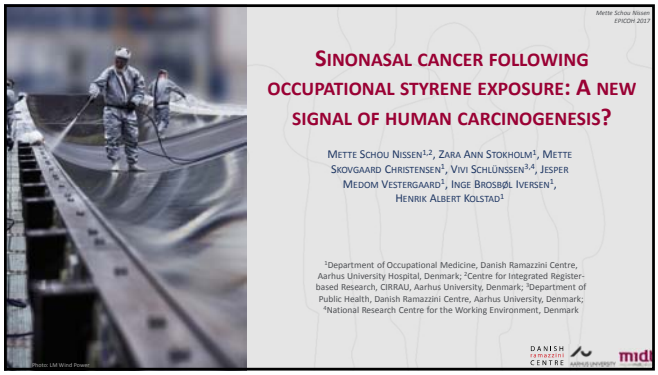
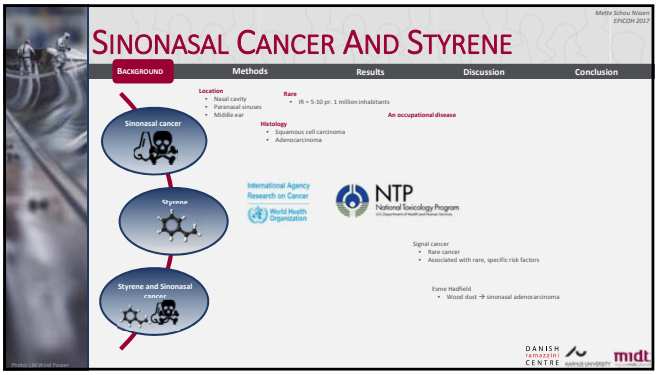


Sinonasal cancer following occupational styrene exposure: A new signal of human carcinogenesis?

Mette Schou Nissen[1,2], Zara Ann Stokholm[1], Mette Skovgaard Christensen[1], Vivi Schlünssen[3,4], Jesper Medom Vestergaard[1], Inge Brosbøl Iversen[1], Henrik Albert Kolstad[1]

[1]Department of Occupational Medicine, Danish Ramazzini Centre, Aarhus University Hospital, Denmark; [2]Centre for Integrated Register-based Research, CIRRAU, Aarhus University, Denmark; [3]Department of Public Health, Danish Ramazzini Centre, Aarhus University, Denmark; [4]National Research Centre for the Working Environment, Denmark



Sinonasal Cancer And Styrene

Sinonasal cancer

Location
- Nasal cavity
- Paranasal sinuses
- Middle ear

Rare
- IR = 5-10 pr. 1 million inhabitants

An occupational disease

Histology
- Squamous cell carcinoma
- Adenocarcinoma

Styrene

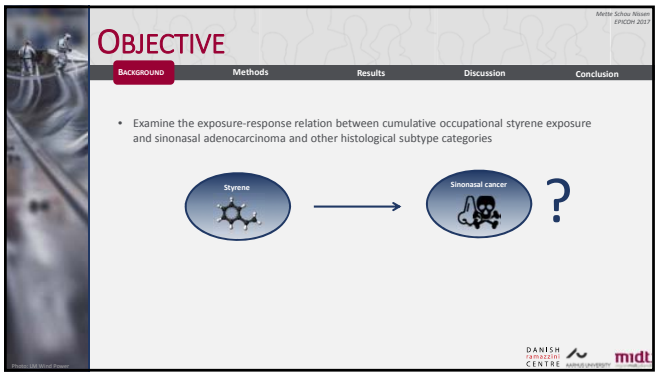
International Agency Research on Cancer
World Health Organization

NTP National Toxicology Program

Styrene and Sinonasal cancer

Signal cancer
- Rare cancer
- Associated with rare, specific risk factors

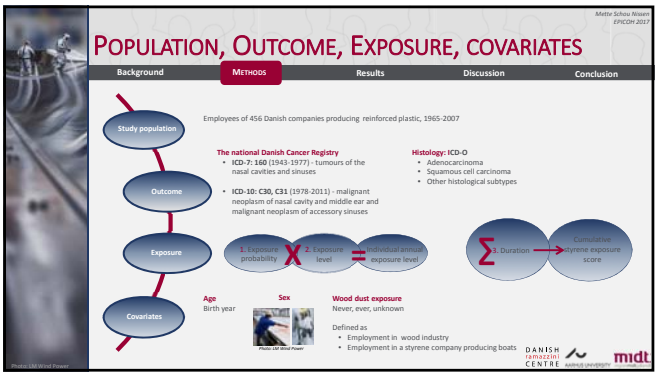
Eime Hadfield
- Wood dust → sinonasal adenocarcinoma



Objective

- Examine the exposure-response relation between cumulative occupational styrene exposure and sinonasal adenocarcinoma and other histological subtype categories

Styrene → Sinonasal cancer ?



