Explain the difference between:

- Case-control vs. Cross Sectional Study Design
- Analytical vs. Descriptive Studies
- Observational vs. Experimental studies
- Strengths vs. limitations of various study designs

An Odds Ratio of 3.3 would imply that there is a protective effect between the exposure and outcome of interest.

A. TRUE

B. FALSE

Which of the following is not true of case-control studies?

A. They are good for studying rare diseases

B. It is difficult to determine temporal sequence

C. They are subject to selection bias

D. They are good for establishing causation

Cross-sectional studies:

A. Allow us to calculate incidence of disease within in a population

B. Often underrepresent long-term diseases

C. Can be both descriptive or analytical

D. Do not allow for the calculation of a measure of effect (e.g. odds ratio)

According to the case-control study on the association between drowning and swimming lessons:

A. Participation in formal swimming lessons was associated with an 88% reduction in drowning in the 1-4 year old age group.

B. Formal swimming lessons had no impact on drowning outcomes

C. Formal swimming lessons and drowning showed an Odds Ratio of 2.4

D. Any exposure to swimming activity – formal or otherwise, decreased the risk of drowning in this population.

Cohort Studies

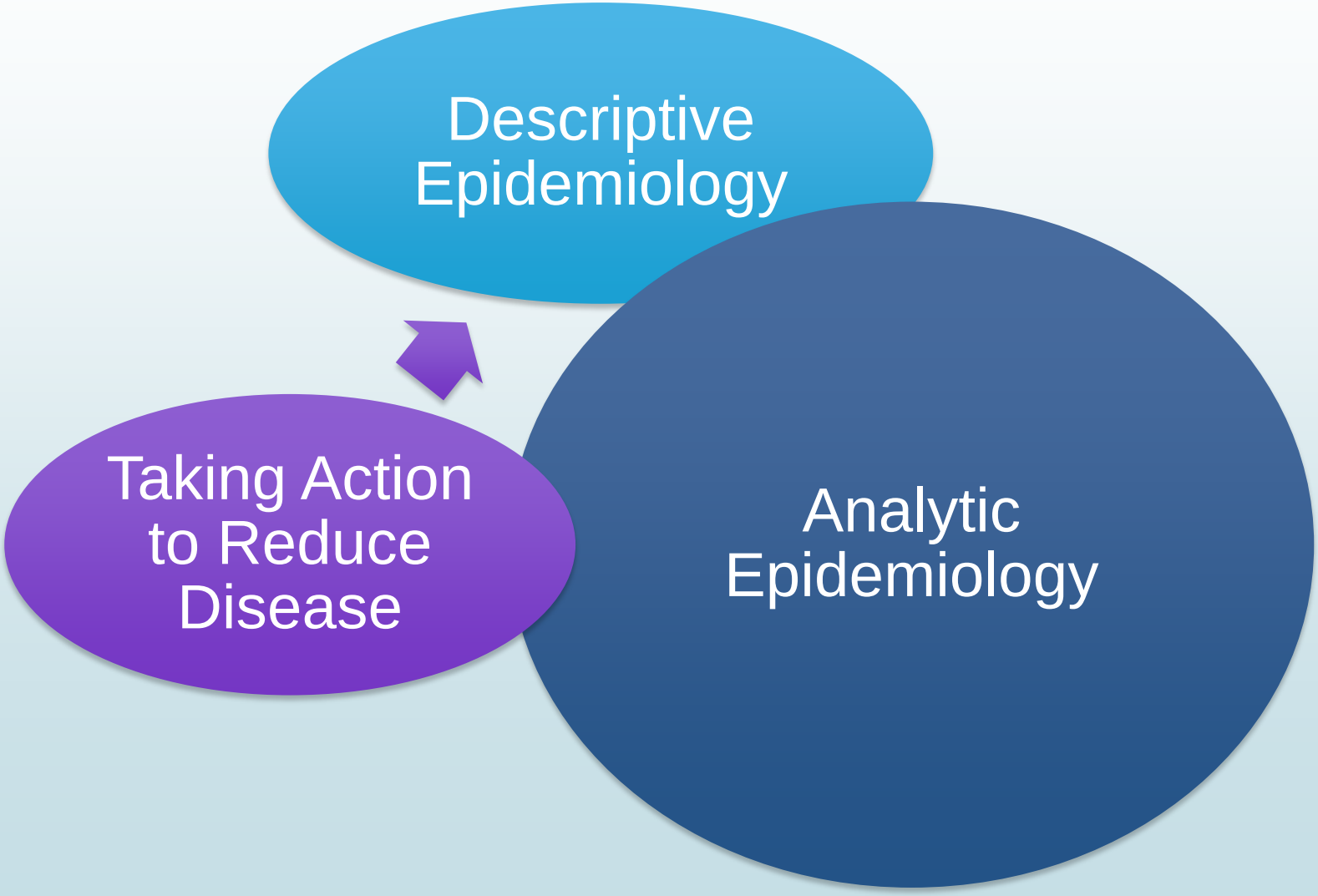
HLSC 2003 Epidemiology

Class 7

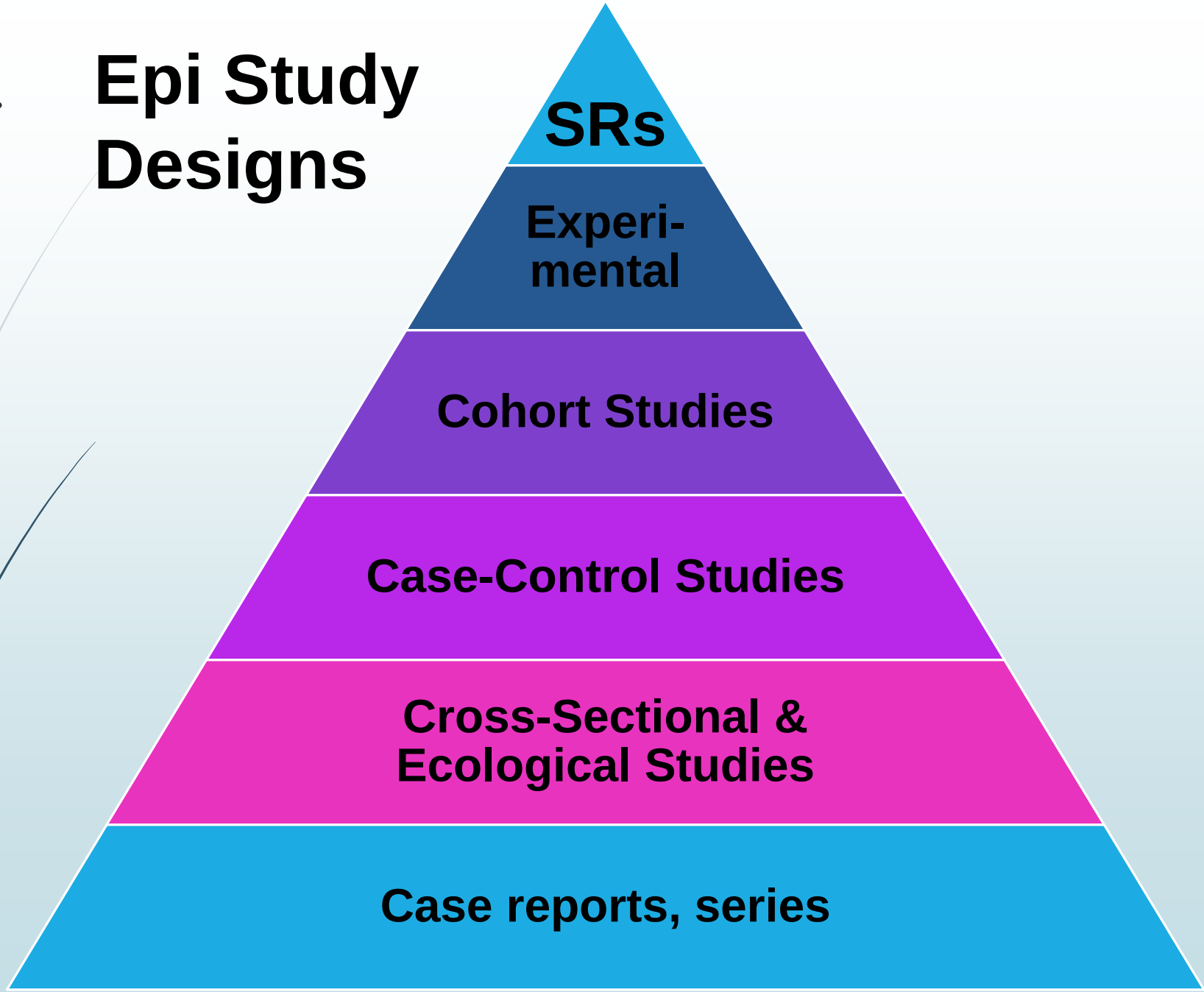
Faculty of health Sciences

University of Lethbridge

Where are we in the epi cycle?



Epi Study Designs



Class 9: Learning Objectives

1. Explain the **goal of a cohort study**, and how it ***differs*** from a case control study.
2. Distinguish between a **prospective** and a **retrospective** cohort study.
3. Calculate and interpret **relative risks**.
4. Discuss the **advantages** and **disadvantages** of cohort studies, and a key source of error.

Cohort Studies:

(also referred to as a prospective or longitudinal studies)

Can be thought of as the **opposite of Case-control studies** (which start with participants WITH the outcome of interest and an unknown exposure status)

- Start with subjects WITHOUT the outcome of interest **and** who are "at risk" for it, then groups them according to their exposure status
- derives incidence (of potentially multiple outcomes) in exposed and unexposed groups
- Studies individuals, not whole populations
- Best design for testing causation, without manipulating exposures (experimental studies)

Cohort Studies: The Basics

A cohort is a population sample group of non-diseased individuals followed over a period of time. The sample is usually placed in 2 groups:

Group 1: Everyone is exposed to risk factor
Group 2: No one is exposed to risk factor

- Best observational design when we cannot ethically or practically manipulate whether people are exposed to a factor or not

- **Cohort Study Goal**: To see if those who choose to be exposed to a risk factor are more likely to develop a certain disease than those who choose not be exposed.

Epi in the News

Feb 2012

House moves can cause poor health later on

Adrian O'Dowd

Add to PDP Print

Wednesday, 8 February 2012

Children of families who move frequently are more likely to develop poor health in later life, according to new research published in the *Journal of Epidemiology and Community Health.*

Scottish researchers found such children were more likely to have poorer overall health, psychological distress, and become heavy drinkers and smokers during adolescence and adulthood.

Researchers led by the Social and Public Health Sciences Unit in Glasgow, assessed the health of 850 people, taking part in the West of Scotland Twenty-07 Study.

This study has tracked the long-term health, based on postcodes, of those aged 15, 35, and 55 in 1987-8 over a period of 20 years.

