



PRINCIPLES OF EPIDEMIOLOGY & OBSERVATIONAL STUDIES

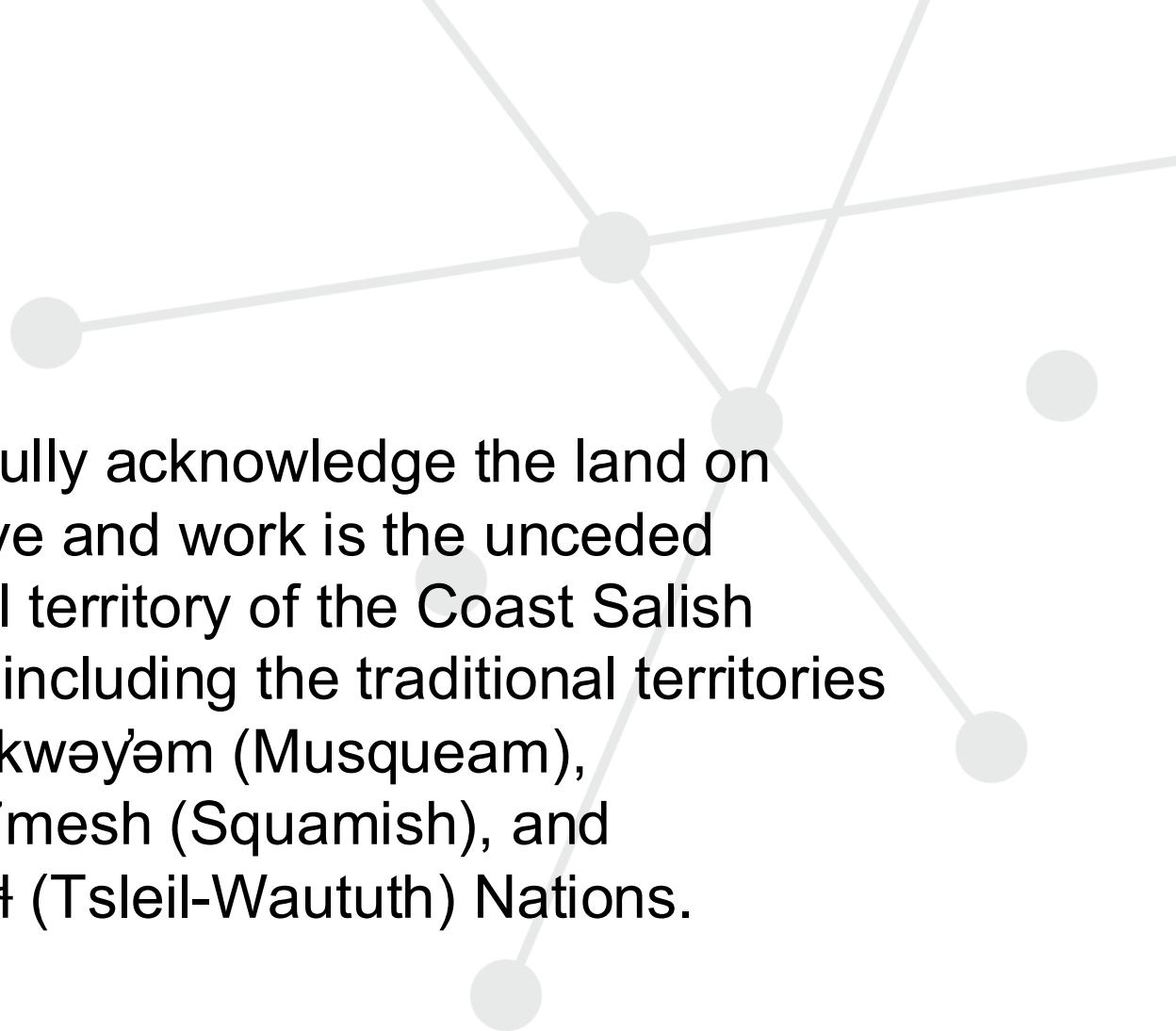
M-J Milloy, PhD

Associate professor, Dep't of Medicine, UBC;
Research scientist, BC Centre on Substance Use



DISCLOSURE

- I am supported by:
 - **United States National Institutes of Health (U01-DA0251525);**
- The University of British Columbia (UBC) has received an unstructured gift from **NG Biomed, Ltd.**, to support me;
- The Canopy Growth professorship in cannabis science was established through arms' length gifts to UBC from **Canopy Growth** and the Government of British Columbia's **Ministry of Mental Health and Addictions**
- I have no personal financial relationships with the cannabis industry



I respectfully acknowledge the land on which I live and work is the unceded traditional territory of the Coast Salish Peoples, including the traditional territories of xʷməθkʷəy̥əm (Musqueam), Skwxwú7mesh (Squamish), and Səl̓ílwətaɬ (Tsleil-Waututh) Nations.

OUTLINE

1. Principles of epidemiology

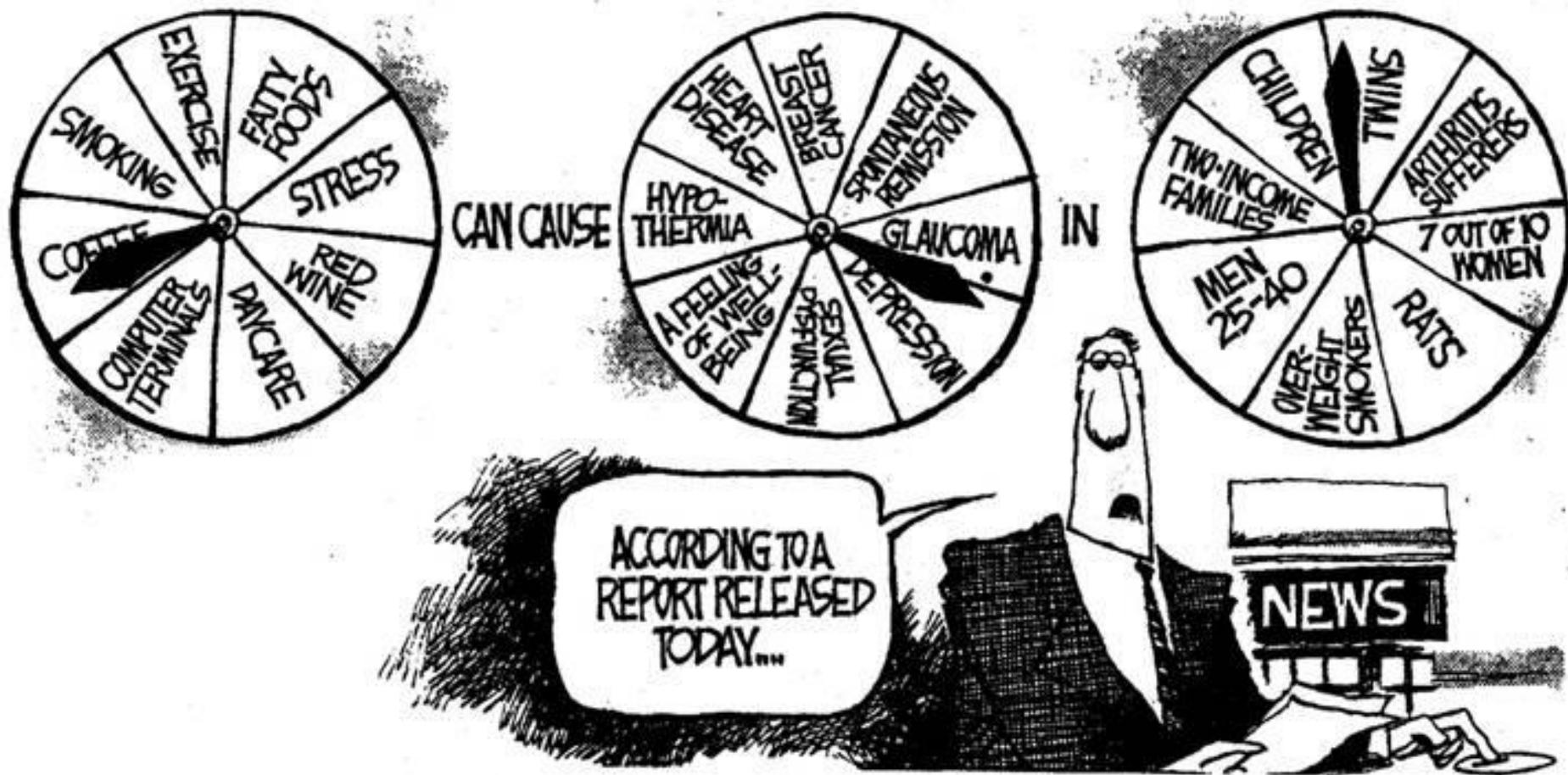
- Definition & history, public health cycle
- Analytic epidemiology: Agent, host, enviro

2. Observational studies

- Study designs (Cross-sectional, case-control)
- Threats to validity (Bias, errors)
- Cohort studies: Vancouver Injection Drug Users Study (VIDUS)

Today's Random Medical News

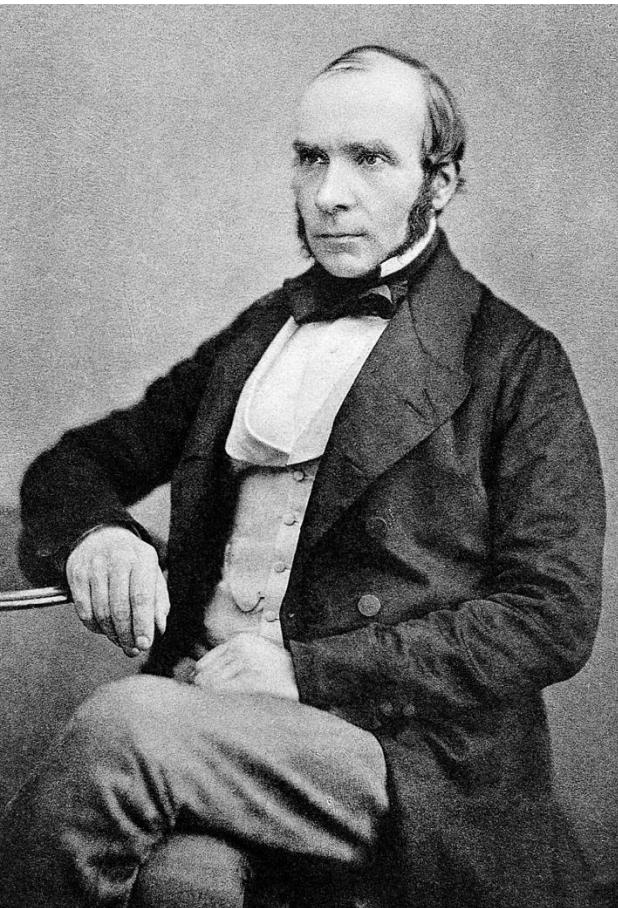
from the New England
Journal of
Panic-Inducing
Gobbledygook





