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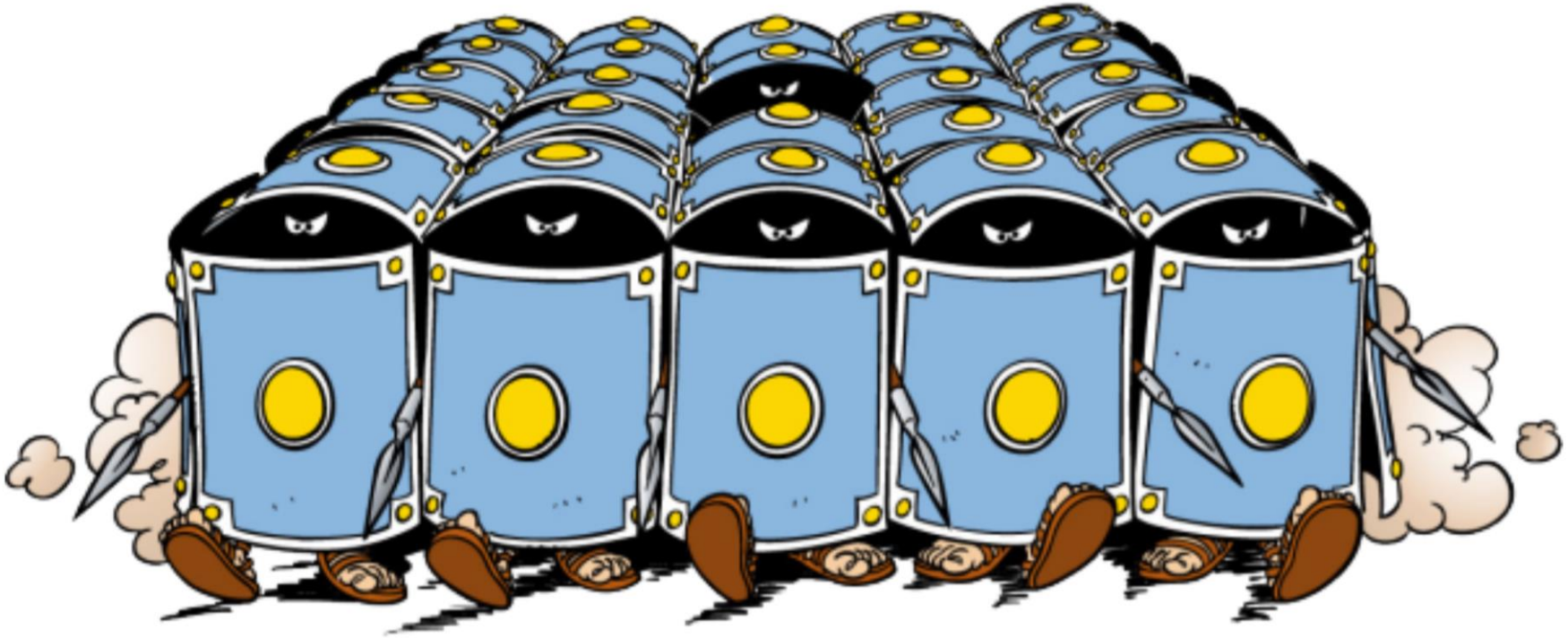
Cohort studies

Maria Albin (made the presentation) & Ingrid Sivesind Mehlum (presenter)

What is a cohort?

