Directed acyclic graphs in Neighborhood and Health research (Social Epidemiology)

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Inference in n'hood & health research

N'hood (neighborhood) and health research has to deal with challenging difficulties:

- N'hood factors are distal causes of health: significant causal distance
- Complex causal chains with variables at multiple levels: cross-level mediating mechanisms
- Selective migration as a source of confounding
- Ecological processes generating interdependence among the n'hood exposures
- Feedback loops and reciprocal interactions

Inference in n'hood & health research

Randomization in n'hood and health research?

(i) of interventions to neighborhoods

(ii) of individuals to neighborhoods

(i) Randomized community trials

- in a limited number of n'hoods → generalizability?
- only applicable to a restricted range of n'hood exposures
- which of the multiple components is influent?

(ii) Residential relocation programs

- in a limited number of n'hoods
- unnatural scenario + ethical issues

→ Interventions often only representative of themselves

→ Observational studies remain a key approach

DAGs: GENERAL RATIONALE

Common problems:

- Imprecise identification of research hypotheses
- Inappropriate selection of adjustment variables

Directed Acyclic Graphs (**DAGs**) allow to:

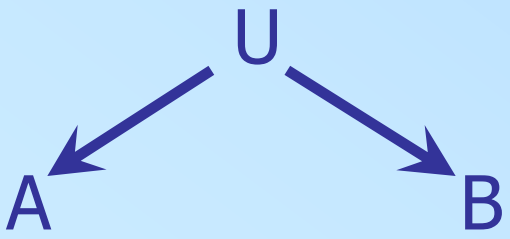
- graphically encode *a priori* assumptions about causal relations between exposure, outcome, and covariates (before data analysis)
  → identify appropriate analytical strategies
- depict alternative sets of causal structures that could give rise to observed associations (after or during data analysis)

Suzuki 2011. Hernán 2004. Glymour 2006

DAGs: STRUCTURE AND BASIC RULES

Causal DAGs are composed of:

- nodes: representing (un)measured variables
  - In our case: individuals as units of analysis (n'hood variables reflect n'hood exposures)
- directed arrows (or edges) between variables (most often single-headed)
  - Arrows can be interpreted as direct causal effects
  - Sequence of directed arrows: indirect effect

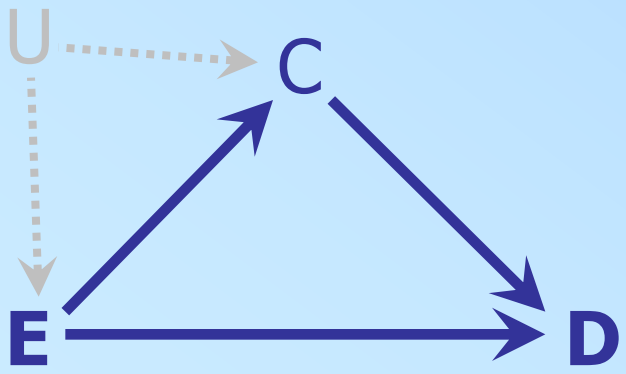


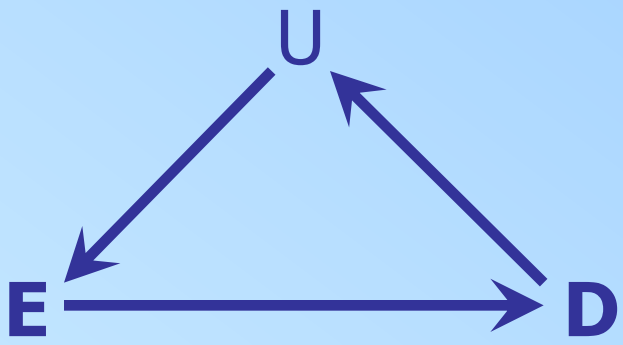
Greenland 1999. Hernán 2004. Glymour 2006

DAGs: STRUCTURE AND BASIC RULES

Formal rules and assumptions of DAGs:

- If two variables in the DAG share a common cause (including an unmeasured one), it has to be reported.
- Acyclic: a variable cannot cause itself (directly or indirectly)





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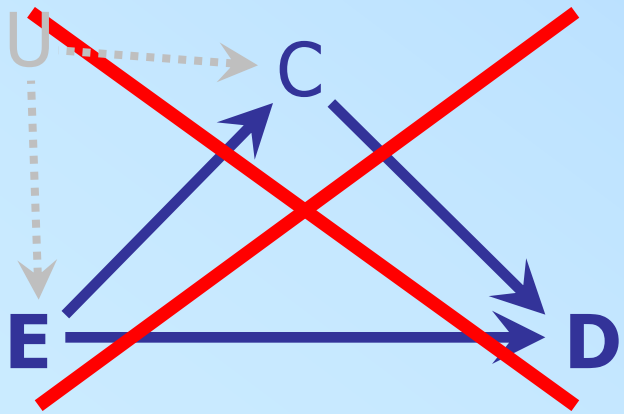

