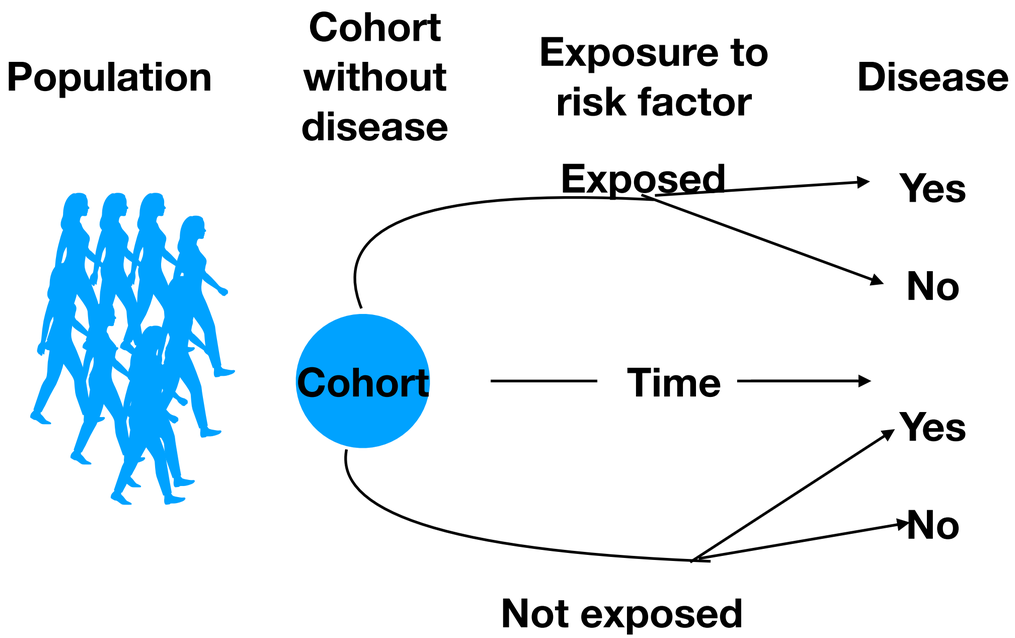
Risk

Exposure to disease

Observational study
Cohort study
Cohort
Exposed group
Unexposed group
Incidence study
Prospective cohort study
Retrospective/ historical cohort study
Case-cohort design
Measure of effect
Absolute risk
Attributable risk
Risk difference
Risk ratio
Population-attributable risk
Population-attributable fraction
Extraneous variable
Covariate
Crude measure of effect
Confounding

Intermediate outcome
Confounding
Intermediate outcome
Confounding variable/ confounder
Controlling
Restriction
Matching
Stratification
Standardization
Multivariable analysis
Logistic regression
Cox proportional hazard model
Unmeasured confounder
Residual confounding
Effect modification
Interaction
Mendelian randomization


Population
Cohort without disease
Exposure to risk factor
Disease
Exposed
Yes
No
Cohort
Time
Yes
No
Not exposed

Retrospective (historical) cohort

+advantage of computerized medical databased and population registries
less time, less expensive, more feasible than prospective.
Cannot undertake studies of factors not recorded in computerized data.
-Lifestyle, social standing and education are often not included.
-Medical care records = information collection not standardized=bias. Large databases useful for studying treatment/outcomes.

Prospective cohort

assess purported risk factors not captured in medical records (eg breast feeding)

Advantages	Disadvantages
All cohort study types	
The only way to establish incidence	Confoinding/bias susceptibility
If persons are exposed, do they get the disease?	
Exposure can be elicited without the bias that might occur if outcome was known on beforehand	
Can assess relationship between exposure and disease	
Retrospective cohort	
More efficient than prospective- data already collected	Range of possible risk factors that can be studied is more narrow than prospective study
Cheaper than prospective	Cannot examine patient charachteristics unavailabnle in data set
Faster than prospective (outcome has occurred)	
Case-cohort	
All advantages of retrospective	All disadvantages of retrospective cohort studies apply
More efficient than retrospective cohort because only a sample of unexposed group analyzed.	Difficult for readers to understand weighing

Express and compare risk: measures of effect

Absolute risk	Incidence of disease in a group initially free of the condition?	I= number of new cases/people
Attributable risk (risk difference)	Incidence if disease attributable to exposure?	AR=Incidence *exposed* - Incidence *unexposed*
Relative risk (risk ratio)	How many times more likely are the exposed to develop the disease?	RR=I *e*/I *ue*
Population-attriutable risk	What is the incidence of disease in a population associated with the prevalence of the risk factor?	AR*p*=AR * Prevalence
Population-attributable fraction	What fraction of the disease in a population is attributable to exposure of the risk factor?	AF*p*=AR*p*/I*t*

Population-attributable risk What is the incidence of disease in a population associated with the prevalence of the risk factor?

