

Economic Analysis for Adding Newborn Screening for OTCD

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Criterion #5

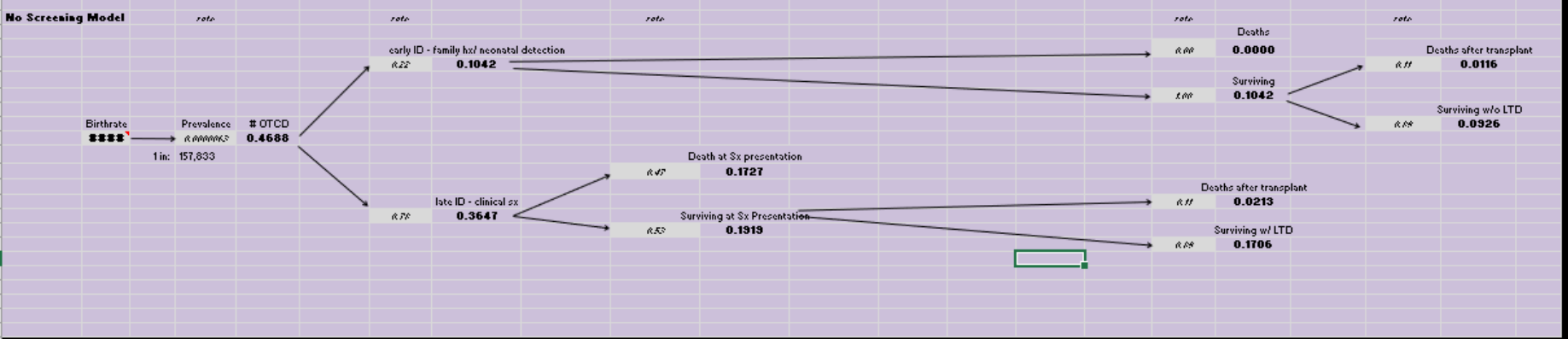
5. Cost-benefit/Cost-effectiveness: The outcomes outweigh the costs of screening. All outcomes, both positive and negative, need to be considered in the analysis. Important considerations to be included in economic analyses include:

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- The positive and negative predictive values of the screening and diagnostic tests.
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- The impact of ambiguous results. For example the emotional and economic impact on the family and medical system.
- Adverse effects or unintended consequences of screening.