A Roman military legion consisted of 10 cohorts, each with 300-600 soldiers



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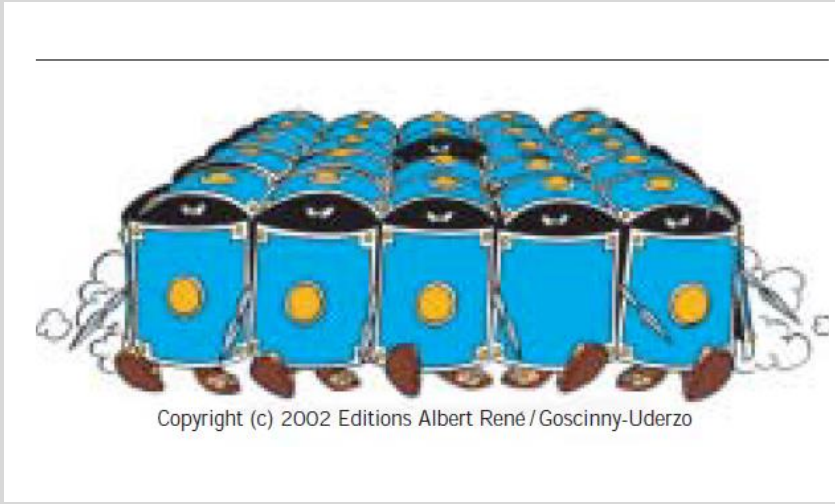
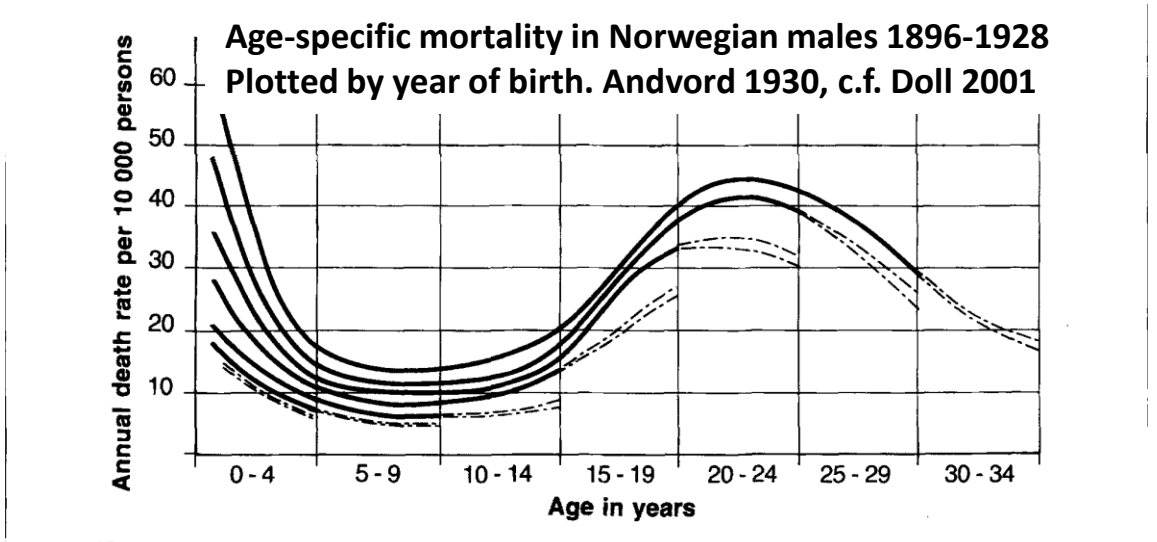
For today

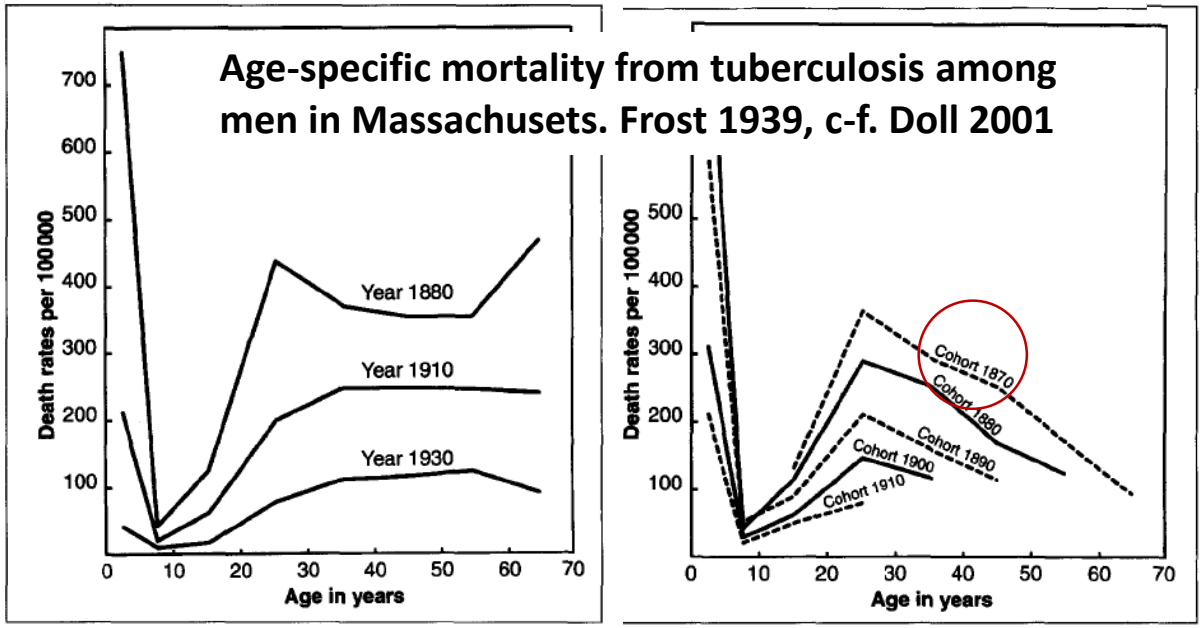
- Cohort design: Why?
- Finding your cohort
- Exposure contrast
- Inclusion criteria
- Effect modification/Susceptible groups
- Usability for risk assessment
- Describing the study for impact
- Challenges and opportunities