Population, Outcome, Exposure, covariates

Study population

Employees of 456 Danish companies producing reinforced plastic, 1965-2007

Outcome

The national Danish Cancer Registry
- ICD-7: 160 (1943-1977) - tumours of the nasal cavities and sinuses
- ICD-10: C30, C31 (1978-2011) - malignant neoplasm of nasal cavity and middle ear and malignant neoplasm of accessory sinuses

Histology: ICD-O
- Adenocarcinoma
- Squamous cell carcinoma
- Other histological subtypes

Exposure

1. Exposure probability X 2. Exposure level = Individual annual exposure level

Σ 3. Duration → Cumulative styrene exposure score

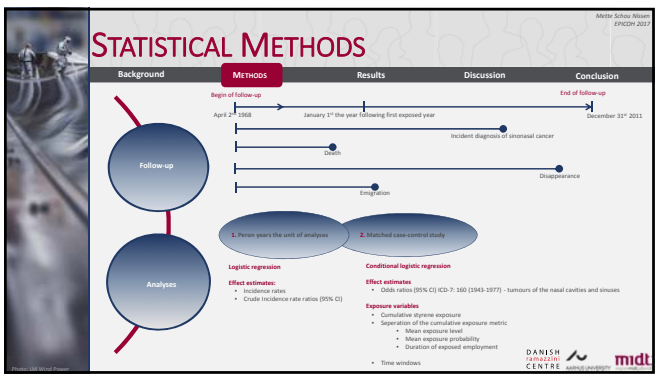
Covariates

Age
Birth year

Sex

Wood dust exposure
Never, ever, unknown

Defined as
- Employment in wood industry
- Employment in a styrene company producing boats



Statistical Methods

Follow-up

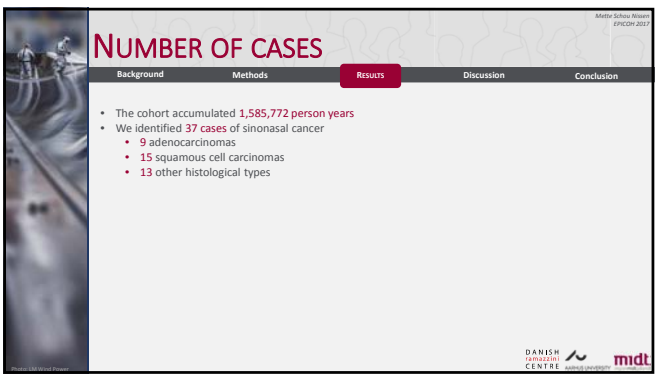
Begin of follow-up: April 2nd 1968 / January 1st the year following first exposed year
End of follow-up: December 31st 2011
Incident diagnosis of sinonasal cancer
Death
Disappearance
Emigration

Analyses

1. Peron years the unit of analyses
Logistic regression
Effect estimates:
- Incidence rates
- Crude Incidence rate ratios (95% CI)

2. Matched case-control study
Conditional logistic regression
Effect estimates
- Odds ratios (95% CI) ICD-7: 160 (1943-1977) - tumours of the nasal cavities and sinuses

Exposure variables
- Cumulative styrene exposure
- Seperation of the cumulative exposure metric
  - Mean exposure level
  - Mean exposure probability
  - Duration of exposed employment
- Time windows



Number of cases

- The cohort accumulated 1,585,772 person years
- We identified 37 cases of sinonasal cancer
  - 9 adenocarcinomas
  - 15 squamous cell carcinomas
  - 13 other histological types

RISK OF SINONASAL CAN

Background | Methods | RESULTS

Unadjusted analyses
- IR
- IRR

Adjusted analyses
- OR

INCIDENCE RATES AND UNADJUSTED INCIDENCE RATE RATIOS with 95% confidence intervals of sinonasal adenocarcinoma, squamous cell carcinoma, and a category of other histological subtypes by cumulative styrene exposure level in the Danish reinforced plastics industry, 1968-2011

