Arbejdsmiljøforskningsfondens årskonference 2019:

Styren eksponering og risiko for kræft

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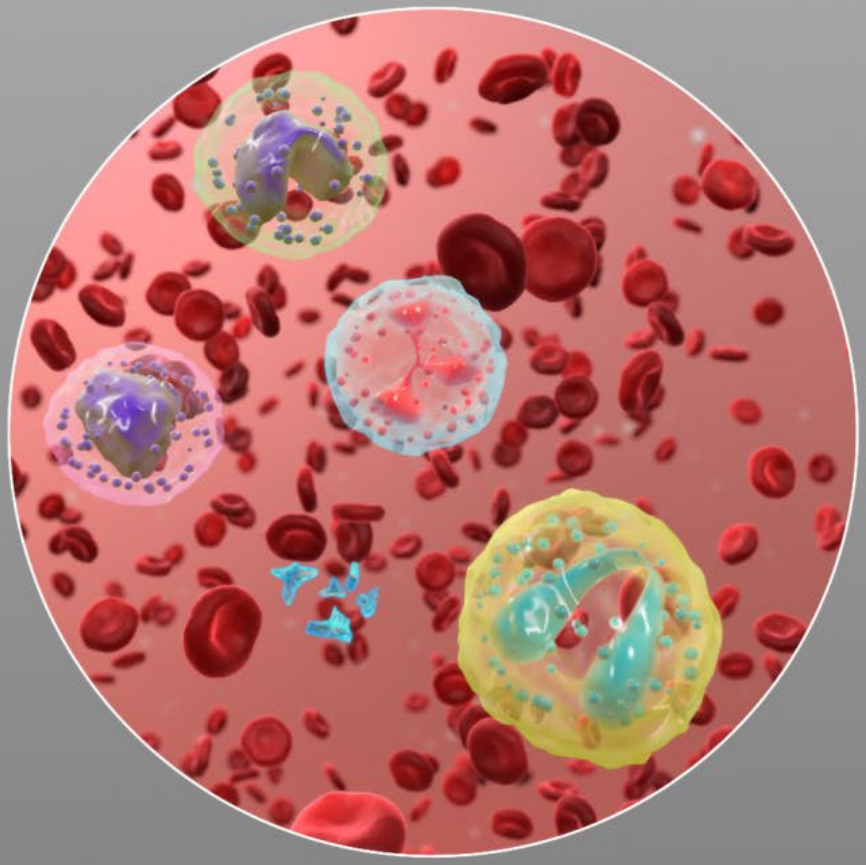
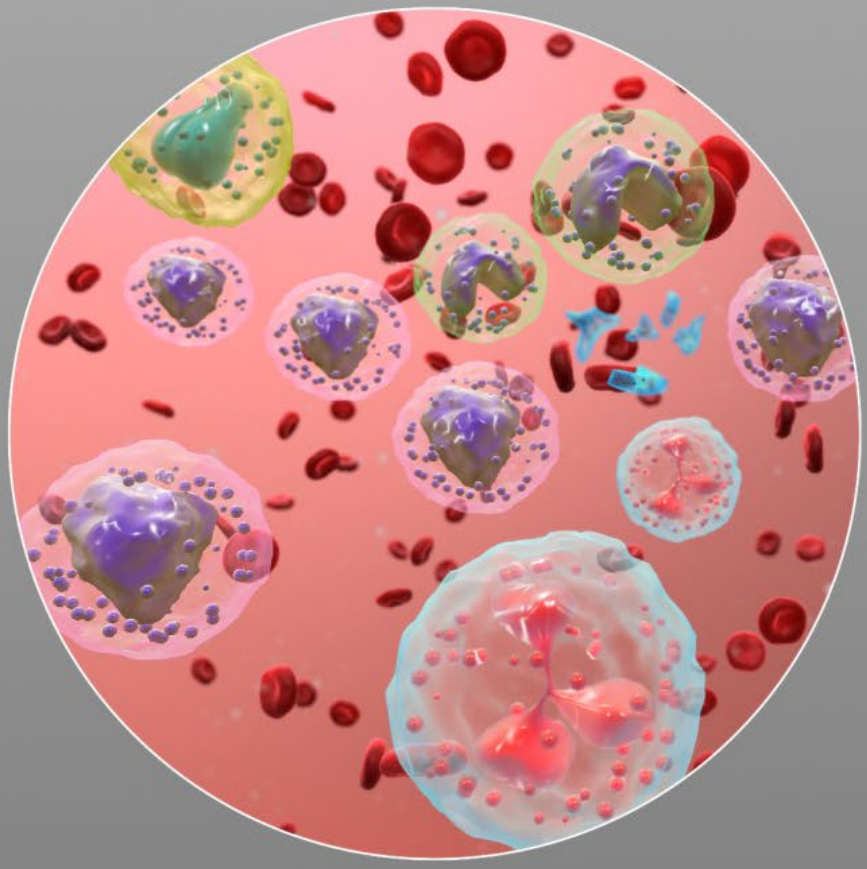
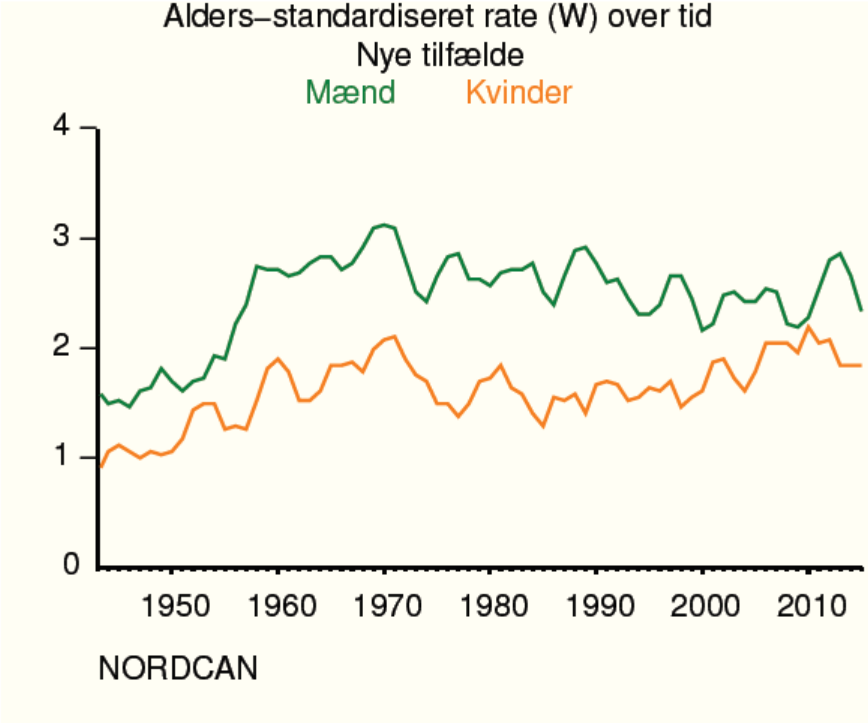