Why a cohort design?

- Efficient for rare exposures when high exposure populations can be accessed
- Incidence of outcome
- Continuous outcome measures
- Change in exposure and outcome over time
- Option to study many outcomes
  - E.g. malignant and non-malignant lung diseases, several cancer sites…
- Communication:
  - Straight forward, well established
- Draw-backs: May be costly, time-consuming…(efficiency an issue)





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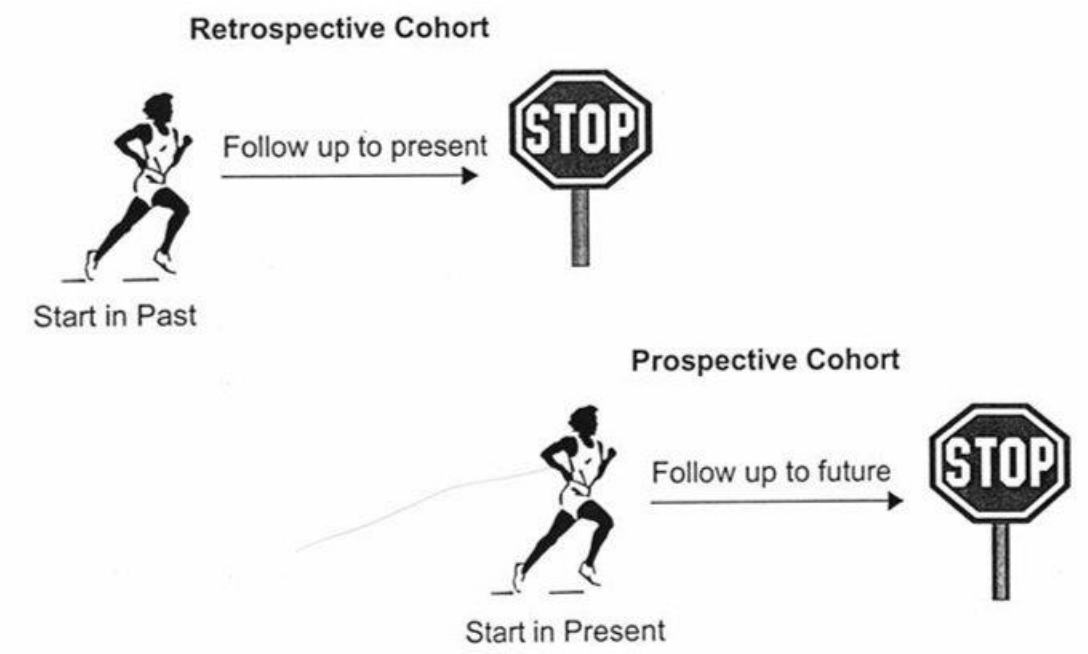
Finding your cohort

- Accessible data on *both* exposure and outcome
- Group with shared property followed over time,
  - many possibilities, e.g. birth cohort, factory cohort, profession, general population….
  - but identification of cohort may be a challenge
    (e.g. in manufacturing vs. service sector)
- Prevalence of exposure of interest may decide your choice

- Two time perspectives (advantages/disadvantages?)
  - Prospective
  - Retrospective

Data already collected



Data collection starts now

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Exploring causes of lung cancer

- 1950s rising incidence – why?
- High proportion of lung cancer at autopsy of workers with asbestosis
  - Indicative, not proof of association

- Asbestos factory with
  - ”Scheduled” (very dusty areas) subject to special regulations since the 1930s
  - Focus on long service (20+ yrs) in such areas (feasible and efficient): 113 men
    - All traced!

