

Cornea CJD Risk Assessment:

Sensitivity Analysis of the Risk Model

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Risk Assessment: Background

European Commission Health and Consumer Protection Directorate-General, Directorate C - Scientific Opinions. Harmonisation of Risk Assessment Procedures in the Scientific Committees Advising the European Commission in the Area of Human and Environmental Health, 26-27 October 2000

Objective

- To provide information on the effect of changes in the risk model by calculating the risk of CJD infection among potential donors under differing sets of assumptions

as a tool to examine the model assumptions, variability, and uncertainty

Sources of Information

CJD Incidence in the U.S.: Holman et al. Emerging Infectious Diseases 2:333-337. Oct.-Dec. 1996.

Age-specific mortality rates: CDC. National Vital Statistics Reports. 47(19), 1999.

Population estimates: U.S. Bureau of the Census, P25-1127, 1995.

Cornea donors: EBAA Report, 1998

Risk Assessment Model

*estimates of infection rate within the donor pool
potential impact of uncertainty in the model*

- diagnosed cases of CJD
- undiagnosed symptomatic CJD
- asymptomatic CJD

Model Variables

- specificity of additional donor screening
- symptomatic cases missed by current screening
- symptomatic cases prior to diagnosis
- asymptomatic cases
- disease prevalence

Calculations

- number of years to detect 1 true positive case by additional screening
- number of donors incorrectly excluded
- number of donors and infected donors in the donor pool during the same time period
- percentage of infected donors detected by additional screening

Parameter 1: Missed Symptomatic Cases

Specificity	Percentage of Missed Cases				
	1	5	10	15	20
80 %	74399	23818	12876	8823	6710
85 %	55799	17864	9657	6617	5033
90 %	37199	11909	6438	4411	3355
95 %	18600	5955	3219	2206	1678
100 %	0	0	0	0	0
years to 1 true positive donors during interval	8.3	2.7	1.4	1.0	0.8
infected donors	371994	119090	64379	44113	33551
percent screened	118	45	30	24	21
	0.8	2.2	3.4	4.2	4.8

Parameter 2: Incubation Period

Specificity	Incubation Period			
	5 yr	10 yr	15 yr	20 yr
80 %	74399	74399	74399	74399
85 %	55799	55799	55799	55799
90 %	37199	37199	37199	37199
95 %	18600	18600	18600	18600
100 %	0	0	0	0
years to 1 true positive	8.33	8.33	8.33	8.33
donors during interval	371994	371994	371994	371994
infected donors	64.5	117.8	171.0	224.3
Percent screened	1.6	0.8	0.6	0.4

Parameter 3: Symptomatic Period

Specificity	Symptomatic Period			
	3 mo	6 mo	9 mo	12 mo
80 %	97196	74399	60264	50643
85 %	72897	55799	45198	37982
90 %	48598	37199	30132	25321
95 %	24299	18600	15066	12661
100 %	0	0	0	0
years to 1 true positive	10.89	8.33	6.75	5.67
donors during interval	485978	371994	301321	253214
infected donors	150	118	98	84
percent screened	0.7	0.8	1.0	1.2

Parameter 4: CJD Prevalence

Specificity	Prevalence*				
	1.00	1.05	1.10	1.15	1.20
80 %	74399	70856	67635	64695	61999
85 %	55799	53142	50726	48521	46499
90 %	37199	35428	33818	32347	31000
95 %	18600	17714	16909	16174	15500
100 %	0	0	0	0	0
years to 1 true positive	8.33	7.94	7.58	7.25	6.94
donors during interval	371994	354280	338177	323473	309995
infected donors	118	118	118	118	118
percent screened	0.8	0.8	0.8	0.8	0.8

* Calculations based on observed prevalence of CJD multiplied by the factor shown.

Conclusions

- Estimates of the number of cornea donors with CJD and the number of donors that may be erroneously excluded by screening vary depending on the model assumptions.
- Uncertainty in the assumed number of cases missed by current screening and in the specificity of additional screening could have a substantial impact on the result of the risk assessment.