

## **A follow-up study of occupational styrene exposure and risk of autoimmune rheumatic diseases**

Supplementary material

Supplementary Table 1. Adjusted incidence rate ratios with 95% confidence interval for systemic sclerosis, rheumatoid arthritis, systemic lupus erythematosus, small vessel vasculitis, and Sjögren's syndrome by duration of employment, mean styrene exposure intensity and mean styrene exposure probability in 59 997 male and 12 215 female workers in the Danish reinforced plastics industry, 1979 to 2012.						
		Men				
		Systemic sclerosis (n=22)	Reumatoid arthritis (n=359)	Systemic lupus erythematosus (n=23)	Small vessel vasculitis (n=61)	Sjögren's syndrome (n=18)
Exposure metric	Person-years	IRR (95 % CI) <sup>a</sup>	IRR (95 % CI) <sup>a</sup>	IRR (95 % CI) <sup>a</sup>	IRR (95 % CI) <sup>a</sup>	IRR (95 % CI) <sup>a</sup>
<b>Duration of employment</b>						
<1 year	585 835	1	1	1	1	1
1-4 years	457 832	0.63 (0.21-1.84)	1.22 (0.96-1.54)	1.42 (0.58-3.51)	1.00 (0.56-1.78)	0.80 (0.28-2.24)
≥5 years	219 230	1.57 (0.59-4.20)	1.33 (1.01-1.74)	1.08 (0.33-3.56)	1.06 (0.55-2.05)	0.68 (0.18-2.55)
Per year (trend)		1.07 (0.99-1.15)	1.02 (1.00-1.04)	0.96 (0.84-1.09)	1.00 (0.95-1.06)	0.86 (0.69-1.08)
<b>Mean exposure intensity</b>						
≤11 mg/m <sup>3</sup>	370 818	1	1	1	1	1
12-39 mg/m <sup>3</sup>	434 564	3.33 (0.72-15.34)	1.25 (0.93-1.68)	0.90 (0.36-2.26)	0.84 (0.41-1.72)	0.47 (0.13-1.63)
≥40 mg/m <sup>3</sup>	457 515	2.52 (0.53-12.01)	1.38 (1.03-1.85)	0.24 (0.06-0.92)	1.24 (0.63-2.42)	0.83 (0.28-2.48)
Per 10 mg/m <sup>3</sup>		1.00 (0.92-1.08)	1.02 (1.00-1.03)	0.87 (0.75-1.02)	1.03 (1.00-1.07)	1.01 (0.93-1.11)
<b>Mean styrene exposure probability</b>						
≤22 %	330 820	1	1	1	1	1
23-56 %	444 077	0.99 (0.35-2.76)	0.97 (0.75-1.26)	1.45 (0.56-3.73)	1.28 (0.68-2.41)	0.32 (0.08-1.21)
≥57 %	488 000	0.98 (0.33-2.88)	1.08 (0.83-1.41)	0.45 (0.13-1.59)	1.11 (0.57-2.17)	0.70 (0.25-1.97)
Per 1 %		0.91 (0.18-4.62)	1.15 (0.78-1.70)	0.35 (0.07-1.80)	1.07 (0.41-2.78)	0.73 (0.13-4.21)