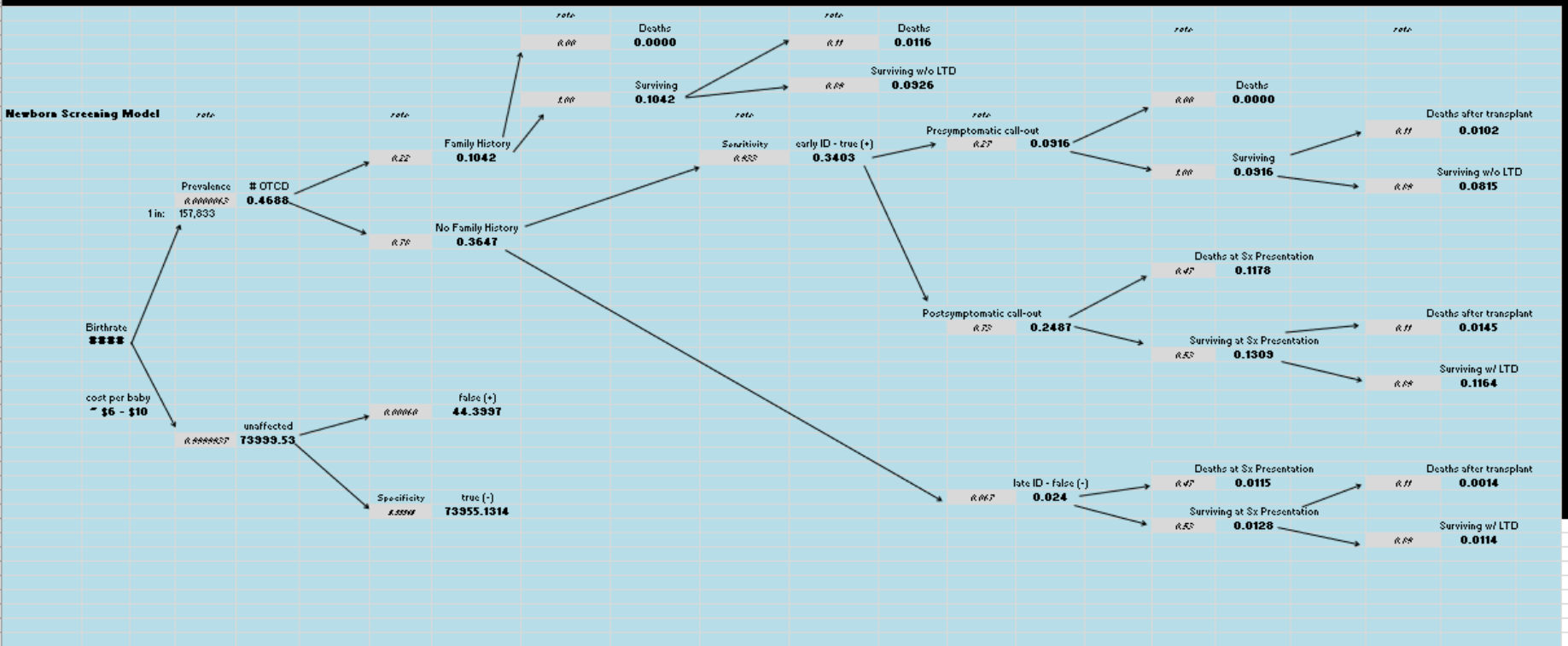
Decision Tree Model

Decision Tree Model

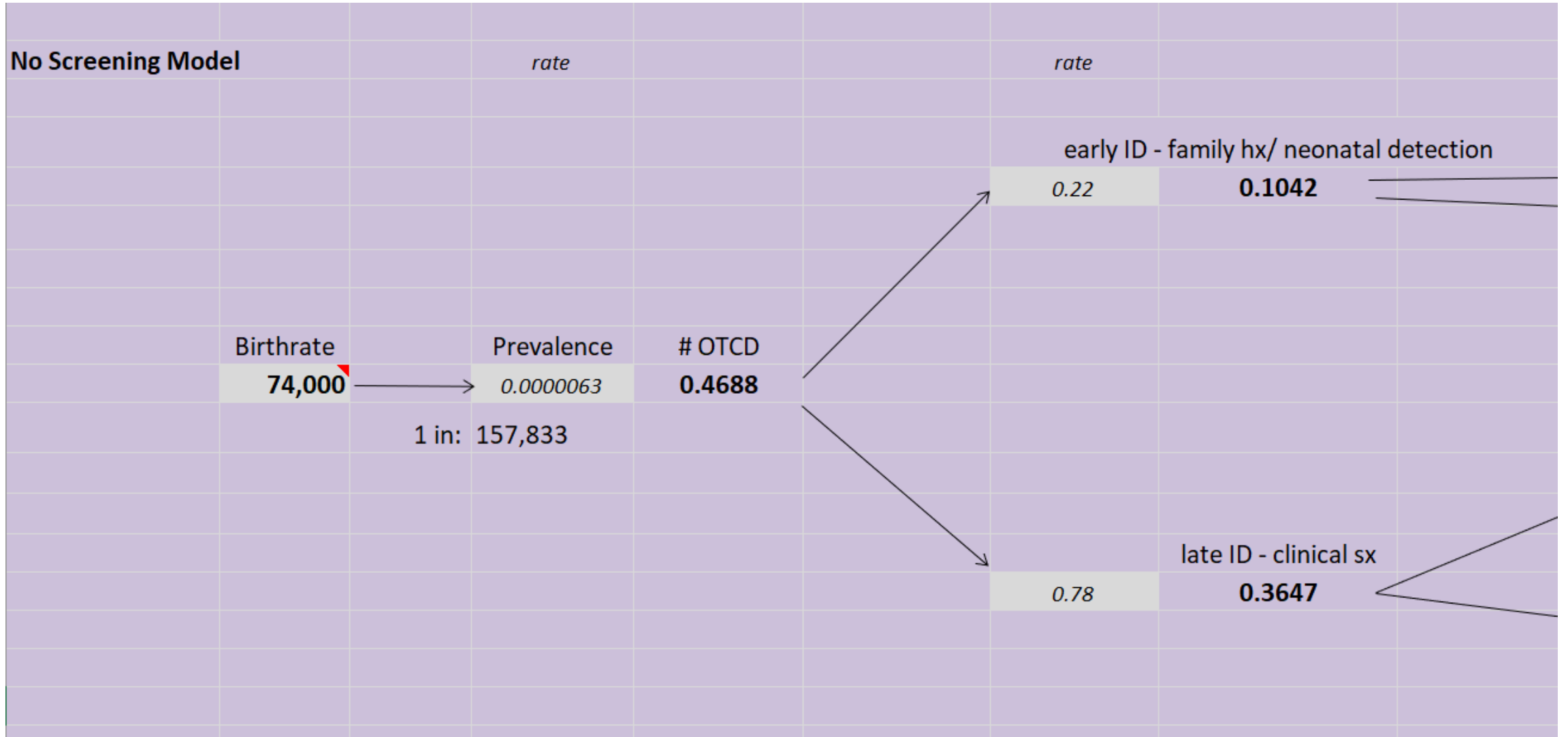
No Screening



Screening



No Screening Model

