SCANDAT

Assessing long-term donor health with transfusion epidemiology

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Disposition

1. The SCANDAT3 database - tool for assessing long-term health effects of blood donation

2. Methodological challenges with assessing long-term donor health

3. Long-term donor health cases

    1) Risk of fracture

    2) Risk of non-Hodgkin lymphoma revisited (unpublished)

    3) Risk for infections (unpublished)

SCANDAT3

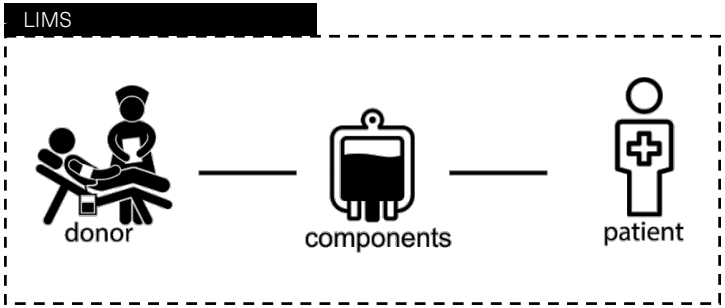
- Scandinavian Donation and Transfusions Database
- Third and latest iteration of the Swedish-Danish collaboration
- Swedish PI Dr. Gustaf Edgren, Danish PI Dr. Henrik Hjalmgrim

SCANDAT is a vein-to-vein database

Scandinavian Donation and Transfusions Database

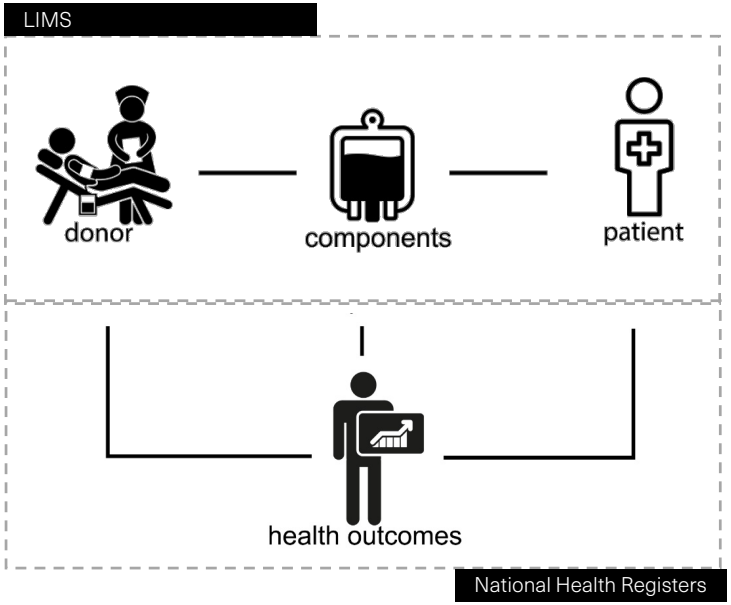
Data from Sweden since the 1960s (complete since 1990s)

Data from Denmark in a separate database since 1970s



SCANDAT is a vein-to-vein database

Scandinavian Donation and Transfusions Database



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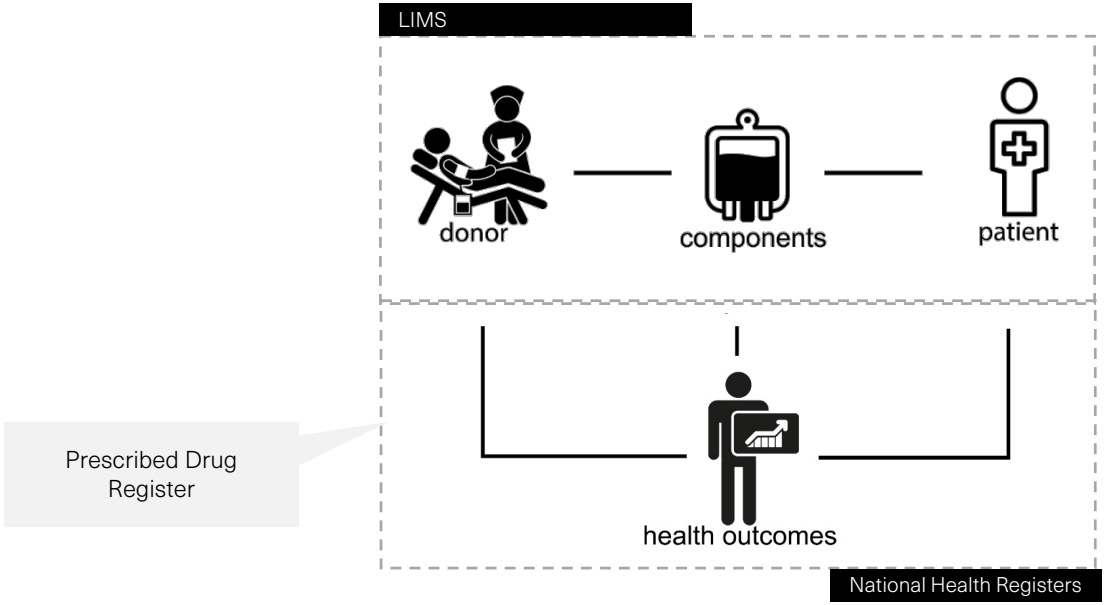

