tables

- We will use the following mortality table data
 - Note that not all ages are in the table
 - Interpolation will handle the gaps

Index	Value
0	0.007
1	0.000315
5	0.00017
15	0.000815
25	0.001036
35	0.002016
45	0.004332
55	0.009409
65	0.02255
75	0.054631
85	0.145933
95	0.25
120	1

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Time Dependence & Tables

- Create table
 - Tree should be open
 - Choose **VALUES > Variables and Tables...**



... or ...

Click toolbar icon

- **Switch to Tables List**

- **Click New Table**

- TreeAge Pro user's manual, Ch. 17

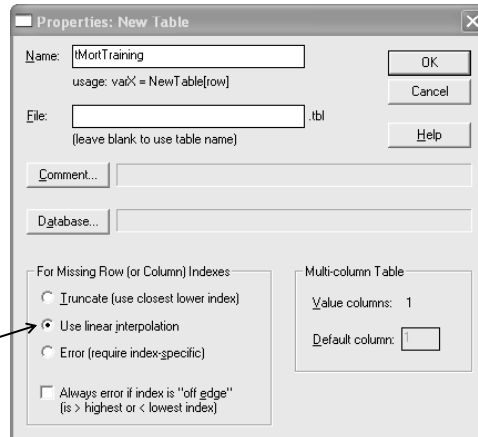
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Time Dependence & Tables

• Set table properties

- Naming rules same as variables
- In separate file initially (*.tbl) in Tables folder
- Handle missing rows via interpolation
- Click OK



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Time Dependence & Tables

• Set table properties

- Lookup method defaults to **linear interpolation** for new tables

- For example, if ...

1	0.000315
5	0.00017

- $tMortTraining[1] = 0.000315$

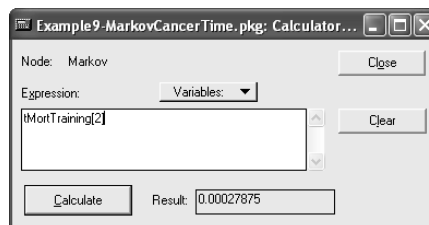
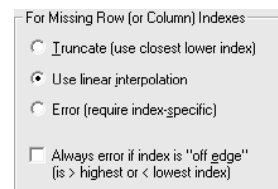
- $tMortTraining[2] = ????$

$$= (Lval) + (Hval - Lval) * (idx - Ldx) / (Hidx - Lidx)$$

$$= .000315 + (.00017 - .000315) * (2 - 1) / (5 - 1)$$

$$= .0027875$$

- If the table has a row for every index value, use Error (require index-specific)



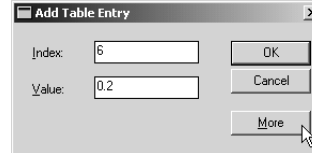
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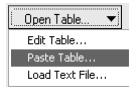
Time Dependence & Tables

• Enter table data

– Can do via Open Table > **Edit Table**



– Quicker to...



• Enter data in Excel and **Paste Table**,

- We'll do this
- Does *not* require Excel module



• Edit in Excel and export back to TreeAge Pro

- Requires Excel module

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Time Dependence & Tables

• Enter table data

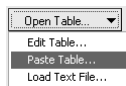
– Enter data in Excel and Copy to clipboard

• Data already entered in tMortTraining-RawData.xls

	A	B
1	Index	Value
2		0 0.007
3		1 0.000315
4		5 0.00017
5		15 0.000815
6		25 0.001036
7		35 0.002016
8		45 0.004332
9		55 0.009409
10		65 0.02255
11		75 0.054631
12		85 0.145933
13		95 0.25
14		120 1

Index	Value
0	0.007
1	0.000315
5	0.00017
15	0.000815
25	0.001036
35	0.002016
45	0.004332
55	0.009409
65	0.02255
75	0.054631
85	0.145933
95	0.25
120	1

– Open Table > Paste Table



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Time Dependence & Tables

- Incorporate table into tree

- Our table is based on age, not `_stage` counter
- Generate age at each cycle from the cohort start age (50) and `_stage`

- Add new variables



- `startAge = 50`
- `Age = startAge + 50`

- At each cycle, age can now be used to lookup background mortality in table

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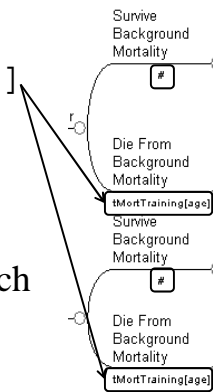
Time Dependence & Tables

- Incorporate table into tree

- Now we can pace the background mortality table lookups in the tree

`Prob = tMortTraining[age]`

- At each cycle, a different mortality probability will be retrieved from the table based on the values of **age**, which is a function of `_stage`