John Snow

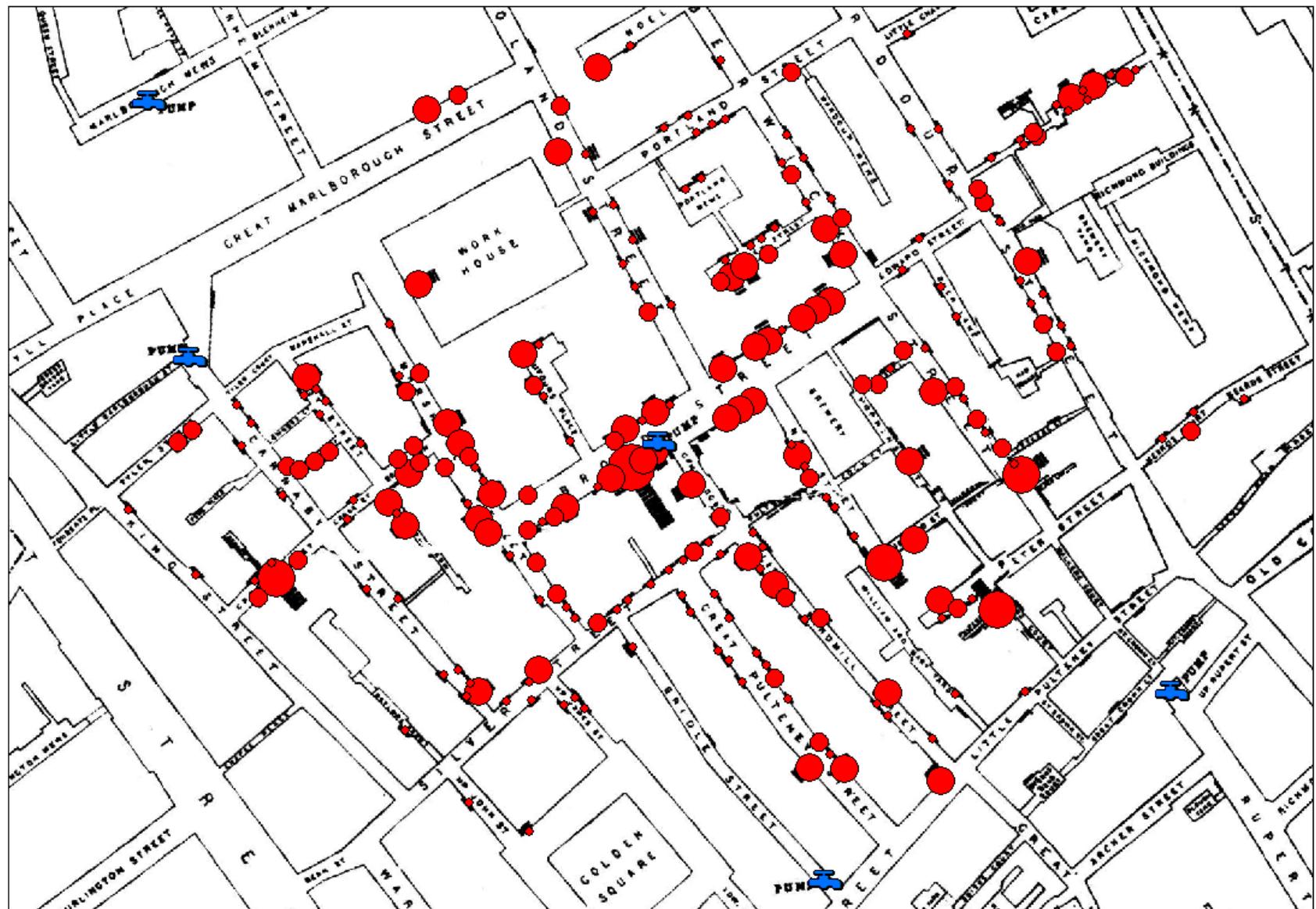




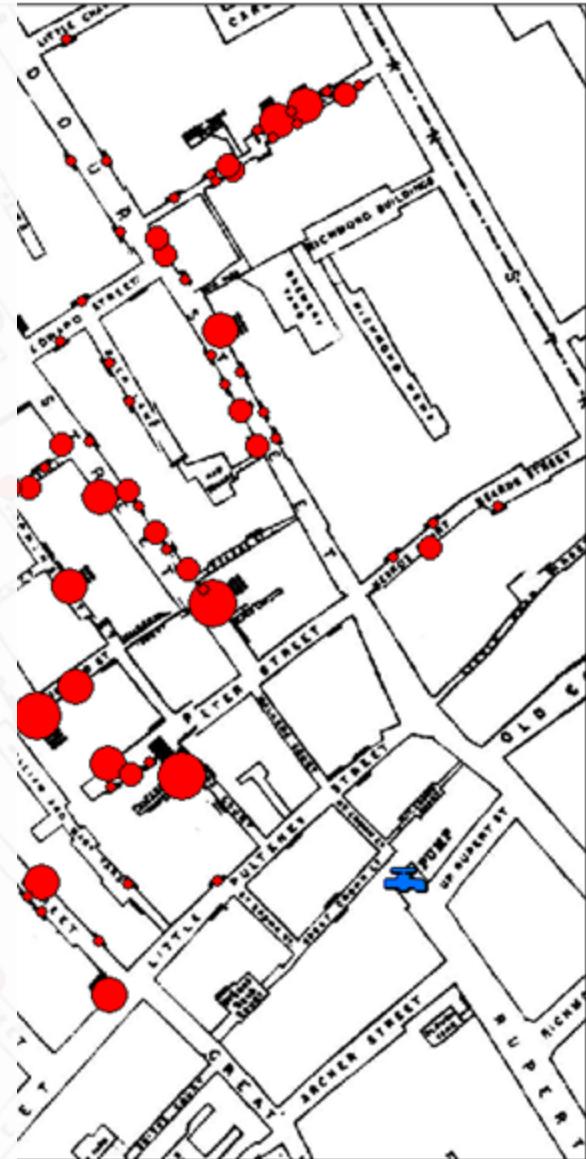
John Snow

Dr. John Snow (1813-1858)

- Considered one of the founders of modern epidemiology
- Snow conducted a novel and effective investigation into cholera outbreaks in Soho, London (1854)
- At the time, cholera was thought to be caused by *miasma*, or noxious vapours arising from rotting materials



I found that nearly all the deaths had taken place within a short distance of the pump. There were only ten deaths in houses situated decidedly nearer to another street-pump. In five of these cases the families of the deceased persons informed me that they always went to the pump in Broad Street, as they preferred the water to that of the pumps which were nearer. In three other cases, the deceased were children who went to school near the pump in Broad Street...



Epidemiology: A Modern Definition

Study of the **occurrence and distribution** of health-related **diseases or events** in specified **populations**, including the study of the **determinants** influencing such states, and the application of this knowledge to **control** the health problem

(Porta M, Last J, Greenland S. A Dictionary of Epidemiology, 2008)

Epidemiology: A Modern Definition

- **Public health:** because of the emphasis on disease prevention
- **Clinical medicine:** because of the emphasis on disease classification and diagnosis (**numerators**)
- **Pathophysiology:** because of the need to understand basic biological mechanisms in disease (**natural history**)
- **Biostatistics:** because of the need to quantify disease frequency and its relationships to antecedents (**denominators, testing hypotheses**)
- **Social sciences:** because of the need to understand the social context in which disease occurs and presents (**social determinants of health phenomena**)

Epidemiology: A Modern Definition

- **Social determinants of health:** “The conditions in the environment in where people are born, live, learn, work, play, worship and age that affect a wide range of health, functioning, and quality-of-life outcomes and risks.” (*US health.gov*)

Social Determinants of Health



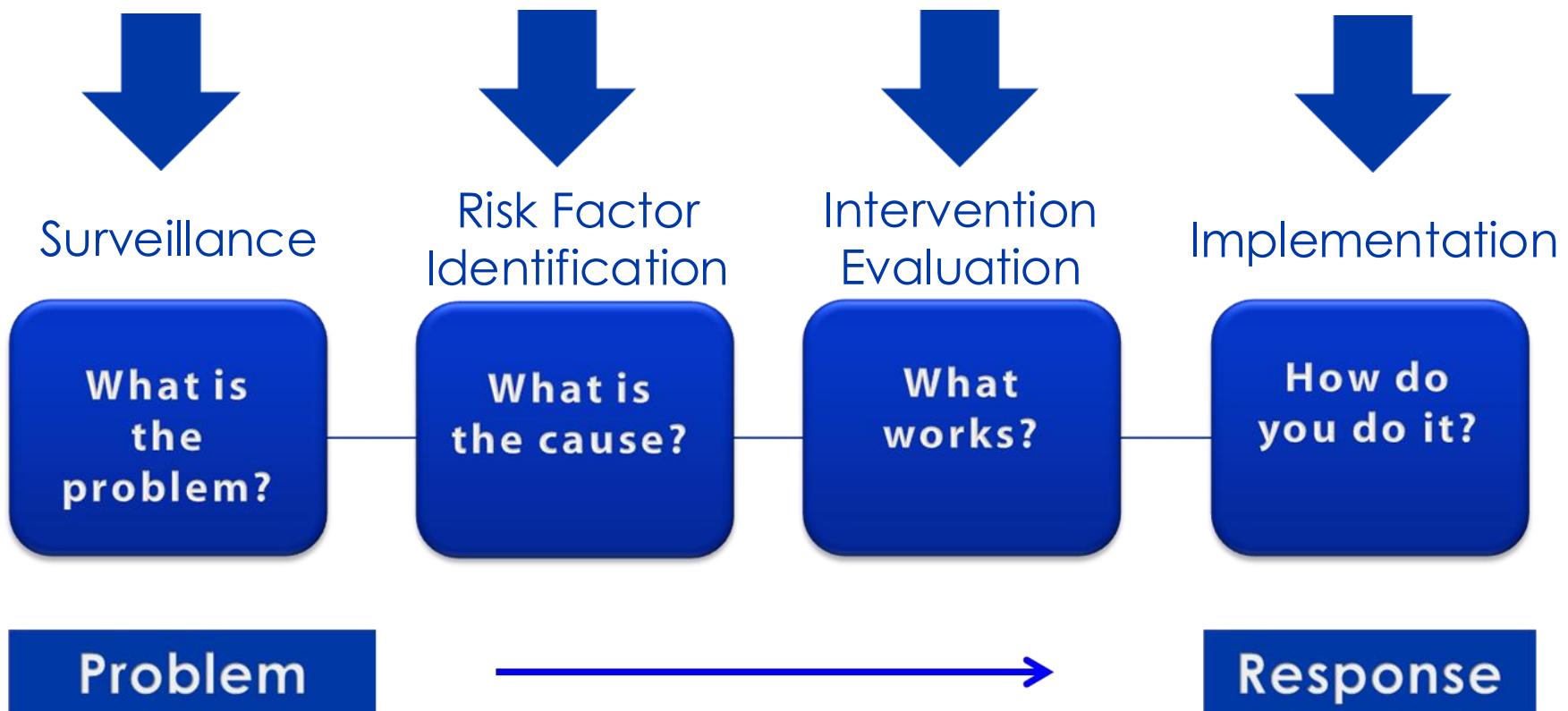
Social Determinants of Health
Copyright-free

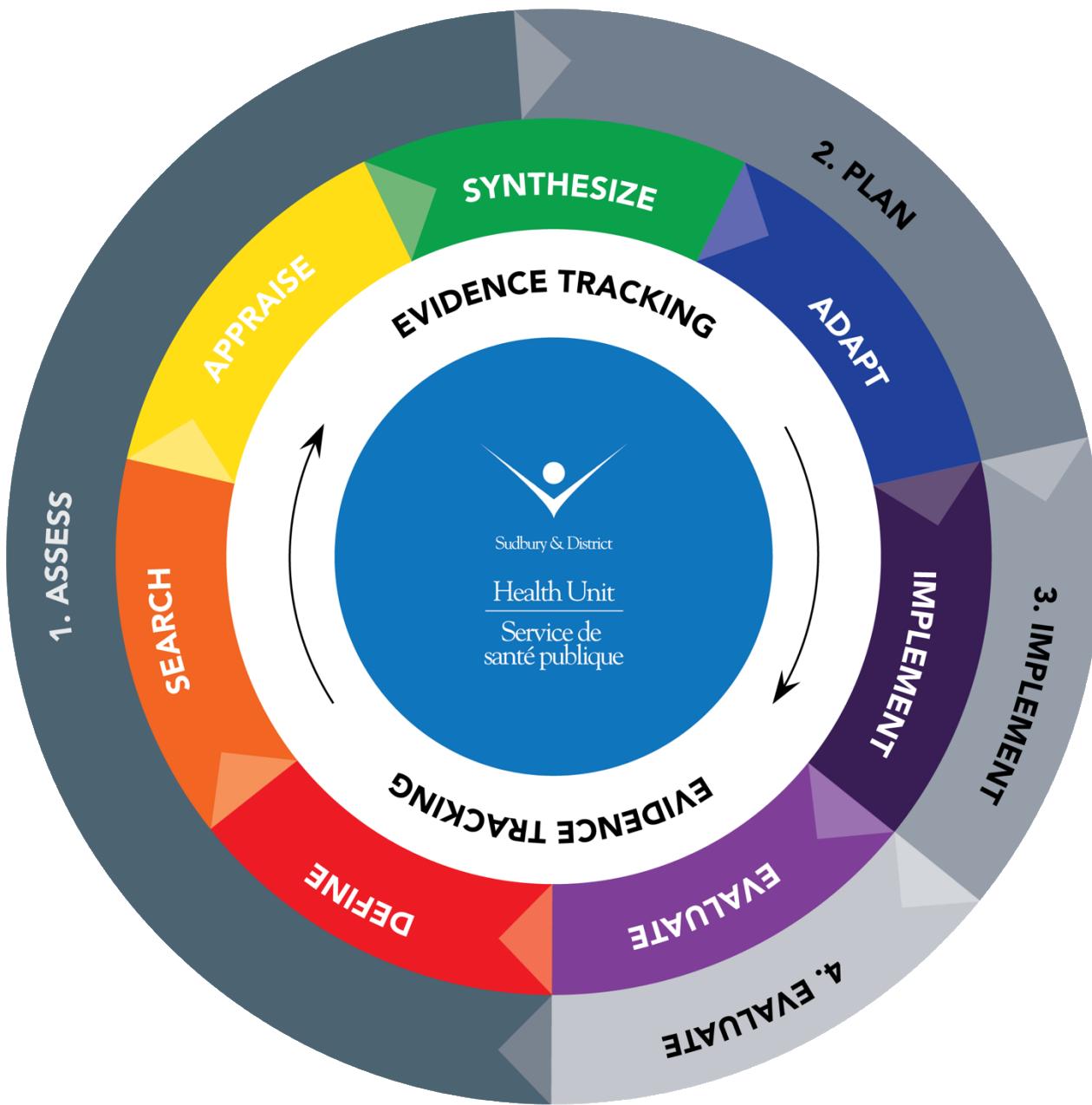
Healthy People 2030

Epidemiology: Objectives

1. To investigate nature/extent of **health-related phenomena** in the community
2. To study **natural history** and prognosis of health-related problems
3. To identify causes and **risk factors**
4. To identify/assist in implementation and evaluation of **interventions**
5. To provide foundation for **public policy**

A Public Health Approach





Epidemiology: Classification

1. Descriptive epidemiology

- Examining distribution of disease (time, person, place)
- Disease surveillance; hypothesis generating

2. Analytic epidemiology

- Testing specific hypotheses about disease causation, e.g., exposure & outcome
- Agent/ host/ environment

EXPOSURE

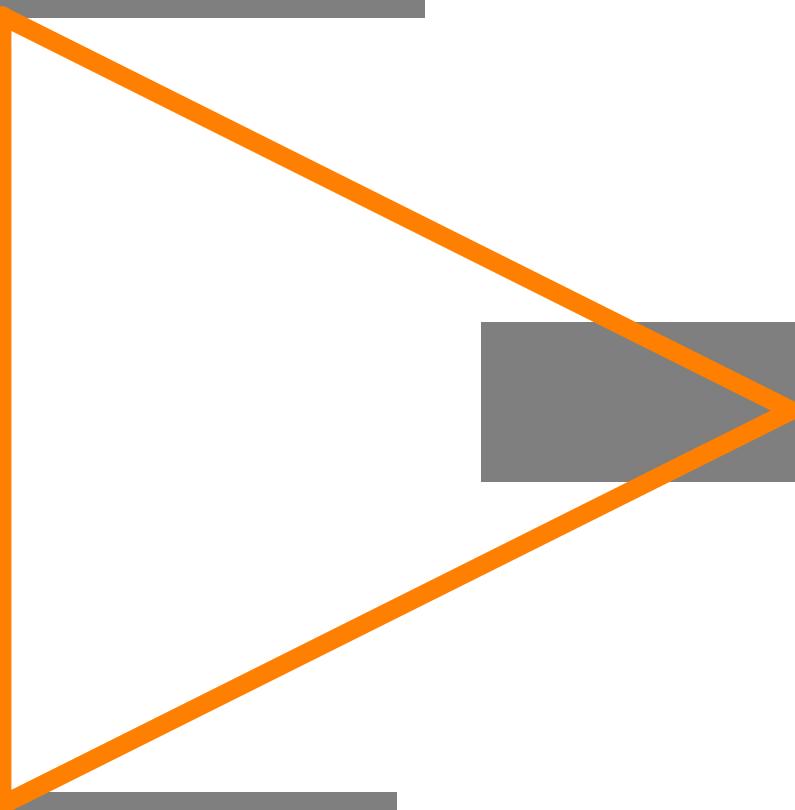


OUTCOME

ENVIRONMENT

AGENT

HOST



HOST/ AGENT/ ENVIRONMENT

AGENTS

- **Biological** (microorganisms, e.g., *Vibrio cholerae*)
- **Physical** (temperature, radiation, physical trauma)
- **Chemical** (toxins, poisons, drugs)
- **Psychological** (experiences, abuse, neglect)
- **Necessary for disease to occur**