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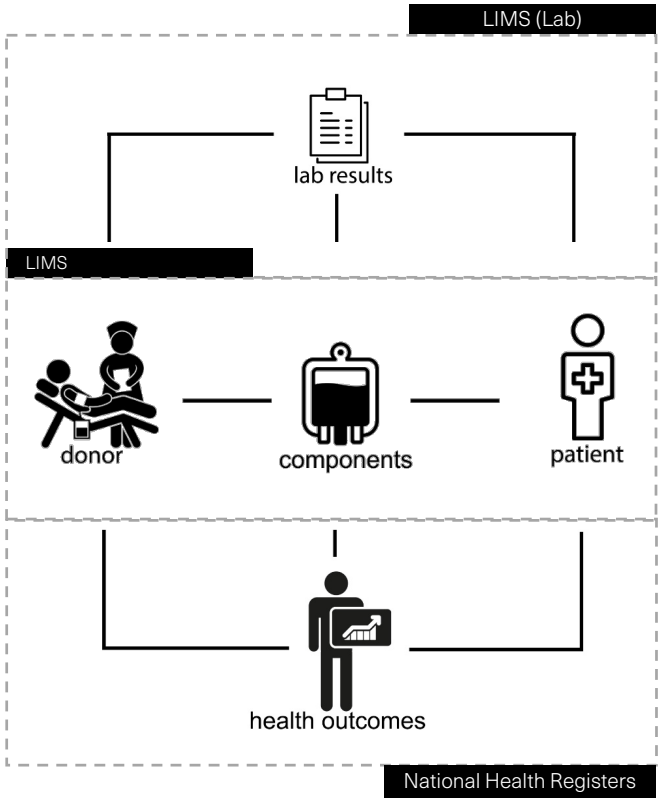
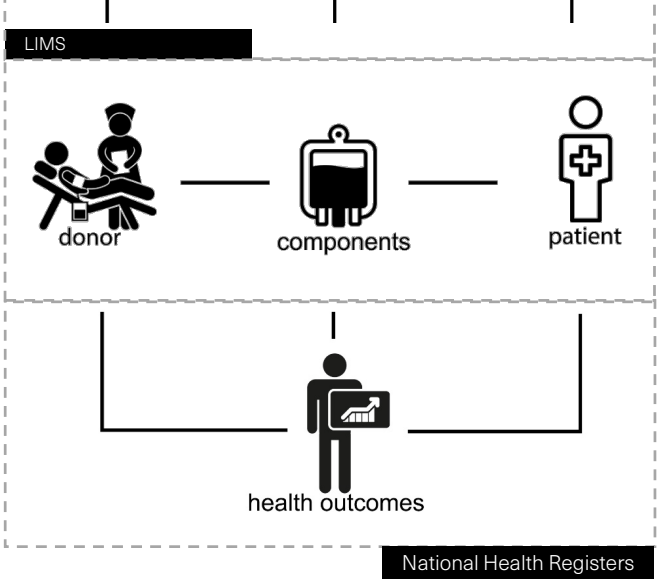




Diagnoses and patient visits

- National Patient Register
- National Cancer Register
- Numerous quality registers

Medical and surgical interventions

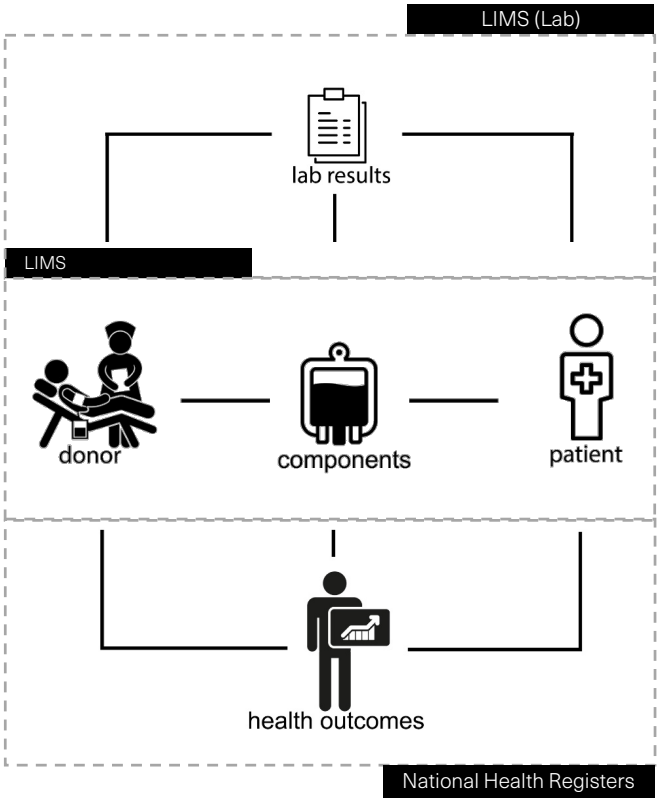
- National Patient Register
- Numerous quality registers

Prescribed Drugs

- National Prescribed Drug Register

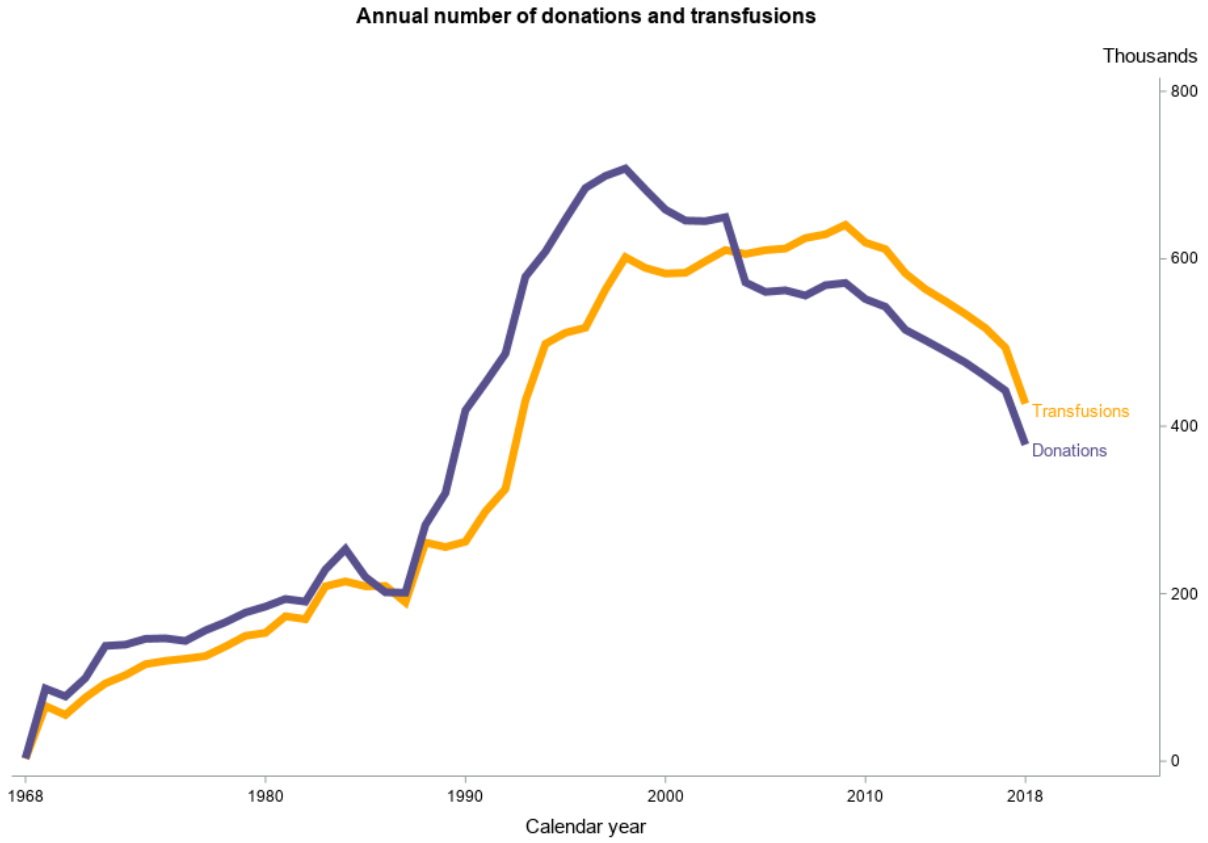
Possibility to link to around 100 other niched national health registers

Scandinavian Donation and Transfusions Database



Potentially a powerful tool for studying long-term donor health and donor hemovigilance!