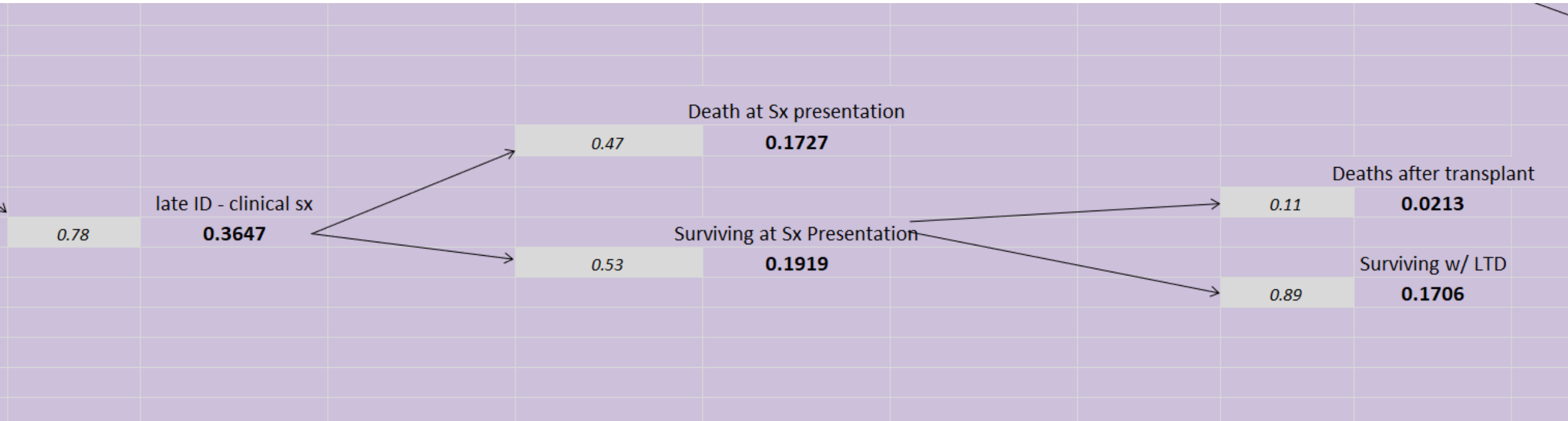


No Screening Model

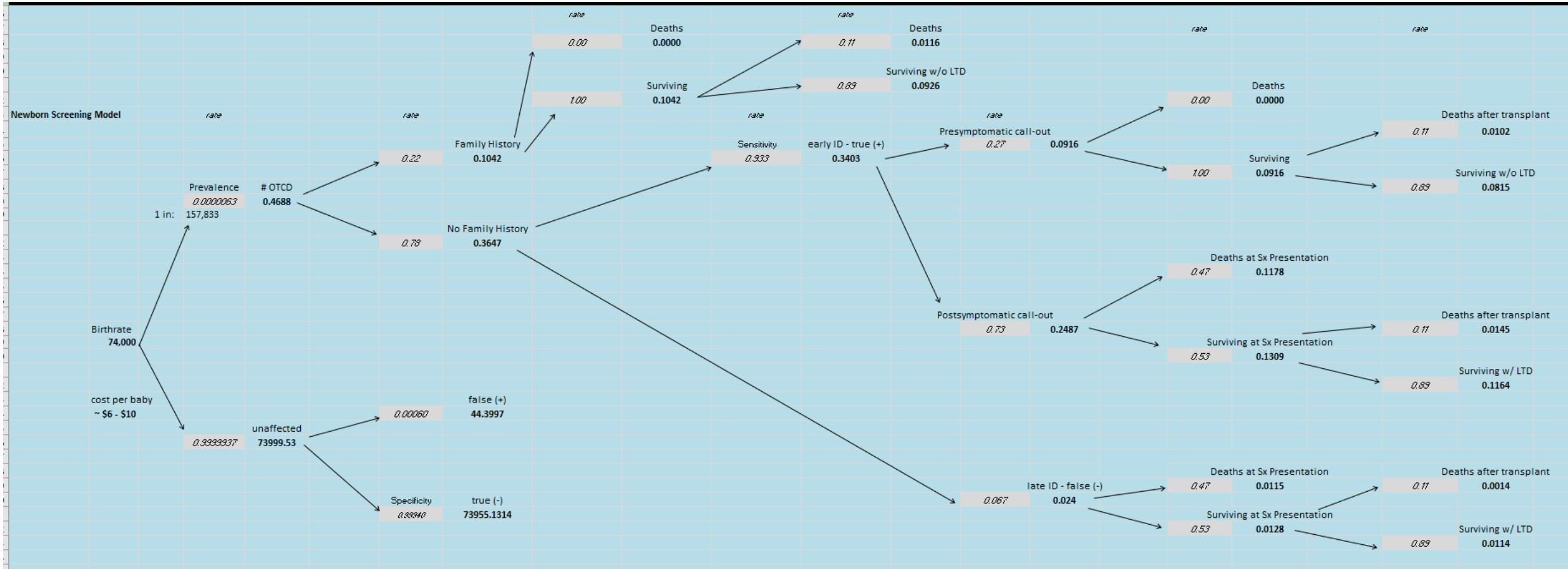
<i>rate</i>		<i>rate</i>		<i>rate</i>		<i>rate</i>	
					Deaths		
early ID - family hx/ neonatal detection				0.00	0.0000		Deaths after transplant
0.22	0.1042					0.11	0.0116
				1.00	Surviving		
					0.1042		Surviving w/o LTD
						0.89	0.0926