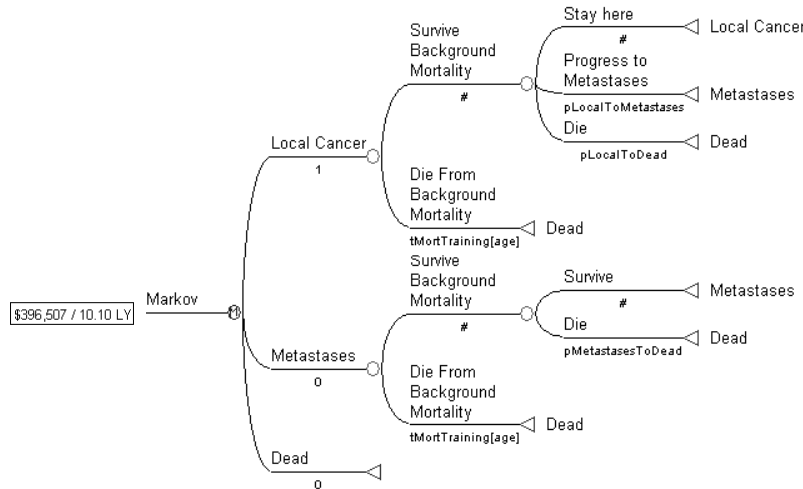


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Time Dependence & Tables





- **Example9-MarkovCancerTime.pkg** (*.pkg vs. *.tre on next slides)



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Time Dependence & Tables

- **Tables management:**
 - TreeAge Pro Users Manual Ch. 17
 - Open tables list via
VALUES > Variables and Tables... 
 - Select table and edit properties and/or data
 - Excel add-in:   Tables 
- **Tables report:**
 - VALUES > Report > Tables Used
 - Shows current Tables directory path and files required by tree

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Time Dependence & Tables

- Table file storage:
 - New tables are stored by default in folder “..\TreeAge Pro\Tables\” (off the installation path)
- To change default folder for table files and/or move table files...
 - Open tables list  and click 
- To save the required tables with tree in a single file...
 - FILE > Save As... Package File (*.pkg)
 - Good for sharing models

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Time Dependence & Tables

- Discounting
 - Standard practice for costs, life expectancy/QALYs in multi-year models
- Discount() function:
 - TreeAge Pro manual, Appendix D, “Functions and Operators”
 - Syntax: “Discount(*value*; *rate*; *time*)”
 - value = base cost (or utility) for one **cycle**
 - rate = discount rate **per period** (usually annual rate)
 - time = number of periods to discount by (usually *_stage*)



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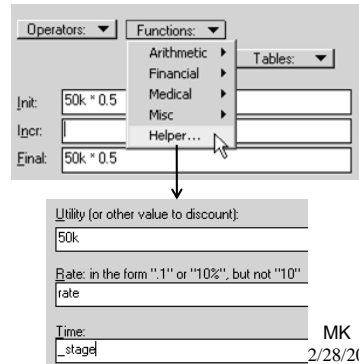
Time Dependence & Tables

- Functions Helper:

- Helps you enter the parameters for a function
- Available in all formula editors
 - Probabilities, payoffs, variable definitions, Markov State Info, etc.

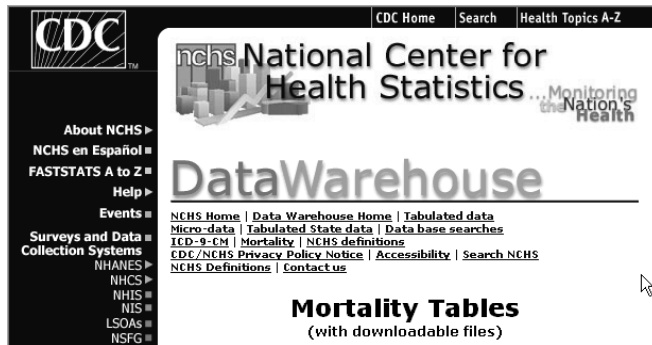
- Edit Markov State Info:

- Click popup Functions > Helper...
- Select "Discount" function
- Opens window to guide parameter entry
- *Initial reward*: no need to discount (cost occurs now)



Time Dependence & Tables

- Data sources?



<http://www.cdc.gov/nchs/datawh/statab/unpubd/mortabs.htm>

- Wikipedia:

External links

- [Canadian Human Mortality Database](#)
- [UK Government Actuary Department's Interim Life Tables](#)
- [US CDC Mortality Reports](#)

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Time Dependence & Tables



- Life tables

National Vital
Statistics Reports



Volume 54, Number 14

April 19, 2006

United States Life Tables, 2003

http://www.cdc.gov/nchs/data/nvsr/nvsr54/nvsr54_14.pdf

	Probability of dying between ages x to $x+1$	Number surviving to age x	Number dying between ages x to $x+1$	Person-years lived between ages x to $x+1$	Total number of person-years lived above age x	Expectation of life at age x
Age	$q(x)$	$l(x)$	$d(x)$	$L(x)$	$T(x)$	$e(x)$
0-1	0.006865	100,000	687	99,394	7,748,865	77.5

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Time Dependence & Tables



- Mortality tables (2003 all cause)

10/07/05

Worktable 23R. Death Rates by 10-year age groups: United States and each State, 2003

[Rates per 100,000 population in specified group. Rates are based on population estimates.]