Unpublished data
Zhao J et al.



Up to 50-years of follow-up!

Unpublished data
Zhao J et al.

Table 1. SCANDAT3 in Numbers

	Donors	Transfusion Recipients	Non-donors / Transfusion Recipients
Sex, N	1 475 262	1 873 447	4 821 591
Male	755 994	825 401	1 976 263
Female	719 268	1 048 046	2 845 328
Age at entry, years (S.D.)	30.82 (11.35)	64.61 (21.38)	39.14 (24.08)
Follow-up, N			
0-4 years	232 581	996 970	1 267 788
5-9 years	197 205	333 979	808 926
10-14 years	163 238	209 271	644 100
16-19 years	180 343	132 956	594 860
20-29 years	353 439	123 263	1 118 628
30-39 years	234 654	51 737	372 011
40+ years	113 802	25 271	15 278
Total follow-up, years	28 638 436	13 582 350	65 613 639

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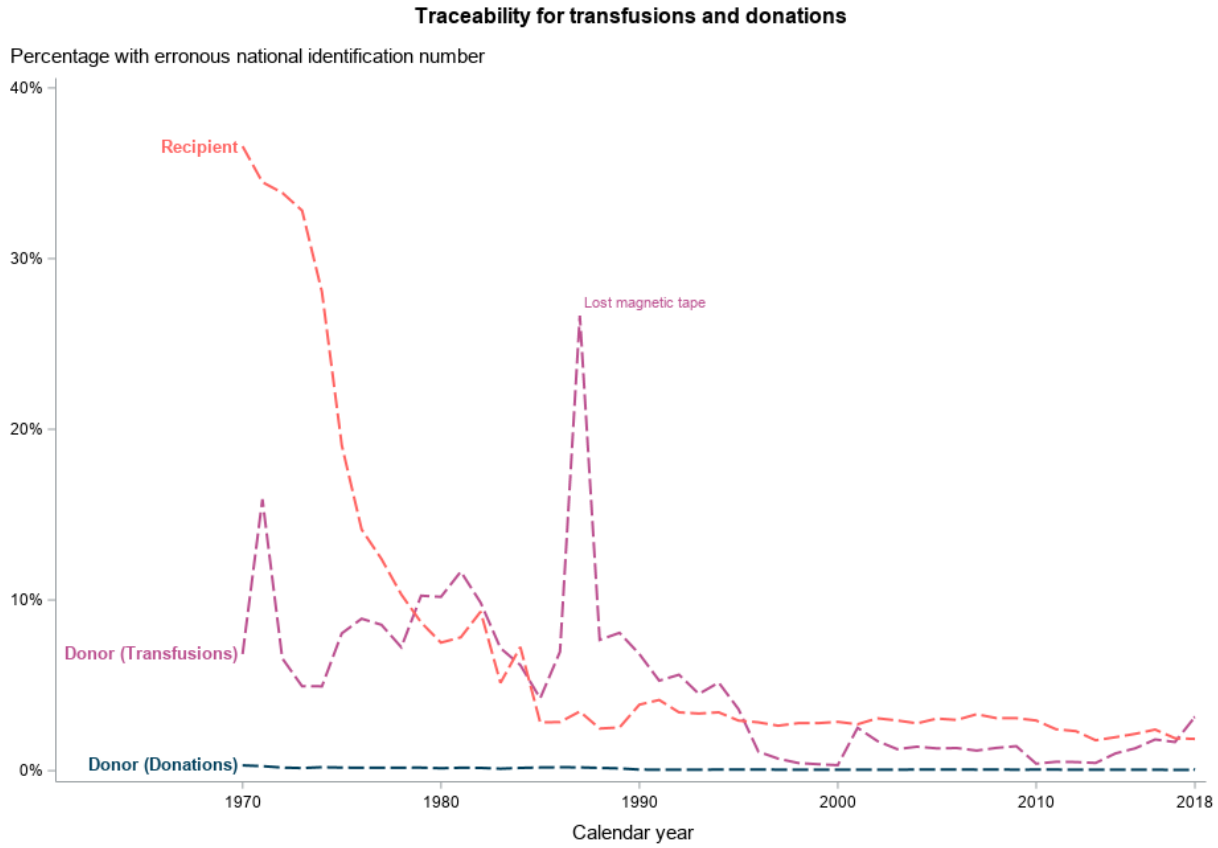
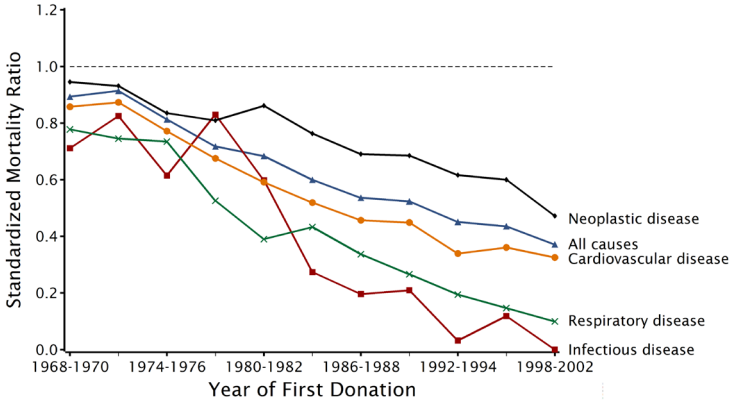