The researchers' analysis included physical health, such as weight, waist: hip ratio, lung function and blood pressure; overall health (meaning a limiting long term illness and subjective assessment of general health); psychological health; and unhealthy behaviours, such as smoking and heavy drinking or illicit drug use.

They found that one in five people had lived at the same address throughout childhood; six out of 10 (59%) had moved once or twice; and a further one in five (21%) had moved at least three times.

Children of single parent/step parent households were significantly more likely to move home as were those with two or three siblings, but children with at least four siblings were more likely to stay put during childhood.

There was no association between the frequency of house moves and physical health measures, but the researchers frequent house moves during childhood were associated with an increased risk of poorer overall health, psychological distress, and heavy drinking and smoking during adolescence and adulthood.

Childhood residential mobility and health in late adolescence and adulthood: findings from the West of Scotland Twenty-07 Study

D Brown[1], M Benzeval[1], V Gayle[2], S Macintyre[1], D O'Reilly[3], A H Leyland[1]

+ Author Affiliations

Correspondence to

Dr D Brown, MRC/CSO Social and Public Health Sciences Unit, 4 Lilybank Gardens, Glasgow G12 8RZ, UK; denise@sphsu.mrc.ac.uk

Accepted 8 October 2011

Published Online First 6 February 2012

Abstract

Background The relationship between childhood residential mobility and health in the UK is not well established; however, research elsewhere suggests that frequent childhood moves may be associated with poorer health outcomes and behaviours. The aim of this paper was to compare people in the West of Scotland who were residentially stable in childhood with those who had moved in terms of a range of health measures.

Methods A total of 850 respondents, followed-up for a period of 20 years, were included in this analysis. Childhood residential mobility was derived from the number of addresses lived at between birth and age 18. Multilevel regression was used to investigate the relationship between childhood residential mobility and health in late adolescence (age 18) and adulthood (age 36), accounting for socio-demographic characteristics and frequency of school moves. The authors examined physical health measures, overall health, psychological distress and health behaviours.

Results Twenty per cent of respondents remained stable during childhood, 59% moved one to two times and 21% moved at least three times. For most health measures (except physical health), there was an increased risk of poor health that remained elevated for frequent movers after adjustment for socio-demographic characteristics and school moves (but was only significant for illegal drug use).

Conclusions Risk of poor health was elevated in adolescence and adulthood with increased residential mobility in childhood, after adjusting for socio-demographic characteristics and school moves. This was true for overall health, psychological distress and health behaviours, but physical health measures were not associated with childhood mobility.

Population-based cohort study in Glasgow, Scotland.

Exposure: Moving **≥3 times** in childhood

Outcomes: Variety of health outcomes in adolescence & adulthood

Cohort Studies: The Basics

- Cohort studies require that we collect data at least twice, and often multiple times (i.e. there is a need for follow-up)
  - **Time 1**: Determine exposure status and ensure they are free of the disease and at risk for it
  - **Time 2+**: Determine if they developed the outcome(s) of interest?

Exposure-Based Cohort Studies

Cohort group members experience a common exposure associated with a specific setting

Examples

- Occupational cohorts
- School cohorts

Incidence of cancer among Nordic airline pilots over five decades: occupational cohort study

Eero Pukkala, Rafael Aspholm, Anssi Auvinen, Harald Eliasch, Maryanne Gundestrup, Tor Haldorsen, Niklas Hammar, Jón Hrafnkelsson, Pentti Kyyrönen, Anette Linnersjö, Vilhjálmur Rafnsson, Hans Storm, Ulf Tveten

Abstract

Objective To assess the incidence of cancer among male airline pilots in the Nordic countries, with special reference to risk related to cosmic radiation.
Design Retrospective cohort study, with follow up of cancer incidence through the national cancer registries.
Setting Denmark, Finland, Iceland, Norway, and Sweden.
Participants 10 032 male airline pilots, with an average follow up of 17 years.
Main outcome measures Standardised incidence ratios, with expected numbers based on national cancer incidence rates; dose-response analysis using Poisson regression.
Results 466 cases of cancer were diagnosed compared with 456 expected. The only significantly increased standardised incidence ratios were for skin cancer: melanoma 2.3 (95% confidence interval 1.7 to 3.0), non-melanoma 2.1 (1.7 to 2.8), basal cell carcinoma 2.5 (1.9 to 3.2). The relative risk of skin cancers increased with the estimated radiation dose.

tional exposure.[1] Flight personnel may also be exposed to electromagnetic fields from cockpit instruments, jet fuel, and substances emanating from materials used in aircraft construction. In addition, it has been suggested that disruptions in sleep-wake cycles associated with flying across time zones may increase the risk of cancer by suppressing secretion of melatonin[2] or by some other hormone related mechanism.

The aim of this paper is to describe cancer incidence among male commercial airline pilots from all five Nordic countries. The presentation of the results and discussion about possible causes will focus on skin cancer and cancers hypothesised in advance to have an association with cosmic radiation.

Methods

We identified national cohorts of airline pilots from various registers in the Nordic countries. In Denmark we enrolled all members of commercial cockpit crew on file since 1946 in the National Clinic of Aviation Medicine, University Hospital, Copenhagen (3790 men).[3] In Finland we included all 793 male pilots who

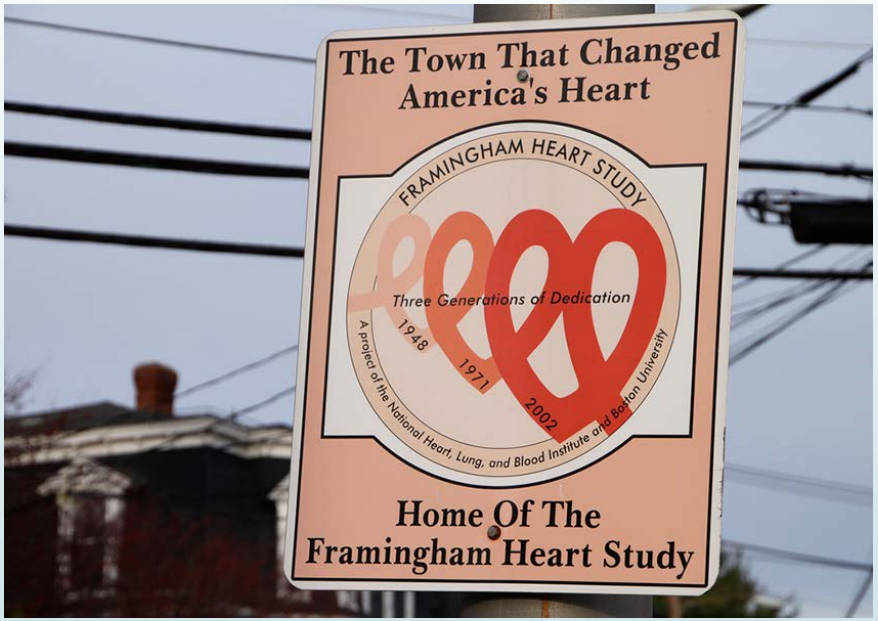
Population-Based Cohort Studies

Cohort group members are exposed to certain environmental and social factors that may influence health.

Examples

- Live in particular place
- Born at a particular time (birth cohorts)
- Origins of the Framingham Study

http://www.framinghamheartstudy.org/



Centre for Longitudinal Studies

Home of the 1958 National Child Development Study, the 1970 British Cohort Study and the Millennium Cohort Study

Leading education and social research
Institute of Education
University of London

Welcome to the 1970 British Cohort Study

The 1970 British Cohort Study (BCS70) follows the lives of more than 17,000 people born in England, Scotland and Wales in a single week of 1970. Over the course of cohort members lives, the BCS70 has collected information on health, physical, educational and social development, and economic circumstances among other factors.

The BCS70 is managed by CLS and funded by the Economic and Social Research Council.

The surveys

Since the birth survey in 1970, there have been seven 'sweeps' of all cohort members at ages 5, 10, 16, 26, 30 and 34. The next survey is planned for 2012, when the cohort members turn 42. CLS is inviting experts in relevant fields to advise on the design of the next survey. For more information, click here.

For more information on each of these surveys, visit our surveys pages.

The data

The data for all BCS70 sweeps is available from the Economic and Social Data Service. For more information, see our accessing the data page.

Support available

This section of our website offers tools and information to help researchers use the data. If you need further support, please contact our user support team.