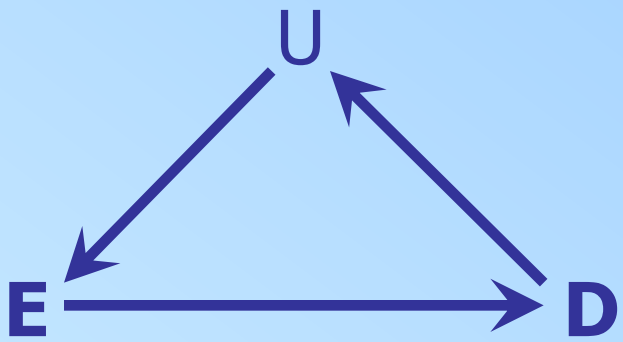

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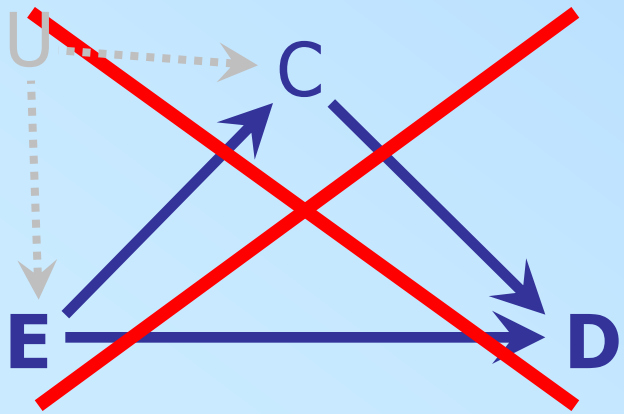

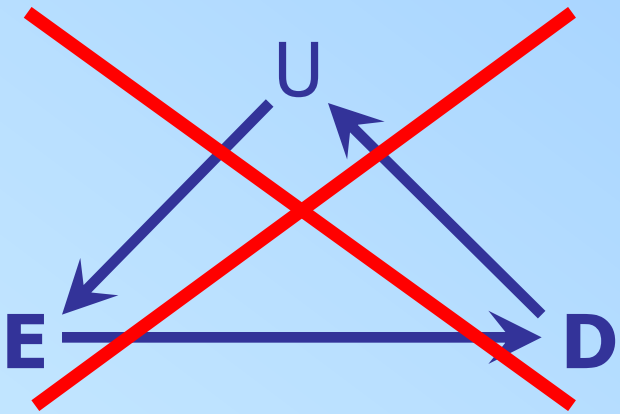

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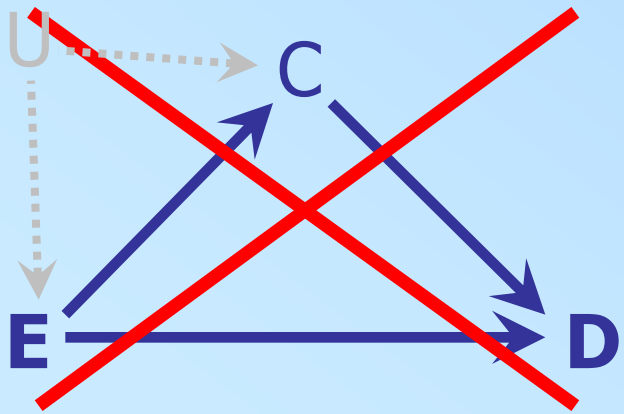
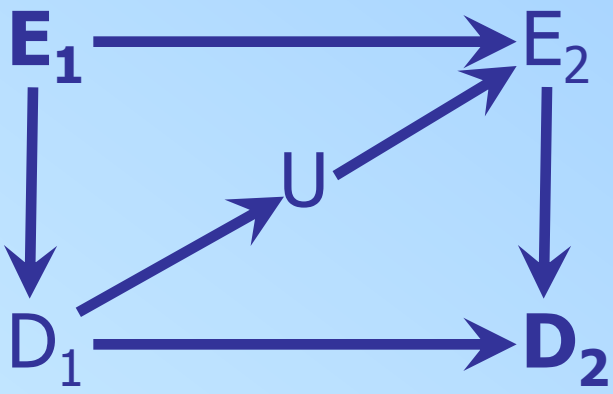
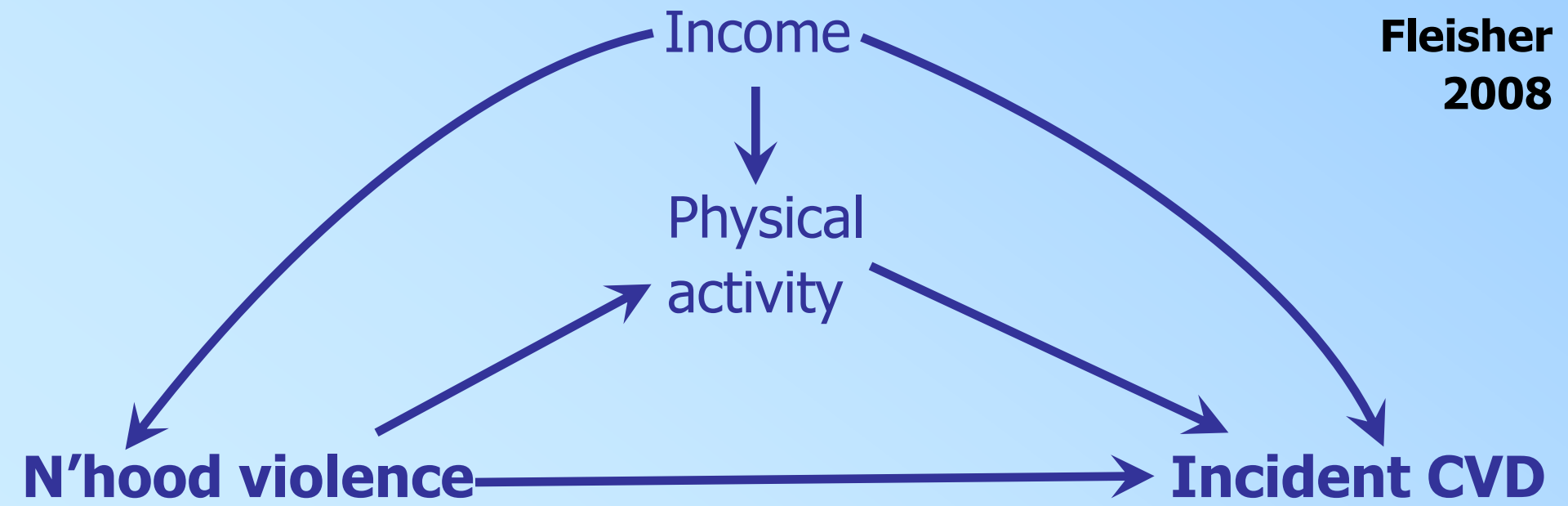