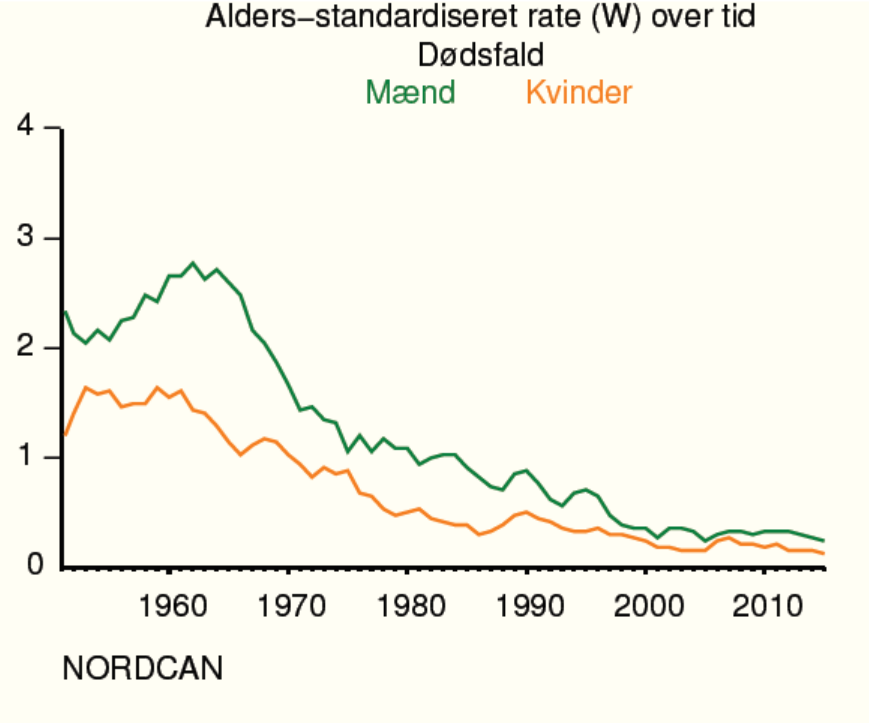
Normal Blood



Leukemia

Hodgkins lymfom, nye tilfælde og dødsfald i befolkningen, 1945-2015





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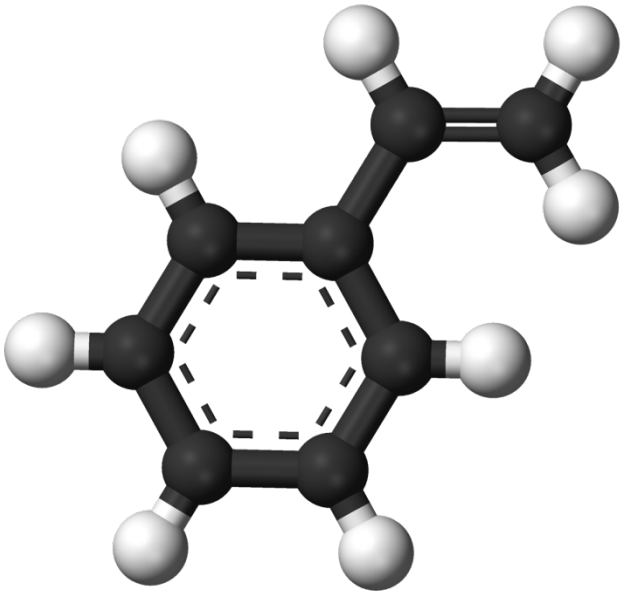