Methodological challenges in assessing donor health

Healthy donor-effect


donor


non-donors



Edgren G, et al. Transfusion, 2007

Methodological challenges in assessing donor health

Healthy donor-effect amongst donors cross-sectionally

Rare donor

Frequent donor

	Men		Women	
	Crude	Adjusted*	Crude	Adjusted*
Good health	1.13 (1.10–1.17)	1.10 (1.07–1.14)	1.16 (1.11–1.20)	1.09 (1.06–1.14)
Poor health	1.01 (0.96–1.07)	1.04 (0.99–1.09)	0.97 (0.91–1.03)	0.97 (0.91–1.03)
Medication use	0.97 (0.95–0.99)	0.94 (0.91–0.96)	1.02 (0.99–1.05)	0.95 (0.93–0.98)
Diagnosed disease	0.98 (0.96–0.99)	0.96 (0.94–0.98)	0.99 (0.97–1.01)	0.95 (0.93–0.97)
Visited GP past 3 months	0.90 (0.88–0.92)	0.93 (0.91–0.95)	0.92 (0.89–0.93)	0.94 (0.92–0.96)
Visited specialist past 12 months	0.89 (0.87–0.91)	0.94 (0.92–0.97)	0.87 (0.85–0.89)	0.93 (0.90–0.96)

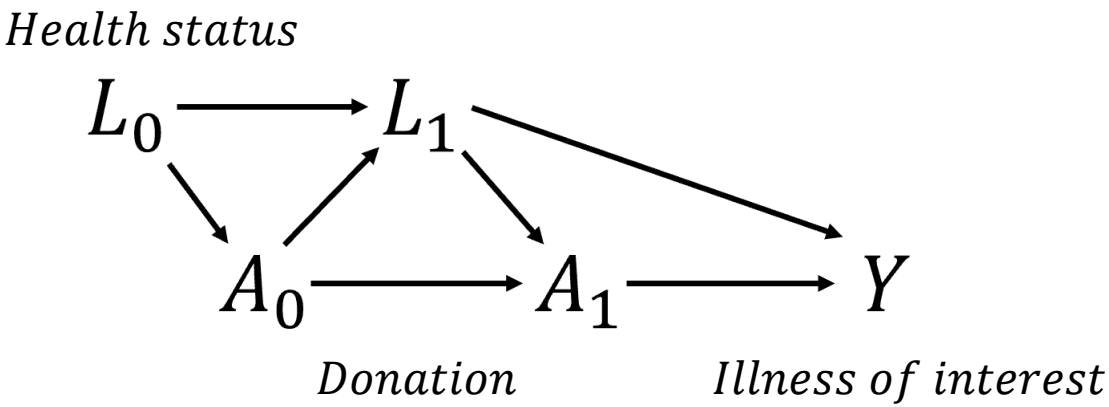
Poisson regression models for associations of self-reported health status with donation intensity; the number of whole blood donation attempts within two years after participating in Donor InSight.
*Adjusted for age, smoking, baseline donation intensity and new donor status.

https://doi.org/10.1371/journal.pone.0186662.t004

Hurk K, et al. PLOS ONE. 2017

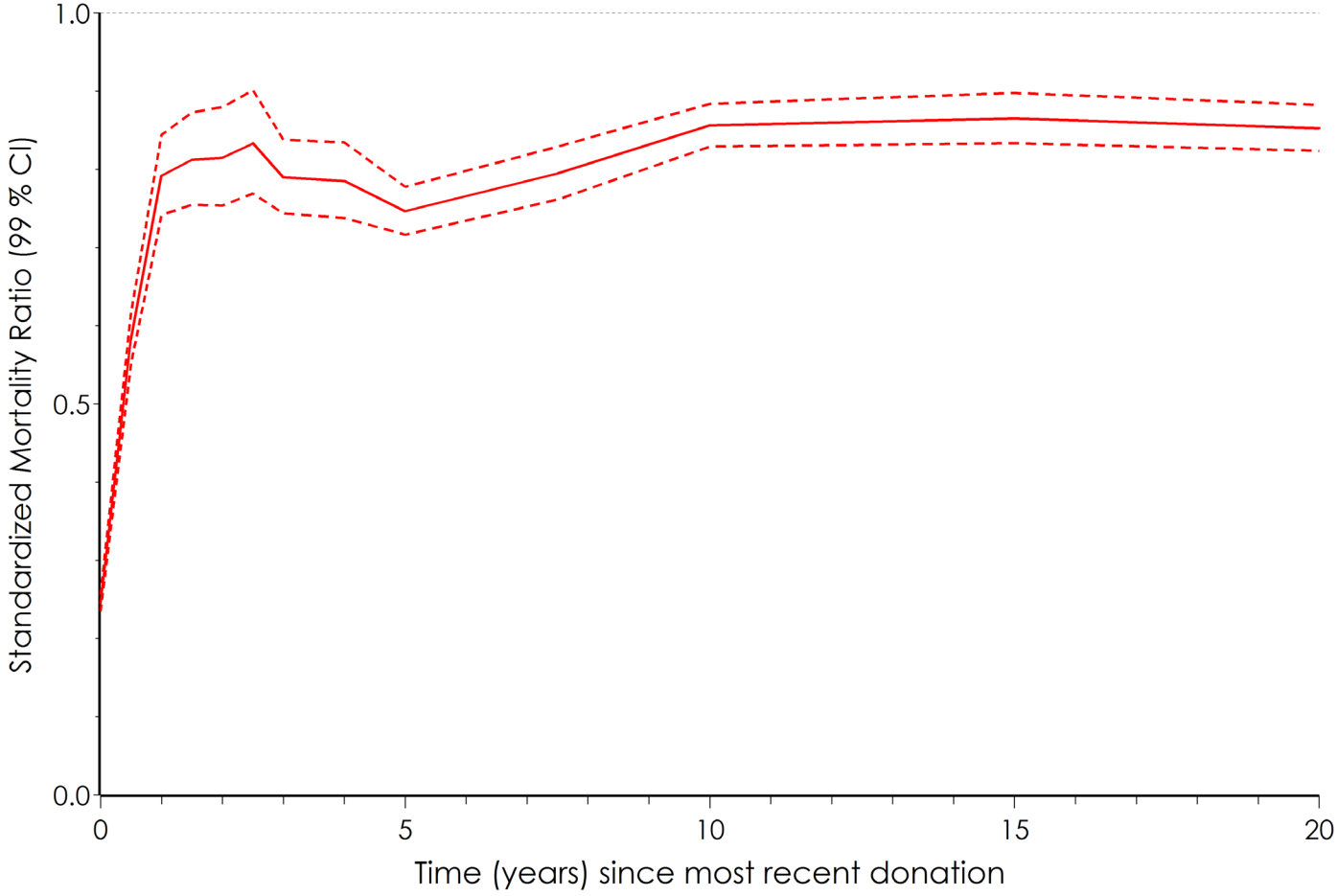
Methodological challenges in assessing donor health