Hernán 2004. Glymour 2006

DAGs: TERMINOLOGY

- A **child** of a variable / a **parent** of a variable
- A **descendant** of a variable / an **ancestor** of a variable
- **A path**: a series of lines connecting two variables, regardless of arrowhead direction



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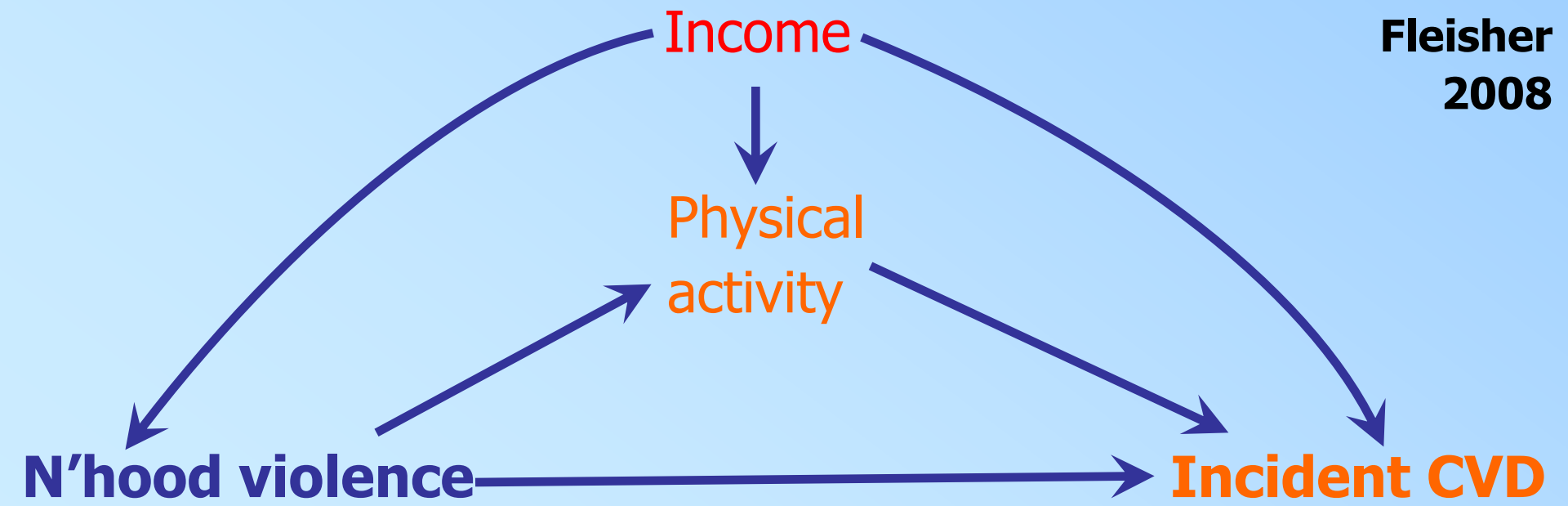

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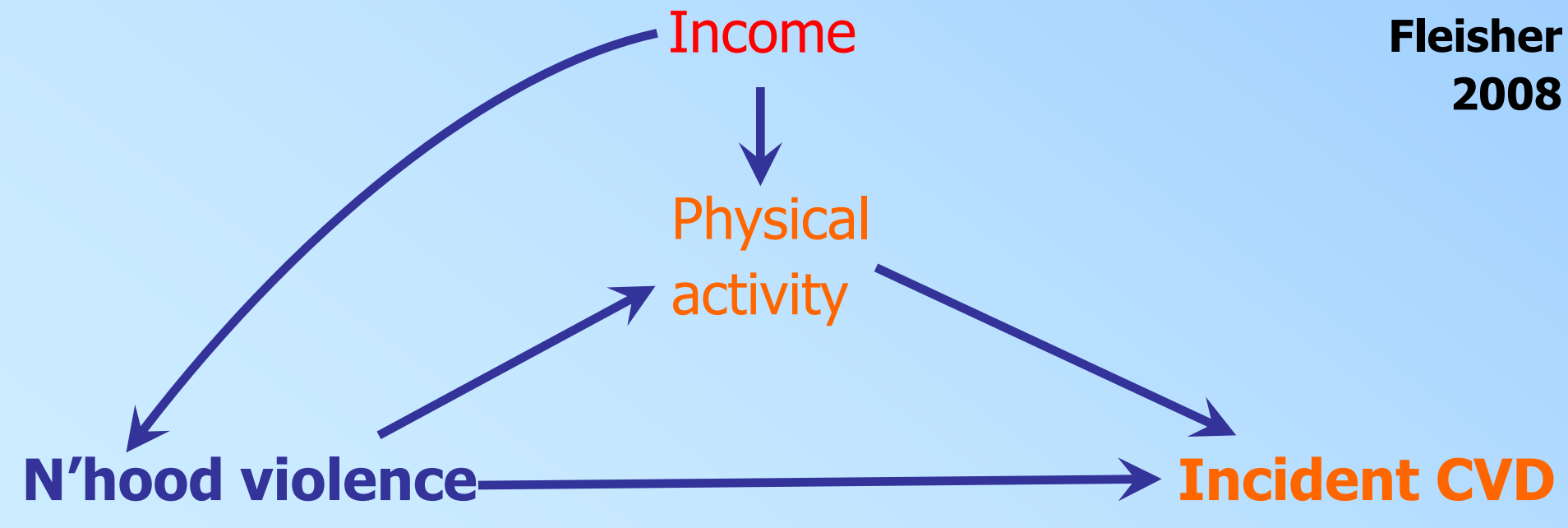