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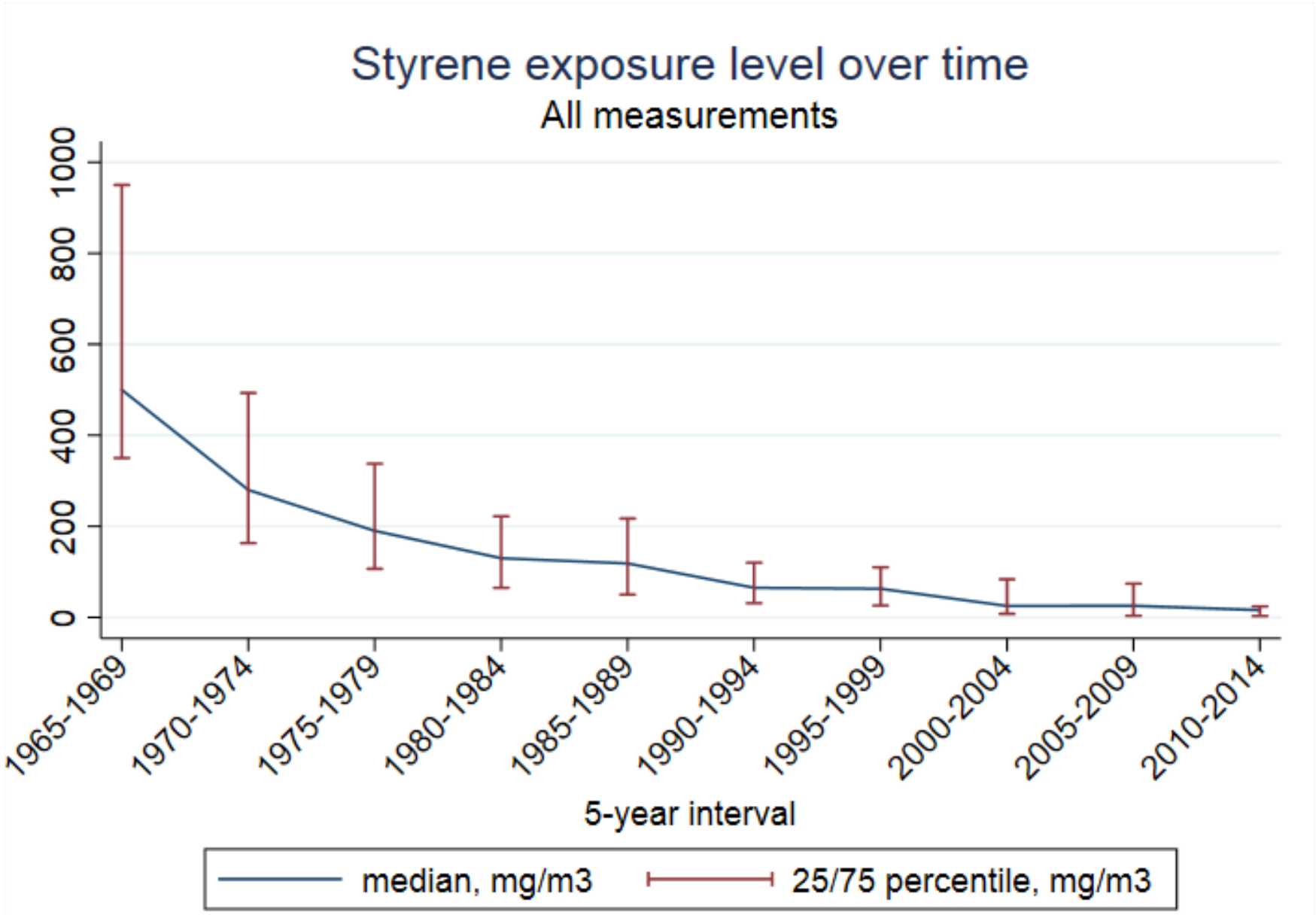
Styrene exposure level over time
All measurements
0
200
400
600
800
1000
1965-1969
1970-1974
1975-1979
1980-1984
1985-1989
1990-1994
1995-1999
2000-2004
2005-2009
2010-2014
5-year interval
median, mg/m3
25/75 percentile, mg/m3

Virksomhedskarakteristika og styren niveau (logaritmerede værdier, mg/m^3)

Company Characteristics	Regression Coefficient[a] (95% CI)
Intercept[b]	1.4 (0.4–2.5)
Main product	
Boats	0.6 (0.3–1.0)
Wind turbine rotor blades	0.3 (-0.1, 0.6)
Main production process	
Lamination	0.6 (0.3, 1.0)
Calendar year	
1970–1979	2.8 (1.7, 3.8)
1980–1989	2.2 (1.2, 3.3)
1990–1999	1.3 (0.0, 2.6)

Eksponeringsniveau for person ansat i virksomhed, som producerede både med laminering i 1970erne: exp(1.4+0.6+0.6+2.8)=221 mg/m^3

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Christensen et al, Epidemiology 2018

Kumuleret styreneksponering og rate ratio (RR) for en række former for leukæmi og lymfekræft

TABLE 3. Incidence Rate Ratios of Lymphohematopoietic Malignancies by Cumulative Styrene Exposure Score Accrued During the Complete Work History in 73,036 Workers of the Danish Reinforced Plastics Industry, 1968–2011

