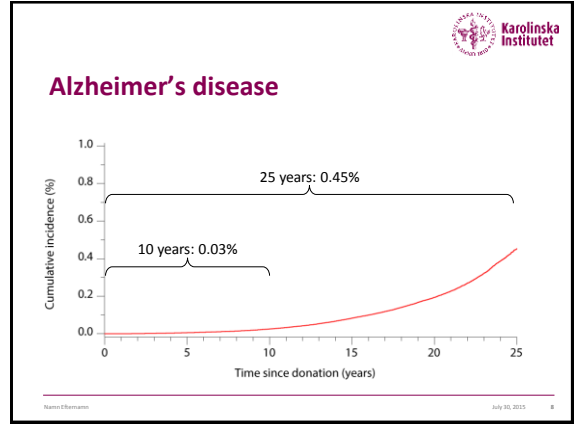

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Conceptual TTI risk model

$$\text{Clinical consequence} \equiv \left[\text{Prevalence of agent in blood donors} \right] \times \left[\text{Infectivity/transmissibility} \right] \times \left[\text{Probability that recipient lives long enough} \right]$$

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Results

$$\text{Clinical consequence} \equiv \left[\text{Prevalence of agent in blood donors} \right] \times \left[\text{Infectivity/transmissibility} \right] \times \left[\text{Probability that recipient lives long enough} \right]$$

Disease	10 yr. cumulative incidence	Expected 10 yr. survival	Expected cases per 100,000 transfusions (5% infect.)	Expected cases per 100,000 patients (5% infect.)
Alzheimer's disease	0.03%	0.3	0.5	2.2
Parkinson's disease	0.03%	0.3	0.4	1.9
Amyotrophic lateral sclerosis	0.02%	0.3	0.3	1.7
Dementia, unspecified	0.08%	0.3	1.2	4.7

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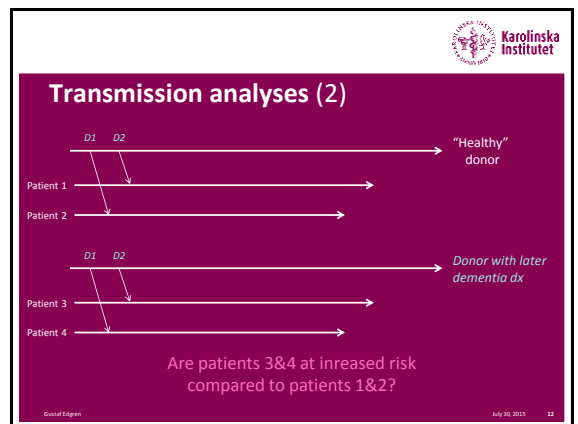
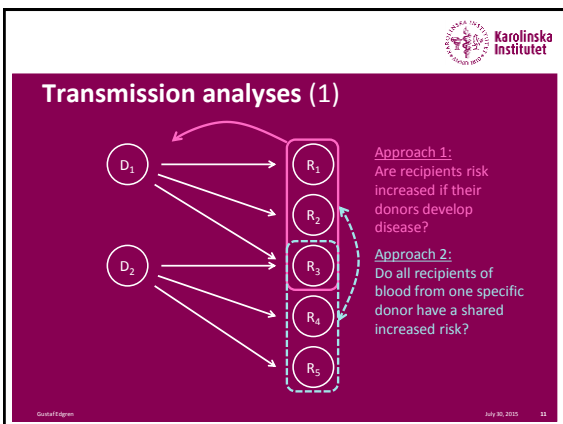
Example: Cancer as a TTD?


The Lancet 2007; 369:1724-30

➤ Risk of cancer after blood transfusion from donors with subclinical cancer: a retrospective cohort study

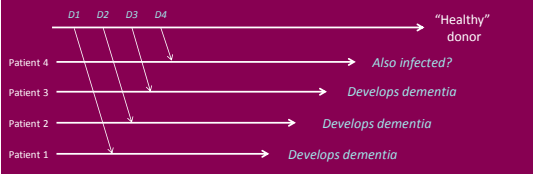
Gustaf Edgren, Henrik Hagglund, Maria Balci, Dong-Nam Tran, Klaus Berglund, Agnete Ohmanell, Kjell Tildestam, Johannes Anders, Agnete Wikman, Conger Jankil, Christo Grady, Louise Wadell, Olaf Nyman, Mads Moller

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Transmission analyses (3)




Do patients 1-4 have a "shared" increased risk?