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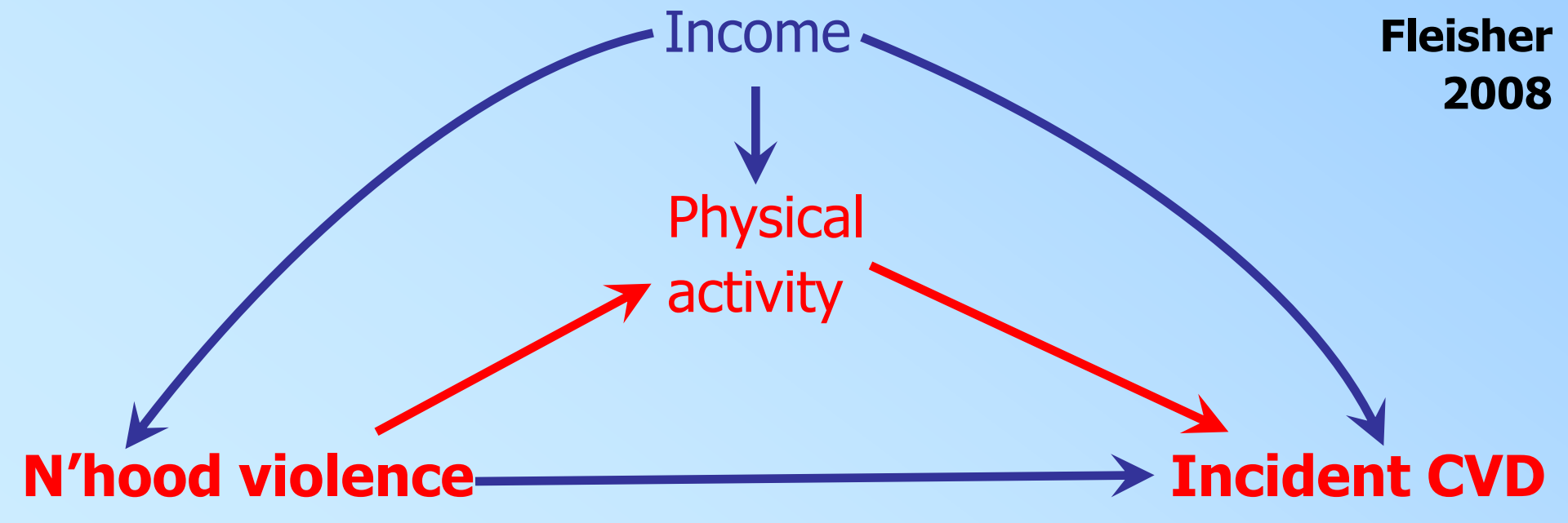

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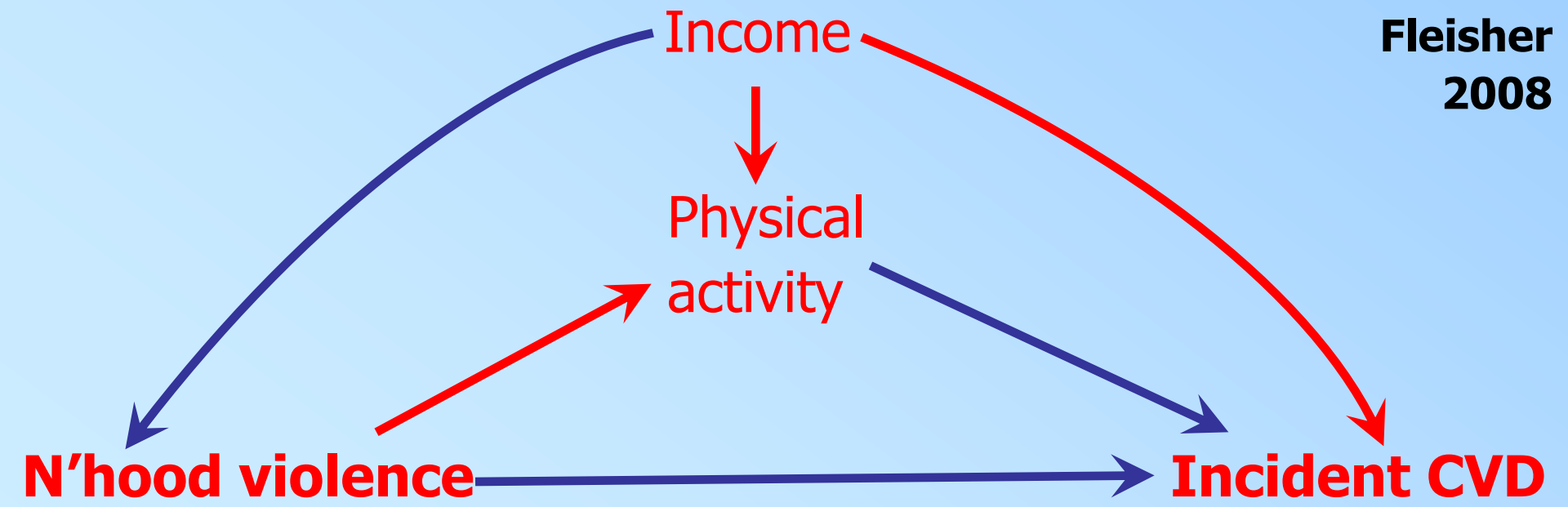