Population-attributable fraction What fraction of the disease in a population is attributable to exposure of the risk factor? Population attributable risk divided by the total incidence if disease in the population. (e.g. smoking: annually contributes to 156 lung cancer deaths for every 100000 men in the population=population-attributable risk; accounts for 82% of all lung cancer death in the population. = The more common a risk factor is, the bigger fraction of diseased associated with the risk factor.

Pitfalls when interpreting attributable and relative risk

Night work and miscarriage: a Danish nationwide register-based cohort study

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Abstract

Objective Observational studies indicate an association between working nights and miscarriage, but inaccurate exposure assessment precludes causal inference. Using payroll data with exact and prospective measurement of night work, the objec was to investigate whether working night shifts during pregnancy increases the risk of miscarriage.

Methods A cohort of 22 744 pregnant women was identified by linking the Danish Working Hour Database (DWHD), which holds payroll data on all Danish public hospital employees, with Danish national registers on births and admissions to hospitals (miscarriage). The risk of miscarriage during pregnancy weeks 4–22 according to measures of night work was analysed using Cox regression with time-varying exposure adjusted for a fixed set of potential confounders.

Results In total 377 896 pregnancy weeks (average 19.7) were available for follow-up. Women who had two or more night shifts the previous week had an increased risk of miscarriage after pregnancy week 8 (HR 1.32 (95% CI 1.07 to 1.62) compared with women, who did not work night shifts. The cumulated number of night shifts during pregnancy weeks 3–21 increased the risk of miscarriages in a dose-dependent pattern.

Conclusions The study corroborates earlier findings that night work during pregnancy may confer an increased risk of miscarriage and indicates a lowest observed threshold level of two night shifts per week.

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HR 1,32 (1,07-1,62)

Workplace

Table 1 Characteristics of the study population according to exposure of night work (n=22 744)

Characteristics	Exposed ≥1registered night shift during pregnancy week 3–21 (n=10 047)	Reference group No registered night shifts during pregnancy week 3–21 (n=12 697)
Outcome of pregnancy, n (%)		
Births	9 089 (90)	11 007 (87)
Miscarriages	740 (8)	1 149 (9)
Molar and ectopic pregnancies	44	96 (1)
Induced abortions	174 (2)	445 (3)
Time for miscarriage (pregnancy week)		
Gestational age, median (min, max)	9.0 (4.0, 21.0)	8.0 (4.0, 21.0)
Follow-up weeks at risk, median (Pct 25, 75)	22 (22,22)	22 (22,22)
Work during pregnancy weeks 3–21, median (Pct 25,75)		

Från 9% till 8% risk…?

When examined condition is common, the attributable risk increases

Confounding

Extraneous variable = *Covariates* are variables that are not the primary studied, but may be part of the study. (E.g. level of education). Term
not perfect – do not by definition co-vary… are not per definition extraneous, but may co-vary

Confounding – threat to validity of observational study. Confounding occurs when exposure is associated with another variable which is itself
related to the outcome -> systematic erroe (bias) where one effect is attributed to the wrong variable. A confopunding variable is:

1) associated with exposure.
2) Associated with disease.
3) Not a part of the causal chain from exposure to disease.

Intermediate outcome=events thar are part of the causal chain from exposure to disease.

Potential confounders? Previous research? Variables that makes sense based on matter knowledge.

Potential confounders?

Identify
Previous research?
Variables that makes sense based on matter knowledge.

Control for confounding
Randomization
Restriction
Matching
Stratification
Simple adjustment
Multivariable adjustment
Beest case/worst case analysis

Confirm
is variable associated with exposure and (separately) disease?
Does crude relationship changes when accounting for potential confounder?

Control for confounding

Randomization
Restriction
Matching
Stratification - data analysis, results presented for subgroups of patients
Simple adjustment - standardization: what would the overall rate of disease be if strata-specific rates were applied to a population made of similar proportions in each stratum?
Multivariable adjustment/multivariable analysis/mathematical modeling - consider effects of many variables simultaneously.
- Logistic regression=used in cohort and case-control studies (dichotomous outcome)
- Cox proportional hazard model=outcome is the time to the event (e.g. survival analyses)

Beest case/worst case analysis

Not one way of dealing with extraneous variables are without limitations
Only identified variables can be modeled

Effect modification
”A finding reported, not a bias avoided”

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