NUMBER OF MAN-YEARS LIVED BY MEN WITH 20 OR MORE YEARS OF WORK IN A "SCHEDULED AREA"

Age (years)	Period					All Periods
	1922–33	1934–38	1939–43	1944–48	1949–53	
30–	0	0·5	1·5	0	0	2
35–	4·5	2	11	17·5	9	44
40–	9·5	16	33·5	48	55	162
45–	9·5	19·5	50	78·5	84	241·5
50–	6·5	25·5	39·5	85	96·5	253
55–	12	6	30	52	85·5	185·5
60–	15	3	5·25	25·5	36	84·75
65–	1	13·5	3	10	21·5	49
70–	0	2	9	3	3·5	17·5
75–79	0	0	1	1·5	0·5	3
All ages	58	88	183·75	321	391·5	1042·25

- Comparison with mortality rates among men in England and Wales in same 5-year age- and calendar-year classes

R Doll Br J Ind Med 1955

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Causes of death in men working 20+ years in ”scheduled” asbestos work (N=113)

	Observed	Expected	p-value	SMR*
Lung cancer - mention of asbestosis - asbestosis not mentioned	11 0	- 0.8	<<0.0001	14
Other respiratory and cardiovascular disease	20	7.6	<0.001	2.6
All causes	39	15	<<0.0001	2.5

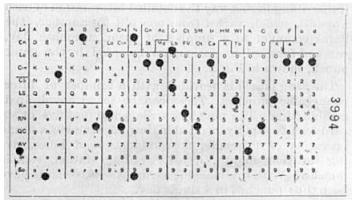
This study established the association between asbestos exposure and lung cancer

*Standardized mortality ratio: Observed/Expected from comparison population (not in original publication)

R Doll Br J Ind Med 1955

Lung cancer and smoking

- Doctors would make a suitable population to study
- Mailed questionnaire to 60,000 doctors
  - 40,000 responded
  - 7 questions
- 53 months of follow-up
- 1854 deaths identified by professional organisations, and Registrars-General (also cause of death)



Doll and Hill 1956

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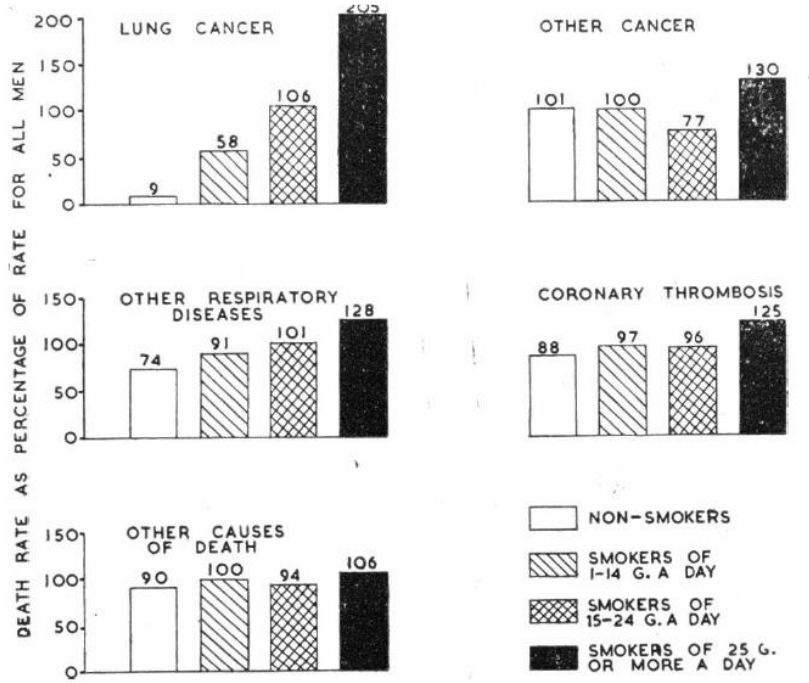
TABLE II.—*Total Number of Man-Years of Exposure by Non-smokers and Smokers of Different Amounts of Tobacco: Men Only, Divided by Age*

Age in Years	Non-Smokers*	All Smokers	Men Smoking a Daily Average of:		
			1–14 g.†	15–24 g.	25 g. or More
Under 35	10,143	25,346	12,548	10,002	2,796
35–44 ..	7,130	34,081	13,625	13,380	7,076
45–54 ..	4,136	28,020	9,477	10,371	8,172
55–64 ..	1,907	18,002	6,333	6,514	5,155
65–74 ..	1,078	11,384	5,201	3,893	2,290
75–84 ..	720	5,711	3,334	1,701	676
85 and over	136	892	616	230	46
All ages	25,250	123,436	51,134	46,091	26,211

* A non-smoker is defined as a person who has never consistently smoked as much as 1 g. of tobacco a day for as long as one year.
† 1 cigarette is equivalent to 1 g. of tobacco.