HOST/ AGENT/ ENVIRONMENT

HOST

- Age, sex, ancestry
- Genetic endowment
- Immunologic status
- Personal behaviours (both protective and susceptible, e.g., using contaminated pump handle)
- *Host factors influence likelihood of disease or its severity*

HOST/ AGENT/ ENVIRONMENT

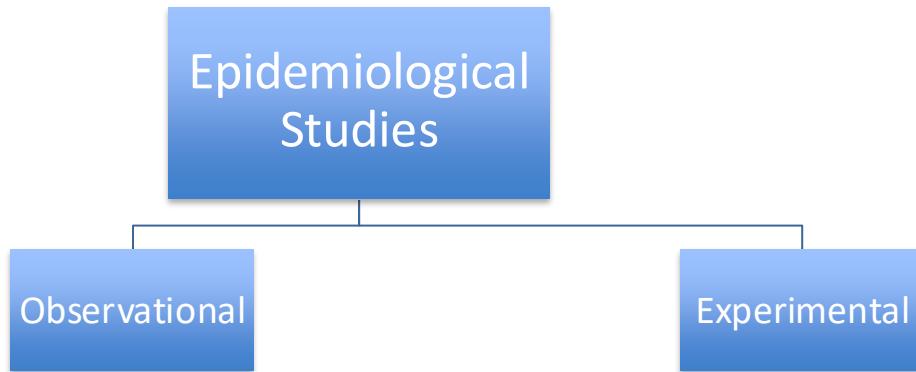
ENVIRONMENT

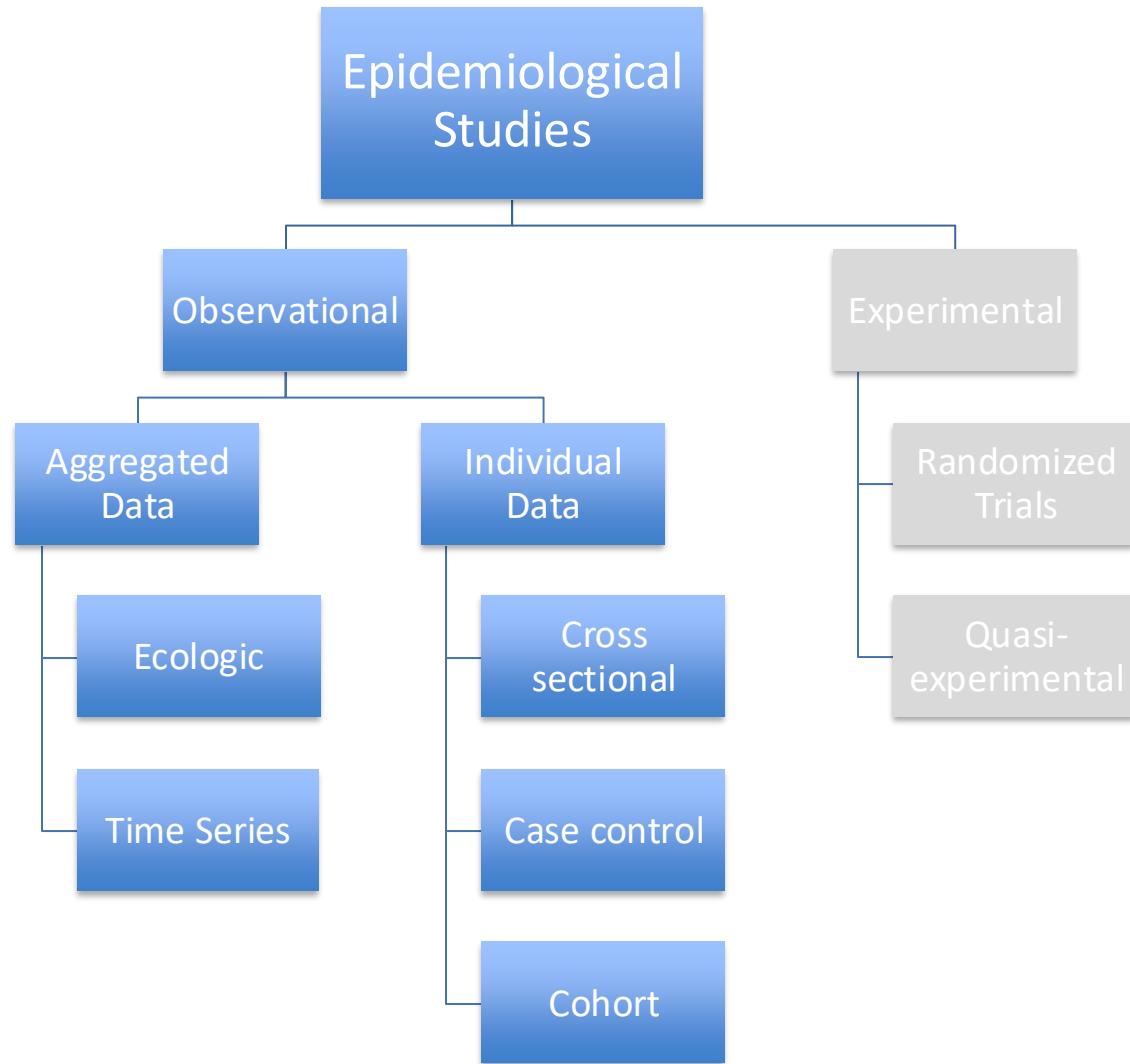
- Housing and other living conditions
- Atmosphere, climate, ecology
- Insect vectors, vehicles (e.g., food, pump handles), viral/bacterial reservoirs
- *Environmental factors mediate relationship between agent and host*

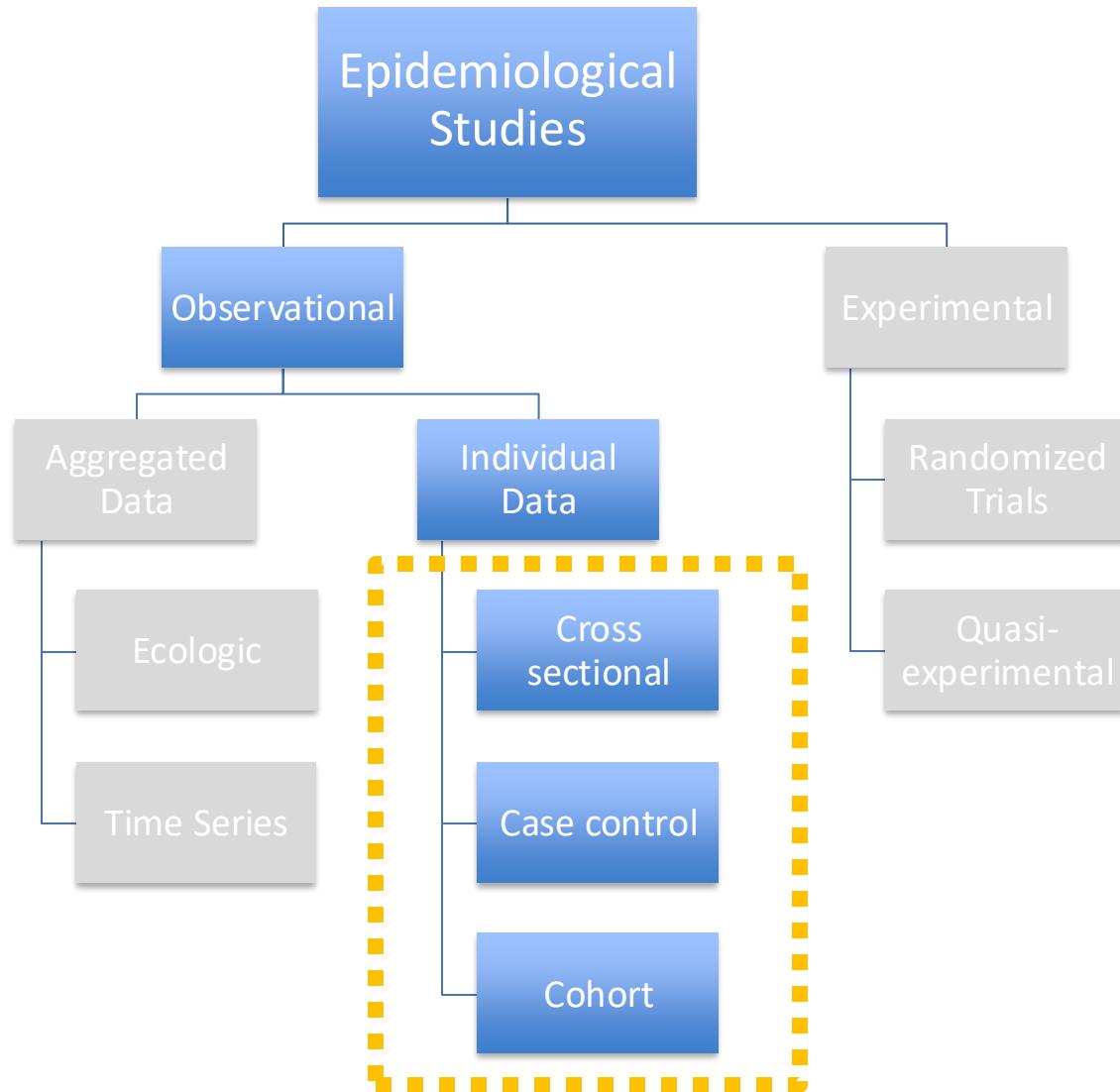
HOST/ AGENT/ ENVIRONMENT

SARS CoV2 pandemic:

- Host:
- Agent:
- Environment:







STUDY DESIGNS

Case-control study

- Exposure/disease assessed at a single point in time
- Population sampled based on disease (i.e., cases) and (non-diseased) controls
- Controls:
 - Must come from same population of interest and
 - Selection independent of exposure of interest
- Hypothesis: Exposure of interest more common among diseased

STUDY DESIGNS

Cross-sectional study

- Measures prevalence of exposure and disease at a single point in time
- Population NOT sampled based on exposure/disease state
- Analysis assesses statistical association between exposure/disease
- Risk: Probability of disease given the exposure of interest in population

National Center for Health Statistics

CDC > NCHS

National Health and Nutrition Examination Survey

About NHANES



What's New



Questionnaires, Datasets, and Related Documentation



Survey Participants



Biospecimen Program



New Content and Proposal Guidelines



Survey Results and Products



Tutorials



Listserv



Information for Health Professionals



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Related Sites

[NHANES Longitudinal Study](#)

[Growth Charts](#)

[Surveys and Data Collection Systems](#)

[NCHS Data Linkage Activities](#)



National Health and Nutrition Examination Survey

2017-2018 Questionnaire Data - Continuous NHANES

[Print](#)

- [NHANES 2017-2018 Questionnaire Variable List](#)
- [Questionnaire Instruments](#)
- [2017-2018 Questionnaire Data Overview](#)
- [SAS Universal Viewer](#)
- [Data User Agreement](#)

| Data File Name | Doc File | Data File | Date Published |
|--|------------------------------|--|----------------|
| Acculturation | ACQ_J.Doc | ACQ_J Data [XPT - 396.3 KB] | February 2020 |
| Alcohol Use | ALQ_J.Doc | ALQ_J Data [XPT - 434.4 KB] | December 2020 |
| Audiometry | AUQ_J.Doc | AUQ_J Data [XPT - 3.9 MB] | July 2020 |
| Blood Pressure & Cholesterol | BPQ_J.Doc | BPQ_J Data [XPT - 531.8 KB] | February 2020 |
| Cardiovascular Health | CDQ_J.Doc | CDQ_J Data [XPT - 518.7 KB] | February 2020 |
| Consumer Behavior | CBQ_J.Doc | CBQ_J Data [XPT - 435.4 KB] | April 2021 |
| Consumer Behavior Phone Follow-up Module - Adult | CBQPFA_J.Doc | CBQPFA_J Data [XPT - 2.7 MB] | June 2021 |
| Consumer Behavior Phone Follow-up Module - Child | CBOPFC_J.Doc | CBOPFC_J Data [XPT - 1.1 MB] | June 2021 |
| Current Health Status | HSQ_J.Doc | HSQ_J Data [XPT - 590.2 KB] | February 2020 |
| Dermatology | DEQ_J.Doc | DEQ_J Data [XPT - 242.4 KB] | February 2020 |
| Diabetes | DIQ_J.Doc | DIQ_J Data [XPT - 3.7 MB] | February 2020 |
| Diet Behavior & Nutrition | DBQ_J.Doc | DBQ_J Data [XPT - 3.3 MB] | February 2020 |

National Health and Nutrition Examination Survey

2017-2018 Data Documentation, Codebook, and Frequencies

Drug Use (DUQ_J)

Data File: DUQ_J.xpt

First Published: February 2020

Last Revised: NA

Component Description

The Drug Use questionnaire (variable name prefix DUQ) focuses on lifetime and current use of marijuana or hashish, cocaine, heroin, and methamphetamine, as well as intravenous use of these and other drugs.

Eligible Sample

Participants aged 12-69 years were eligible; however, only data from participants aged 18-69 are included in this file for public release. Data collected for participants aged 12-17 years are available through the NCHS Research Data Center (RDC). Mentally impaired participants, or participants who were unable to understand English, Spanish, Korean, Vietnamese, or Chinese (traditional/Mandarin, simplified/Mandarin, and traditional/Cantonese) were excluded from the DUQ.

Interview Setting and Mode of Administration

The DUQ was administered at the Mobile Examination Center (MEC) during the MEC Interview. For participants aged 12 to 69, questions were self-administered using the Audio Computer-Assisted Self-Interview (ACASI) system.

The ACASI was conducted in one of the following languages: English, Spanish, Korean, Vietnamese, or Chinese (traditional/Mandarin, simplified/Mandarin, and traditional/Cantonese).

The ACASI enables participants both to hear questions through headphones and read questions on the computer screen. Participants moved at their own speed and touched the screen to indicate their responses. No proxy respondents or translators were used during the ACASI.

Quality Assurance & Quality Control

For details on the QA/QC process for this component, please refer to the MEC Interviewer Procedures manual on the [NHANES website](#).

Data Processing and Editing

The data were edited for completeness, consistency, and illogical values.

To decrease the risk of disclosure, additional "bottom" summary codes were implemented for six variables in 2017-2018. For the age of first use variables (DUQ210, DUQ213, DUQ260, DUQ300, DUQ340, DUQ390), participants who reported an age less than or equal to 11 years were coded as "11 years or younger."

In addition, the new variable DUD380F includes participants who reported injecting steroids or "any other drug" (i.e., other than cocaine, heroin, or methamphetamine, which are asked about separately) using a needle. In prior cycles, these frequencies were available separately in variables DUQ380D and DUQ380E, respectively.