Contact us

For more information about the BCS70, please contact Alice Sullivan, Principal

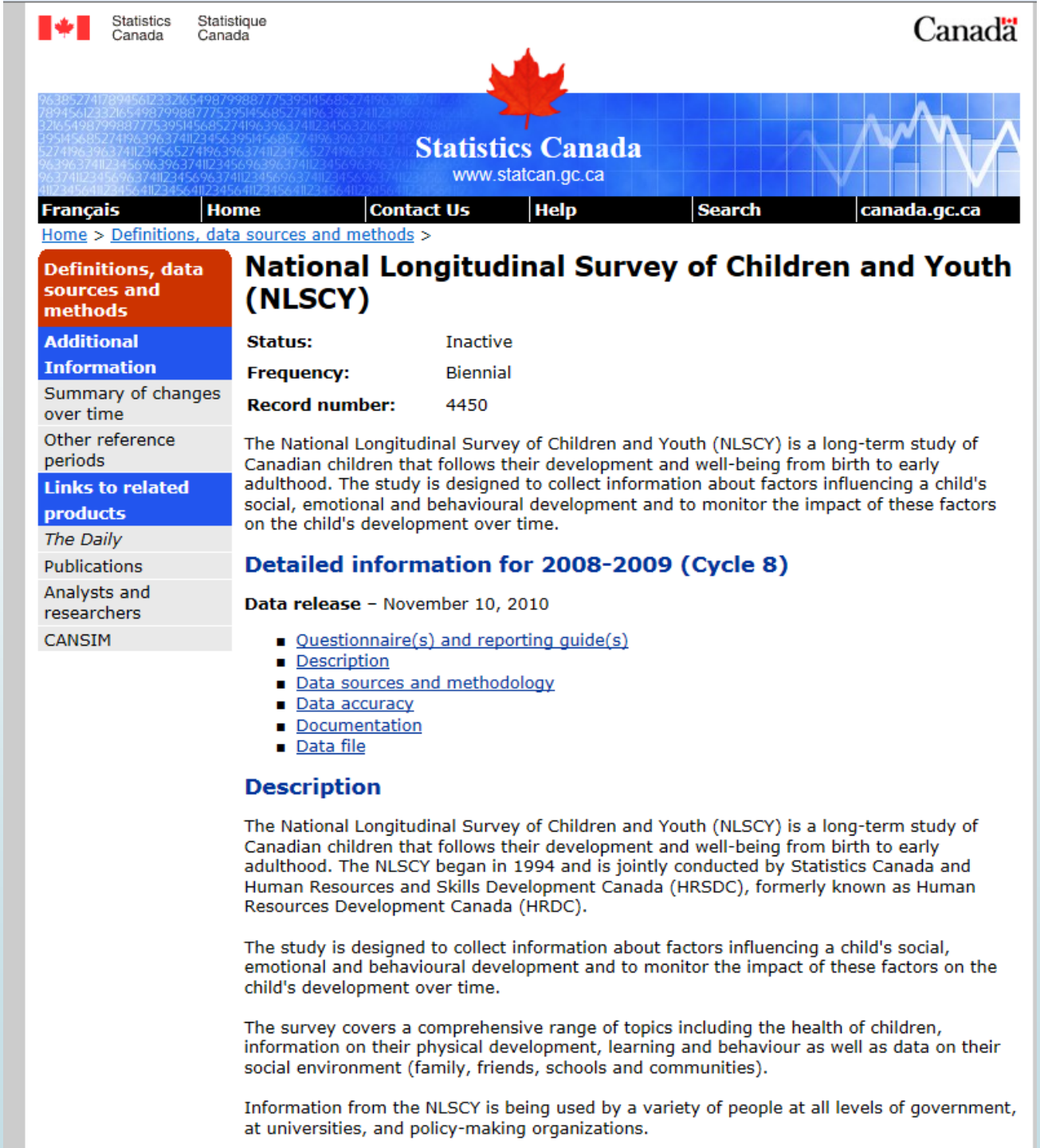
Tell us about your research

We ask researchers to contact us whenever they publish research using the cohort data. With up-to-date records, we can help other researchers avoid duplication and also demonstrate to funders how useful the data is to the research community.

Useful links

- Economic and Social Data Service

In Canada



Statistics Canada Statistique Canada

Canada

Statistics Canada
www.statcan.gc.ca

Français | Home | Contact Us | Help | Search | canada.gc.ca

Home > Definitions, data sources and methods >

Definitions, data sources and methods

Additional Information

- Summary of changes over time
- Other reference periods

Links to related products

- *The Daily*
- Publications
- Analysts and researchers
- CANSIM

National Longitudinal Survey of Children and Youth (NLSCY)

Status: Inactive

Frequency: Biennial

Record number: 4450

The National Longitudinal Survey of Children and Youth (NLSCY) is a long-term study of Canadian children that follows their development and well-being from birth to early adulthood. The study is designed to collect information about factors influencing a child's social, emotional and behavioural development and to monitor the impact of these factors on the child's development over time.

Detailed information for 2008-2009 (Cycle 8)

Data release – November 10, 2010

- Questionnaire(s) and reporting guide(s)
- Description
- Data sources and methodology
- Data accuracy
- Documentation
- Data file

Description

The National Longitudinal Survey of Children and Youth (NLSCY) is a long-term study of Canadian children that follows their development and well-being from birth to early adulthood. The NLSCY began in 1994 and is jointly conducted by Statistics Canada and Human Resources and Skills Development Canada (HRSDC), formerly known as Human Resources Development Canada (HRDC).

The study is designed to collect information about factors influencing a child's social, emotional and behavioural development and to monitor the impact of these factors on the child's development over time.

The survey covers a comprehensive range of topics including the health of children, information on their physical development, learning and behaviour as well as data on their social environment (family, friends, schools and communities).

Information from the NLSCY is being used by a variety of people at all levels of government, at universities, and policy-making organizations.

Font Size + - | Language en fr | Search

Member Login | Contact Us | Facebook | Site Map

clsa élcv

Canadian Longitudinal Study on Aging
Étude longitudinale canadienne sur le vieillissement

CLSA Project | CLSA Team | Participants | Privacy | Project Sites | Partners | Researchers | News

In Canada

Watch our videos

Canadian Longitudinal
Study on Aging

12553 Participants so far — 50,000 goal

Our Mission

Transforming everyday life into extraordinary ideas

The Canadian Longitudinal Study on Aging (CLSA) is a large, national, long-term study that will follow approximately 50,000 men and women between the ages of 45 and 85 for at least 20 years. The study will collect information on the changing biological, medical, psychological, social, lifestyle and economic aspects of people's lives. These factors will be studied in order to understand how, individually and in combination, they have an impact in both maintaining health and in the development of disease and disability as people age. The CLSA will be one of the most comprehensive studies of its kind undertaken to date, not only in Canada but around the world.

News

Oct 4th

Aging study data collection site opens in Surrey

The Canadian Longitudinal Study on Aging (CLSA) is unfolding at 11 major universities and in communities across the country.

Government of Canada

Population-Based Cohort Studies

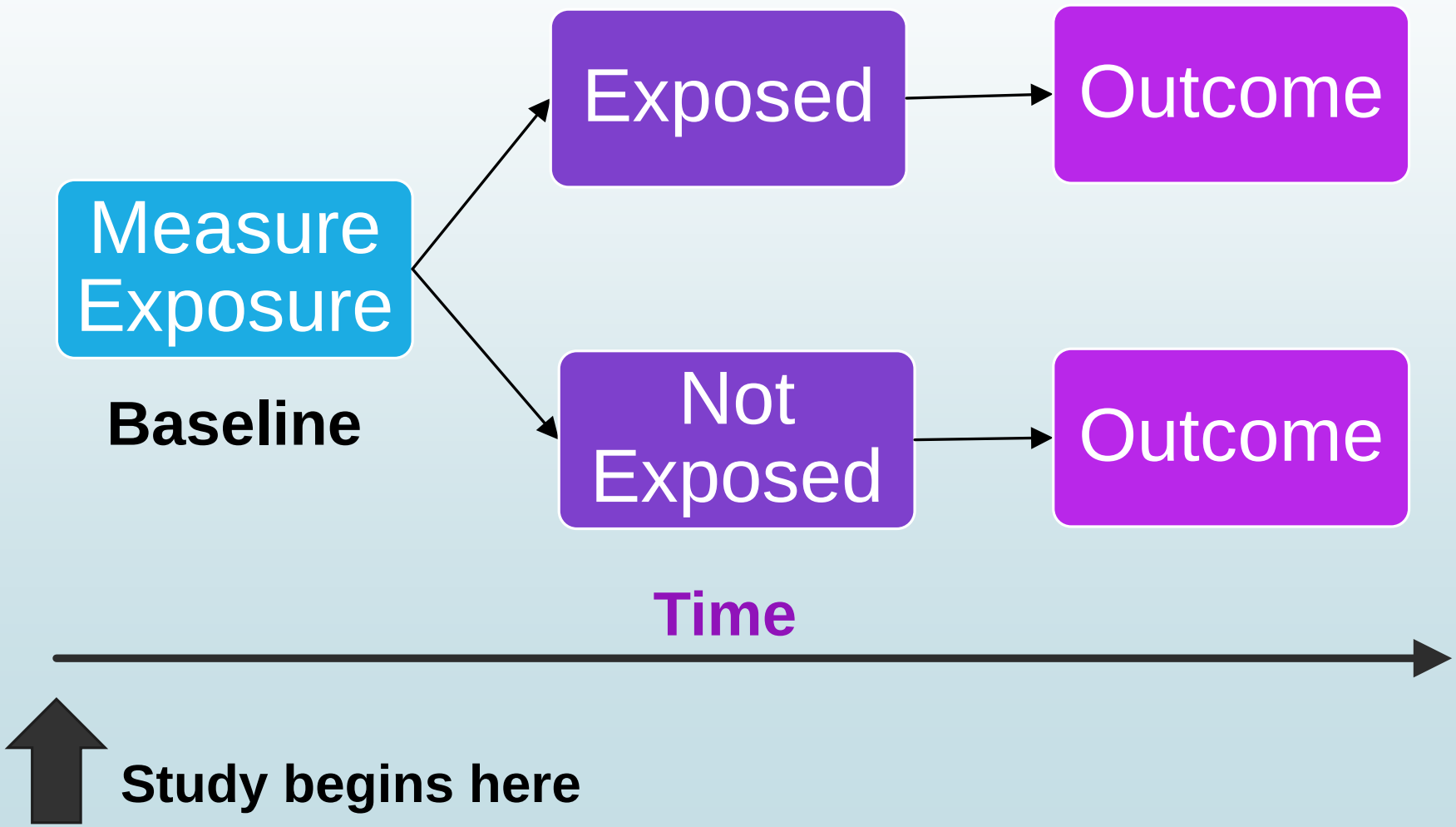
- Birth cohorts – entire population born in specific time is exposed to a particular risk factor
- Example: Smoking - The Tobacco Story in Canada
- Height of smoking in North America: 1960s: Link

Cohort Studies
Timing of Data Collection

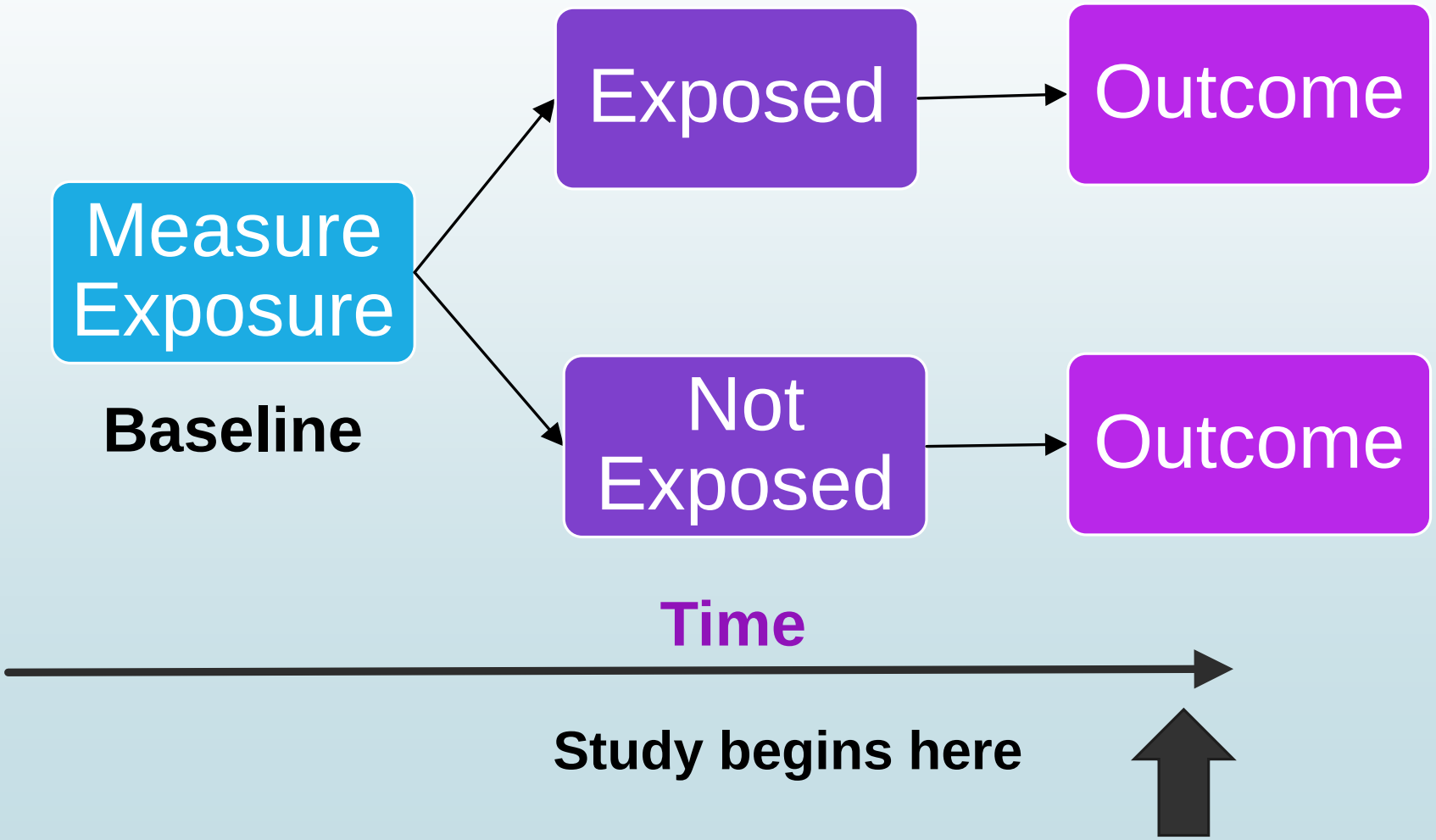
- The basic feature of all cohort studies is measurement of exposure and follow-up for disease.
- Depending on when data is collected, this can happen in 2 ways:

1. **Prospective cohort studies** – exposure level in present, then wait to see if they develop disease in future.
2. **Retrospective cohort studies** – we have data on their exposure levels in the past. Then we contact them in present to see if they developed disease.

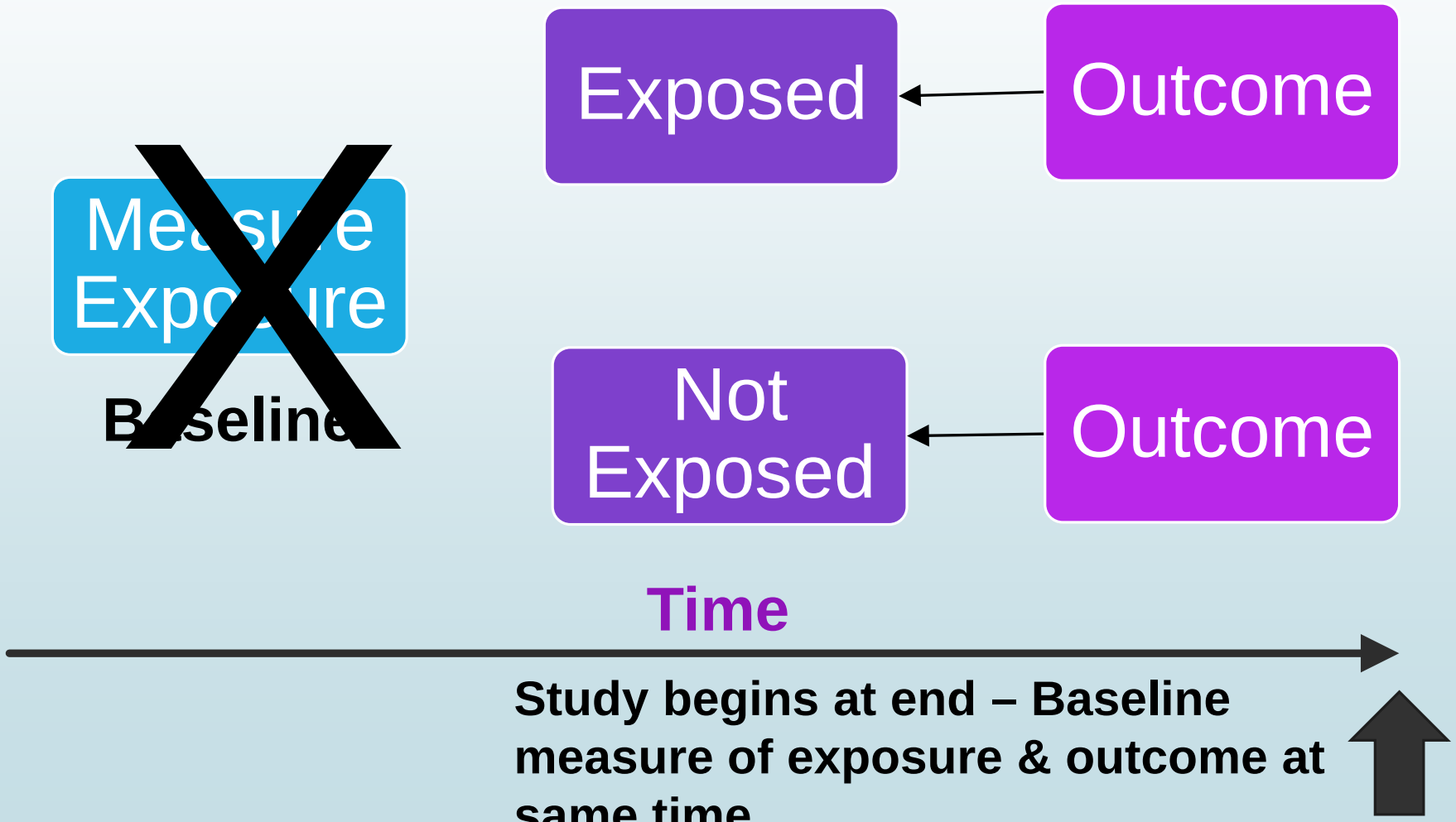
Prospective Cohort Study (i.e. longitudinal study)



Retrospective Cohort Study *(i.e. historical cohort study)*



Case Control Study



Retrospective Cohort vs. Case Control Study

Case Control Study

- **Start in present** with those with the disease (data collection 1).
- **In present** - ask about their exposure in past or use biomarkers to tell us about their past (all during data collection 1).
- Did your parents move a lot when you were little?

Retrospective Cohort Study

- **Start investigating the past** with those exposed and disease-free (data collection 1).
- **Re-contact in present** to see if they developed the disease (data collection 2).

Advantages of Retrospective Cohort Studies

- Using administrative data that has already been collected.
- Large amount of follow-up (person-years) may be accrued that you can use.
- The amount of exposure data collected can be quite extensive and available to the investigator at minimal cost.

Cohort Studies
Timing of Data Collection

DESIGN	PAST	PRESENT	FUTURE
Prospective		E ⇒	D
Retrospective	E ⇒	D	
Case-Control	E ⇐	D	

E = exposure; D = disease

Size and Cost of the Cohort

- The larger the size of the cohort, the better the evidence it can provide, **but** larger cohorts are more costly.
- Amount of money available often determines size of a cohort study.
- Larger studies are more demanding than smaller ones due to data collection and data management.

LINK

OP/ED | 2/04/2013 @ 8:00AM | 210 views

What Caused A Billion Dollar Federal Study Of Child Health To Implode?

+ Comment Now + Follow Comments

After 10 years and $1 billion, an ambitious, federally-funded study of child health has not gotten off the ground, and outside observers say it is in serious trouble. Outsized expectations, bureaucratic rigidity, and lack of strong scientific leadership — all played a role in creating "a national embarrassment."

During the past twenty years, the notion that early life exposures may have a profound influence on health in childhood and beyond has gained increasing acceptance among scientists. Over this same period concern about possible effects of exposure to environmental toxins, including pesticides and heavy metals, has become ever more pervasive.

These two developments provided the impetus for a major federal undertaking to examine the effects of early life exposures by following a large cohort of children from pregnancy to adulthood.

Cohort Studies: Measures of Association

Relative Risk

- A **relative risk** provides a **measure of association** between an exposure and a health outcome.
- A relative risk is the **ratio of the incidence of disease in the exposed group to the incidence in the non-exposed group**.

- Relative Risk =

$$\frac{\text{Incidence in the exposed}}{\text{incidence in the unexposed}}$$

Prostate Cancer

- Sample a population of 4400 men in Alberta without prostate cancer.
- Followed for 5 yrs to determine the cumulative incidence of prostate cancer.
- At end of the follow-up 156 men had developed the cancer.

The cumulative incidence is:

Numerator = _____

Denominator =

How to Select Exposures?

Turn to the research literature - In cohort studies, we can only select **1 risk factor** so we select it carefully based on good evidence from animal studies, cross-sectional and case-control studies.

Prostate Cancer Prostatic Dis. 2009;12(3):215-26. Epub 2009 Apr 7.

Vitamin D and prostate cancer risk: a review of the epidemiological literature.