Healthy donor-effect amongst donors time-dependently



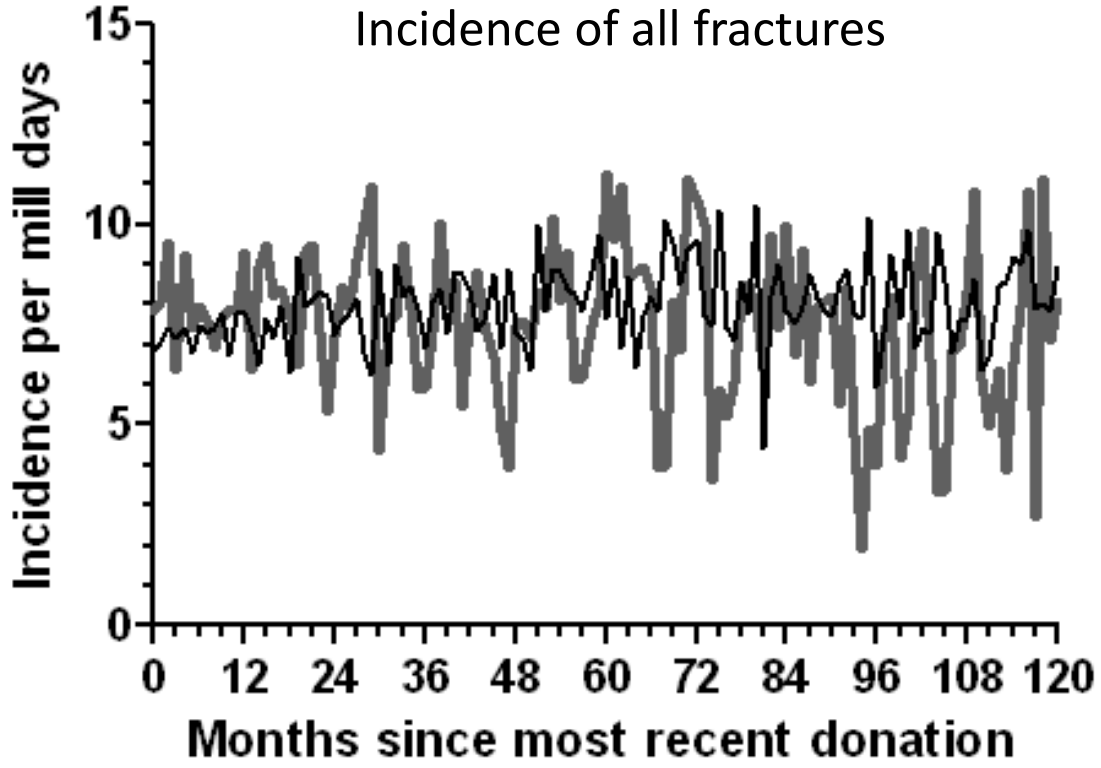
Methodological challenges in assessing donor health

Healthy donor-effect amongst donors time-dependently



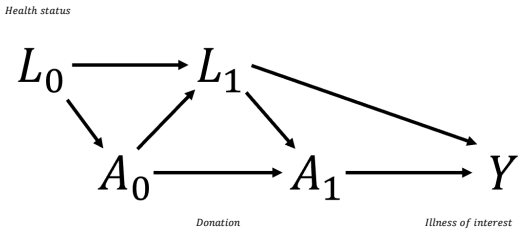
Methodological challenges in assessing donor health

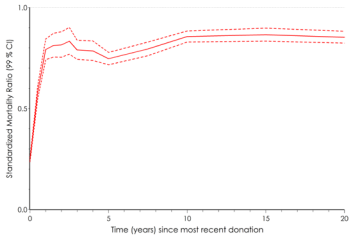
Healthy donor-effect amongst donors time-dependently

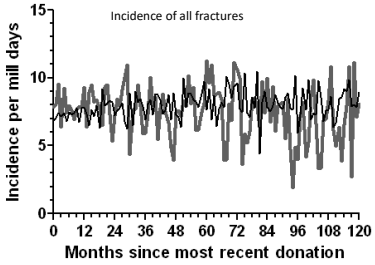


Grau K, et al. Transfusion, 2016

Methodological challenges in assessing donor health







Grau K, et al. Transfusion, 2016

The healthy donor-effect is, in practice, time-dependent confounding, **sometimes.**

Potential analytical approaches

- Use time since last donation as time-axis in survival models
- Investigate conditions without prodromal symptoms
- Separate exposure and outcome time periods
- Compare with a suitable control group, i.e. other donation type or other equipment?
- More complex modelling?

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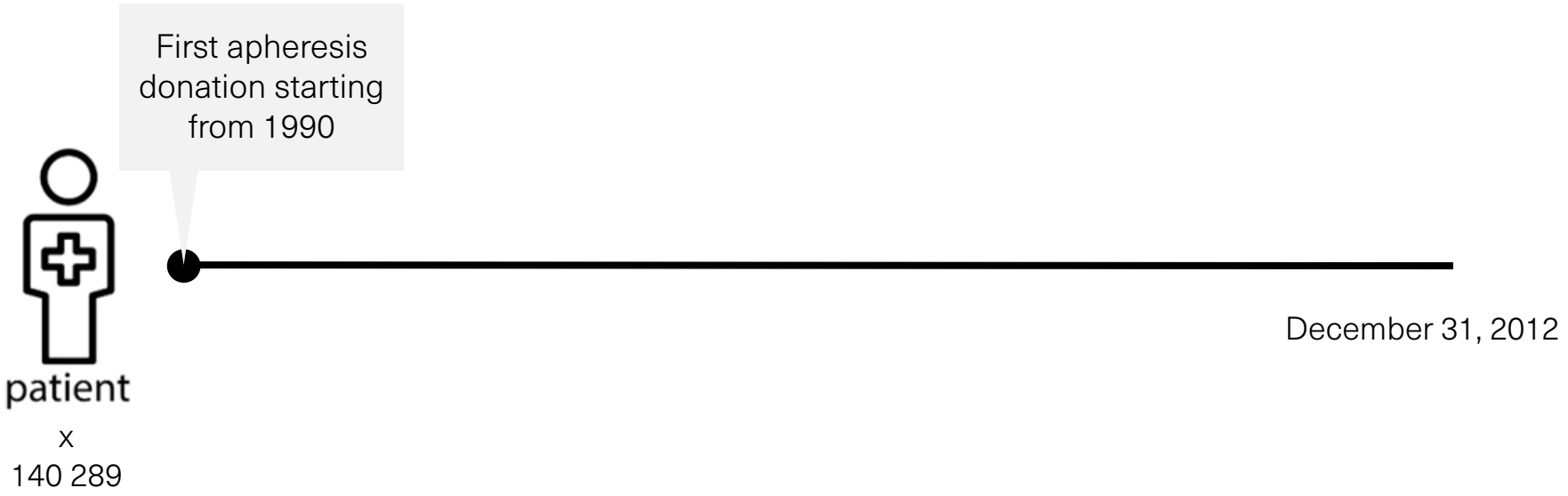
Grau et al. Transfusion, 2016