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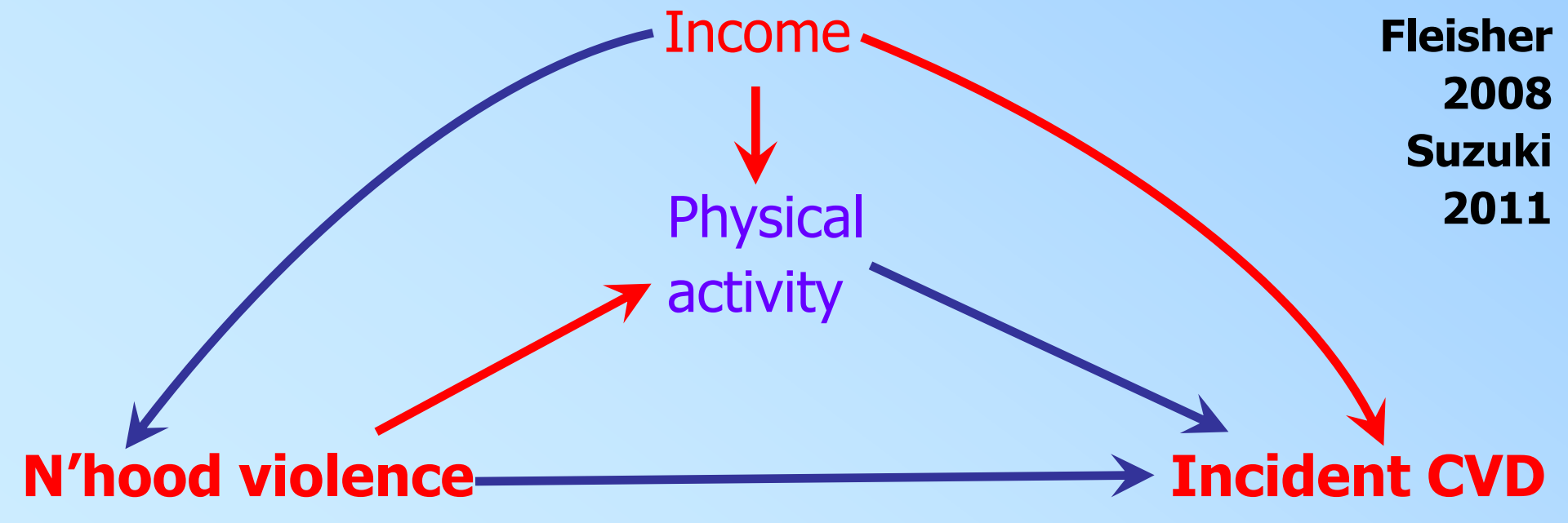
DAGs: TERMINOLOGY

- **A collider on a path**: a variable with two arrows into it (common effect): where two arrows "collide"
- **Unblocked path**: sequence of arrows connecting two variables that does not contain a collider



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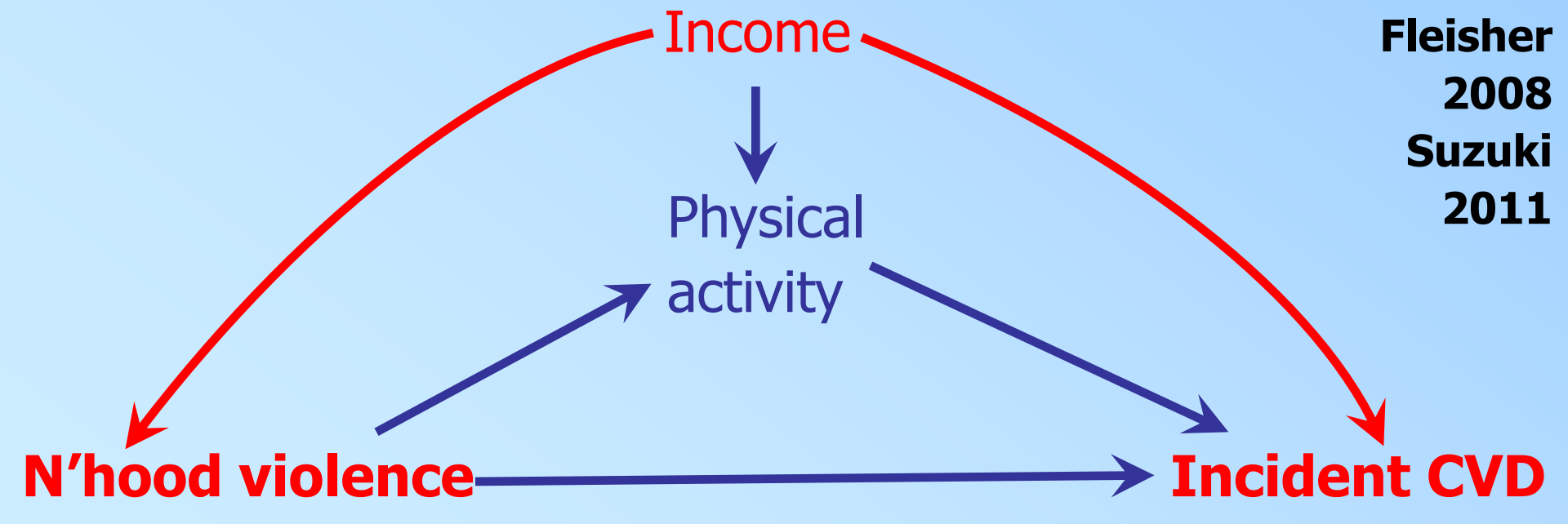