		Women				
		Systemic sclerosis (n=9)	Reumatoid arthritis (n=168)	Systemic lupus erythematosus (n=15)	Small vessel vasculitis (n=19)	Sjögren's syndrome (n=24)
Exposure metric	Person-year	IRR (95 % CI) <sup>a</sup>	IRR (95 % CI) <sup>a</sup>	IRR (95 % CI) <sup>a</sup>	IRR (95 % CI) <sup>a</sup>	IRR (95 % CI) <sup>a</sup>
Duration of employment						
<1 year	106 014	1	1	1	1	1
1-4 years	101 133	0.26 (0.03-2.38)	1.00 (0.72-1.38)	1.22 (0.41-3.64)	2.82 (0.90-8.89)	0.94 (0.38-2.32)
≥5 years	45 082	2.53 (0.61-10.56)	0.51 (0.31-0.84)	0.85 (0.17-4.28)	2.04 (0.50-8.23)	1.04 (0.35-3.09)
Per year (trend)		1.08 (0.96-1.21)	0.97 (0.93-1.02)	1.01 (0.87-1.17)	1.03 (0.93-1.13)	0.98 (0.87-1.10)
Mean exposure intensity						
≤11 mg/m <sup>3</sup>	152 658	1	1	1	1	1
12-39 mg/m <sup>3</sup>	60 677	0.52 (0.06-4.66)	1.25 (0.87-1.78)	2.34 (0.77-7.11)	0.38 (0.11-1.34)	0.88 (0.33-2.32)
≥40 mg/m <sup>3</sup>	38 894	2.63 (0.57-12.00)	1.20 (0.78-1.84)	0.60 (0.07-5.02)	-	1.04 (0.33-3.24)
Per 10 mg/m <sup>3</sup>		1.14 (1.01-1.29)	1.03 (0.98-1.08)	0.96 (0.78-1.19)	0.47 (0.24-0.94)	0.96 (0.82-1.12)
Mean styrene exposure probability						
≤22 %	163 041	1	1	1	1	1
23-56 %	54 142	2.30 (0.51-10.39)	0.97 (0.65-1.45)	0.59 (0.13-2.70)	0.69 (0.20-2.42)	1.19 (0.47-3.04)
≥57 %	35 046	2.81 (0.48-16.42)	1.54 (1.01-2.35)	1.24 (0.32-4.75)	0.77 (0.17-3.50)	0.33 (0.04-2.56)
Per 1 %		5.53 (0.38-80.54)	2.09 (1.07-4.08)	1.42 (0.16-12.74)	0.47 (0.04-4.93)	0.47 (0.06-4.03)

<sup>a</sup> Adjusted for age, calendar year, educational level

- : no observations

Supplementary table 2. Adjusted <sup>1</sup> incidence rate ratios with 95% confidence interval for systemic sclerosis, rheumatoid arthritis, systemic lupus erythematosus, primary systemic vasculitis, and Sjögren's syndrome by cumulated styrene exposure in windows of time of exposure in 59 997 male and 12 215 female workers in the Danish reinforced plastics industry, 1979 to 2012.						
		Men				
		Systemic sclerosis (n=22)	Rheumatoid arthritis (n=359)	Systemic lupus erythematosus (n=23)	Small vessel vasculitis (n=61)	Sjögren's syndrome (n=18)
Cumulated styrene exposure in time windows	Person- years	IRR (95 % CI) <sup>a</sup>	IRR (95 % CI) <sup>a</sup>	IRR (95 % CI) <sup>a</sup>	IRR (95 % CI) <sup>a</sup>	IRR (95 % CI) <sup>a</sup>
1-5 years						
Unexposed <sup>b</sup>	941 804	1	1	1	1	1
1-16 mg/m <sup>3</sup> -years	148 753	1.89 (0.53-6.73)	0.96 (0.64-1.43)	0.30 (0.04-2.30)	0.43 (0.10-1.77)	0.51 (0.07-3.93)
≥17 mg/m <sup>3</sup> -years	172 340	0.97 (0.20-4.56)	1.04 (0.68-1.58)	-	0.91 (0.33-2.50)	0.97 (0.11-8.32)
Per 100 mg/m <sup>3</sup>		0.92 (0.40-2.13)	1.03 (0.86-1.23)	n.a	1.05 (0.73-1.49)	n.a
6-10 years						
Unexposed <sup>b</sup>	935 384	1	1	1	1	1
1-23 mg/m <sup>3</sup> -years	151 523	1.59 (0.46-5.51)	0.73 (0.49-1.11)	1.67 (0.55-5.09)	0.32 (0.08-1.33)	2.47 (0.78-7.83)
≥24 mg/m <sup>3</sup> -years	175 990	0.31 (0.04-2.45)	1.02 (0.69-1.49)	0.36 (0.05-2.84)	0.51 (0.17-1.50)	2.86 (0.52-15.67)
Per 100 mg/m <sup>3</sup>		1.05 (0.68-1.63)	1.01 (0.87-1.17)	0.09 (0.00-9.47)	0.90 (0.58-1.40)	1.08 (0.51-2.25)
11-15 years						
Unexposed <sup>b</sup>	969 997	1	1	1	1	1
1-32 mg/m <sup>3</sup> -years	135 108	1.38 (0.31-6.12)	1.03 (0.72-1.48)	1.82 (0.61-5.46)	0.48 (0.15-1.54)	0.97 (0.22-4.27)
≥33 mg/m <sup>3</sup> -years	157 792	2.55 (0.93-6.96)	1.09 (0.78-1.53)	-	0.69 (0.26-1.80)	-
Per 100 mg/m <sup>3</sup>		1.10 (0.80-1.51)	1.05 (0.94-1.16)	0.16 (0.01-4.86)	1.05 (0.81-1.35)	n.a
≥16 years						
Unexposed <sup>b</sup>	733 858	1	1	1	-	1
1-49 mg/m <sup>3</sup> -years	245 006	0.51 (0.14-1.86)	1.15 (0.87-1.53)	2.67 (0.95-7.54)	2.62 (1.27-5.40)	0.38 (0.10-1.39)
≥50 mg/m <sup>3</sup> -years	284 033	0.87 (0.32-2.36)	1.34 (1.04-1.74)	1.46 (0.46-4.58)	2.37 (1.16-4.84)	0.42 (0.13-1.37)
Per 100 mg/m <sup>3</sup>		1.04 (0.92-1.17)	1.02 (0.99-1.05)	0.87 (0.61-1.24)	1.05 (1.00-1.11)	0.73 (0.41-1.31)