	Cumulative Styrene Exposure Score[a]							
	1–17 mg/m³-years (Reference)	18–70 mg/m³-years			≥ 71 mg/m³-years			
Malignancy	No. of cases[b]	No. of cases[b]	Crude RR	Adjusted RR[c] (95% CI)	No. of cases[b]	Crude RR	Adjusted RR[c] (95% CI)	P_{trend}[d]
All lymphohematopoietic malignancies	182	220	1.2	0.9 (0.8, 1.1)	263	1.4	0.9 (0.8, 1.1)	0.42
All myeloid malignancies	48	57	1.2	0.9 (0.6, 1.3)	78	1.6	0.9 (0.7, 1.4)	0.86
All myeloid leukemias	22	22	1.0	0.8 (0.4, 1.4)	40	1.8	1.1 (0.6, 2.0)	0.83
Acute myeloid leukemia	12	12	1.0	0.8 (0.3, 1.7)	26	2.2	1.4 (0.7, 2.8)	0.28
Chronic myeloid leukemia	6	7	1.2	0.7 (0.2, 2.2)	11	1.8	0.9 (0.3, 2.6)	0.99
Myelodysplastic syndrome	10	14	1.4	0.9 (0.4, 2.0)	13	1.3	0.6 (0.3, 1.4)	0.39
Polycythemia vera	12	14	1.4	0.9 (0.4, 2.0)	18	1.5	0.9 (0.4, 2.0)	0.86
All lymphoid malignancies	133	161	1.2	0.9 (0.7, 1.2)	182	1.4	0.9 (0.7, 1.1)	0.36
Hodgkin lymphoma	16	16	1.0	1.0 (0.5, 2.1)	25	1.6	1.6 (0.8, 2.2)	0.15
All non-Hodgkin lymphoma	67	80	1.2	0.9 (0.7, 1.3)	89	1.3	0.9 (0.7, 1.3)	0.58
B-cell lymphoma	49	62	1.3	1.0 (0.7, 1.5)	63	1.3	0.9 (0.6, 1.3)	0.46
Follicular B-cell lymphoma	11	13	1.2	1.0 (0.4, 2.2)	11	1.0	0.7 (0.3, 1.8)	0.46
Diffuse B-cell lymphoma	31	44	1.4	1.1 (0.7, 1.7)	45	1.5	0.9 (0.6, 1.5)	0.72
T-cell lymphoma	n.r.	n.r.	1.3	1.1 (0.3, 5.2)	n.r.	4.3	3.2 (0.9, 11.8)	0.04
Other or nonspecific lymphomas	15	14	0.9	0.8 (0.4, 1.7)	12	0.9	0.7 (0.3, 1.4)	0.29
Multiple myeloma	19	20	1.0	0.8 (0.4, 1.5)	30	1.6	0.9 (0.5, 1.7)	0.91
All lymphoid leukemias	29	40	1.4	0.9 (0.6, 1.5)	33	1.2	0.6 (0.4, 1.0)	0.04
All chronic lymphoid leukemias	24	30	1.3	0.8 (0.5, 1.4)	27	1.1	0.6 (0.3, 1.9)	0.04
Chronic B-cell lymphoid leukemia	21	28	1.3	0.9 (0.5, 1.6)	25	1.2	0.6 (0.3, 1.1)	0.08
All B-cell–derived lymphoid malignancies	107	131	1.2	1.0 (0.8, 1.3)	148	1.4	1.0 (0.7, 1.2)	0.69
All T-cell–derived lymphoid malignancies	5	4	0.8	0.7 (0.2, 2.5)	13	0.6	1.8 (0.6, 5.2)	0.18

Kumuleret styren eksponering og rate ratio (RR) for akut myeloid leukæmi, Hodgkins lymfom og T-celle lymfom

	Kumuleret styren eksponering						
	1-17 mg/m^3-år		18-70 mg/m^3–år		≥71 mg/m^3-år		P trend
Sygdom	N	RR	N	RR (95%CI)	N	RR (95%CI)	
Akut myeloid leukemi	12	1	12	0.8 (0.3-1.7)	26	1.4 (0.7-2.8)	0.28
Hodgkins lymfom	16	1	16	1.0 (0.5-2.1)	25	1.6 (0.8-2.2)	0.15
T-celle lymfom	n.r.	1	n.r.	1.1 (0.3-5.1)	n.r.	3.2 (0.9-11.8)	0.04