The flowchart illustrates the progression of a 'No Screening Model'. It starts with an initial rate of 0.22 for 'early ID - family hx/ neonatal detection', which results in a rate of 0.1042. This rate then branches into two paths: one leading to 'Deaths' with a rate of 0.00 and a count of 0.0000, and another leading to 'Surviving' with a rate of 1.00 and a count of 0.1042. The 'Surviving' path further branches into 'Deaths after transplant' with a rate of 0.11 and a count of 0.0116, and 'Surviving w/o LTD' with a rate of 0.89 and a count of 0.0926.

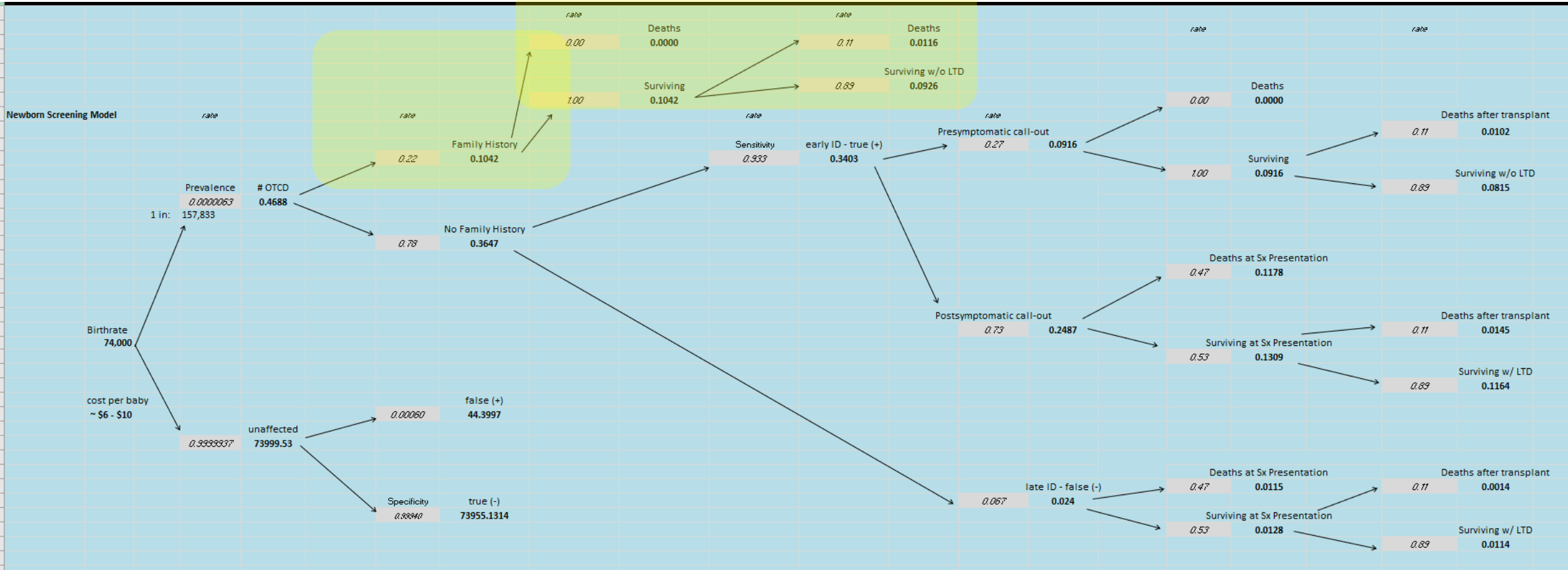
No Screening Model



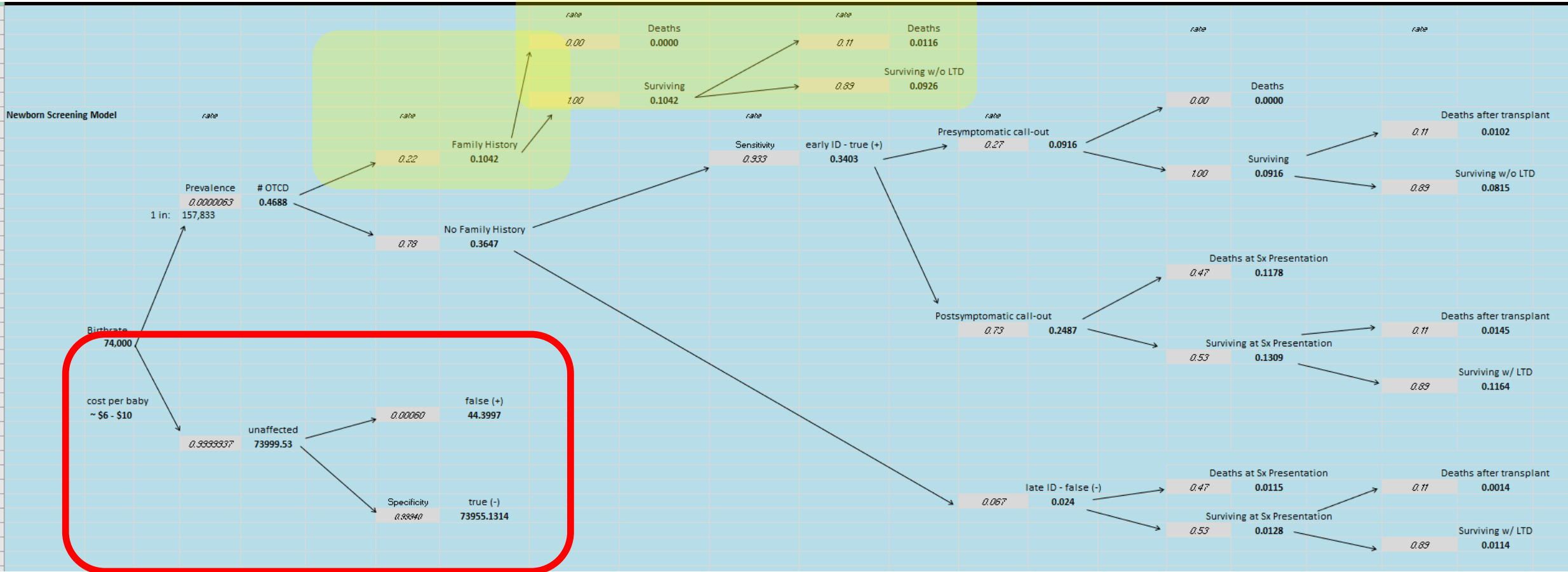
Newborn Screening Model



Newborn Screening Model



Newborn Screening Model

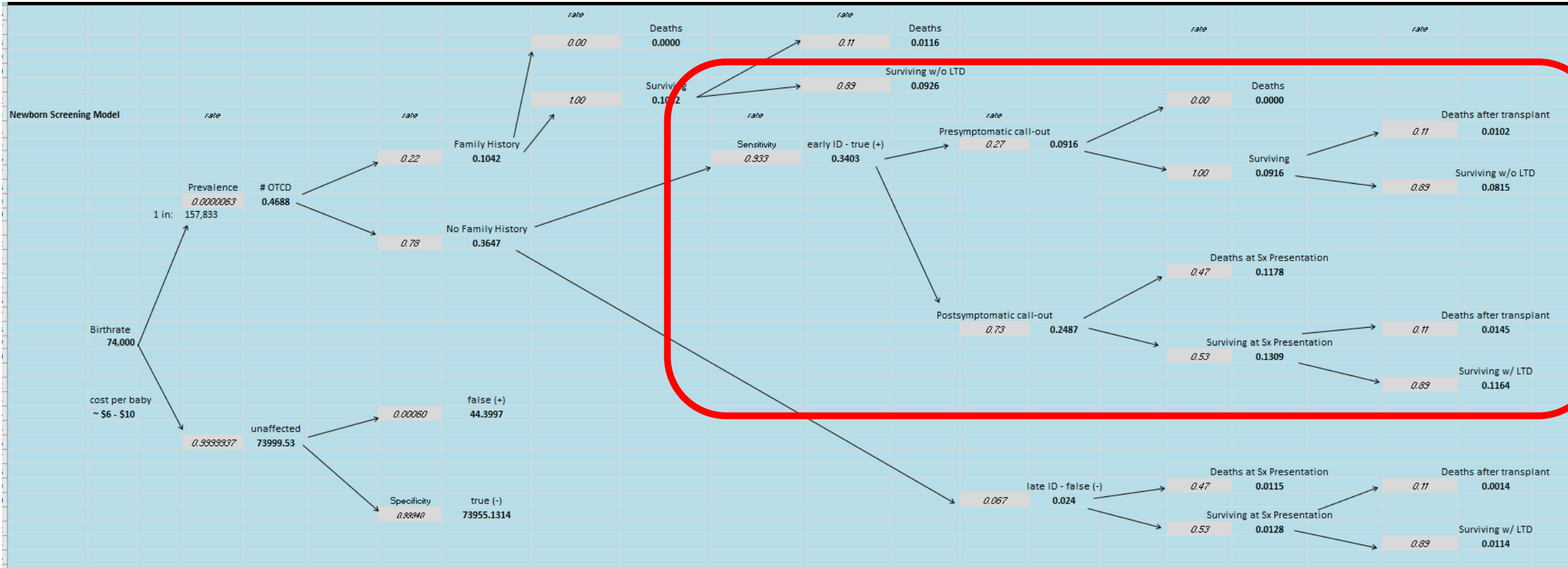


Newborn Screening Model

					false (+)
				0.00060	44.3997
		unaffected			
	0.9999937	73999.53			
				Specificity	true (-)
				0.99940	73955.1314

The diagram illustrates a grid-based model for newborn screening. The grid is a 12x6 table. The cell at row 3, column 2 contains the text 'unaffected' and the value '73999.53'. Two arrows originate from this cell: one points to the cell at row 2, column 4 containing '0.00060', and the other points to the cell at row 10, column 4 containing 'Specificity' and '0.99940'. The cell at row 1, column 5 contains 'false (+)' and '44.3997'. The cell at row 10, column 5 contains 'true (-)' and '73955.1314'. The cells containing '0.9999937' (row 3, column 1) and '0.00060' (row 2, column 4) are highlighted with a light gray background.