		Women				
		Systemic sclerosis (n=9)	Rheumatoid arthritis (n=168)	Systemic lupus erythematosus (n=15)	Small vessel vasculitis (n=19)	Sjögren's syndrome (n=24)
Cumulated styrene exposure in time windows	Person- years	IRR (95 % CI) <sup>a</sup>	IRR (95 % CI) <sup>a</sup>	IRR (95 % CI) <sup>a</sup>	IRR (95 % CI) <sup>a</sup>	IRR (95 % CI) <sup>a</sup>
1-5 years						
Unexposed <sup>b</sup>	187 474	1	1	1	1	1
1-16 mg/m <sup>3</sup> -years	44 164	-	0.86 (0.53-1.41)	1.24 (0.37-4.16)	2.17 (0.66-7.14)	1.84 (0.60-5.60)
≥17 mg/m <sup>3</sup> -years	20 591	-	0.50 (0.20-1.25)	-	3.73 (0.75-18.65)	-
Per 100 mg/m <sup>3</sup>		-	0.40 (0.09-1.70)	0.22 (0.00-123.12)	1.25 (0.40-3.89)	n.a
6-10 years						
Unexposed <sup>b</sup>	188 395	1	1	1	1	1
1-23 mg/m <sup>3</sup> -years	44 142	3.18 (0.70-14.48)	0.93 (0.58-1.47)	0.26 (0.03-2.02)	1.78 (0.56-5.61)	1.08 (0.31-3.72)
≥24 mg/m <sup>3</sup> -years	19 692	2.54 (0.25-25.60)	1.02 (0.51-2.02)	-	1.15 (0.14-9.58)	-
Per 100 mg/m <sup>3</sup>		1.21 (0.42-3.48)	0.82 (0.48-1.40)	n.a	0.78 (0.12-5.17)	n.a
11-15 years						
Unexposed <sup>b</sup>	197 366	1	1	1	1	1
1-32 mg/m <sup>3</sup> -years	38 785	0.71 (0.08-6.13)	0.50 (0.27-0.90)	1.89 (0.59-6.03)	1.70 (0.55-5.21)	1.56 (0.52-4.63)
≥33 mg/m <sup>3</sup> -years	16 078	7.01 (0.99-49.90)	1.05 (0.55-1.98)	-	-	-
Per 100 mg/m <sup>3</sup>		2.06 (1.56-2.72)	0.99 (0.71-1.38)	0.59 (0.05-6.52)	0.18 (0.00-23.29)	0.67 (0.07-6.60)
≥16 years						
Unexposed <sup>b</sup>	152 022	1	1	1	1	1
1-49 mg/m <sup>3</sup> -years	69 439	0.68 (0.12-4.01)	0.98 (0.67-1.41)	2.42 (0.76-7.69)	0.77 (0.28-2.11)	0.26 (0.08-0.79)
≥50 mg/m <sup>3</sup> -years	30 768	1.66 (0.26-10.74)	1.22 (0.79-1.88)	-	0.22 (0.03-1.77)	0.80 (0.30-2.18)
Per 100 mg/m <sup>3</sup>		0.89 (0.36-2.20)	1.05 (0.96-1.15)	0.68 (0.18-2.61)	0.06 (0.00-2.03)	0.77 (0.40-1.46)

<sup>a</sup> Adjusted for age, calendar year, educational level

<sup>b</sup> Unexposed refers to exposed person-years that lies outside the time window of interest

n.a: not applicable

- : no observations