Apheresis donation and risk of fracture



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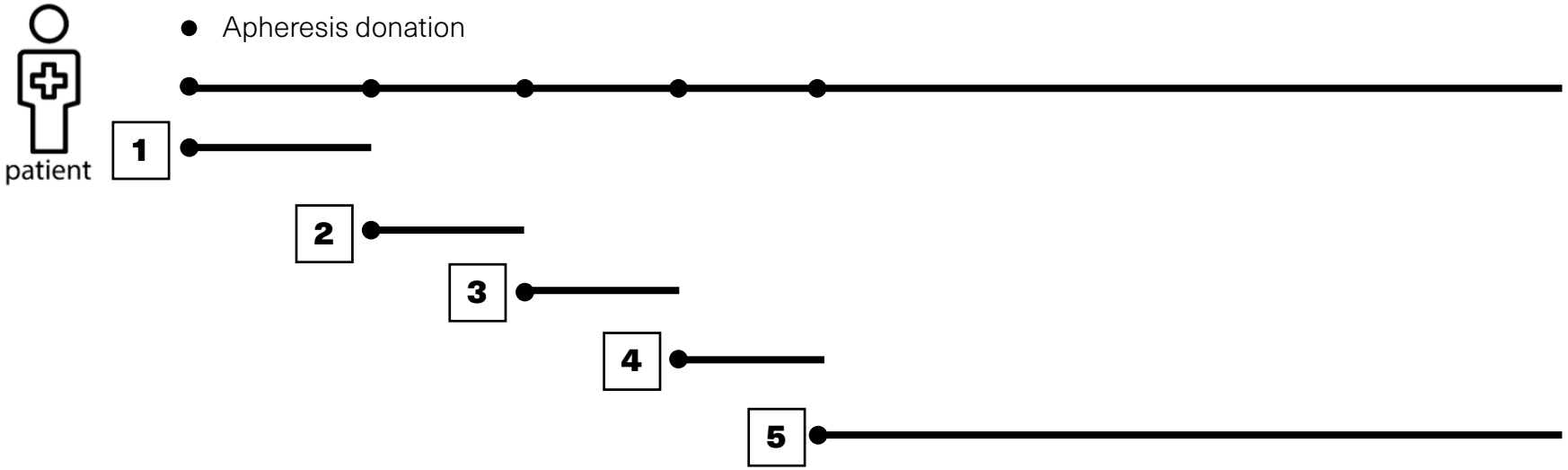
Grau et al. Transfusion, 2016

Apheresis as time-dependent exposure



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Grau et al. Transfusion, 2016

Table 2. Incidence rate ratios of fracture and osteoporosis related fracture in apheresis donors by cumulative number of apheresis donations and stratified by sex.

	Number of apheresis donations				
	1 - 8	9-24	25 - 49	50 - 99	≥ 100
Both sexes	Incidence rate ratios (95% confidence interval)				
All fractures	1.03 (0.99-1.06)	1.00 (ref)	0.99 (0.94-1.04)	0.96 (0.91-1.01)	0.98 (0.91-1.05)
Osteoporosis related fractures	1.05 (1.00-1.11)	1.00 (ref)	1.01 (0.94-1.08)	1.02 (0.94-1.11)	1.03 (0.93-1.15)
Women					
All fractures	1.06 (0.98-1.14)	1.00 (ref)	1.03 (0.94-1.13)	1.00 (0.89-1.12)	1.00 (0.86-1.16)
Osteoporosis related fractures	1.06 (0.98-1.14)	1.00 (ref)	1.03 (0.94-1.13)	1.00 (0.89-1.12)	1.00 (0.86-1.16)
Men					
All fractures	1.05 (0.96-1.14)	1.00 (ref)	0.98 (0.87-1.09)	1.04 (0.92-1.18)	1.06 (0.92-1.23)
Osteoporosis related fractures	1.05 (0.96-1.14)	1.00 (ref)	0.98 (0.87-1.09)	1.04 (0.92-1.18)	1.06 (0.92-1.23)

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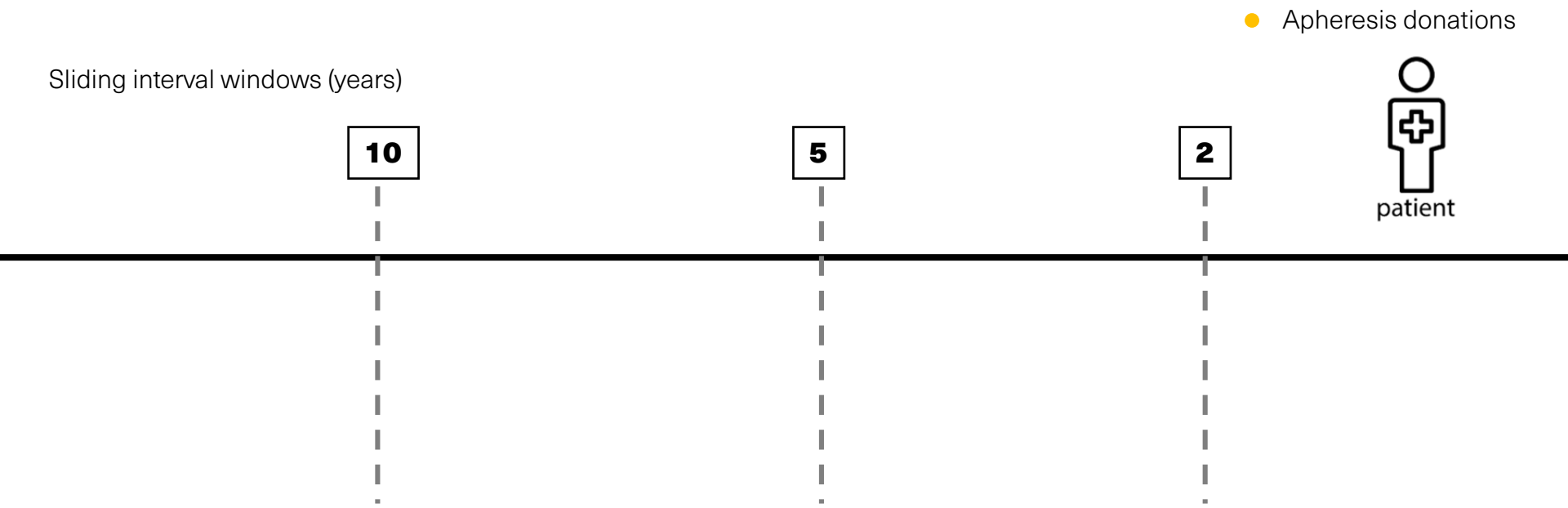
Grau et al.
Transfusion, 2016