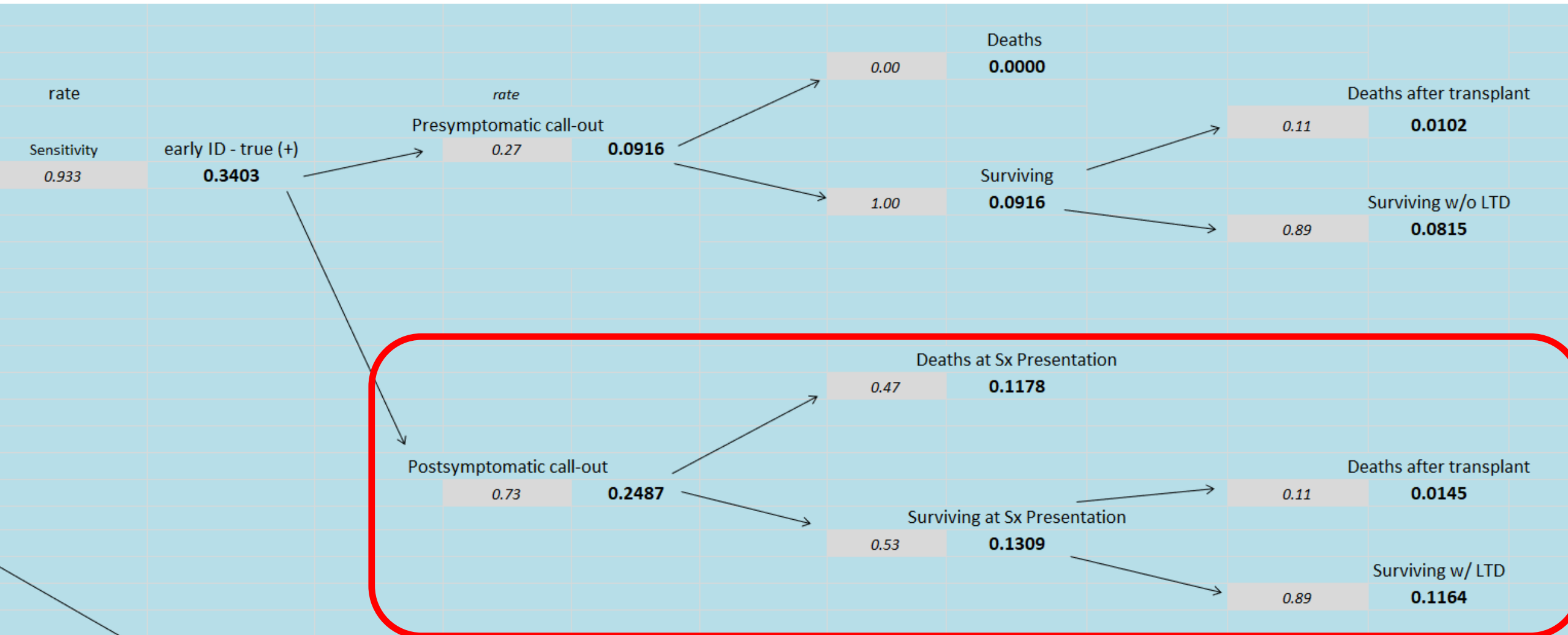
Newborn Screening Model



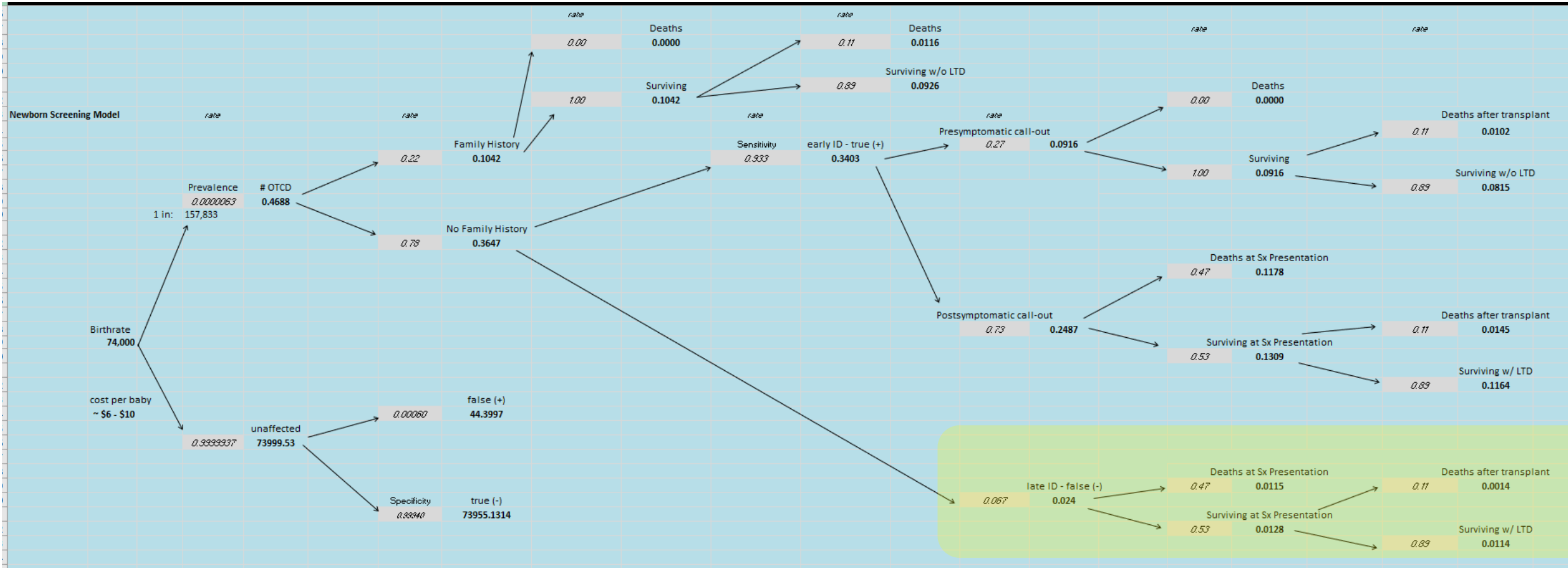
Newborn Screening Model



Newborn Screening Model



Newborn Screening Model



No Screening vs. Screening

No Screening	Deaths		0.2056
	Surviving w/ LTD		0.1706
	Surviving w/o LTD		0.0926
	Early Tx costs	\$	181,422.06
	Late Tx costs	\$	334,198.53
	Total tx costs	\$	515,620.58