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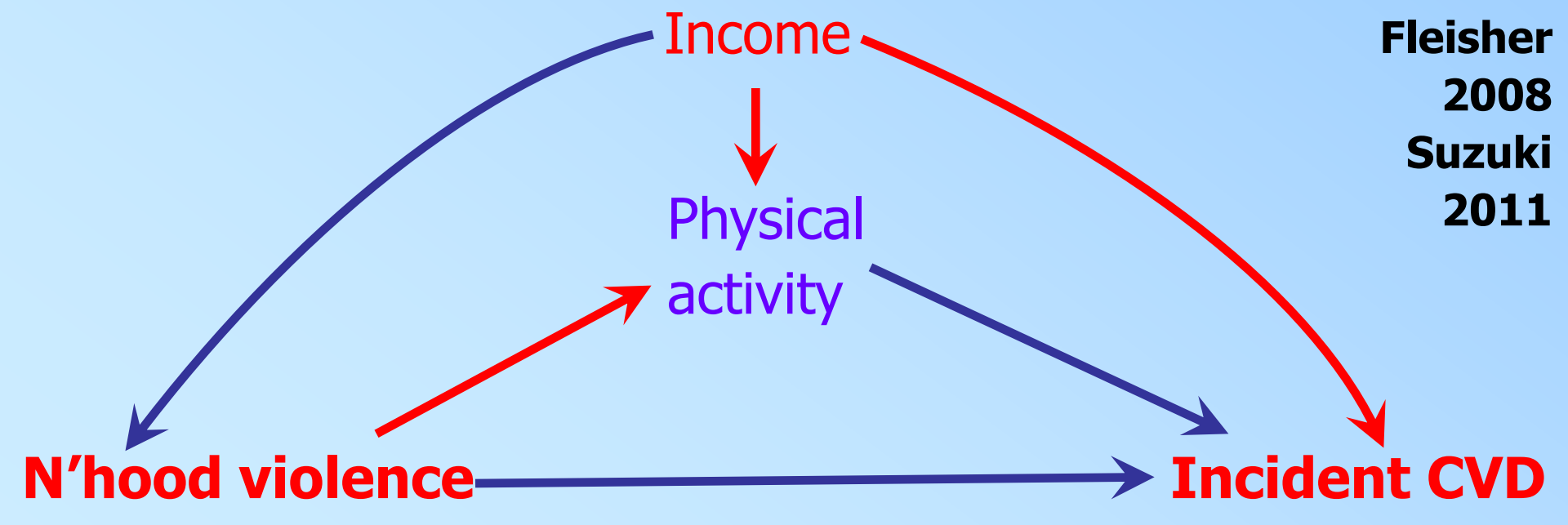

Fleisher 2008
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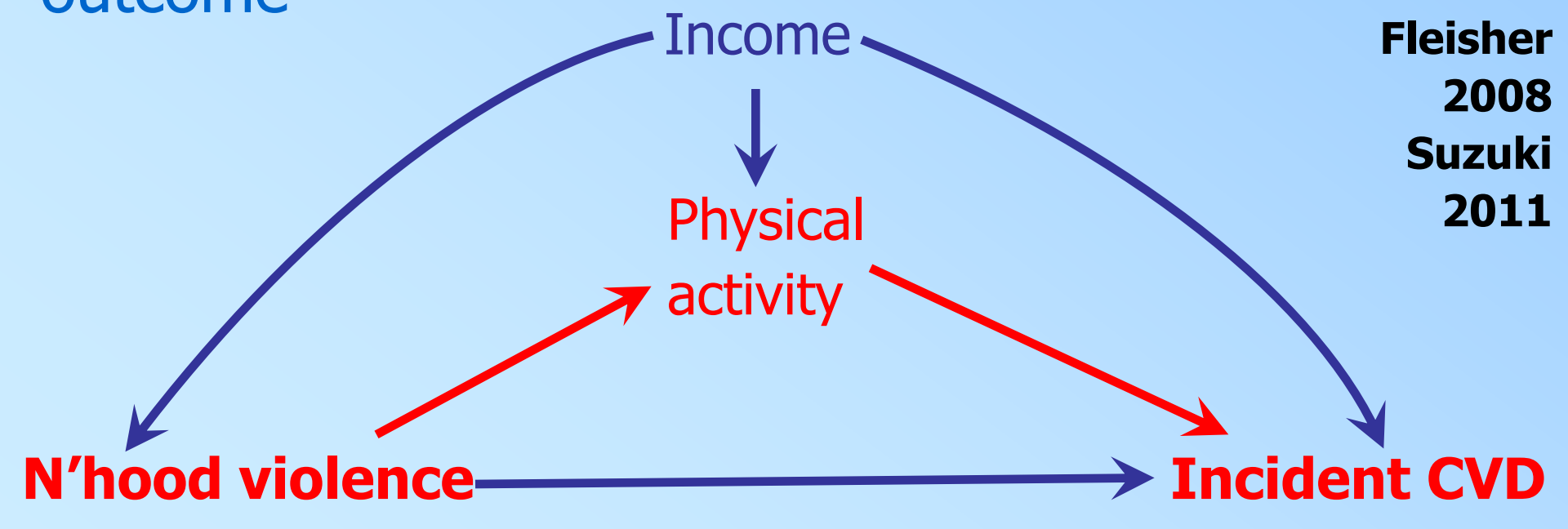
DAGs: TERMINOLOGY