Relationship between death rate, expressed as a percentage of the rate for all men, and the amount smoked, for five disease groups.

Hair dressers and risk of asthma

- Recruitment?
  - Self-employed or small employer
  - Low unionization
- Registries of examinations from vocational training schools
  - Survey sent to 7000+ female hairdressers and age-matched population referents (1:1)
    - Periods of work as hairdresser
    - Asthma diagnosis (year)

Asthma incidence per 1000 p-yrs

• Hairdresser, all years	3.5
• Working as hairdresser	3.9
• Other years	2.9
• Referents, all years	3.2

Three conclusions:

- Including unexposed years as exposed would attenuate the risk (exposure misclassification)
- Higher risk during exposed than unexposed years support association with exposure
- Moderately increased asthma incidence during hairdressing work

Albin et al. 2002

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Lung function in hairdressers

- Systematic enrolment of hairdressing salons in community (Hebron) in 2008
- Survey with spirometry (N=170) repeated in 2013 (N=161)
- Internal comparisons
- Greater yearly decline in FVC and FEV_1 when working as a hairdresser during follow-up
  - Current (n=133): FVC: -35 ml (95% CI: -44, -26), FEV_1: -31 ml (95% CI: -25, -36)
  - Former (n=28): FVC: -6 ml (95% CI:-27, +16), FEV_1: -11 ml (95% CI: -26, +3)
- High exposures (as indicated by ammonia levels)!

(Nemer et al. 2015)

Exposure contrast

- Ideally only grade of exposure differs between your exposed population and the reference population
  - Unexposed population within cohort? (Unexposed time under follow-up)
  - For rare outcomes a large reference population may be needed (malformations, rare cancers) – national general population only possibility?
- For some occupations, selection into exposure may be conditional on NOT having the outcome of interest, and selection out of exposure on having preconditions for it
  - Some jobs may have routines which are preventive (e.g. physical fitness requirements, smoking not permitted in factory area)
  - Investigating risk for cardiovascular disease or COPD in firefighters – how would you find a group to compare with?

Detailed exposure information AND power

Untapped sources – routinely collected information

- Night shift work – administrative register
- Incidence of cerebrovascular disease increased with
  - Night shifts* (0.3% per shift)
  - 3+ consecutive nights* (1.8% per time)
  - Quick returns from nights* (0.6% per time)
  - Years worked with nights (8% per year)
- Effect of consecutive nights and quick returns independent from number of night shifts
- May inform scheduling of work

Bigert et al. 2022

Case-cohort/nested case-control approach

- Solution when needed exposure information has high cost/person
  - e.g. analyses of biological samples
  - detailed case-by-case exposure assessment by occupational hygienist (e.g. job tasks)
- Keep all cases
- Select sample of non-cases from same cohort
  - matched (case-control)
  - unmatched subcohort (case-cohort)

* Exposure preceding year

Left-truncation: What happened in the cohort population before observation starts?

Employment time

- Minimum employment time for inclusion can reduce loss to follow-up
- But employment duration is related to health
  - Susceptible individuals may have disappeared
  - Seniority may also protect from doing worst tasks
- First exposure year(s) may have highest risk for asthma/eczema
  - Consider including apprentices/new employees/entering vocational training