Area	All ages 1/ year	Under 1 year 2/ year	1-4 years	5-14 years	15-24 years	25-34 years	35- 74 years
United States...	841.9	700.0	31.5	17.0	81.5	103.6	201
Alabama.....	1,038.0	876.8	40.3	21.4	108.5	147.4	288
Alaska.....	490.1	731.5	*	35.7	117.7	128.5	209
Wyoming.....	832.3	611.0	*	*	93.4	117.2	256

* Figure does not meet standards of reliability or precision.

0.0 Quantity more than zero but less than 0.05.

1/ Figures for age not stated included in "all ages" but not distributed among age groups.

2/ Death rates for "Under 1 year" (based on population estimates) differ from infant mortality rates.

Source: CDC/NCHS, National Vital Statistics System, Mortality.

http://www.cdc.gov/nchs/data/statab/mortfinal2003_worktable23r.pdf

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Time-in-State and Tunnels



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Time-in-State and Tunnels



- In the previous section, we looked at factors that depend on time
 - **time**-dependent $y = f(_stage)$
- Now we will look at factors that depend on time-in-state
 - How long a patient has been in a certain state can affect that patient's transitions, etc.
 - For example, the likelihood of metastases may depend on how long the patient has had local cancer
 - Time-in-state dependent $y = f(_tunnel)$

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Time-in-State and Tunnels

- This introduces the concept of a **tunnel** within TreeAge Pro
- A tunnel is a like fixed sequence of temporary states
 - temporary state 1 (entry point)
 - temporary state 2 (next cycle)
 - ...
 - temporary state N
- At each temporary state...
 - Transition probabilities, rewards, etc. can differ based on the use of the `_tunnel` counter

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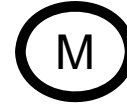
Time-in-State and Tunnels

- Tunnel implementation in TreeAge Pro:
 - Temporary states are collapsed into one actual state with its rewards and transition subtree
 - Internally the temporary state position is tracked using the time-in-state counter: `_tunnel`
 - If the patient stays in the same state, the `_tunnel` increments by 1 each cycle
 - Probabilities, rewards, etc. can be functions of `_tunnel`
 - Reports (e.g., Markov Cohort Analysis) can expand into separate columns for each temporary state

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Time-in-State and Tunnels



- Why use tunnels?
 - Progressive disease (like cancer):
 - Length of time a patient will spend in a particular disease stage (e.g., localized tumor) is uncertain
 - Probability of transitioning to next disease stage (e.g., metastases) may increase or decrease over time
 - not age-dependent, but time-in-state dependent
 - Infectious disease:
 - Time since infection may affect prognosis

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Time-in-State and Tunnels



- TreeAge Pro tunnels are...
 - Like a real tunnel...
 - One entry point (temp. #1)
 - Predefined length (max # = N)
 - $1 \rightarrow 2 \rightarrow \dots \rightarrow N \rightarrow N \rightarrow N$
 - Unlike a real tunnel...
 - Can “exit” to **other** states from any temporary state



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Time-in-State and Tunnels



- To implement tunnels:
 1. Select a state
 2. Open Markov State Info
 3. Check the box to make the state a “tunnel state”
 4. Set the number of temporary states
 - For speed, use the minimum number of temporary states that is necessary to handle all transitions, rewards, etc. within the state
 - If patient returns to state beyond max tunnels, `_tunnel` value remains at max
 5. Incorporate the `_tunnel` counter into expressions for transitions, rewards, etc.

Tunnel Info
 Tunnel state
temporary_states: (max. value for _tunnel)

```
Prob = TableName[_tunnel]
```

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Time-in-State and Tunnels



- Example 10: Now we will incorporate tunnels into our Cancer model....
 - Start with Example9-MarkovCancerTime.pkg and save to new file
 - Change the following transition probabilities from fixed to time-in-state dependent (probability data on next slide)
 - Progression from Local to Metastases
 - Death from Metastases

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Time-in-State and Tunnels

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- Example 10:

- Progression from Local to Metastases

- Place in model as table
- Probability max is 0.5 in the 10th cycle, remains 0.5 in next cycles
- tLocalToMetastases-RawData.xls