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Grau et al. Transfusion, 2016

Table 3. Incidence rate ratios of all fractures in apheresis donors by number of apheresis donations in past time window, overall and stratified by sex.

	Number of apheresis donations in time window			
Past 2 years	1-3	4-7	8-15	≥16
	Incidence rate ratios (95% confidence interval)			
Both sexes	1.00 (0.92 - 1.08)	1.00 (ref)	0.95 (0.87 - 1.04)	0.94 (0.85 - 1.03)
Women	1.00 (0.88 - 1.14)	1.00 (ref)	0.98 (0.85 - 1.14)	0.89 (0.76 - 1.05)
Men	0.99 (0,90 - 1,10)	1.00 (ref)	0.93 (0.84 - 1.04)	0.96 (0.85 - 1.09)
Past 5 years	1-9	10-19	20-39	≥40
Both sexes	1.05 (0.99 - 1.12)	1.00 (ref)	1.05 (0.97 - 1.13)	0.97 (0.88 - 1.06)
Women	1.09 (0.99 - 1.21)	1.00 (ref)	1.08 (0.95 - 1.23)	0.97 (0.83 - 1.13)
Men	1.03 (0.95 - 1.11)	1.00 (ref)	1.03 (0.93 - 1.13)	0.97 (0.86 - 1.08)
Past 10 years	1-19	20-39	40-79	≥80
Both sexes	0.99 (0.94 - 1.04)	1.00 (ref)	0.94 (0.88 - 1.01)	0.95 (0.87 - 1.04)
Women	0.97 (0.90 - 1.05)	1.00 (ref)	0.92 (0.82 - 1.03)	0.92 (0.79 - 1.08)
Men	1.01 (0.94 - 1.07)	1.00 (ref)	0.96 (0.88 - 1.05)	0.96 (0.86 - 1.08)

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Grau et al. Transfusion, 2016

Conclusions

No evidence of any association between number of apheresis donations and risk of fractures

- No difference in effects in men/women
- No age interaction, i.e. no increased effects also in older donors
- No difference when analyzing only plasma or platelet apheresis

Limitations

- No data on calcium supplementation
- Small effect?
- Healthy donor effect?

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Edgren et al.
JNCI, 2008

Apheresis donation and risk of malignancy

- Nested case control study using conditional logistic regression
- Cases were blood donors that were diagnosed with a malignancy
- Matched on sex, age, and county of residence

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Edgren et al.
JNCI, 2008

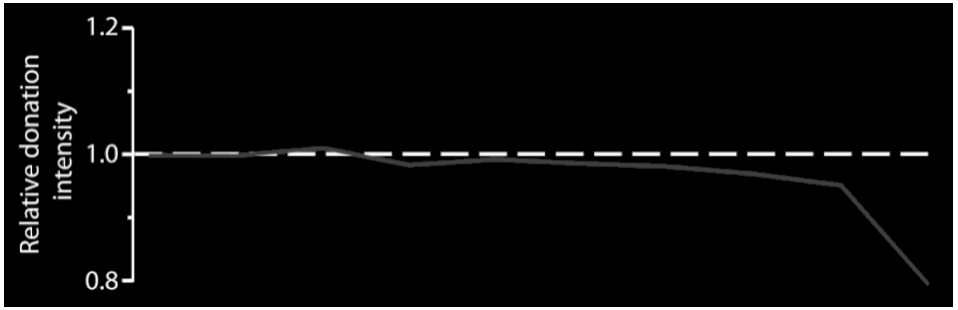
Apheresis donation and risk of malignancy

Index date, t_0

t_0 – 12 yrs.

t_0 – 7 yrs.

t_0 – 2 yrs.



case

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Edgren et al. JNCI, 2008

SCANDAT1 Nested case-control study (1968-2002)

Cancer overall	Number of donations				
3-12 years before diagnosis	1-8	9-16	17-25	>25	P for trend
Both sexes	1.00 (ref)	0.98 (0.91-1.05)	0.97 (0.89-1.05)	0.99 (0.90-1.10)	0.84
Women	1.00 (ref)	0.96 (0.86-1.07)	0.99 (0.87-1.13)	0.98 (0.83-1.17)	0.78
Men	1.00 (ref)	0.99 (0.90-1.09)	0.96 (0.86-1.07)	1.00 (0.88-1.13)	0.68

Non-Hodgkin lymphoma	Number of apheresis donations			
3-12 years before diagnosis	1-8	9-25	>25	P for trend
Both sexes	1.00 (ref)	0.47 (0.15-1.52)	2.14 (1.22-3.74)	0.05

risk. There was some suggestion that the risk of non-Hodgkin lymphoma might be increased among frequent plasma donors who began donating before 1986, but the dose–risk trend was erratic and the data not very convincing.

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Unpublished data
Zhao J et al.