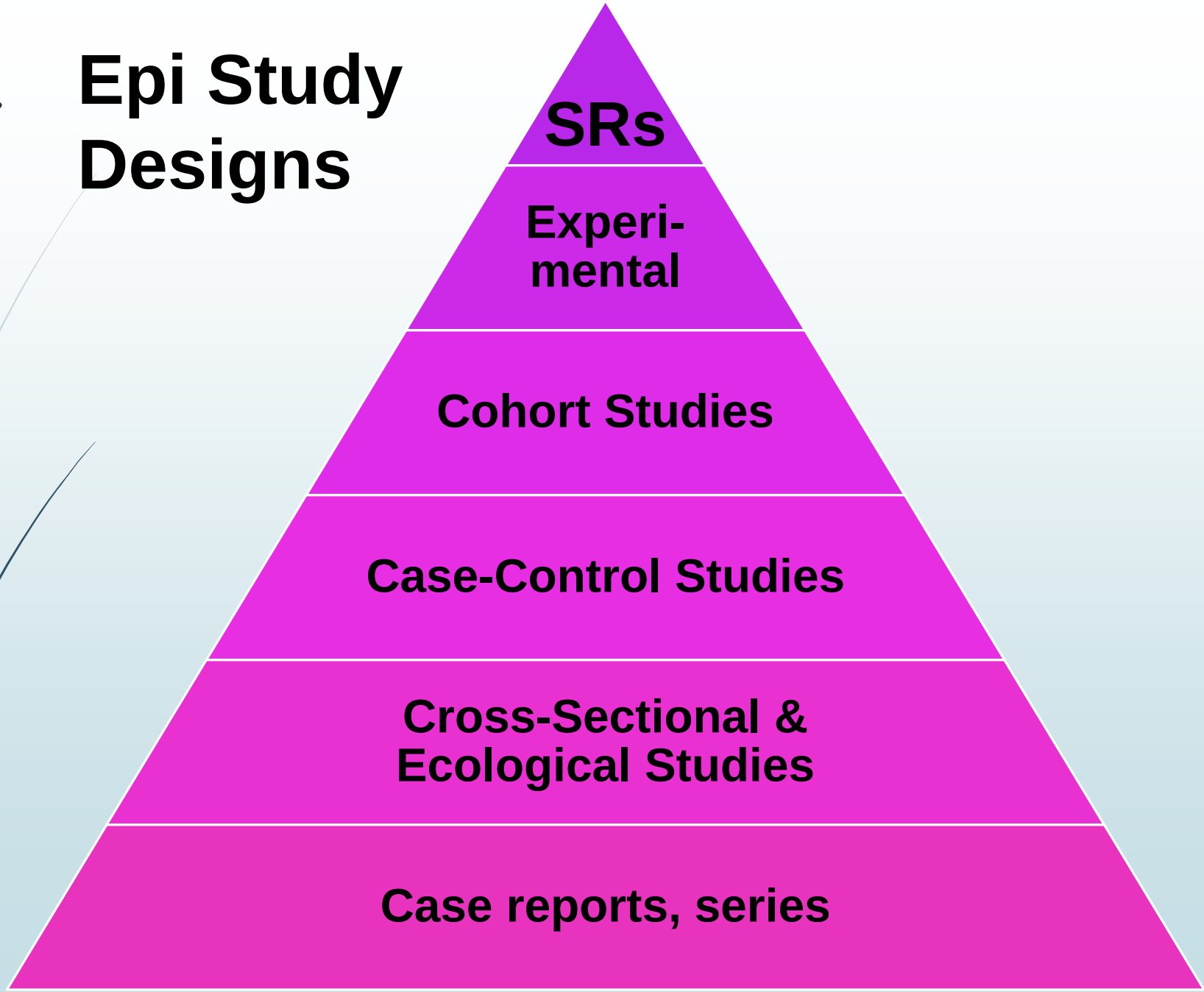
Gupta D, Lammersfeld CA, Trukova K, Lis CG.

Cancer Treatment Centers of America, Midwestern Regional Medical Center, Zion, IL 60099, USA. gupta_digant@yahoo.com

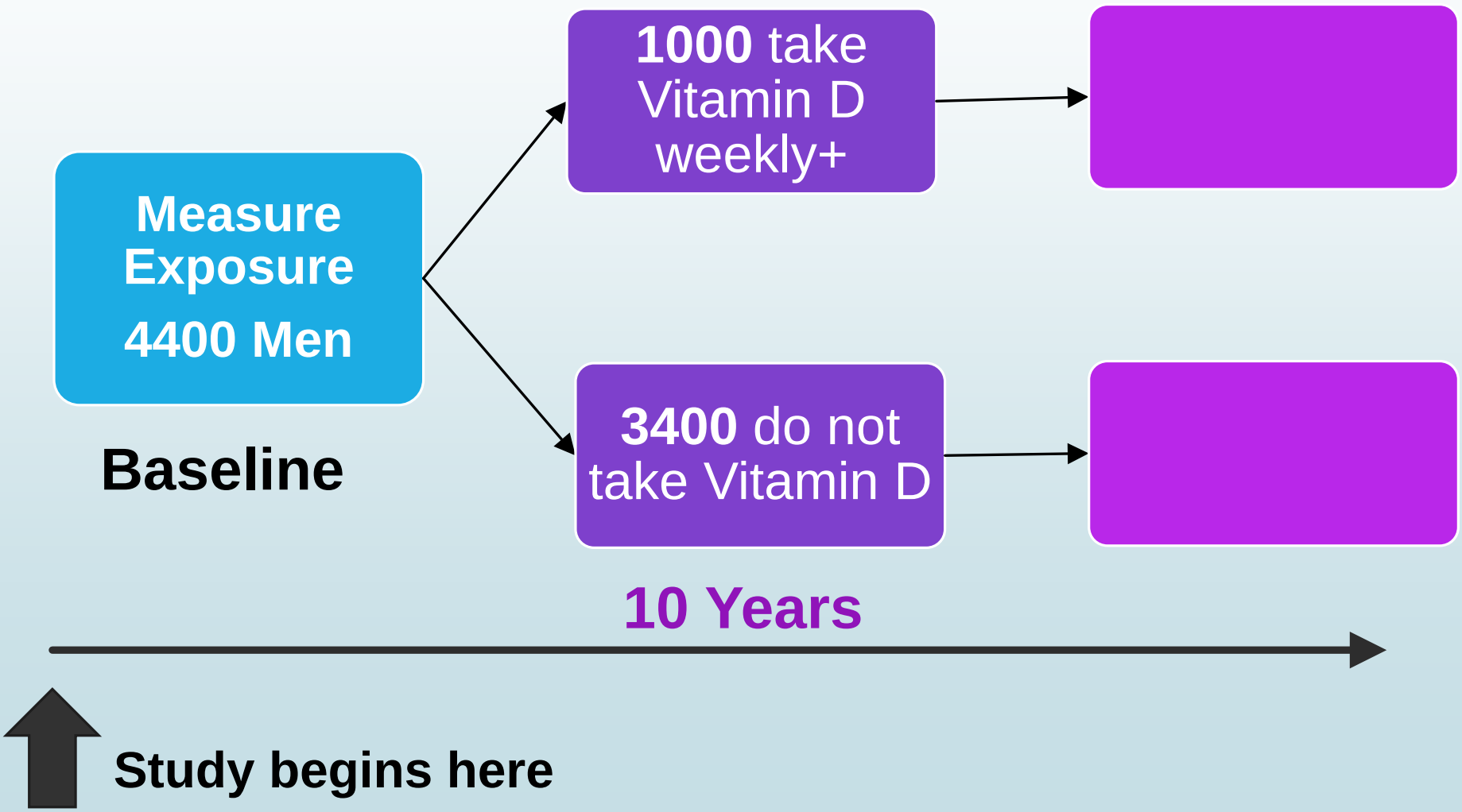
Abstract

Prostate cancer is the most commonly diagnosed cancer in the United States. Prostate cells contain vitamin D receptors as well as enzymes necessary for vitamin D metabolism. Vitamin D metabolites have an antiproliferative and a pro-differentiating effect on prostate cancer cell lines in vitro and in vivo. As a result, there has been an emerging interest in the potential role of vitamin D in the etiology of prostate cancer. This review summarizes all available epidemiological literature on the association between dietary vitamin D, circulating levels of vitamin D and sunlight exposure in relation to prostate cancer risk. To place these studies in context, we also provide some background information on vitamin D, such as its dietary sources, metabolism, optimal levels, hypovitaminosis and relationship with the prostate.