Analytic Notes

Please refer to the NHANES Analytic Guidelines and the on-line NHANES Tutorial for further details on the use of sample weights and other analytic issues.

Information on drug use is collected from all participants aged 12-69 years. Only data from participants aged 18-69 are included in this data file. A special use data file for participants aged 12-17, DUQY_J_R, is available through the NCHS Research Data Center (RDC).

Codebook and Frequencies

TABLE OF CONTENTS

- Component Description
- Eligible Sample
- Interview Setting and Mode of Administration
- Quality Assurance & Quality Control
- Data Processing and Editing
- Analytic Notes
- Codebook
 - SEQN - Respondent sequence number
 - DUQ200 - Ever used marijuana or hashish
 - DUQ210 - Age when first tried marijuana
 - DUQ211 - Used marijuana every month for a year?
 - DUQ213 - Age started regularly using marijuana
 - DUQ215Q - Time since last used marijuana regularly
 - DUQ215U - Time since used marijuana regularly/unit
 - DUQ217 - How often would you use marijuana?
 - DUQ219 - How many joints or pipes smoke in a day?
 - DUQ220Q - Last time used marijuana or hashish
 - DUQ220U - Last time used marijuana or hashish/unit
 - DUQ230 - # days used marijuana or hashish/month
 - DUQ240 - Ever used cocaine/heroin/methamphetamine
 - DUQ250 - Ever use any form of cocaine
 - DUQ260 - Age first used cocaine
 - DUQ270Q - Last time you used cocaine, in any form
 - DUQ270U - Last time you used cocaine/unit
 - DUQ272 - # of time you used cocaine
 - DUQ280 - # of days used cocaine/month
 - DUQ290 - Ever used heroin
 - DUQ300 - Age first used heroin
 - DUQ310Q - Last time used heroin
 - DUQ310U - Last time used heroin/unit
 - DUQ320 - # of days used heroin/month
 - DUQ330 - Ever used methamphetamine
 - DUQ340 - Age first used methamphetamine
 - DUQ350Q - Last time used methamphetamine
 - DUQ350U - Last time used methamphetamine/unit
 - DUQ352 - # times used methamphetamine
 - DUQ360 - # days used methamphetamine/month
 - DUQ370 - Ever use a needle to inject illegal drug
 - DUQ380A - Drugs injected - Cocaine

DUQ200 - Ever used marijuana or hashish

| | |
|-----------------------|---|
| Variable Name: | DUQ200 |
| SAS Label: | Ever used marijuana or hashish |
| English Text: | The following questions ask about use of drugs not prescribed by a doctor. Please remember that your answers to these questions are strictly confidential. The first questions are about marijuana and hashish. Marijuana is also called pot or grass. Marijuana is usually smoked, either in cigarettes, called joints, or in a pipe. It is sometimes cooked in food. Hashish is a form of marijuana that is also called 'hash.' It is usually smoked in a pipe. Another form of hashish is hash oil. Have you ever, even once, used marijuana or hashish? |
| Target: | Both males and females 18 YEARS - 59 YEARS |

| Code or Value | Value Description | Count | Cumulative | Skip to Item |
|---------------|-------------------|-------|------------|--------------|
| 1 | Yes | 1738 | 1738 | |
| 2 | No | 1461 | 3199 | DUQ240 |
| 7 | Refused | 0 | 3199 | DUQ240 |
| 9 | Don't know | 1 | 3200 | DUQ240 |
| . | Missing | 1372 | 4572 | |

vietnamese, or Chinese (traditional/Mandarin, simplified/Mandarin, and traditional/Cantonese).

The ACASI enables participants both to hear questions through headphones and read questions on the computer screen. Participants moved at their own speed and touched the screen to indicate their responses. No proxy respondents or translators were used during the ACASI.

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In addition, the new variable DUD380F includes participants who reported injecting steroids or "any other drug" (i.e., other than cocaine, heroin, or methamphetamine, which are asked about separately) using a needle. In prior cycles, these frequencies were available separately in variables DUQ380D and DUQ380E, respectively.

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 - DUQ220Q - Last time used marijuana or hashish
 - DUQ220U - Last time used marijuana or hashish/unit
 - DUQ230 - # days used marijuana or hashish/month
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 - DUQ260 - Age first used cocaine
 - DUQ270Q - Last time you used cocaine, in any form
 - DUQ270U - Last time you used cocaine/unit
 - DUQ272 - # of time you used cocaine
 - DUQ280 - # of days used cocaine/month
 - DUQ290 - Ever used heroin
 - DUQ300 - Age first used heroin
 - DUQ310Q - Last time used heroin
 - DUQ310U - Last time used heroin/unit
 - DUQ320 - # of days used heroin/month
 - DUQ330 - Ever used methamphetamine
 - DUQ340 - Age first used methamphetamine
 - DUQ350Q - Last time used methamphetamine
 - DUQ350U - Last time used methamphetamine/unit
 - DUQ352 - # times used methamphetamine
 - DUQ360 - # days used methamphetamine/month
 - DUQ370 - Ever use a needle to inject illegal drug
 - DUQ380A - Drugs Injected - Cocaine

DUQ200 - Ever used marijuana or hashish

Variable Name: DUQ200
SAS Label: Ever used marijuana or hashish

English Text: The following questions ask about use of drugs not prescribed by a doctor. Please remember that your answers to these questions are strictly confidential. The first questions are about marijuana and hashish. Marijuana is also called pot or grass. Marijuana is usually smoked, either in cigarettes, called joints, or in a pipe. It is sometimes cooked in food. Hashish is a form of marijuana that is also called 'hash.' It is usually smoked in a pipe. Another form of hashish is hash oil. Have you ever, even once, used marijuana or hashish?

Target: Both males and females 18 YEARS - 59 YEARS

| Code or Value | Value Description | Count | Cumulative | Skip to Item |
|---------------|-------------------|-------|------------|--------------|
| 1 | Yes | 1738 | 1738 | |
| 2 | No | 1461 | 3199 | DUQ240 |
| 7 | Refused | 0 | 3199 | DUQ240 |
| 9 | Don't know | 1 | 3200 | DUQ240 |
| . | Missing | 1372 | 4572 | |

vietnamese, or Chinese (traditional/Mandarin, simplified/M.

The ACASI enables participants both to hear questions through speakers and to see questions on the computer screen. Participants moved at their own pace to answer questions. Participants were asked to move their mouse to the screen to indicate their responses. No proxy respondents or ACASI.

Quality Assurance & Quality Control

For details on the QA/QC process for this component, please refer to the Quality Assurance and Quality Control Procedures manual on the NHANES website.

Data Processing and Editing

The data were edited for completeness, consistency, and internal validity.

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In addition, the new variable DUD380F includes participant "any other drug" (i.e., other than cocaine, heroin, or methamphetamine) about separately) using a needle. In prior cycles, these items were included in variables DUQ380D and DUQ380E, respectively.

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 - DUQ217 - How often would you use marijuana?
 - DUQ219 - How many joints or pipes smoke in a day?
 - DUQ220Q - Last time used marijuana or hashish
 - DUQ220U - Last time used marijuana or hashish/unit
 - DUQ230 - # days used marijuana or

DUQ370 - Ever use a needle to inject illegal drug

Variable Name: DUQ370

SAS Label: Ever use a needle to inject illegal drug

English Text: The following questions are about the different ways that certain drugs can be used. Have you ever, even once, used a needle to inject a drug not prescribed by a doctor?

Target: Both males and females 18 YEARS - 69 YEARS

| Code or Value | Value Description | Count | Cumulative | Skip to Item |
|---------------|-------------------|-------|------------|--------------|
| 1 | Yes | 106 | 106 | |
| 2 | No | 4042 | 4148 | DUQ426 |
| 7 | Refused | 1 | 4149 | DUQ426 |
| 9 | Don't know | 4 | 4153 | DUQ426 |
| . | Missing | 419 | 4572 | |

```
1 library(haven)
2 library(epitools)
3 setwd("~/Downloads")
4
5 xs <- as.data.frame(read_xpt("DUQ_J.XPT"))
6 xs <- xs[is.na(xs$DUQ200) == FALSE, ] # restrict to non-missing rows on DUQ200
7 xs <- xs[xs$DUQ200 != 9, ]
8
9 table(xs$DUQ200) # table: DUQ200: Ever used cannabis?
10 prop.table(table(xs$DUQ200))
11
12 table(xs$DUQ370) # table: Ever injected illegal drugs?
13 prop.table(table(xs$DUQ370))
14
15 table(xs$DUQ200 == 1, xs$DUQ370 == 1) # Crosstabulation: Cannabis x Injected
16
17 epitab(xs$DUQ200 == 1, xs$DUQ370 == 1) # Predictor/Exposure (Cannabis) x Outcome (Injection)
18
19
20
21
22
23
```

```

> table(xs$DUQ200) # table: DUQ200: Ever used cannabis?
1   2
1738 1461
> prop.table(table(xs$DUQ200))

1       2
0.5432948 0.4567052
>
> table(xs$DUQ370) # table: Ever injected illegal drugs?

1   2
72 3126
> prop.table(table(xs$DUQ370))

1       2
0.02251407 0.97748593
>
> table(xs$DUQ200 == 1, xs$DUQ370 == 1) # Crosstabulation: Cannabis x Injected

    FALSE  TRUE
FALSE  1457     4
TRUE   1669    68
>
> epitab(xs$DUQ200 == 1, xs$DUQ370 == 1) # Predictor/Exposure (Cannabis) x Outcome (Injection)
$tab
      Outcome
Predictor FALSE      p0  TRUE      p1 oddsratio    lower    upper      p.value
    FALSE  1457 0.4660909     4 0.05555556  1.00000      NA      NA        NA
    TRUE   1669 0.5339091    68 0.94444444 14.84062 5.400705 40.78062 3.584561e-14

```

THREATS TO VALIDITY

BIAS: Systematic error in the design, conduct or analysis of a study which effects the estimates of association between exposure and disease.

THREATS TO VALIDITY

Selection bias: Error in **ascertainment of study subjects** such that incorrect association observed

- Who takes part in a study, who refuses?
- Are social strata (age, gender, race) adequately represented?
- Can findings in sample be generalized to the population as a whole?
- Survivorship bias

THREATS TO VALIDITY

Information bias: Data gathered about outcome or exposure is incorrect, e.g.:

- Inaccuracy/imprecision of diagnostic tests or medical records
- Social desirability bias (?)
- Recall bias (?)

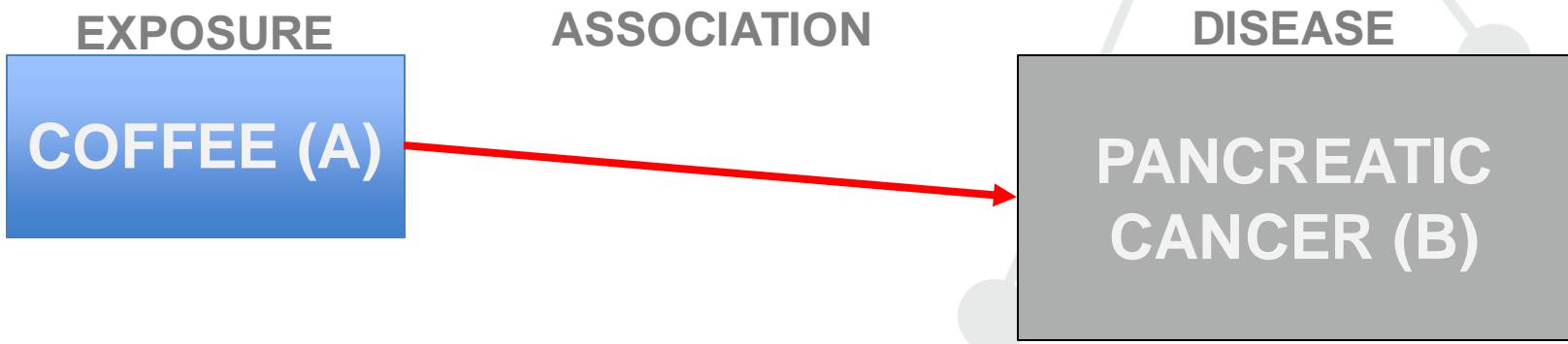
CONSIDERATIONS

Confounding: Identification of **non-causal statistical association** between exposure and outcome as a result of third variable

- e.g.: In a study of factor A is a cause of disease B, a third factor (X) is a confounder if:
 1. Factor X is a known risk factor for Disease B, and
 2. Factor X is associated with Factor A, but is not the result of factor A

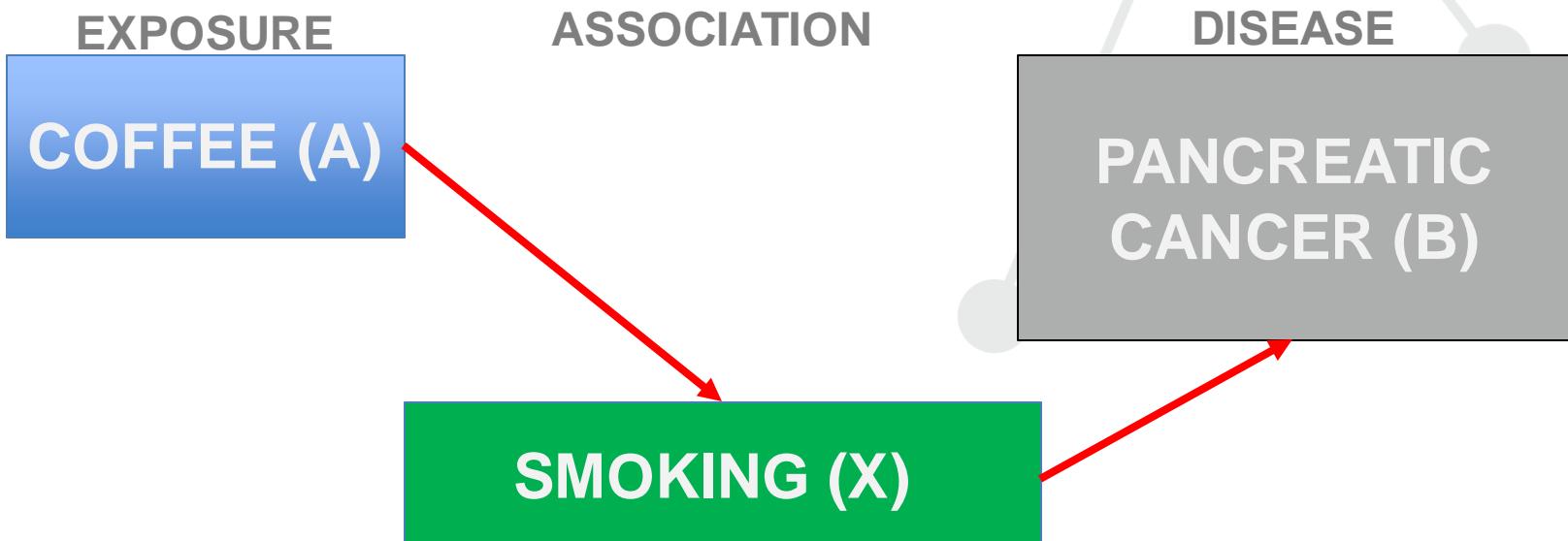
CONSIDERATIONS

Confounding: Identification of non-causal statistical association between exposure and outcome as a result of third variable