Cumulated styrene exposure level (mg/m³-years)	Adenocarcinoma (n=9) IR*	Adenocarcinoma (n=9) IRR (95% CI)	Squamous cell carcinoma (n=15) IR*	Squamous cell carcinoma (n=15) IRR (95% CI)	Other histological subtypes (n=13) IR*	Other histological subtypes (n=13) IRR (95% CI)
Low (<37.26)	0.13	1.00 (reference)	0.63	1.00 (reference)	0.76	1.00 (reference)
High (≥37.26)	1.01	8.00 (1.00-63.97)	1.26	2.00 (0.68-5.85)	0.88	1.17 (0.39-3.47)
P_{trend}†		0.005		0.623		0.531

Abbreviations: IR=incidence rate; IRR=incidence rate ratio; CI=confidence interval
*Per 100 000 person-years
†Two-sided P-value for linear test for trend conducted with a continuous exposure variable

Odds ratios with 95% confidence intervals of sinonasal adenocarcinoma, squamous cell carcinoma, and a group of other histological subtypes by styrene exposure level in the Danish reinforced plastics industry, 1968-2011

	Adenocarcinoma (n=9) OR* (95% CI)	Squamous cell carcinoma (n=15) OR* (95% CI)	Other histological subtypes (n=13) OR* (95% CI)
Cumulated styrene exposure level (mg/m³-years)†			
Low (<37.26)	1.00 (reference)	1.00 (reference)	1.00 (reference)
High (≥37.26)	5.11 (0.58-45.12)	1.15 (0.34-3.89)	0.74 (0.22-2.42)
P_{trend}‡	0.207	0.840	0.255
Mean exposure level (mg/m³-years)§			
Low (<25.3)	1.00 (reference)	1.00 (reference)	1.00 (reference)
High (≥25.3)	2.06 (0.38-11.25)	0.43 (0.14-1.32)	0.45 (0.13-1.53)
P_{trend}‡	0.119	0.731	0.485
Mean exposure probability (%)§			
Low (<15.5)	1.00 (reference)	1.00 (reference)	1.00 (reference)
High (≥15.5)	1.82 (0.39-8.45)	1.46 (0.47-4.20)	0.94 (0.20-3.04)
P_{trend}‡	0.098	0.858	0.374
Duration of exposed employment (years)			
<5	1 (reference)	1.00 (reference)	1.00 (reference)
≥5	2.30 (0.64-9.73)	0.96 (0.26-3.55)	0.24 (0.03-1.95)
P_{trend}‡	0.251	0.680	0.583

Abbreviations: OR=odds ratio; CI=confidence interval
*Cases and controls are matched on age (birth year), sex, and employment in wood industry (never, ever, unknown)
†Categories were generated according to the person-year median
‡Two-sided P-value for linear test for trend conducted with a continuous exposure variable

TIME WINDOWS

Mette Schou Nissen EPICOH 2017

Background | Methods | RESULTS | Discussion | Conclusion

TIME WINDOWS. Odds ratios with 95% confidence intervals of sinonasal adenocarcinoma by styrene exposure received during the prior <15, 15-29 and >30 years in the Danish reinforced plastics industry, 1968-2011

Styrene exposure	>15 years prior OR* (95% CI)	15-29 years prior OR* (95% CI)	≥30 years prior OR* (95% CI)
Never exposed	1. 00 (reference)	1. 00 (reference)	1. 00 (reference)
Ever exposed	3.88 (0.71-21.05)	0.80 (0.18-3.67)	0.43 (0.06-3.33)

Abbreviations: OR=odds ratio; CI=confidence interval
*Cases and controls are matched on age (birth year), sex, and employment in wood industry (never, ever, unknown)

STRENGTHS AND LIMITATIONS

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Background | Methods | Results | DISCUSSION | Conclusion

The National Danish Registers	Large population and long follow-up → studying the risk of rare cancers Complete and validated topographic and morphologic cancer information → histology-specific analysis
Information bias	Outcome- and exposure-information independent of the participants → misclassification expected to be non-differential and unlikely to explain our findings
Selection bias	High coverage of the registries → recruitment and follow-up almost complete → reduced risk of selection bias
Confounding	Wood dust: Employment in wood industry a crude proxy for wood dust exposure → Residual confounding? Other risk factors : Nickel, leather-dust, formaldehyde? Tobacco smoking? → unmeasured
Major limitation	Small number of cases

CONCLUSION

Mette Schou Nissen EPICOH 2017

Background | Methods | Results | Discussion | CONCLUSION

- Suggestive of an increased risk of sinonasal adenocarcinoma following high-level styrene exposure
- It may signal a carcinogenic effect
- No firm conclusions can be drawn

SINONASAL CANCER FOLLOWING OCCUPATIONAL STYRENE EXPOSURE: A NEW SIGNAL OF HUMAN CARCINOGENESIS?

- MAYBE