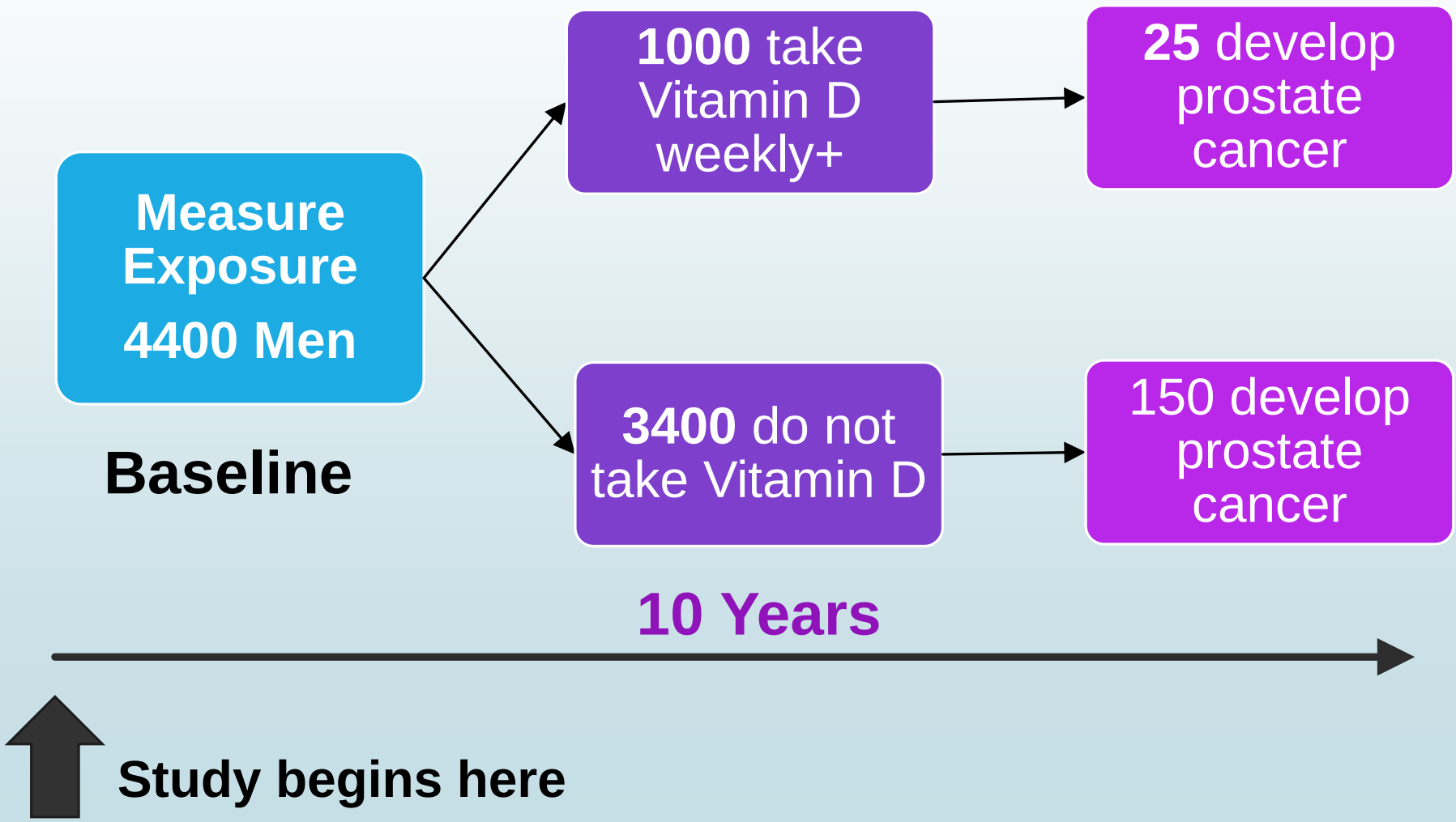
Epi Study Designs



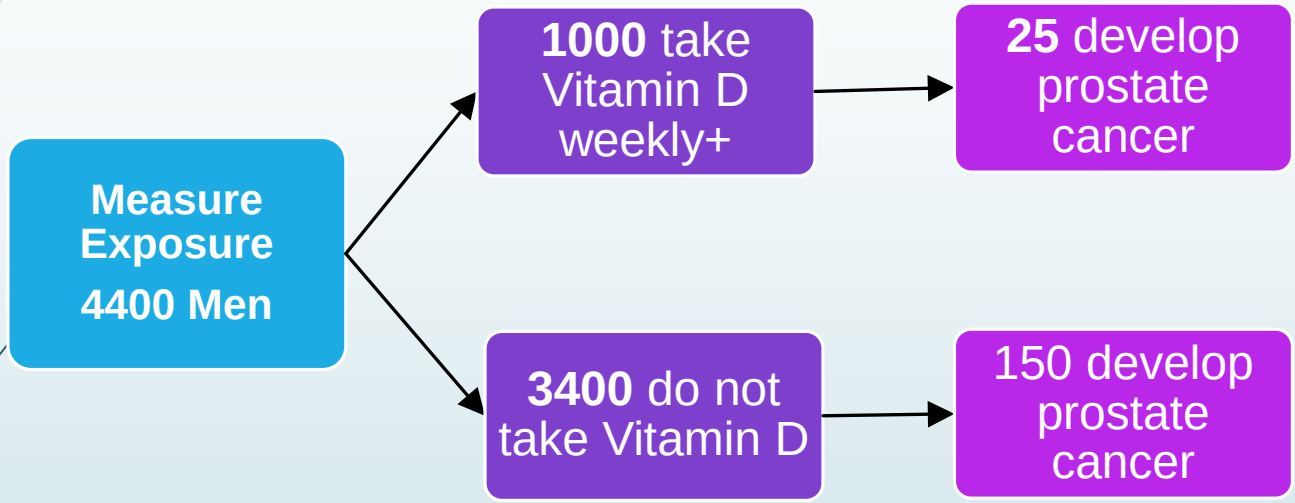
Calculate the Relative Risk



Prospective Cohort Study



Relative Risk Calculation



Incidence in the exposed group = 25/1000 = 0.025

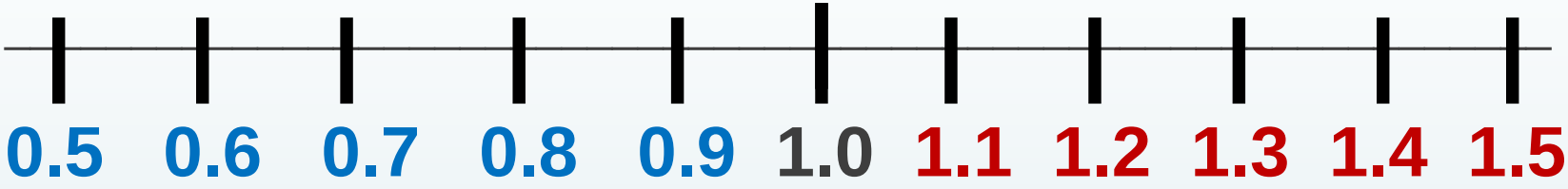
Incidence in the unexposed group =150/3400 = 0.044

Relative Risk =

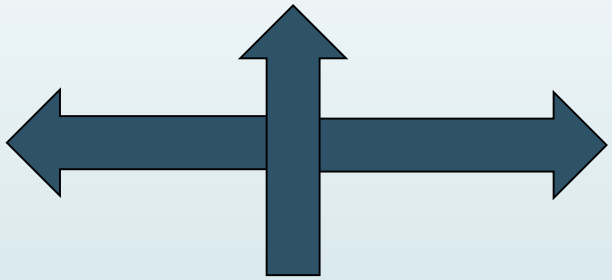
$$\frac{\text{Incidence in the exposed (0.025)}}{\text{incidence in the unexposed (0.044)}}$$

$$= \frac{0.025}{0.044} = 0.57$$

Relative Risk Ratio Interpretation



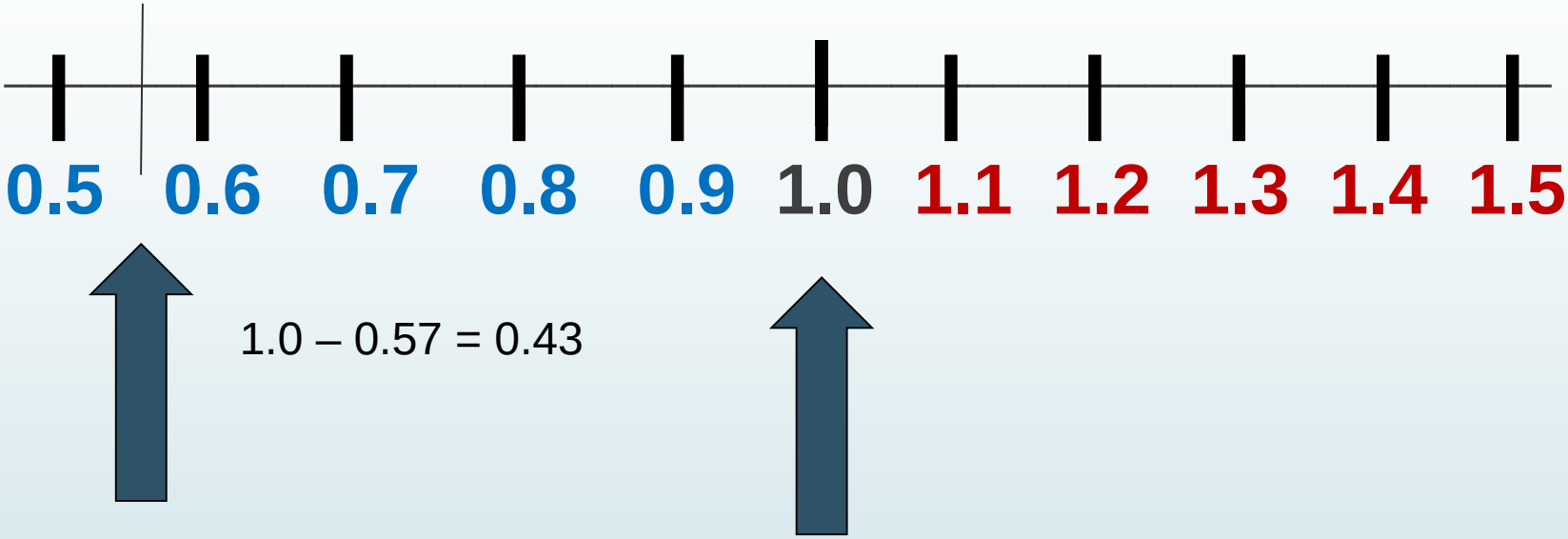
Negative association; possibly protective



Positive association; possibly causal

Exposure has no effect on disease

Relative Risk Ratio Interpretation



Men exposed to Vitamin D are **43% <u>LESS</u>** likely to get prostate cancer

Exposure has no effect on disease

Relative Risk Calculation 2X2 table

	Developed Prostate Cancer	Did NOT develop Prostate Cancer	Total
Took Vitamin D (exposed)	(a)	(b)	(a+b)
Did not take Vitamin D (not exposed)	(c)	(d)	(c+d)
Total	(a+c)	(b+d)	n

$$\text{Relative Risk} = \frac{a/a+b}{c/c+d}$$

(incidence in the exposed)

(incidence in the unexposed)

OR, RR, HR Interpretation

RR, OR or HR Above 1	Below 1	Interpretation
5.0 and up	0.3 and lower	Strong association
2.0 – 4.0	0.6 – 0.4	Moderate association
Under 2.0	0.7 and up	Weak association

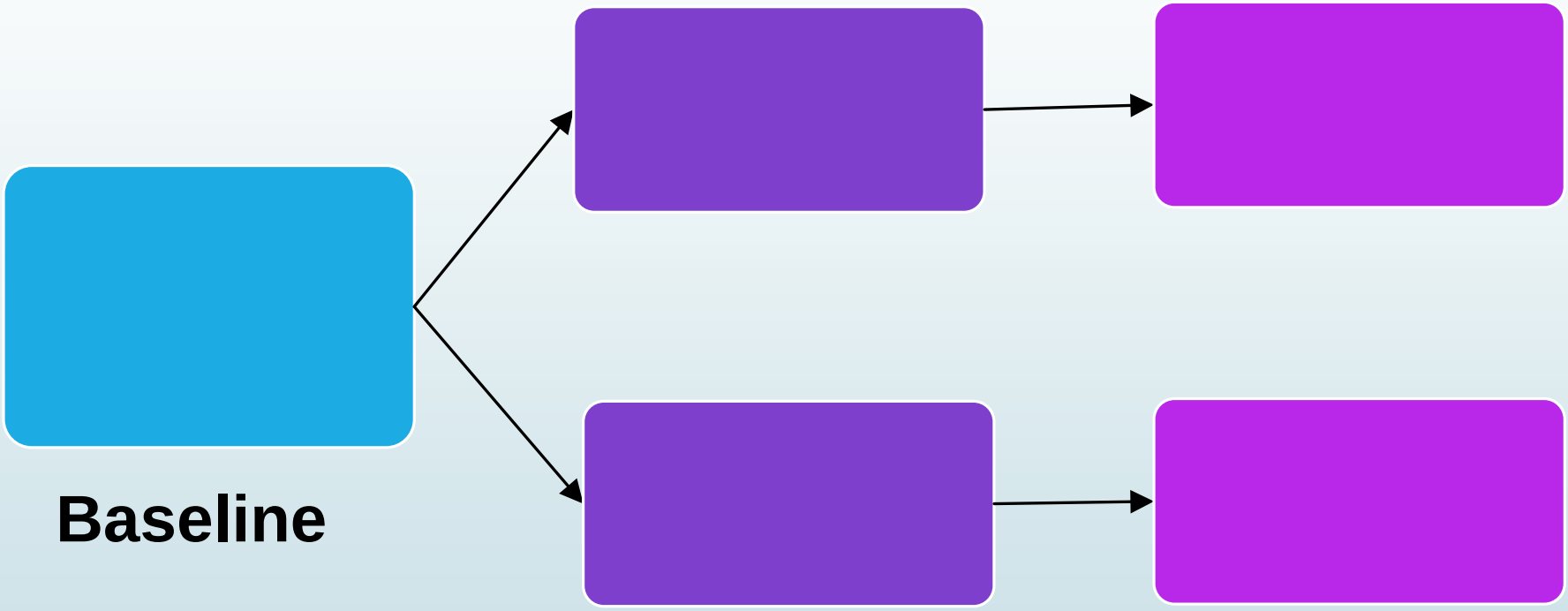
Use the following information to calculate a relative risk and interpret it:

- 850 children followed for 20 years
  - **Exposure**: Frequent moving in childhood (3+ times)
  - **Outcome**: Drug addiction in adulthood

- **Exposed**: 200 kids move 3+ times during study
- **Unexposed**: 650 kids move 0-2 times during study

- 30 exposed and 60 unexposed children are drug addicted at the end of study. Is frequent moving in childhood a risk factor for drug addiction in adulthood?