Screening	Deaths		0.1671
	Surviving w/ LTD		0.1277
	Surviving w/o LTD		0.1741
	Early Tx costs		\$340,980.43
	Late Tx costs		\$250,220.44
	Total tx costs		\$591,200.87

Treatment Costs

	Year One Costs	Subsequent Year Costs
Monitoring Labs	\$9,476.40	\$1579.40
Dialysis	\$4,916.40	
Liver Transplant	\$1,714,952	

Total Costs: 1,741,284.00

Shift: Benefits vs. Costs

SHIFT		
Benefits	Deaths averted	0.039
	LTD averted	0.043
	Value of LTD prevented	\$ 64,303.58
	Value of a life	\$11,600,000
	Value of lives saved	\$447,552.89
	less tx costs	(\$75,580.28)
	TOTAL Benefits	\$371,972.61

Costs:

Estimated cost of screening per baby of \$6.00-\$10.00.

This integrates the cost of an overnight courier service and program staffing.

Costs	costs of screening	\$	594,241
	costs: false(+) dx	\$	38,938.55
	TOTAL costs	\$	633,179.55

Costs:

The Suite of Diagnostic Tests for OTCD:

Test	Average Cost
Blood Ammonia	\$150.00
Plasma Amino Acid	\$250.00
Urine Organic Acid	\$477.00

Total: \$877.00 per false positive

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Benefit/Cost ratio	0.59
net benefit	(\$261,206.95)

Sensitivity Analysis

	B/C ratio
	0.59
	base
birthrate	74,000
birth prevalence - 1 in:	157,833
% with OTCD family hx	0.22
sensitivity	93.33%
specificity	99.94%
Pre-Sx Callout Mortality	0.00
Post-Sx Callout Mortality	0.47
Treatment Cost	\$1,741,284.00
Value of a life	\$11,600,000.00
cost of NBS test	~ \$6 - \$10
cost of false (+)	\$877.00
% call out postsymptoms (NBS)	73.08%

Sensitivity Analysis

		B/C ratio			
	B/C ratio swing		0.59		B/C ratio swing
		low	base	high	
birthrate	0.56	63.000	74.000	85.000	0.61
birth prevalence - 1 in:	0.47	197,292	157,833	17,000	5.45
% with OTCD family hx	0.61	0.19	0.22	0.25	0.57
sensitivity	0.55	86.67%	93.33%	100.00%	0.63
specificity	0.56	99.90%	99.94%	100.00%	0.63
Pre-Sx Callout Mortality	0.59	0.00	0.00	0.02	0.56
Post-Sx Callout Mortality	0.46	0.37	0.47	0.57	0.71
Treatment Cost	0.65	\$870,642.00	\$1,741,284.00	\$6,965,136.02	0.23
Value of a life	0.47	\$9,600,000.00	\$11,600,000.00	\$13,600,000.00	0.71
cost of NBS test	0.77	\$ 6.00	~ \$6 - \$10	\$10	0.48
cost of false (+)	0.61	\$ 438.50	\$877.00	\$8,770.00	0.38
% call out postsymptoms (NBS)	1.18	46.15%	73.08%	86.54%	0.29

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Variability of Clinical Presentation



- We don't know if childhood or later onset forms of OTCD will be detected by NBS.

Neonatal Onset	Childhood Onset (1m-16yr)	Later Onset (> 16yr)
N= 27	N= 52	N= 11

Data from Brassier et al. 2015 study of 90 OTCD patients

Ambiguous Results

- Ambiguous results
 - Low Citrulline is not specific to OTCD
 - Other genetic disorders affecting the urea cycle (CPS1, NAGS)
 - Mitochondrial disorders
 - False positives
 - Prematurity, protein restriction, intestinal pathologies
 - Impact to families
 - Impact to the medical system

Unintended Consequences of Screening

- Impact of the system failing
 - Expectation that screening will work
 - Families of babies with OTCD
 - Medical providers
 - Newborn screening staff
- Risk for litigation
 - What can the agency do to mitigate this risk?

Acknowledgements

Thank you to,

- Dr. Gregory Enns
- Dr. Angela Sun
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- Dr. Neela Sahai
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- New England Newborn Screening
- WA Newborn Screening
- Puerto Rico Newborn Screening
- UW School of Public Health

Questions
and
Discussion