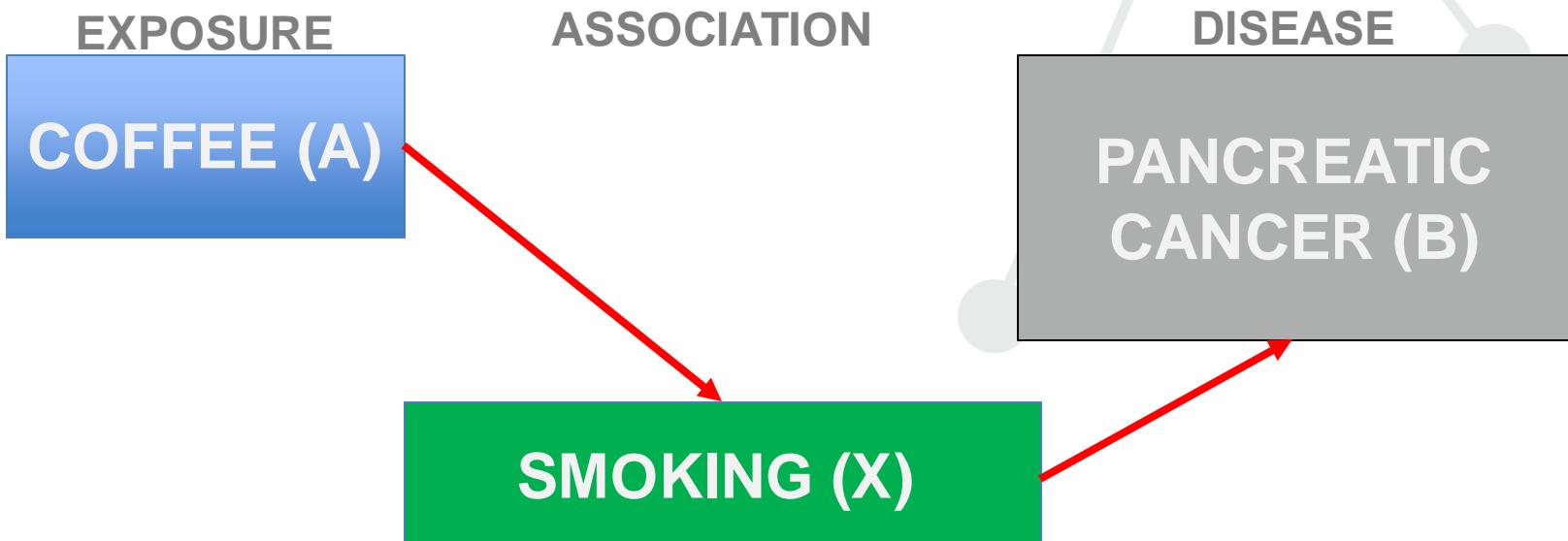
CONSIDERATIONS

Confounding: Identification of non-causal statistical association between exposure and outcome as a result of third variable



CONSIDERATIONS

Confounding: The observed statistical association (coffee > cancer) is a result of confounding by smoking, a cause of cancer and statistically associated with coffee drinking



CONSIDERATIONS

Mediation: Causation via an intervening variable

Moderation: Third variable makes relationship weaker or stronger

CASE STUDY: VIDUS





Balmoral 159 Hastings



New Zealand 235 Main



Gees Royal 237 Main



Siam Hotel W Hastings



Walton Hotel
261 E Hastings



American 928 Main St



The Beacon 7 W. Hastings



Evergreen 333 Columbia



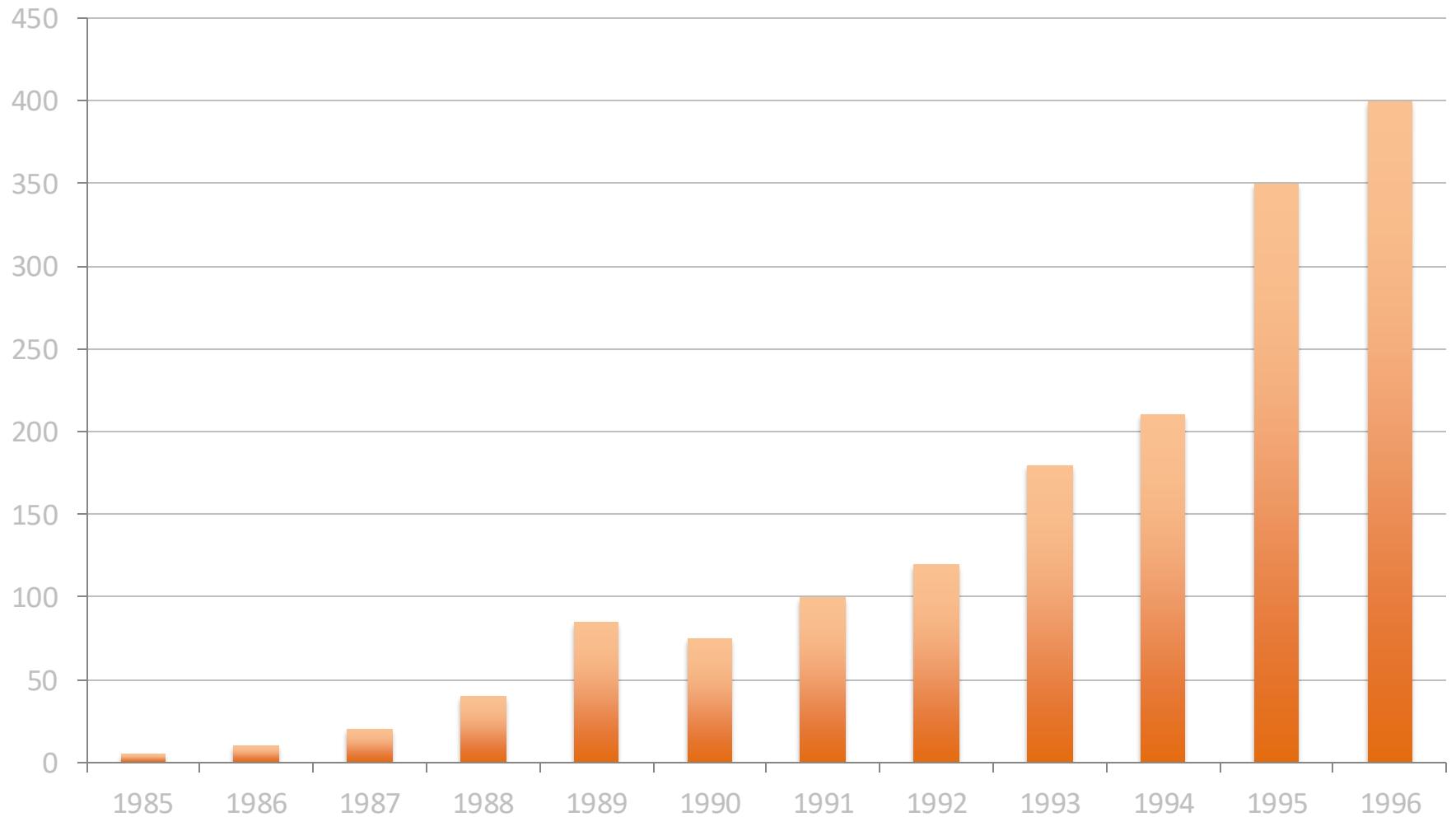
Golden Crown
116 W Hastings



Gastown 110 Water St







Vancouver's raging HIV epidemic most rampant in developed world

Nearly half the 6,000 to 10,000 addicts in Downtown Eastside are infected, AIDS expert says.

MARGARET MCNAUL

Star Staff Writer

The HIV epidemic raging in the heart of Vancouver is now established as the most rampant in the developed world.

Close to half the 6,000 to 10,000 addicts who frequent the seedy streets and back alleys in the Downtown Eastside are believed to be infected with the AIDS-causing virus, which passes from drug users to drug user via the use of needles.

Thousands more in Surrey and New Westminster, where the virus is known to be spreading, are also threatened, as are native Indian communities around the province and young drug users.

"Basically, I don't think it gets any worse," said senior AIDS researcher Dr. Martin Schechter, whose team is documenting how a poison mixture of drugs, despair and poverty is fueling the epidemic.

According to studies at the B.C. Centre for Excellence in HIV/AIDS, the infection rate among injecting drug users in Vancouver has been rising at close to 20 per cent per year. "What that means is that out of every 1,000 people who are negative at the beginning of the year, 200 will become infected by the



GRIEVE WARNING: Dr. Dave Patric, who is charting the HIV epidemic in Vancouver, stands behind Carnegie Centre at Main and Hastings, where signs of drug use are all.

end of the year," said Schechter, who is co-director of the centre.

"This is the highest incidence rate we know of in the developed world."

Bangkok, Edinburgh, and New York City experienced similar infection

rates when the virus swept through their injection drug using communities, but he said Vancouver's rate is highest.

Patric, who is charting the HIV epidemic in Vancouver, said the city's infection rates are the highest in the developed world.

"It's not a very good way to get well known," said Schechter, referring to the

way the Vancouver epidemic is attracting attention from around the world.

People with new infections, if untreated, will go on to develop AIDS in five to 10 years.

15 cents 11/97 Price in Seattle, A2

HIV outbreak among people who inject drugs (PWID) in Vancouver

- 1988: HIV prevalence ~ 1%
- 1996: Vancouver NEP exchanged 3 million needles; ranked top 3 in NA by US CDC
- Explosive outbreak of HIV began in mid-1990s
- HIV prevalence reached >25% in 18 months
- Public health disaster/scientific questions

Agent/ Host/ Environment

- Agent?
- Host?
- Environment?

AIDS. 1997 Jul;11(8):F59-65.

Needle exchange is not enough: lessons from the Vancouver injecting drug use study.

Strathdee SA¹, Patrick DM, Currie SL, Cornelisse PG, Rekart ML, Montaner JS, Schechter MT, O'Shaughnessy MV.

Author information

Abstract

OBJECTIVE: To describe prevalence and incidence of HIV-1, hepatitis C virus (HCV) and risk behaviours in a prospective cohort of injecting drugs users (IDU).

SETTING: Vancouver, which introduced a needle exchange programme (NEP) in 1988, and currently exchanges over 2 million needles per year.

DESIGN: IDU who had injected illicit drugs within the previous month were recruited through street outreach. At baseline and semi-annually, subjects underwent serology for HIV-1 and HCV, and questionnaires on demographics, behaviours and NEP attendance were completed. Logistic regression analysis was used to identify determinants of HIV prevalence.

RESULTS: Of 1006 IDU, 65% were men, and either white (65%) or Native (27%). Prevalence rates of HIV-1 and HCV were 23 and 88%, respectively. The majority (92%) had attended Vancouver's NEP, which was the most important syringe source for 78%. Identical proportions of known HIV-positive and HIV-negative IDU reported lending used syringes (40%). Of HIV-negative IDU, 39% borrowed used needles within the previous 6 months. Relative to HIV-negative IDU, HIV-positive IDU were more likely to frequently inject cocaine (72 versus 62%; $P < 0.001$). Independent predictors of HIV-positive serostatus were low education, unstable housing, commercial sex, borrowing needles, being an established IDU, injecting with others, and frequent NEP attendance. Based on 24 seroconversions among 257 follow-up visits, estimated HIV incidence was 18.6 per 100 person-years (95% confidence interval, 11.1-26.0).

CONCLUSIONS: Despite having the largest NEP in North America, Vancouver has been experiencing an ongoing HIV epidemic. Whereas NEP are crucial for sterile syringe provision, they should be considered one component of a comprehensive programme including counselling, support and education.

Study type? Exposure? Outcome?