Calculate the relative risk



Baseline

Study time frame:

Relative Risk =

Interpretation =

Error in Cohort Studies

- **Loss to Follow up** is the Biggest source of selection bias in cohort studies.
- **Misclassification** may occur if people are wrongly classified based on exposure status (especially if their exposure status changes)

Cohort Studies: Strengths & Weaknesses

Strengths

- Can study rare exposures
- Can examine multiple outcomes
- Measures incidence – know temporal sequence of E and D

Weaknesses

- Poor choice when a disease is rare.
- Difficult to select an appropriate unexposed control group.
- Loss to follow up
- Expensive!!
- Time consuming
- Misclassification - biasing outcome status based on exposure status

A final word on Cohort Studies

- Long term cohort studies of childhood health provide understanding of the association between early life exposures and adult health outcomes.
- This is called a “life course perspective” in epidemiology
- E.g. Hiroshima and Nagasaki (intrauterine exposure to radiation)
- Large Cohort studies may start with multiple hypothesis (but these may changed and data may not be available)

Epi in the News

Huge 40-year, 180,000 woman cohort shows flavanols can reduce ovarian cancer risk

By Nicola Cottam, 02-Sep-2014

Post a comment

Related tags: Polymeric flavonoids, Flavanones, Flavonols, Anthocyanins, Flavan-3-ols, Flavones, Ovarian cancer, Polymer

Related topics: Botanicals, Phood, Research, Antioxidants, carotenoids, Phytochemicals, plant extracts, Cancer risk reduction

Regular consumption of flavanols and flavanone bioactive compounds, found in tea, citrus

Common Sources of Flavonoids

Background

- Diet rich in fruit & vegetables associated with decreased ovarian cancer in ecological studies.
- **How?** **Flavonoids** – Plant compounds that modulate cell signaling and cancer-inflammation pathways in the body.
- **Case control studies** report inverse association between flavonoids and ovarian cancer.
- Previous cohort studies found no effect – but small sample sizes & limited range of flavonoids measured.

Tea and Cancer

Abstract

Tea is one of the most popular beverages consumed worldwide. The relationship between tea consumption and human cancer incidence is an important concern. This topic has been studied in different populations by many investigators, but no clear-cut conclusion can be drawn. Whereas some studies have shown a protective effect of tea consumption against certain types of cancers, other studies have indicated an opposite effect. Our purpose is to provide a critical review of this topic, covering basic chemistry and biochemical activity of tea, epidemiologic investigations, and laboratory studies, as well as possible directions for future research. Studies have demonstrated either a lack of association between tea consumption and cancer incidence at specific organ sites or inconsistent results. On the other hand, many laboratory studies have demonstrated inhibitory effects of tea preparations and tea polyphenols against tumor formation and growth. This inhibitory activity is believed to be mainly due to the antioxidative and possible antiproliferative effects of polyphenolic compounds in green and black tea. These polyphenolics may also inhibit carcinogenesis by blocking the endogenous formation of N-nitroso compounds, suppressing the activation of carcinogens, and trapping of genotoxic agents. The effect of tea consumption on cancer is likely to depend on the causative factors of the specific cancer. Therefore, a protective effect observed on a certain cancer with a specific population may not be observable with a cancer of a different etiology. On the basis of this concept, we suggest future laboratory and epidemiologic studies to elucidate the relationship between tea consumption and human cancer risk. [J Natl Cancer Inst 85: 1038–1049, 1993]

« Previous | Next Article »
Table of Contents

This Article
JNCI J Natl Cancer Inst (1993) 85 (13): 1038-1049.
doi: 10.1093/jnci/85.13.1038

» Abstract *Free*
Full Text (PDF) *Free*

- Classifications
REVIEW

- Services
Alert me when cited
Alert me if corrected
Find similar articles
Similar articles in PubMed
Add to my archive
Download citation
Request Permissions

+ Citing Articles
+ Google Scholar
+ PubMed
- Share
What's this?

J Cell Biochem Suppl. 1995;23:200-7.

The epidemiology of ovarian cancer.

Tortolero-Luna G[1], Mitchell MF.

Author information

Abstract

Ovarian cancer is the second most common cancer of the female reproductive system and the leading cause of death from gynecologic malignancies. In 1995, 26,600 women will be diagnosed with ovarian cancer in the U.S., and 14,500 women will die from the disease. Between 1986-1900, the overall age-adjusted incidence was 14.3/100,000 women; mortality was 7.8/100,000 women. Ovarian cancer, rare before age 40, increases steeply thereafter and peaks at ages 65-75. Incidence and mortality rates are higher among white women than among African-American women. Over the last three decades, ovarian cancer incidence has remained stable in high-risk countries, while an increasing trend has been reported in low-risk countries. Despite recent advancements in treatment, the overall five-year survival rates continues to be low (39%). Over 70% of ovarian tumors are diagnosed when regional or distant involvement has already occurred, causing survival rates to remain stable. The etiology of ovarian cancer is poorly understood. Most studies have focused on the epidemiology of invasive epithelial ovarian tumors, while few have explored the epidemiology of epithelial tumors of low malignant potential and nonepithelial tumors. Factors associated with an increased risk for invasive epithelial ovarian cancer include age, race, nulliparity, family history of ovarian cancer, and history of endometrial or breast cancer. Factors associated with a reduced risk are history of one or more full-term pregnancies, use of oral contraceptives, history of breast feeding, tubal ligation, and hysterectomy. Other factors such as infertility drugs, hormone replacement therapy, age at menarche, age at menopause, dietary factors, lactose intolerance, talc use, coffee and alcohol consumption have been suggested, but their role is still inconclusive.

PMID: 8747397 [PubMed - indexed for MEDLINE]

Int. J. Cancer: **123**, 895–898 (2008)

Flavonoids and ovarian cancer risk: A case–control study in Italy

Marta Rossi[1]*, Eva Negri[1], Pagona Lagiou[2], Renato Talamini[3], Luigino Dal Maso[3], Maurizio Montella[4], Silvia Franceschi[5] and Carlo La Vecchia[1,6]

[1]*Dipartimento di Epidemiologia, Istituto di Ricerche Farmacologiche "Mario Negri", Milan, Italy*
[2]*Department of Hygiene and Epidemiology, University of Athens Medical School, Goudi, Athens, Greece*
[3]*Unità di Epidemiologia e Biostatistica, Centro di Riferimento Oncologico, Aviano (PN), Italy*
[4]*Servizio di Epidemiologia, Istituto Tumori "Fondazione Pascale", Naples, Italy*
[5]*Epidemiology and Biology Cluster, International Agency for Research on Cancer, Lyon Cedex, France*
[6]*Istituto di Statistica Medica e Biometria "G. A. Maccacaro", Università degli Studi di Milano, Milan, Italy*

Flavonoids belong to a vast group of polyphenols widely distributed in all foods of plant origin. Because of their antioxidant, antimutagenic and antiproliferative properties, they have been hypothesized to contribute to the favorable effects of fruit and vegetables against cancer. The aim of this study is to investigate the relation of 6 classes of flavonoids (flavan-3-ols, flavanones, flavonols, flavones, anthocyanidins and isoflavones) with ovarian cancer risk, using data from a multicentric case–control study conducted in Italy between 1992 and 1999. The study included 1,031 cases with incident, histologically confirmed epithelial ovarian cancer and 2,411 controls admitted for acute, nonneoplastic conditions to major hospitals in the same catchment areas. In logistic regression models including study center, education, year of interview, parity, oral contraceptive use and family history of ovarian or breast cancer or both, an inverse relation with significant trend in risk was found between ovarian cancer and flavonols [odds ratio (OR), 0.63; 95% confidence intervals (CI) 0.47–0.84] as well as isoflavones (OR, 0.51; 95% CI, 0.37–0.69), comparing the highest *versus* the lowest quintile. Further adjustment for fruit and vegetable intake did not modify these associations, suggesting that isoflavones and flavonols may have a distinct role in explaining the effect of fruit and vegetable against ovarian cancer. On the basis of our findings and the relevant literature, we infer that isoflavones, and perhaps flavonols, may have favorable effects with respect to ovarian cancer risk.

Key words: flavonoids; ovarian cancer; isoflavones; case–control study; risk factors

Flavonoids belong to a vast group of polyphenols that are widely distributed in all foods of plant origin such as fruit, vegeta-

Italy and the urban area of Naples in southern Italy.[24] Briefly, cases were 1,031 women (median age 56, range 18–79 years) admitted to the major teaching and general hospitals in the areas under study with incident, histologically confirmed epithelial ovarian cancer. Controls were 2,411 women (median age 57, range 18–79 years) admitted to the same network of hospitals as the cases for acute, nonmalignant and nongynecological conditions, unrelated to hormonal or digestive tract diseases or to long-term modifications of diet. Of these, 26% were admitted for traumas, 28% for nontraumatic orthopedic disorders, 15% for surgical conditions and 31% for miscellaneous other illnesses including eye, ear, nose, throat and dental disorders. Less than 4% of cases and controls approached refused interview.

Centrally trained interviewers administered a standard questionnaire to cases and controls during their hospital stay. The questionnaire included information on sociodemographic factors and lifestyle habits, anthropometric variables, history of cancer in first-degree relatives, menstrual and reproductive factors, use of oral contraceptives (OC) and hormone replacement therapy. The subjects' usual diet during 2 years before cancer diagnosis or hospital admission was investigated by means of a reproducible and valid food frequency questionnaire (FFQ).[25,26] The FFQ included 78 foods or food groups, plus questions aimed at assessing fat intake and general dietary habits. Subjects were asked to indicate their average weekly consumption of single food items or food groups. Information on occasional intakes, *i.e.*, lower than once a week but at least once per month, was also collected. This was arbitrarily coded as 0.5 per week. Frequencies were translated into daily consumption of each food item or beverage category, and these quantities were converted into average daily intakes of 6 classes

Intake of dietary flavonoids and risk of epithelial ovarian cancer[1–4]

Aedín Cassidy, Tianyi Huang, Megan S Rice, Eric B Rimm, and Shelley S Tworoger

ABSTRACT

Background: The impact of different dietary flavonoid subclasses on risk of epithelial ovarian cancer is unclear with limited previous studies that have focused on only a few compounds.

Objective: We prospectively examined associations between habitual flavonoid subclass intake and risk of ovarian cancer.