- **Unblocked directed path**: sequence of directed arrows
- **Unblocked backdoor path**: an unblocked path that begins with an arrow pointing into the exposure and ends in an arrow pointing into the outcome



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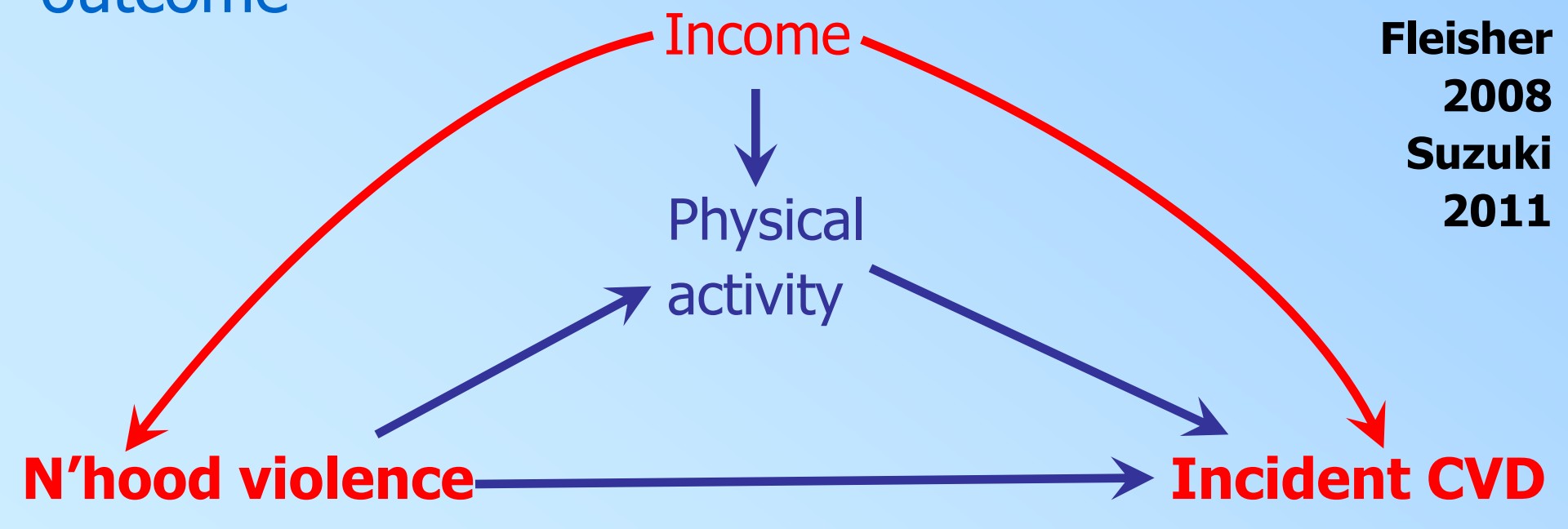


Fleisher 2008
Suzuki 2011

D-SEPARATION RULES

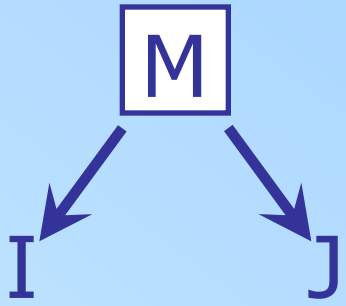
Pearl 2000

… or how to read the statistical independencies implied by the causal assumptions encoded in the DAG
= rules of dependence / independence of the nodes

Causal chain

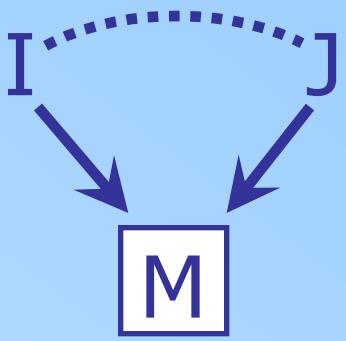
I and J independent conditional on M (d-separated): directed path blocked