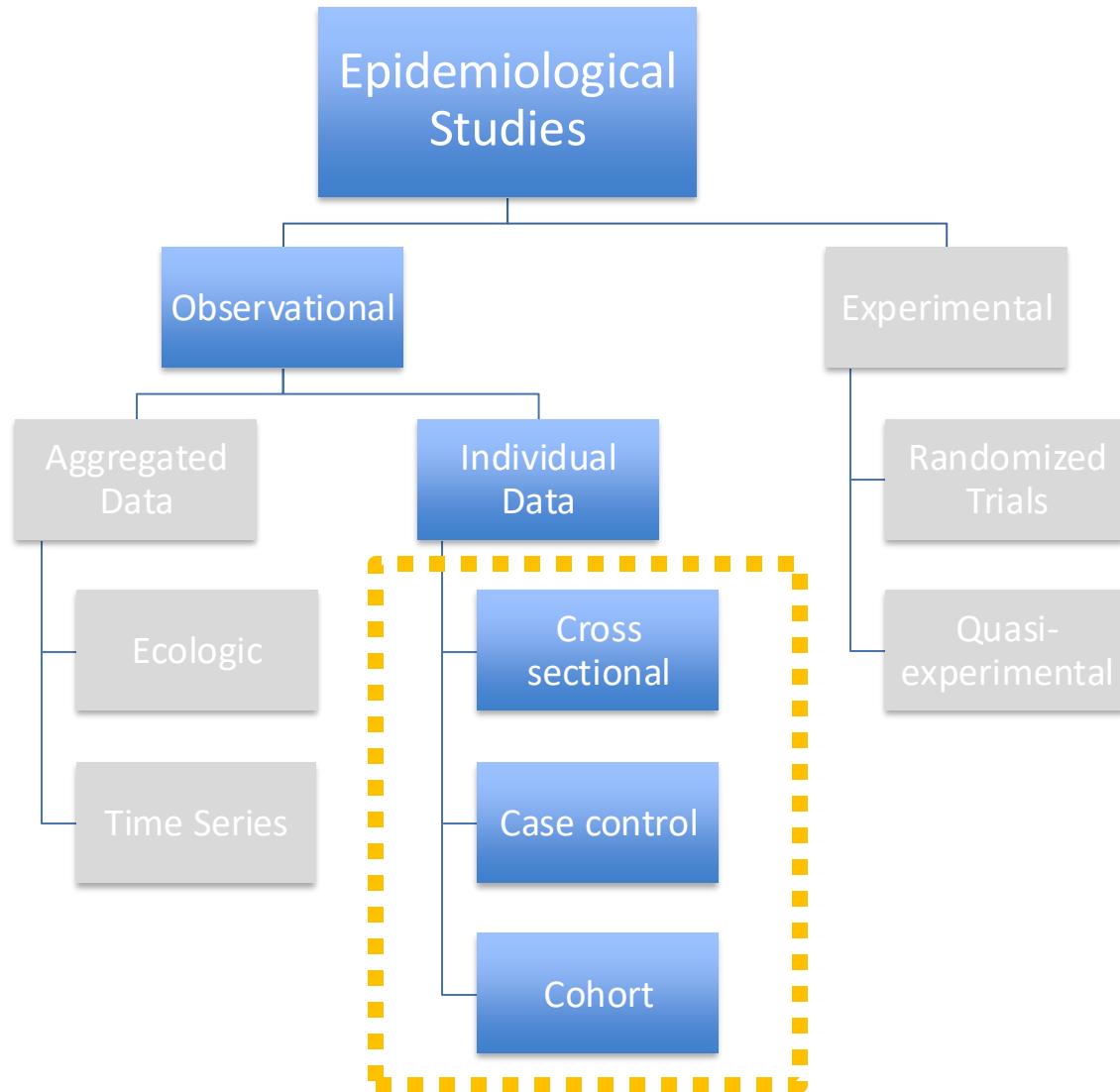
Table 2. Final multivariate logistic regression model of predictors of HIV-positive serostatus at baseline among injecting drug users (IDU) in Vancouver.

| Variable | Adjusted odds ratio (95% CI) | P |
|---|------------------------------|-------|
| Unstable housing* | 1.61 (1.15–2.98) | 0.005 |
| Education (< high school) | 1.79 (1.14–2.82) | 0.006 |
| Commercial sex* | 1.66 (1.18–2.35) | 0.008 |
| Ever used borrowed needles | 1.49 (1.04–2.14) | 0.03 |
| Inject with others* | 1.62 (1.13–2.32) | 0.008 |
| Established injector [†] | 2.24 (1.34–3.74) | 0.002 |
| Frequent NEP* attendance (more than once per week) | 1.68 (1.13–2.5) | 0.011 |

*Based on previous 6 months. [†]First injection >2 years previously.
NEP, Needle exchange programme.

Limitations

- Unclear temporal relationships between outcome and exposure (exposure precede outcome?);
- Why positive relationship between using needle exchange and having HIV?
- Possible sources of bias?



COHORT

- Ancient Roman military unit; persons banded together
- Group of persons with a common statistical characteristics, i.e., birth date, occupation, sex
- “Any defined group of individuals who are followed over a given time period,” Szklo & Nieto



DEFINITION

Cohort study:

In a cohort study, a group of healthy people at risk (cohort) is identified and followed over a certain time period to ascertain the occurrence of health-related events in order to investigate if the incidence of an event is related to a specific exposure.

Key: **Exposure precedes outcome**

Basic cohort approach:

1. Cohort defined and sampled
2. Participants are observed to ascertain exposure status (*baseline*)
3. Time passes...
4. Participants are re-observed to ascertain outcome status (*follow-up*)

COHORT DEFINITION

Who is included in a cohort?

- General population:
 - Whole population (Framingham, MA)
 - Representative sample
- Special group
 - Occupation (Nurses Health Study)
 - Exposure (VIDUS)

EXPOSURE/OUTCOME

How to measure variables (exposures, outcomes, and other factors)?

- Participants interviews/questionnaires
- Medical record review
- Medical examinations/tests
- Surveillance records (e.g., vaccination)
- Administrative data (e.g., social assistance records)

FOLLOW-UP

- Follow-up: Observation period(s) following baseline assessment
- Keeping participants in study after baseline key to study validity!
- Threat to validity: “Loss to follow-up”
 - Common sources of LTFU: Death, migration, study withdrawal
 - Can imperil statistical power & validity
 - Differential vs. non-differential

ANALYSIS

Relative Risk (RR)

- Measure of statistical association between exposure and outcome; or, risk of disease given an exposure
- $RR = \text{Probability of event in exposed} : \text{Probability of event in unexposed}$
- $RR = \text{Incidence of disease in exposed} : \text{Incidence of disease in unexposed}$
- *Example: What is relationship between living in unstable housing and acquiring HIV infection?*

ANALYSIS

Relative Risk (RR)

| | | DISEASE (HIV acquisition) | |
|--------------------------------|-----|---------------------------|----|
| | | YES | NO |
| EXPOSURE (Unstable housing) | YES | a | b |
| | NO | c | d |

= —————

ANALYSIS

Relative Risk (RR)