Design: We followed 171,940 Nurses' Health Study and Nurses' Health Study II participants to examine associations between intakes of total flavonoids and their subclasses (flavanones, flavonols, anthocyanins, flavan-3-ols, flavones, and polymeric flavonoids) and risk of ovarian cancer by using Cox proportional hazards models. Intake was calculated from validated food-frequency questionnaires collected every 4 y.

Results: During 16–22 y of follow-up, 723 cases of ovarian cancer were confirmed through medical records. In pooled multivariate-adjusted analyses, total flavonoids were not statistically significantly associated with ovarian cancer risk (HR for the top compared with the bottom quintile: 0.85; 95% CI: 0.66, 1.09; *P*-trend = 0.17). However, participants in the highest quintiles of flavonol and flavanone intakes had modestly lower risk of ovarian cancer than that of participants in the lowest quintile, although the *P*-trend was not significant [HRs: 0.76 (95% CI: 0.59, 0.98; *P*-trend = 0.11) and 0.79 (95% CI: 0.63,1.00; *P*-trend = 0.26), respectively]. The association for flavanone intake was stronger for serous invasive and poorly differentiated tumors (comparable HR: 0.68; 95% CI: 0.50, 0.92; *P*-heterogeneity = 0.10, *P*-trend = 0.07) compared with nonserous and less-aggressive tumors. Intakes of other subclasses were not significantly associated with risk. In food-based analyses used to compare subjects who consumed >1 with ≤1 cup black tea/d, the HR was 0.68 (95% CI: 0.51, 0.90; $P < 0.01$).

Flavonoids are present in many foods and beverages including fruit, vegetables, tea, and wine. Flavonoid subclasses commonly consumed in the United States include flavanones, flavonols, anthocyanins, flavan-3-ols, flavones, and polymeric flavonoids. Relatively few studies have examined the association between these compounds and ovarian cancer risk. Case-control studies generally have reported inverse associations between flavonols and flavones and risk of ovarian cancer (15–17). Our previous prospective analysis of 5 specific compounds in these classes also observed suggestive inverse associations (18). However, a subsequent prospective study, which examined associations of flavones and some flavonols across several cancer sites, observed no associations with ovarian cancer (19). Previous studies were limited by relatively small case numbers, and because, until recently, food databases did not contain the comprehensive range of flavonoids present in the diet, no previous studies, to our knowledge, have examined the full range of flavonoid subclasses in relation to ovarian cancer risk. Therefore, we examined the association of 6 flavonoid subclasses, total flavonoid intake, and their main food sources with risk of epithelial ovarian cancer in the Nurses' Health Study (NHS)[5] and Nurses' Health Study II (NHSII), including an examination by tumor subtypes, with more than twice the number of cases than in our previous analysis (18).

SUBJECTS AND METHODS

Study population

The NHS commenced in 1976 when 121,700 US women aged

LINK

culated from validated food-frequency questionnaires collected every 4 y.
Results: During 16–22 y of follow-up, 723 cases of ovarian cancer were confirmed through medical records. In pooled multivariate-adjusted analyses, total flavonoids were not statistically significantly associated with ovarian cancer risk (HR for the top compared with the bottom quintile: 0.85; 95% CI: 0.66, 1.09; *P*-trend = 0.17). However, participants in the highest quintiles of flavonol and flavanone intakes had modestly lower risk of ovarian cancer than that of participants in the lowest quintile, although the *P*-trend was not significant [HRs: 0.76 (95% CI: 0.59, 0.98; *P*-trend = 0.11) and 0.79 (95% CI: 0.63,1.00; *P*-trend = 0.26), respectively]. The association for flavanone intake was stronger for serous invasive and poorly differentiated tumors (comparable HR: 0.68; 95% CI: 0.50, 0.92; *P*-heterogeneity = 0.10, *P*-trend = 0.07) compared with non-serous and less-aggressive tumors. Intakes of other subclasses were not significantly associated with risk. In food-based analyses used to compare subjects who consumed >1 with ≤1 cup black tea/d, the HR was 0.68 (95% CI: 0.51, 0.90; $P < 0.01$).

Questions

1. Is this an incidence or a prevalence study?

2. How many cases of cancer developed during the study? _____. The study followed 171,940 women for 2,268,423 person-years. The incidence rate of ovarian cancer in this population is:

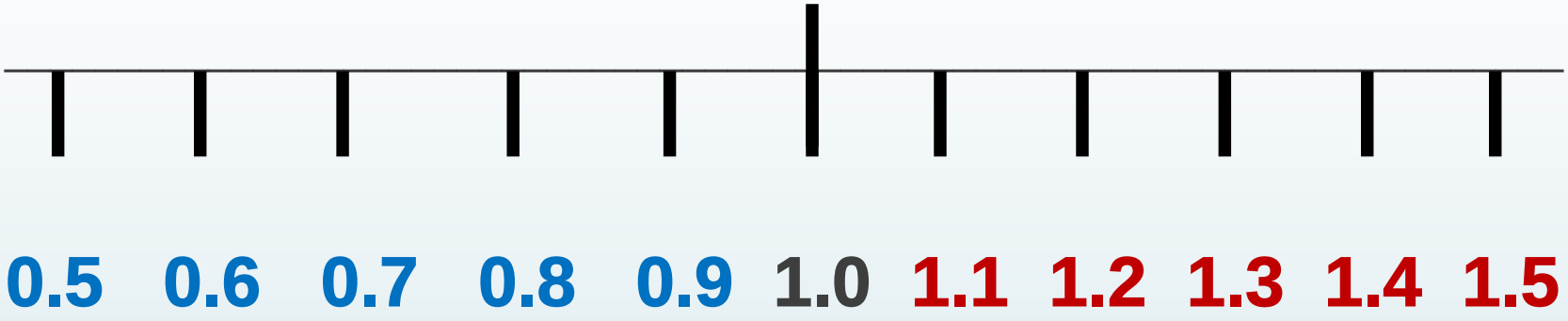
3. The cumulative incidence of ovarian cancer in this group is:

4. Participants were classified into quintiles based on flavonoid intake. The top quintile of flavanol intake was said to have a modestly lower risk of cancer (HR: 0.76). Based on this HR, what is the reported % reduced risk for the highest quintile of flavanol intake in this study group?

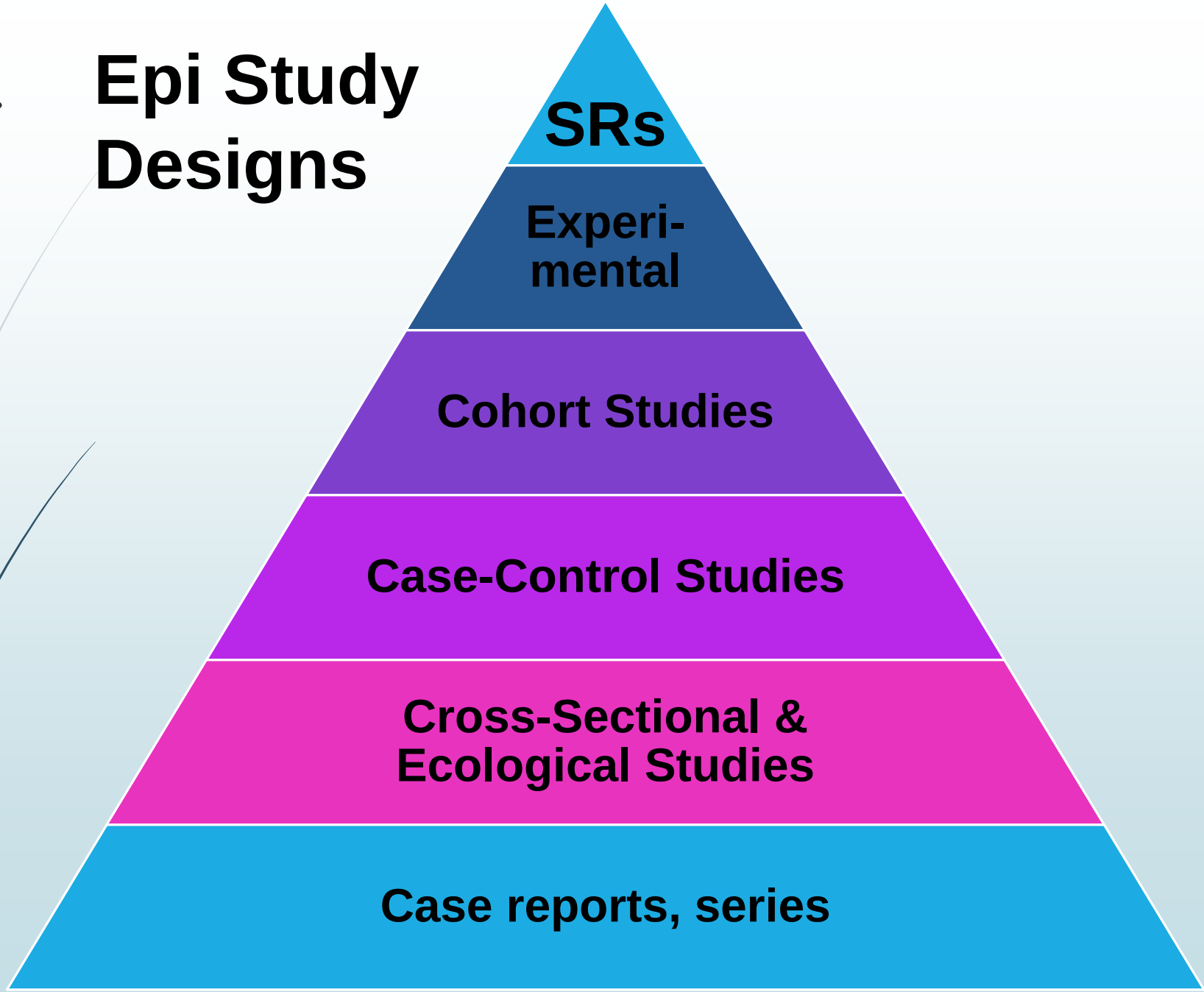
5. Are these findings correctly characterized as modestly lower risk?

6. Is the media providing an accurate picture of the findings?

HR, OR, RR Interpretation



Epi Study Designs



Assignment 2

20 minutes

Quiz 1 next class

Approximately 33 questions

- 11 multiple choice
- 15 short answer
- 8 calculations

*Bring a calculator (cell phones not permitted)

*Material covered will be all classes up to and including Jan 28th (with the exception of Odds Ratio and Relative Risk calculations/interpretation)

Answers to slide 55

1. Incidence

2. 723

Incidence rate: 723/2,268,423 = 0.00031872 * 100 000 = 32 per 100 000 person years

3. 24%

4. Cumulative Incidence: 723/171 940 = 0.0042 * 100 000 = 420 cases per 100 000 people

5. No, there is a weak association according to the measure of effect outlined.