Justeret for køn, alder og kalenderår

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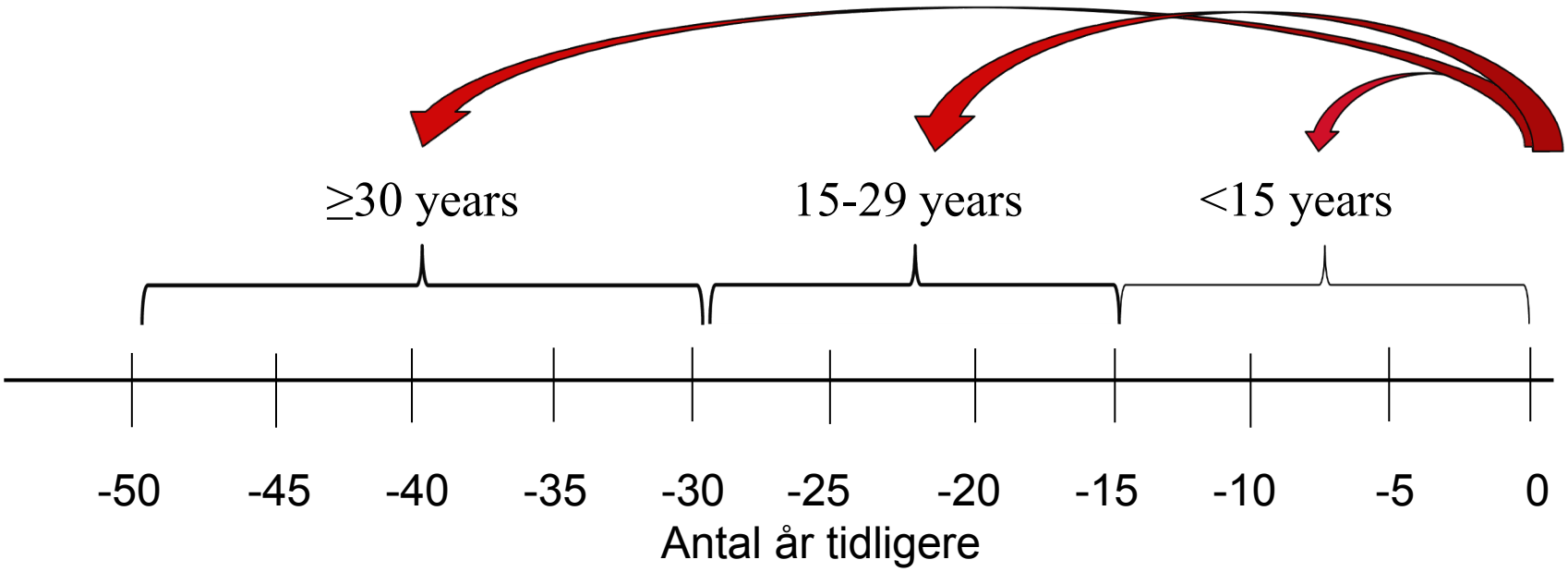
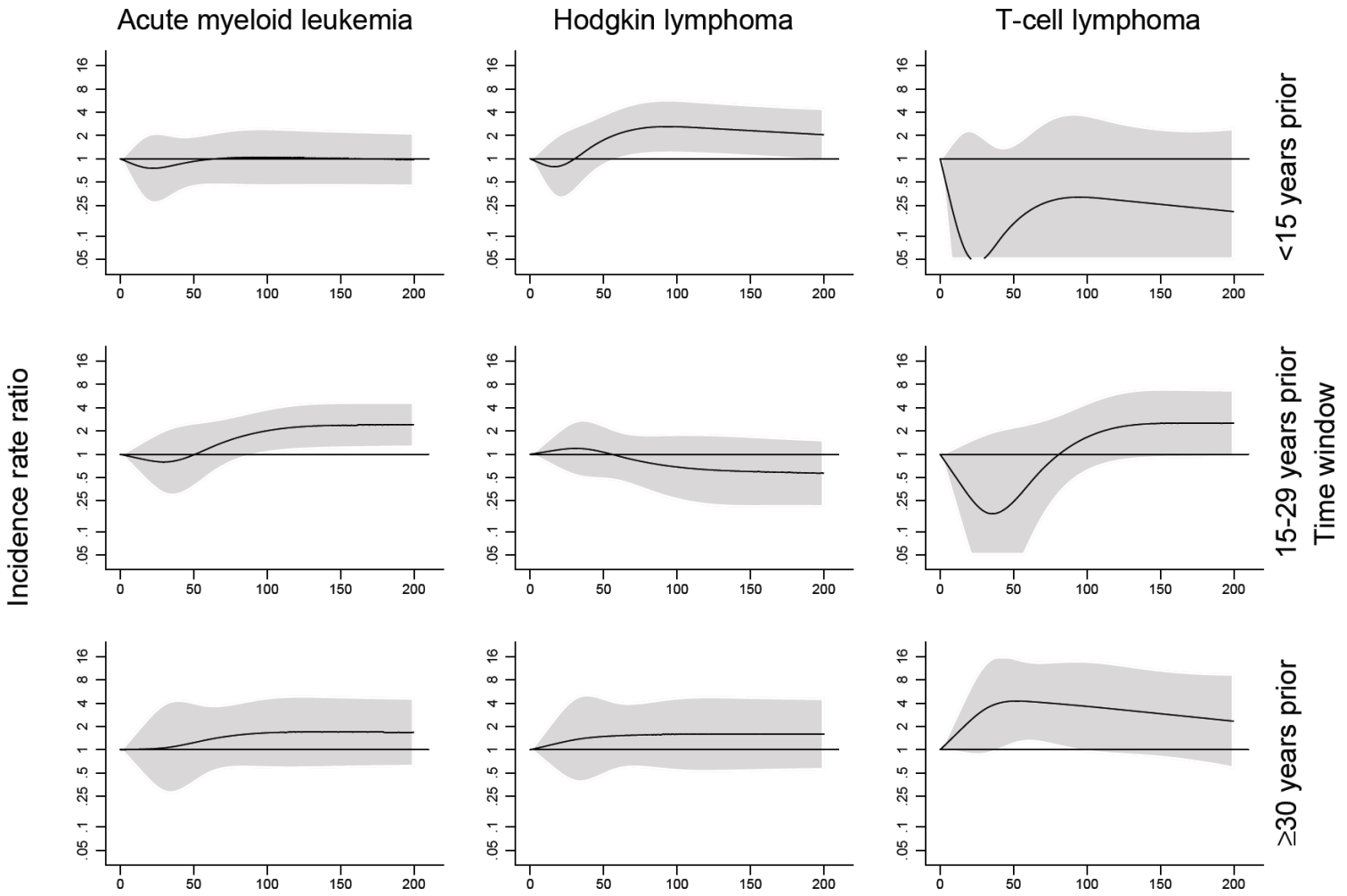
Christensen et al, Epidemiology, 2018