| | | DISEASE | |
|----------|-----|---------|----|
| | | YES | NO |
| EXPOSURE | YES | a | b |
| | NO | c | d |

$$\text{RR} = \frac{a/d}{b/c} = \frac{ad}{bc}$$

Step 1. Assemble cohort



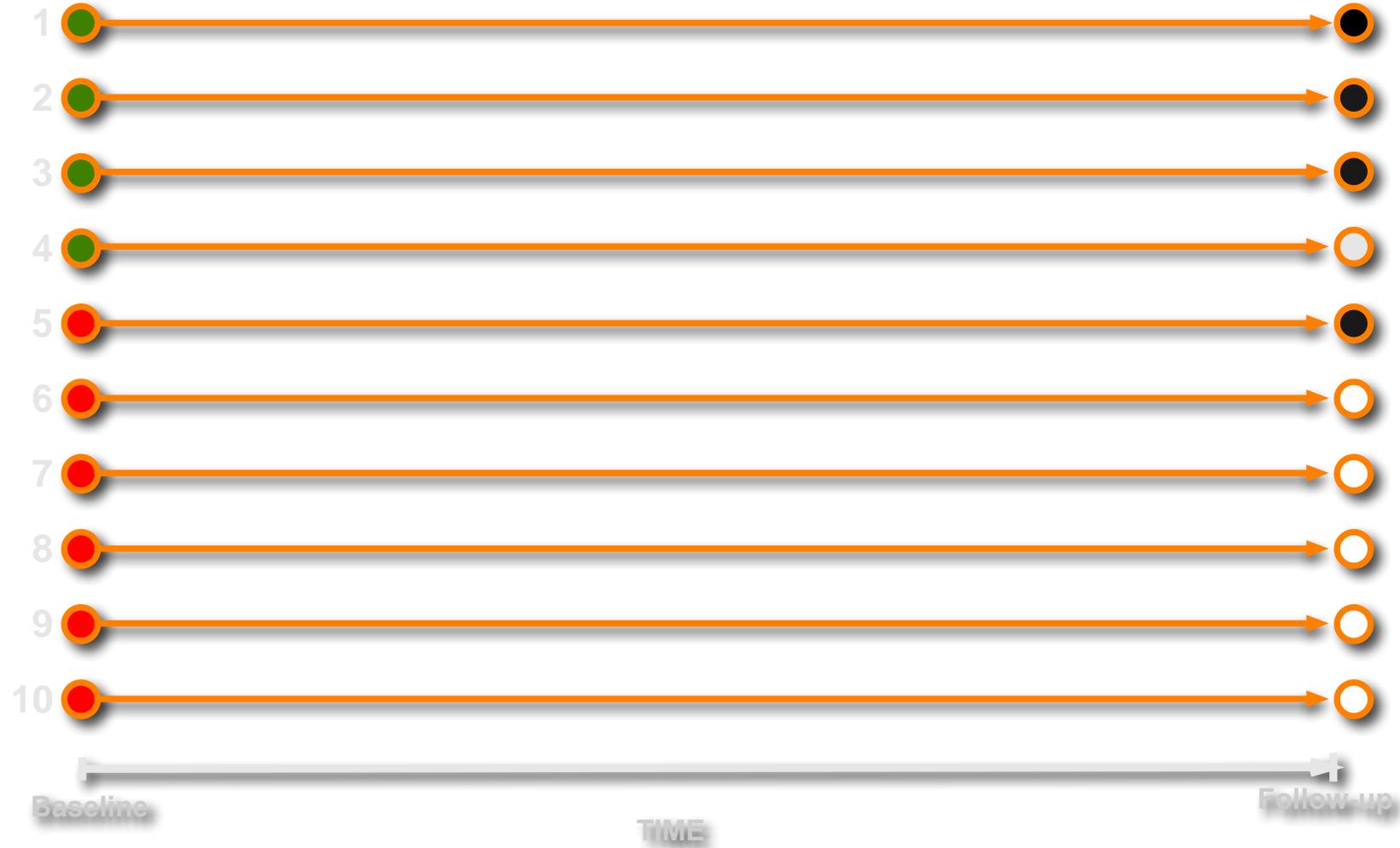
2. Baseline measurement



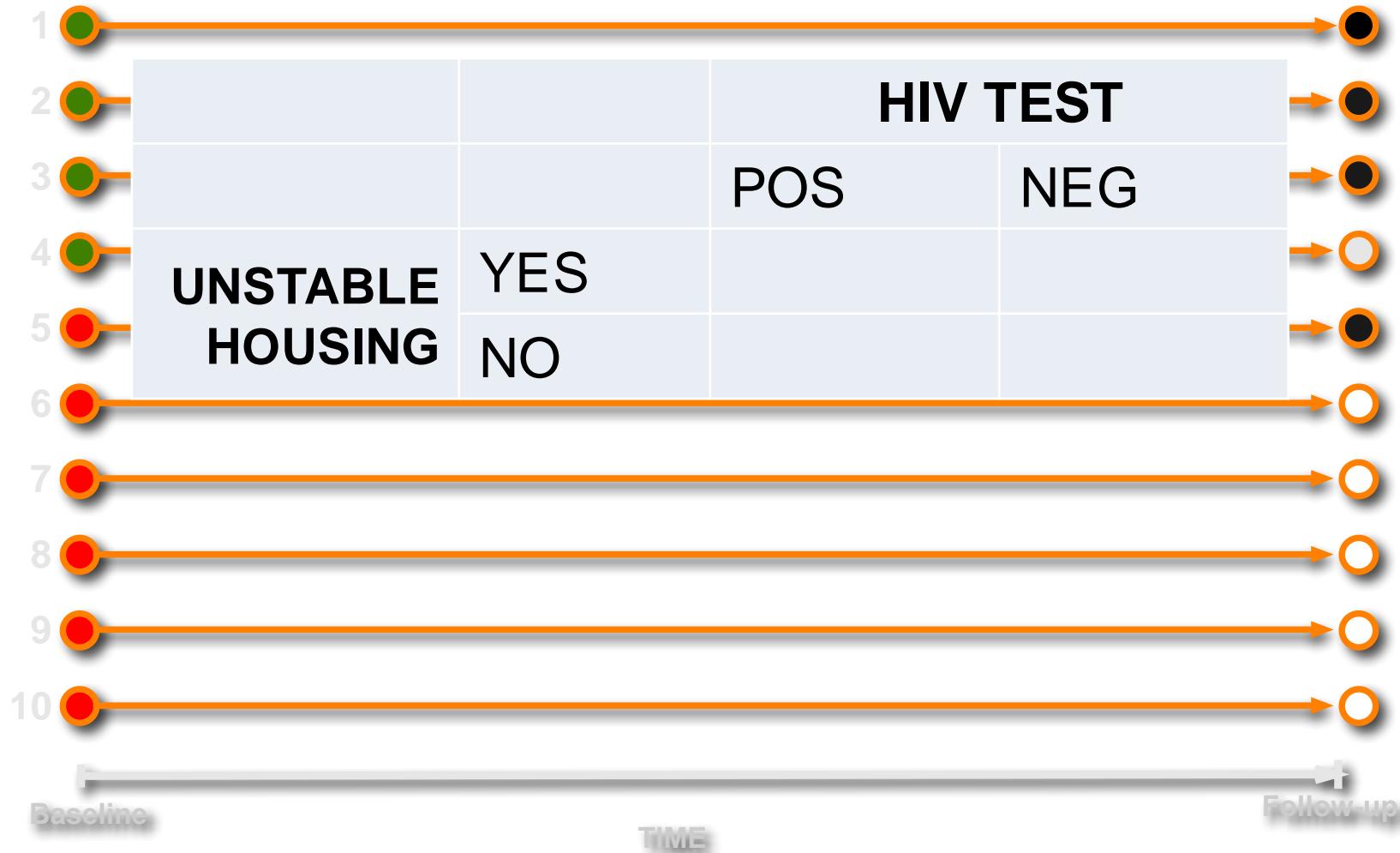
3. Time passes



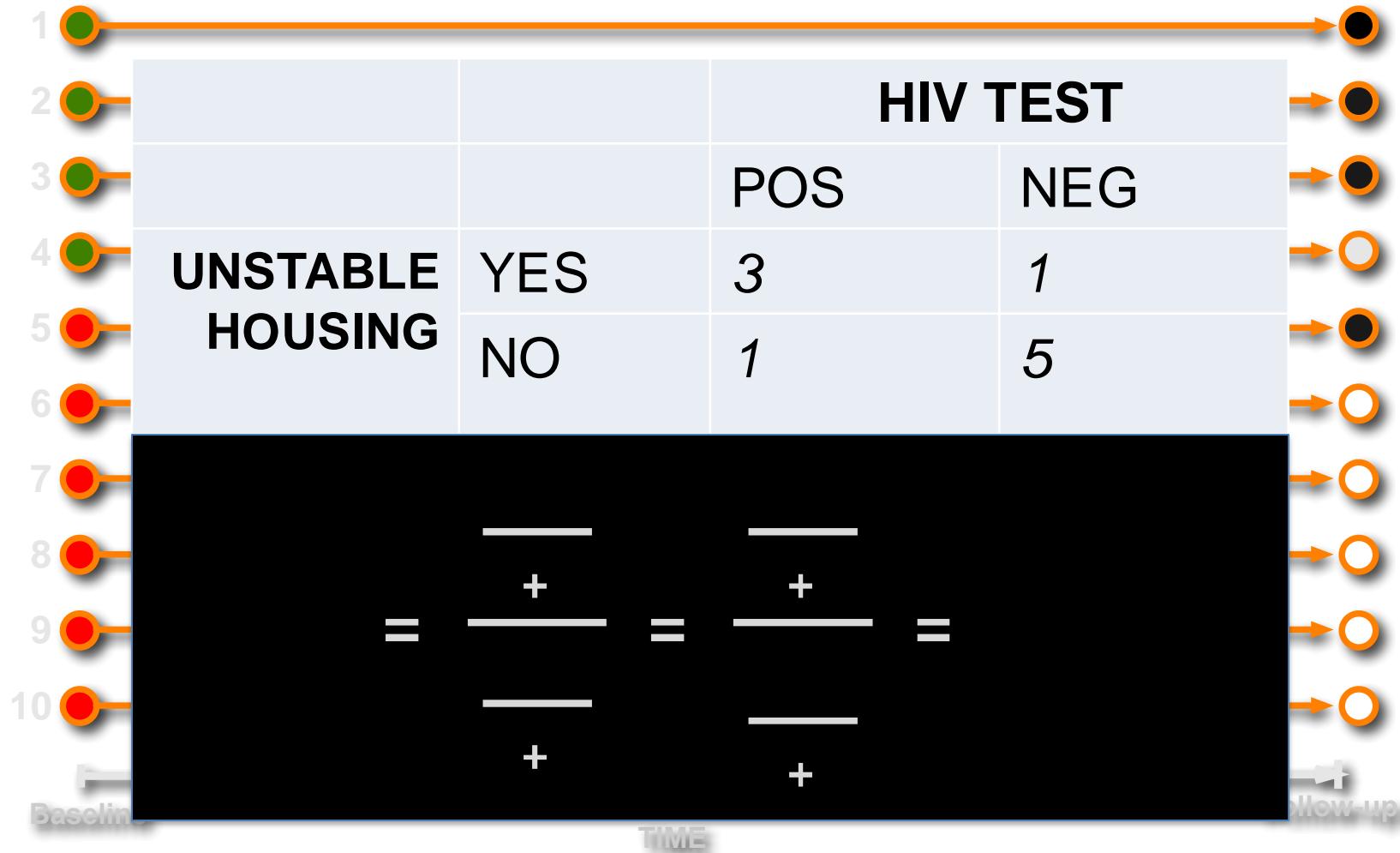
4. Outcome assessment



5. Analysis



5. Analysis



Relative Risk: Interpretation

- Relative Risk typically expressed with 95% Confidence Interval
 - e.g., RR = 1.20, 95% CI: 1.05-1.35, p-value < 0.05
- RR > 1 = Exposed individuals more likely to get disease
- RR < 1 = Exposed individuals less likely to get disease

Relative Risk: Interpretation

- Relative Risk typically expressed with 95% Confidence Interval
 - i.e., RR = 1.20, 95% CI: 1.05 – 1.35, p-value < 0.05

$$= \frac{\overline{\text{+}}}{\overline{\text{-}}} = \frac{\overline{\text{+}}}{\overline{\text{-}}} =$$
$$\frac{\overline{\text{-}}}{\text{+}}$$

PRO/RETRO

Prospective cohort

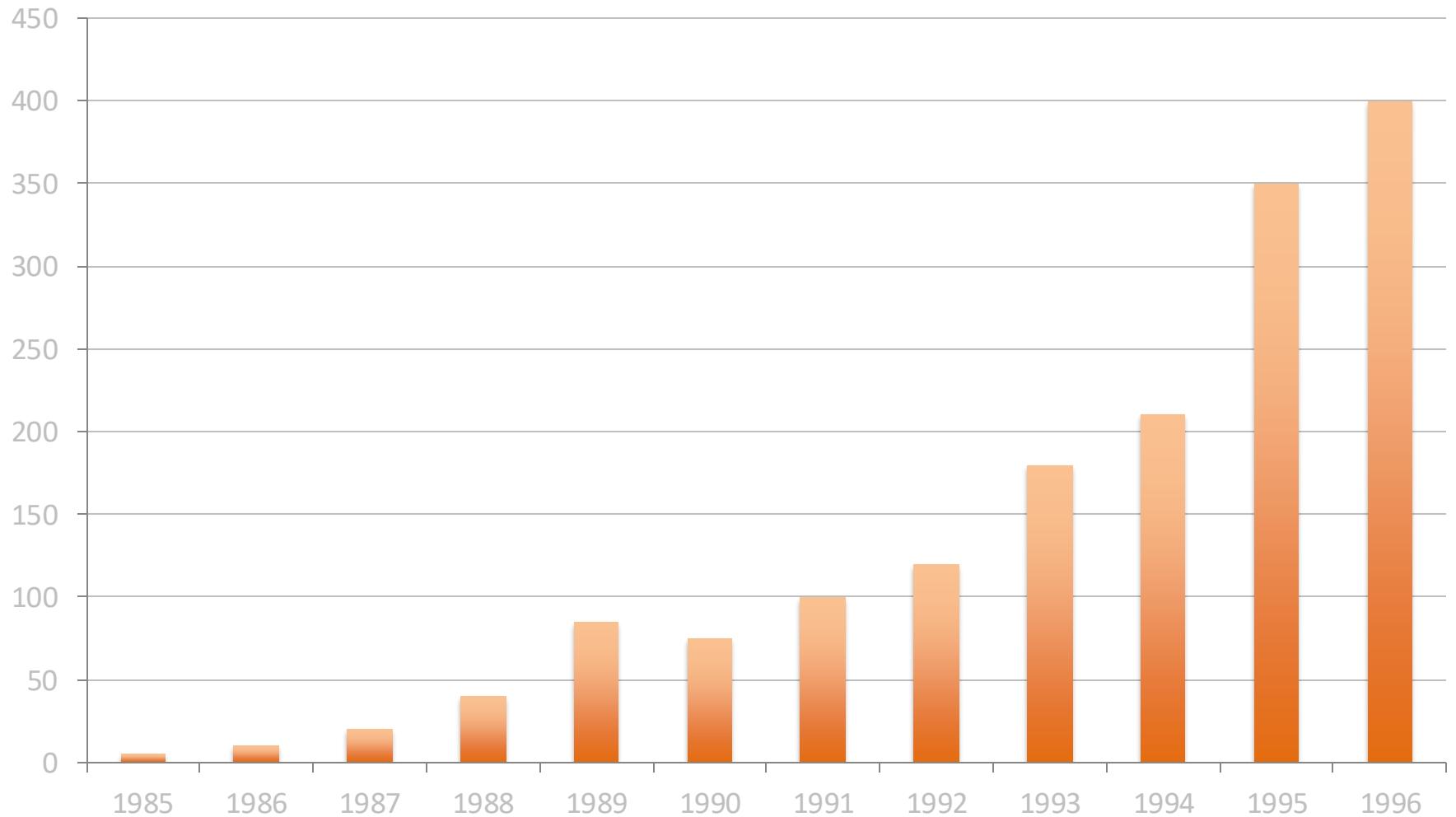
- Outcomes have not occurred when study commences
- More flexible but far more costly

Retrospective cohort

- Outcomes have already occurred
- Cohort defined by existing records, i.e., medical charts, administrative data
 - Example: Danish immunization studies
- Less costly but less flexible

LONGITUDINAL COHORTS

- Longitudinal cohort: Cohort study involving > 1 observation per unit of analysis
 - i.e., multiple observations per individual
- Longitudinal cohorts are the gold standard of observational studies



VIDUS: Definition

Vancouver Injection Drug User Study

- Open longitudinal prospective cohort
- Recruitment began May 5, 1996; recruitment and follow-up ongoing to this day
- Primary objective: HIV incidence study
 - What are the risk factors behind the explosive outbreak of HIV infection among IDU in Vancouver's Downtown Eastside, a site with extensive HIV prevention services?

VIDUS: Methods

- Community-recruited
 - e.g., staff solicit for participants in open drug scene, low-barrier social services, etc.
- Inclusion criteria:
 - Any injection drug use last 30 days
 - Aged \geq 18 years
- Exclusion criteria:
 - Unable to provide informed consent

VIDUS: Methods

At baseline and every six months:

- Participants complete interviewer-administered questionnaire
 - Baseline: Lifetime and recent exposures
 - Follow-up: Recent exposures
- Nurse examination including blood draw for HIV antibody status, urinalysis

Vancouver Injection Drug Users Study (VIDUS) Baseline Questionnaire

INTERVIEWER:

DATE OF INTERVIEW:

(mm/dd/yy)

START TIME:

END TIME:

CODE:

INTERVIEWER NOTES:

a) Where was the respondent recruited from?

At all:

Most important:

(check all that apply)

(check

- Clinic (eg. DCHC)
- Detox.....
- Doctor.....
- Hospital.....
- Needle exchange.....
- Other agency (eg. VNHS, etc.).....
- Other participant.....
- Street nurse.....
- Study staff.....
- Treatment program.....
- Word of mouth.....
- Other (specify): _____

b) Where is the interview being carried out?

- VIDUS office
- Public place (specify: _____)
- Community agency
- Other (specify: _____)

c) Is this interview being carried out where anyone
can overhear?

The Vancouver Injection Drug Users Study (VIDUS)

CODE:

ALL RESPONDENTS

A: Current Demographics

READ:

The first set of questions are about your family background.

11. What is your **date of birth**?

(mm/dd/yy)

A6. Were you **born** in Canada?

- Yes
- No:

If no, what **country** you were born in?

What **year** did you come to Canada?

• Only ask about gender if necessary to clarify.

12. What was your **biological gender** at birth?

- Male
- Female

13. What **gender** do you identify yourself as?

Check one only:

- Male
- Female
- Transgender

14. What kind of **relationship** are you in right now?

- Legally married
- Widowed
- Separated

A7. What **country** were your parents born in?

MOTHER: _____

- Don't know

FATHER: _____

- Don't know

A8. Do you live in Vancouver (the Lower Mainland) **right now**?

- Yes
- No:

{ If no, notify Sue

A9. How long ago did you move to Vancouver (the Lower Mainland?)



Main Questionnaire Follow-Up 28 / 23

**VIDUS II / ACCESS
FU 28**

VIDUS II Code: H05-50234

ACCESS Code: H05-50233

**ARYS II
FU 23**

ARYS II Code: H04-50160

Participant Date of Birth: _____

Participant Last Study Visit: _____
(month)

Interviewer: _____

Date of Interview: _____

READ:

Thank you for coming in today and contributing to this study. As we go through the interview together, in mind that there are **no wrong answers**. It's very important that you answer as honestly as you can your information to **help create positive change** for people who use drugs.

We realize some of these questions are sensitive. If you do not want to answer a question, just let me know. We will move on. It is better for you to **refuse to answer** a question than to give a false answer. False answers limit the quality of our data and limit our ability to advocate for positive change.

We take your **privacy very seriously**. All the information that you provide will only be kept between me. We never report any individual information.

If there are any questions you don't understand, please stop me and **ask for clarification**. The interview will last about an hour. If you need a break, let me know and we can stop for a short rest before we finish the interview.

Remove and shred this page after data cleaning.

C6. Over the last 6 months, what were your sources of income?

| Last 6 mos (Check all that apply.) | (Read out list.) Income source | Most important (Check one only.) | How many weeks? | | | | How much weekly? |
|--|--|---|--------------------------|--------------------------|--------------------------|--------------------------|---------------------|
| | | | 1 to 6 | 7 to 12 | 13 to 18 | More than 18 | |
| <input type="checkbox"/> | Regular job | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | \$ |
| <input type="checkbox"/> | Temporary work | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | \$ |
| <input type="checkbox"/> | Self-employed | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | \$ |
| <input type="checkbox"/> | Recycling (binning, buy/sell) | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | \$ |
| <input type="checkbox"/> | Squeegying | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | \$ |
| <input type="checkbox"/> | Panhandling | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | \$ |
| <input type="checkbox"/> | Income assistance | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | |
| <input type="checkbox"/> | CPP or EI | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | |
| <input type="checkbox"/> | GST rebate | <input type="checkbox"/> | N/A | | | | N/A |
| <input type="checkbox"/> | Parent, friend, relative, partner | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | \$ |
| <input type="checkbox"/> | Theft, robbing or stealing | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | \$ |
| <input type="checkbox"/> | Selling needles | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | \$ |
| <input type="checkbox"/> | Selling cigarettes / tobacco | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | \$ |
| <input type="checkbox"/> | Selling drugs (Reassure confidentiality.) | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | \$ |
| <input type="checkbox"/> | Cocaine | | | | | | |
| <input type="checkbox"/> | Crack cocaine | | | | | | |
| <input type="checkbox"/> | Ecstasy / MDMA / Molly | | | | | | |
| <input type="checkbox"/> | Heroin | | | | | | |
| <input type="checkbox"/> | Cannabis, hash, pot | | | | | | |
| <input type="checkbox"/> | Crystal meth | | | | | | |
| <input type="checkbox"/> | Benzos | | | | | | |
| <input type="checkbox"/> | Methadose | | | | | | |
| <input type="checkbox"/> | Suboxone | | | | | | |
| <input type="checkbox"/> | Prescription opioids | | | | | | |
| <input type="checkbox"/> | Other drug: _____ | | | | | | |
| <input type="checkbox"/> | Other drug: _____ | | | | | | |
| <input type="checkbox"/> | Other criminal activity | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | \$ |
| <input type="checkbox"/> | Sex for money | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | \$ |
| <input type="checkbox"/> | Stipend | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | \$ |
| <input type="checkbox"/> | Other: _____ | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | \$ |