Conclusions

- Earlier erratic findings were likely due to benign conditions (mostly MGUS) that share the same ICD7 code as non-Hodgkin lymphoma

- If this is the case, this result likely reflect a screening effect

- We will redo the original study, now with greater ability to exclude benign conditions

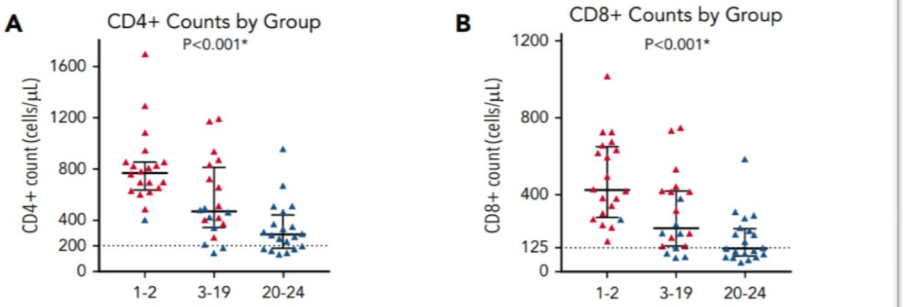
Apheresis donation and risk of infection

Gansner et al. Blood, 2019.

TRANSFUSION MEDICINE

Plateletpheresis-associated lymphopenia in frequent platelet donors

Gansner et al. Blood, 2019.



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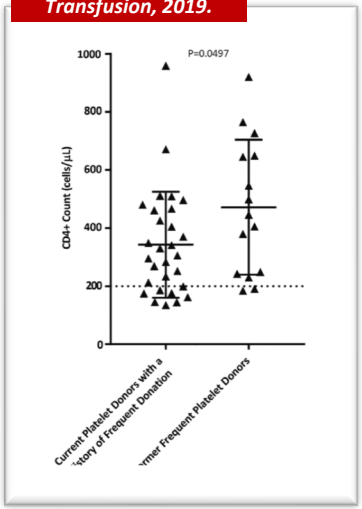

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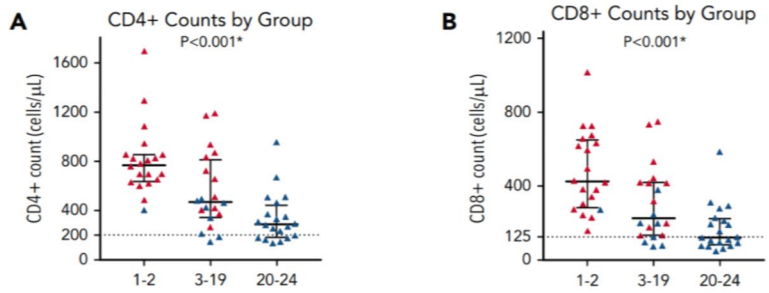

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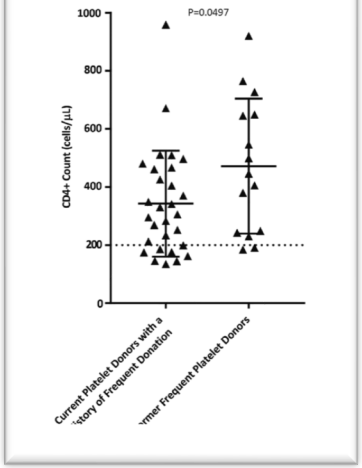

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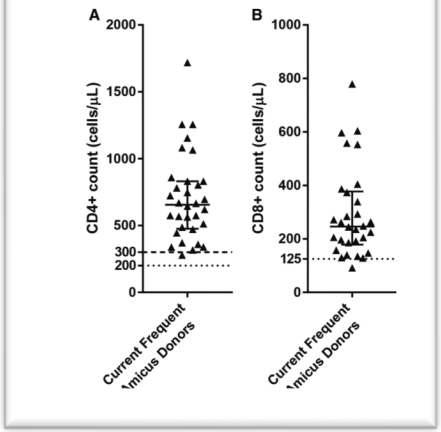

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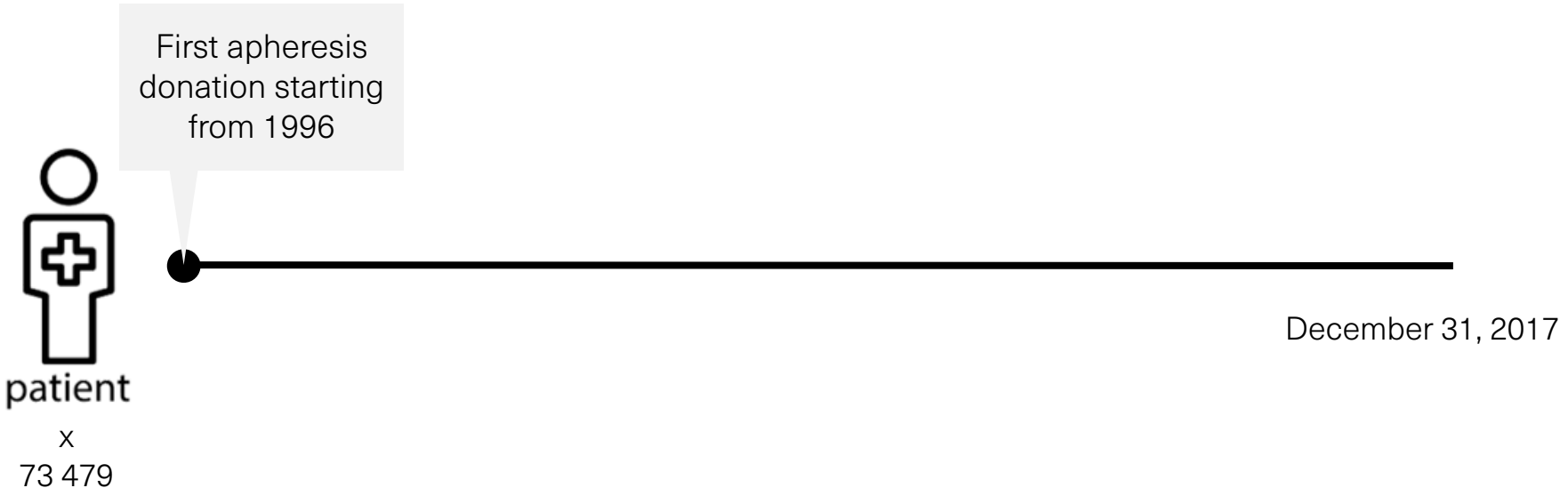

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Summary

- The newly completed SCANDAT3 offers up to 50 years of follow-up for studying long-term donor health in Sweden and Denmark
- Studies on donor health can be methodologically challenging due to the healthy donor effect and time-dependent self-selection
- No apparent increased risk for fractures following apheresis donation
- Preliminary data show no association with increased risk for infections
- Earlier study showing association with NHL is likely due to imprecision in ICD7, and we plan to redo the study with greater diagnostic precision