Analyse af eksponeringsvinduer



Kumuleret styren eksponering <15, 15-29, ≥30 år tidligere og RR for akut myeloid leukæmi, Hodgkin lymfom og T-celle lymfom



Christensen et al, Epidemiology, 2018

Styreneksponering og odds ratio (OR) for adenokarcinom og pladecellekarcinom i næse og bihuler

Styren eksponering	Adenokarcinom (N=9)		Pladecellekarcinom (N=15)	
	OR	95% CI	OR	95% CI
Kumuleret eksponering				
<37 mg/m^3	1		1	
≥37 mg/m^3-år	5.1	0.6-45.1	1.2	0.3-3.9
Gennemsnitlig eksponering				
<23 mg/m^3	1		1	
≥23 mg/m^3	2.1	0.4-11.3	0.4	0.1-1.3
Eksponeringsvarighed				
<5 år	1		1	
≥5 år	2.5	0.6-9.7	1.0	0.3-3.6

Justeret for alder, køn og ansættelse i træindustri

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Nissen et al, OEM, 2018

Styrker og svagheder

Styrker

- Kvantitative mål for styren eksponering
- Detaljerede sygdomsoplysninger
- Interne analyser i studiepopulationen
- Komplette data og ingen selvrapportering

Svagheder

- Ingen oplysninger om tobak
- Lille studiepopulation (n=73.000 deltagere)

Konklusion

- Muligvis forøget risiko for akut myeloid leukæmi og adenokarcinom i næse og bihuler efter erhvervsmæssig eksponering for styren
- IARC, WHO, opgraderede styren fra mulig til sandsynlig kræftfremkaldende for mennesker i 2018
- Målinger af arbejdsmiljøet kombineret med de unikke danske registre er guld værd
- Fundene må efterprøves i en anden, stor population eksponeret for styren

Perspektiver: Styreneksponeret mega-kohorte med >100.000 deltagere og 3 millioner person-år

Studie	Virksomheder	Ansatte	Follow-up	Person-år
Finland	157	2.085	1958-2016	45.000
Italy, Liguria	3	1.438	1969-2016	30.000
Italy, Emilia Romagna	98	5.818	1956-2016	10.000
United Kingdom, MRC	8	7.970	1947-2012	274.047
United Kingdom, HSE	51	1.749	1961-2016	60.000
Washington State	2	5.201	1959-2016	203.404
US	30	15.826	1948-2016	600.000
Denmark	443	72.292	1968-2016	1.800.000
Total	792	112.379	1947-2016	3.000.000

Cancer Incidence in Workers Exposed to Styrene in the Danish-reinforced Plastics Industry, 1968–2012

Mette Skovgaard Christensen,[a,b] Johnni Hansen,[c] Cecilia Høst Ramlau-Hansen,[d] Gunnar Toft,[a,e] and Henrik Kolstad[a]

(*Epidemiology* 2017;28: 300–310)

Styrene Exposure and Risk of Lymphohematopoietic Malignancies in 73,036 Reinforced Plastics Workers

Mette Skovgaard Christensen,[a,b] Jesper Medom Vestergaard,[a] Francesco d'Amore,[c] Jette Sønderskov Gørløv,[d] Gunnar Toft,[a,e] Cecilia Høst Ramlau-Hansen,[f] Zara Ann Stokholm,[a] Inge Brosbøl Iversen,[a] Mette Schou Nissen,[a] Henrik Albert Kolstad[a]

(*Epidemiology* 2018;29: 342–351)

Sinonasal adenocarcinoma following styrene exposure in the reinforced plastics industry

Mette Schou Nissen,[1] Zara Ann Stokholm,[1] Mette Skovgaard Christensen, Vivi Schlünssen,[2,3] Jesper Medom Vestergaard,[1] Inge Brosbøl Iversen,[1] Henrik Albert Kolstad[1]

Occup Environ Med 2018;**75**:412–414.

Cancer mortality in an international cohort of reinforced plastics workers exposed to styrene: a reanalysis

Dana Loomis,[1,2] Neela Guha,[1] Manolis Kogevinas,[3,4,5,6] Vincenzo Fontana,[7] Valerio Gennaro,[7] Henrik A Kolstad,[8] Damien Martin McElvenny,[9] Markku Sallmén,[10] Rodolfo Saracci[1]

Occup Environ Med 2018;**0**:1–6.

Carcinogenicity of quinoline, styrene, and styrene-7,8-oxide

In March, 2018, a Working Group of 23 scientists from 12 countries met at the International Agency for Research on Cancer (IARC) in Lyon,

mutations[5] and chromosomal damage in rodents and in vitro (upon metabolic activation), but no human data on cancer mechanisms were available. The

cancer, was increased in one large cohort of reinforced plastics workers,[11] but cases were few and chance and confounding could not be discounted.

Lancet Oncol 2018
Published Online
April 18, 2018
http://dx.doi.org/10.1016/S1470-2045(18)30316-4