VIDUS: Methods

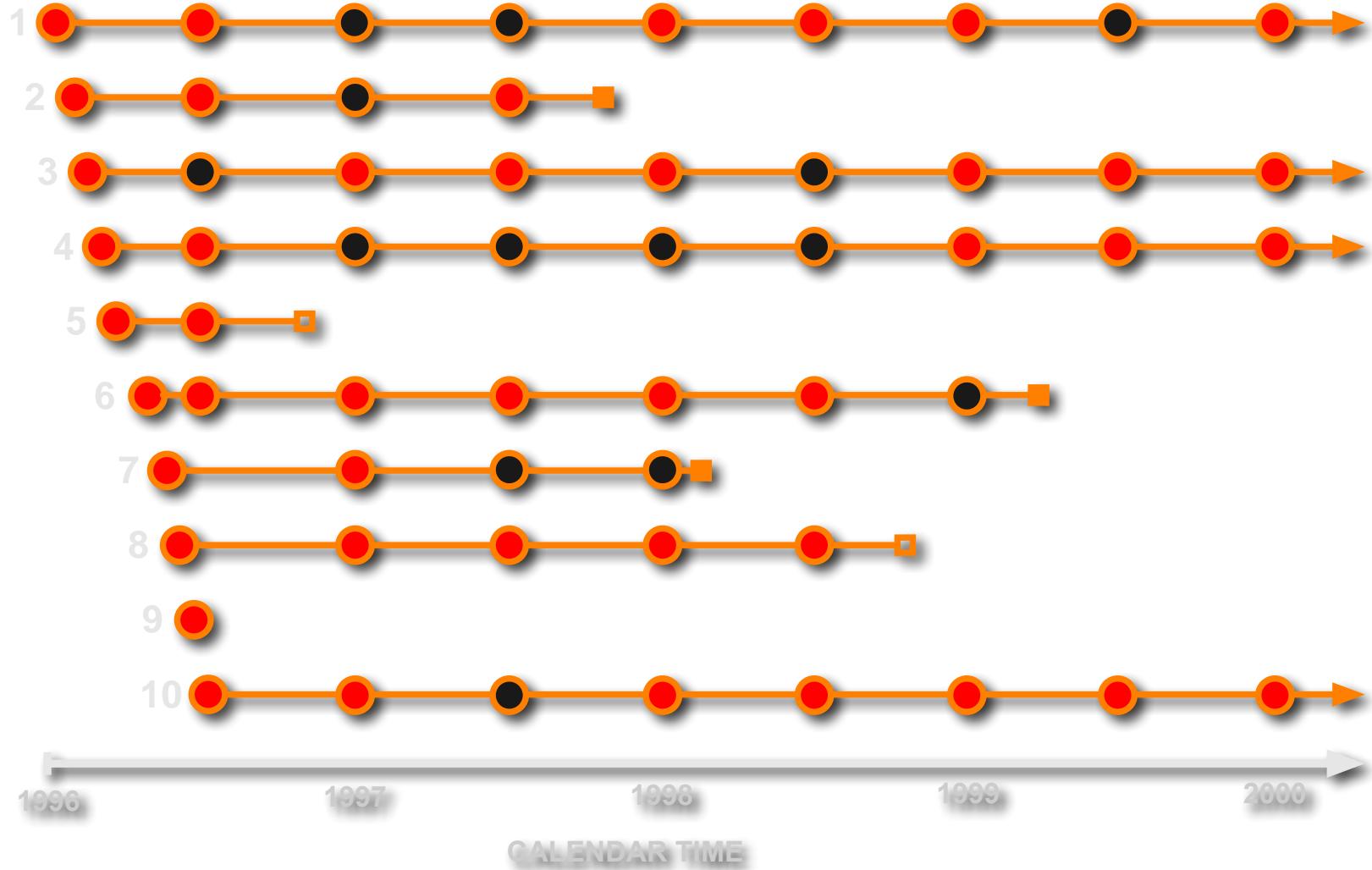
Questionnaire elicits information on:

- Socio-demographics
- Injection and non-injection drug-use behaviours (ever, last six months)
- Housing and homelessness
- Incarceration
- Policing
- Alcohol and drug treatment
- Violence
- Sexual experiences (paid and non-)

VIDUS: Methods

Realities of running a longitudinal prospective cohort

- Not all people recruited at study start: baseline not synchronized to calendar time
- Analyses must account for different amounts of observation time
 - Withdraw from study
 - Lost to follow-up
 - Death
- Some characteristics fixed (e.g., birthplace); other exposures vary over time (e.g., recent behaviours)
- Missing data (interviews, tests)





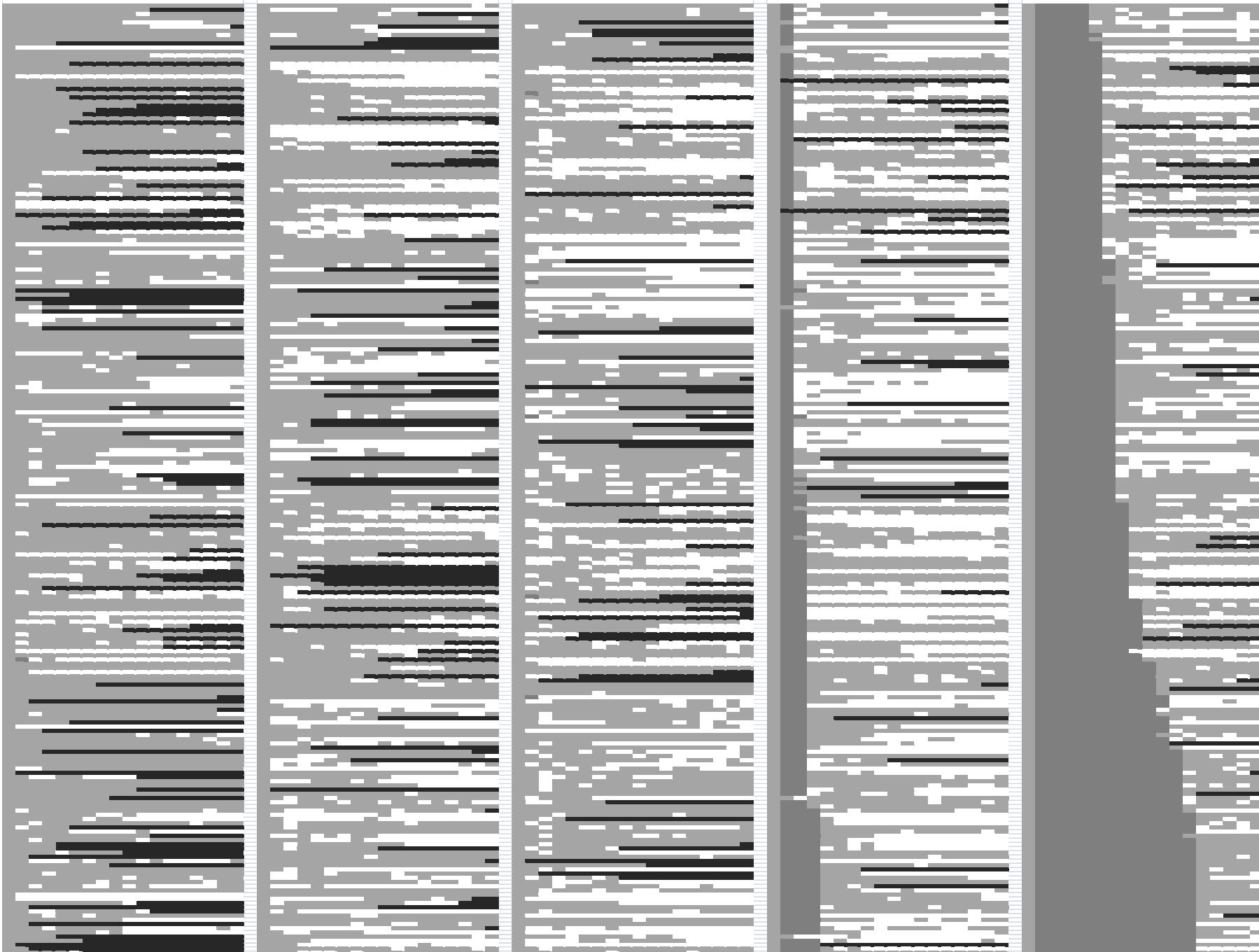
ID 1-320

ID 321-640

ID 641-962

ID 963-1282

ID 1282-1603



VIDUS: Analysis

Analytic technique must incorporate:

- Differing amounts of observation time;
- Time-varying and time-fixed exposures;
- Multiple observations per person
(longitudinal);
- Correlated observations
- Missing data and censoring
- Adjustment for covariates

Intensive injection cocaine use as the primary risk factor in the Vancouver HIV-1 epidemic

**Mark W. Tyndall^{a,b}, Sue Currie^a, Patricia Spittal^{a,b}, Kathy Li^a,
Evan Wood^{a,b}, Michael V. O'Shaughnessy^{a,c} and
Martin T. Schechter^{a,b}**

Objectives: The explosive and ongoing injecting drug use-related HIV-1 epidemic in Vancouver continues to receive international attention. This study was conducted to determine how patterns of cocaine use influence the risk of HIV infection.

Methods: The Vancouver Injection Drug Users Study is an open prospective cohort of injecting drug users that began in May 1996. At enrollment and at semi-annual follow-up visits an interviewer administers a detailed semi-structured questionnaire. Cox proportional hazards models were used to determine behavioral and drug use patterns reported in the 6 months prior to HIV seroconversion.

Results: One-hundred and nine incident HIV infections have been observed during a mean follow-up of 31 months, from 940 HIV-seronegative participants. During the 6 months prior to seroconversion, predictors of HIV infection were injecting cocaine use [adjusted hazards ratio (AHR), 3.72], incarceration (AHR, 2.74), unstable housing (AHR, 2.36), methadone maintenance treatment (AHR, 1.98), and Aboriginal ethnicity (AHR, 1.78). Injecting cocaine use was predictive of HIV infection in a dose-dependent fashion. Compared with infrequent cocaine users, participants who averaged more than three injections per day were seven times more likely to contract HIV. In addition, the time to HIV infection was accelerated among regular cocaine injectors independent of concurrent heroin use.

Conclusions: Injecting cocaine use was a strong, dose-dependent predictor of HIV seroconversion in this poly-drug using population. Injection cocaine users remain particularly vulnerable to HIV infection and treatment options for cocaine dependency

VIDUS: Seroconversion analysis

- **Analytic sample:** Participants who are HIV-negative at baseline interview
- **Outcome:** Time to positive HIV test
- **Hazard Ratio:** Incidence in exposed over incidence in unexposed
- **Cox extended hazards model:** Outputs are estimates of relative hazards associated with each exposure

Table 2. Drug use, sexual behaviors, and demographic factors as predictors of HIV seroconversion.

| Variable | Bivariate hazards ratio (95% CI) | P | Adjusted hazards ratio (95% CI) | P |
|---|----------------------------------|-------|---------------------------------|-------|
| Injection cocaine use (> 1/week) ^a | 4.29 (2.88–6.39) | 0.001 | 3.72 (2.44–5.67) | 0.001 |
| Incarceration ^a | 5.10 (3.36–7.74) | 0.001 | 2.74 (1.81–4.15) | 0.001 |
| Unstable housing ^a | 3.80 (2.57–5.63) | 0.001 | 2.36 (1.57–3.54) | 0.001 |
| Methadone treatment ^a | 2.75 (1.46–5.22) | 0.002 | 1.98 (1.05–3.73) | 0.03 |
| Aboriginal ethnicity | 2.19 (1.45–3.30) | 0.001 | 1.78 (1.19–2.69) | 0.006 |
| Female sex | 1.47 (0.98–2.21) | 0.06 | 1.15 (0.72–1.83) | 0.55 |
| Received payment for sex ^a | 2.67 (1.55–4.59) | 0.001 | 1.05 (0.55–2.01) | 0.89 |
| Lifetime sex partners (> 20) | 2.50 (1.68–3.71) | 0.001 | 0.97 (0.63–1.48) | 0.87 |
| Injection Heroin use (> 1/week) ^a | 1.24 (0.83–1.85) | 0.29 | 0.85 (0.56–1.29) | 0.45 |
| Crack cocaine use (> 1/week) ^a | 0.76 (0.48–1.21) | 0.24 | 0.47 (0.30–0.75) | 0.001 |

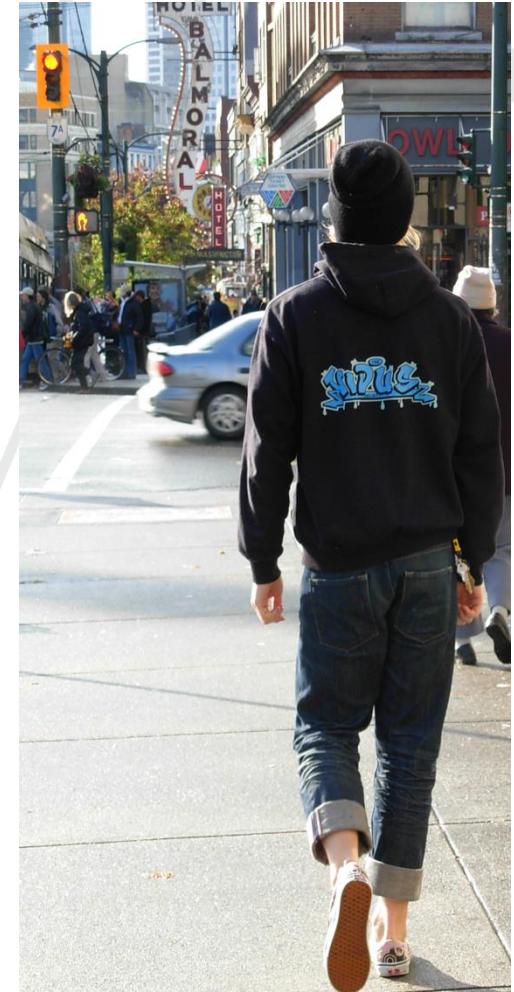
^aDenotes activities reported in the follow-up visit that occurred closest to the time of HIV seroconversion. CI, Confidence interval.

injection. Injecting cocaine use was predictive of HIV infection in a dose-dependent fashion. Compared with infrequent cocaine users, participants who averaged more than three injections per day were seven times more likely to contract HIV. In addition, the time to HIV infection was accelerated among regular cocaine injectors independent of concurrent heroin use.

Conclusions: Injecting cocaine use was a strong, dose-dependent predictor of HIV seroconversion in this poly-drug using population. Injection cocaine users remain particularly vulnerable to HIV infection and treatment options for cocaine dependency

Evidence/action (part of public health cycle) using VIDUS findings:

- Expansion of needle exchange & methadone
- Reforms to policing and incarceration practices
- Addressing overdose risk factors
- Benefits of Insite, supervised injection facility and other forms of harm reduction
- Scale-up of antiretroviral therapy for HIV+ people who use drugs



CONSIDERATIONS

COHORT STRENGTHS

- Estimate incidence and risk = stronger evidence for causal inference
- Temporal relationships can be clearly observed
- More statistical power = greater precision of effect measures, ability to analyse rarer exposures/outcomes
- Repeated measures can reduce bias
- Possible to model disease trajectories (i.e., susceptible, infected, recovered)
- Possible to simultaneously model host/agent/environment interactions

CONSIDERATIONS

COHORT WEAKNESSES

- Loss to follow-up, especially non-random, and survival bias
- Accounting for missing data
- Difficulty of consistent data collection over time
- Time and cost, especially for rare outcomes
- Longitudinal studies: Standard regression models not usable

CONCLUSIONS

Basics of epidemiologic inquiry

1. Concerned with the occurrence and distribution of disease in populations
2. Descriptive or analytic; observational or experimental
3. Often considers the relationship between exposures and outcomes
4. Study designs include cross-sectional and cohorts