Index	Probability
1	0.05
2	0.1
3	0.15
4	0.2
5	0.25
6	0.3
7	0.35
8	0.4
9	0.45
10	0.5

- Death from Metastases

- Use If() function in model

Index	Probability
1	.5
2	1

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Time-in-State and Tunnels

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- Example 10: Do as exercise

1. Create table for progression from Local to Metastases
2. Make Local and Metastases tunnel states
 - How many tunnels for each?
3. Modify the definitions for the existing variables pLocalToMetastases and pMetastasesToDead
4. Rerun Markov Cohort Analysis

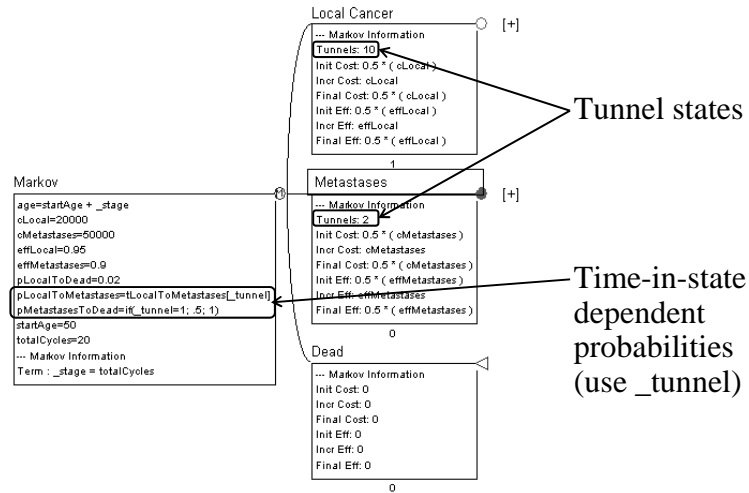
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Time-in-State and Tunnels



- Example 10:



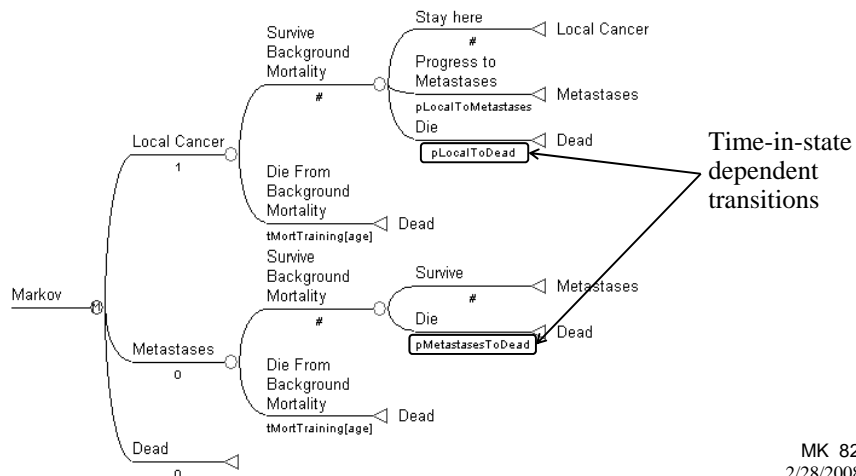
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Time-in-State and Tunnels



- Example 10:



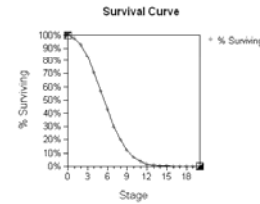
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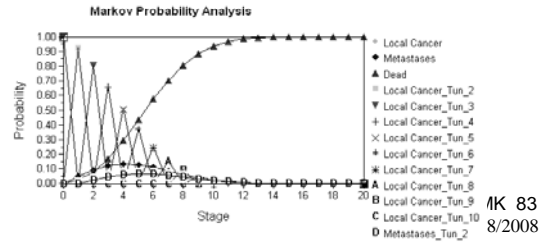
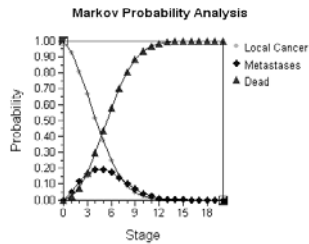
Time-in-State and Tunnels

● Analysis > Markov Cohort

- Prompt with option to “collapse” temporary states into a single tunnel state
- Otherwise, reports and graphs are the same



Not collapsed



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Time-in-State and Tunnels


● After tunnels...

- Dimensions other than or in addition to “time-in-state”:
 - Non homogeneous cohort
 - Distribution of ages
 - Distribution of demographics (gender, etc.)
 - Tumor types
 - Tracking events
- More dimensions may contraindicate use of tunnels, favoring trackers...
 - Next modules

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Markov Models & Time



- Questions?
 - Time Dependence & Tables 
 - Time-In-State & Tunnels 