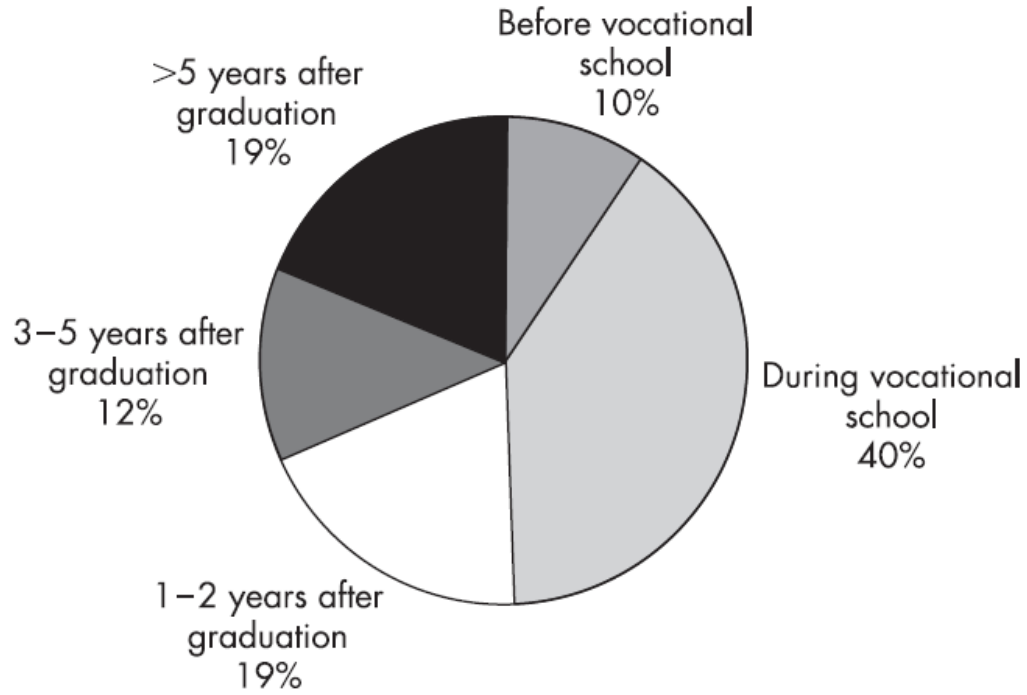

Figure 1 The proportion of hairdressers who reported onset of hand eczema during different time periods.

Lind et al 2007

Susceptible groups – handle with care

Hand eczema in hairdressers

- Twofold incidence compared to population controls (24 vs 10 per 1000 person-years)
- Interaction with atopy
  - 4-fold excess risk for skin atopy + hairdressing
  - But, removing all atopic subjects would only reduce the cases with 10% (not a viable solution!)

	IR (cases/1000 person-years)	
	Childhood eczema	No childhood eczema
Hairdressers	43.9 (112)	21.3 (437)
Population controls	19.0 (164)	8.1 (445)

Policy implications

- Hairdressing is a high-risk occupation for hand eczema.
- To prevent hand eczema in hairdressers, reduction of skin-damaging exposure is essential.
- A history of childhood eczema increases the individual risk of hand eczema, but is not a major risk factor for hand eczema among hairdressers.

Lind et al 2007

Usability for risk assessment

- Exposure metric
  - Preventive measures from ”low, medium, high”?
    - As close to measurable metric as possible
  - Cumulative measure also problematic if dose-rate is an issue
- Outcome metric
  - Relative risks useful to establish association
  - Excess risk more useful for quantitative risk assessment
    - Informs discussions on OELs
    - Especially for low-level (virtually no-threshold) effects: Not only cancer!

Describing the study – and having impact

- Reporting the study
  - STROBE checklist for cohort studies
    - Reduces risk for misunderstandings

- Keywords (finding the study)
  - Should be easy to find for systematic review

Cohort studies – new challenges and opportunities

- A new world of work – new ways to identify study populations
- New technologies – new options for exposure assessment
- Extended collaborations (e.g. OMEGA-NET)
- One exposure – multiple effects (without thresholds)
- New methods for data sharing/pooling

References

- Albin M, Rylander L, Mikoczy Z,et al. Incidence of asthma in female Swedish hairdressers. Occup Environ Med 2002;59:119-23
- Bigert C, Kader M, Andersson T,et al. Night and shift work and incidence of cerebrovascular disease - a prospective cohort study of healthcare employees in Stockholm. Scand J Work Environ Health. 2022;48:31-40.
- Doll R. Cohort studies: history of the method I. Prospective cohort studies. Soz Präventivmed 2001;46:75-86
- Doll R. Cohort studies: history of the method II. Retrospective cohort studies. Soz Präventivmed 2001:46;152-160
- Doll R. Mortality from lung cancer in asbestos workers. Br J Ind Med 1955;12:81-6
- Lind ML, Albin M, Brisman J,et al. Incidence of hand eczema in female Swedish hairdressers. Occup Environ Med. 2007;64:191-5
- Nemer M, Kristensen P, Nijem K, et al. Lung function and respiratory symptoms among female hairdressers in Palestine: a 5-year prospective study. BMJ Open. 2015 Oct 15;5(10):e007857.
- STROBE guidelines (https://www.strobe-statement.org/checklists/)