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SCANDAT 2



- Data on 1.7 million donors and 2.1 million patients in Sweden and Denmark since 1960's and 1980's, respectively
- Ability to track transfusions between donors and their respective recipients
- Linkages with a range of health outcome registers providing follow-up for various health outcomes through 2012


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Methods

- Retrospective cohort analysis based on SCANDAT2 database
- All patients followed from first transfusion until death or diagnosis of neurodegenerative disease (Dementia, Alzheimer's, Parkinson's, or ALS)
- Two sets of analyses:
 - Transmission analyses, assessing effect of receiving blood from diseased donor
 - Cluster analyses, assessing if certain donors' blood increases risk (without donor necessarily becoming ill)
- Methods validated using chronic hepatitis

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Validation analyses: transmission of chronic hepatitis

- Relative risk before 1992 = 8.36 (95% CI, 7.25-9.63)
- Relative risk after 1992 = 1.19 (95% CI, 0.72-1.95)

Number of patients with a later hepatitis diagnosis the donor has donated blood to	RR of chronic hepatitis in "next" recipient (before 1992)	RR of chronic hepatitis in "next" recipient (after 1992)
No prior recipients	1.0 (ref)	1.00 (ref)
1-4 recipients	1.32 (1.19-1.46)	1.07 (0.97-1.20)
≥5 recipients	3.33 (2.55-4.36)	1.29 (0.76-2.22)

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Overall dementia transmission

- Overall relative risk, relative risk = 1.04 (95% CI, 0.99-1.09)
- <5 year latency, relative risk = 1.05 (95% CI, 0.89-1.22)
- Young onset in donor (<65 yrs), relative risk = 1.05 (95% CI, 0.97-1.14)

Number of patients with later dementia the donor has donated blood to	Relative risk of dementia in "next" recipient
No prior recipients	1.00 (ref)
1-4 recipients	1.01 (0.99-1.03)
5-9 recipients	1.03 (0.98-1.07)
≥10 recipients	1.06 (0.87-1.30)

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Alzheimer's disease transmission

- Overall relative risk, relative risk = 0.99 (95% CI, 0.85-1.15)
- <10 year latency, relative risk = 0.73 (95% CI, 0.38-1.41)
- Young onset in donor (<65 yrs), relative risk = 0.79 (95% CI, 0.56-1.11)

Number of patients with later AD the donor has donated blood to	Relative risk of AD in "next" recipient
No prior recipients	1.00 (ref)
1-3 recipients	1.01 (0.98-1.04)
≥4 recipients	1.14 (0.81-1.60)

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Parkinson's disease transmission

- Overall relative risk, relative risk = 0.94 (95% CI, 0.78-1.13)
- <10 year latency, relative risk = 1.10 (95% CI, 0.83-1.47)
- Young onset in donor (<65 yrs), relative risk = 0.88 (95% CI, 0.66-1.16)

Number of patients with later PD the donor has donated blood to	Relative risk of PD in "next" recipient
No prior recipients	1.00 (ref)
1-2 recipients	1.01 (0.98-1.04)
≥3 recipients	1.14 (0.81-1.60)

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ALS transmission

- Overall relative risk, relative risk = 1.83 (95% CI, 0.87-3.88)
- <10 year latency, relative risk = 2.25 (95% CI, 0.84-6.05)
- Young onset in donor (<65 yrs), relative risk = 1.21 (95% CI, 0.39-3.79)

Number of patients with later ALS the donor has donated blood to	Relative risk of ALS in "next" recipient
No prior recipients	1.00 (ref)
1 recipient	0.95 (0.69-1.31)
2 recipients	0.00 (n.e.)


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Conclusions

- Analyses based on SCANDAT2 indicate that even with (speculatively) high transmission rates, possible consequences on transfusion safety are limited
- Although recent animal model data suggest a prion-related etiology behind a range of neurodegenerative diseases, we find no sign of such transmission

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