Causal fork



I and J independent conditional on M (d-separated): backdoor path blocked

Inverted fork

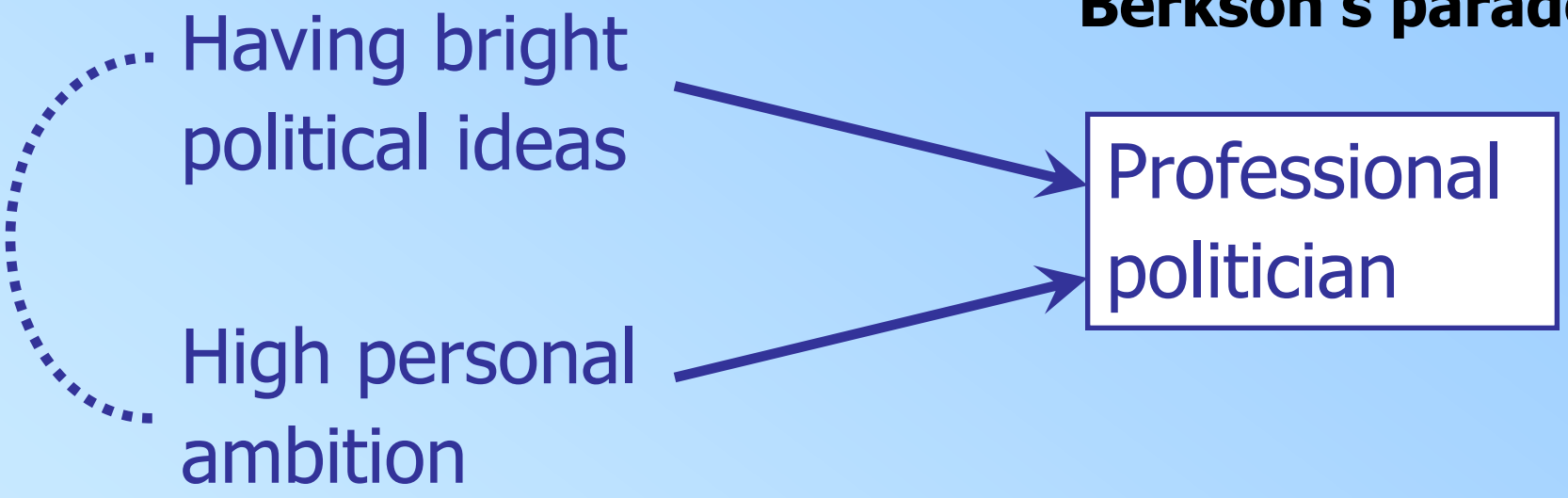


I and J dependent conditional on M (d-connected): M is a collider

CONDITIONING ON A COLLIDER

Conditioning on a common effect of two variables induces an association between those variables.

"Berkson's paradox"

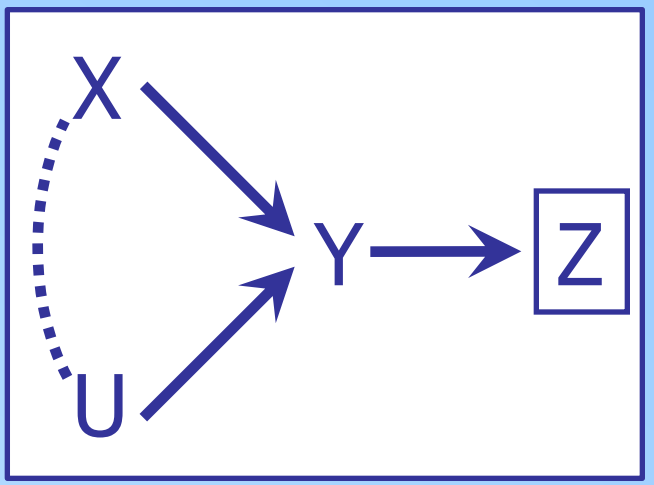


- Having bright political ideas and a high personal ambition are not associated in the whole population.
- Among professional politicians: if becoming a professional politician is not explained by one's bright ideas, then personal ambition is likely to be present…

D-SEPARATION RULES

The d-separation rules imply the following:

- XY marginally dependent
- XZ marginally dependent
- XZ independent conditional on Y
- XU marginally independent
- XU dependent conditional on Y
- XU dependent conditional on Z



Pearl 2000
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The Causal Markov Assumption: if we hold constant the direct causes of Y, any variable Z will be independent of Y, unless Z is an effect of Y

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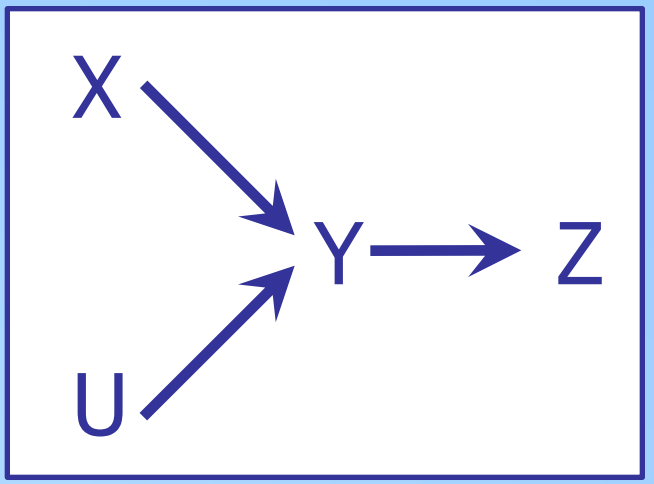

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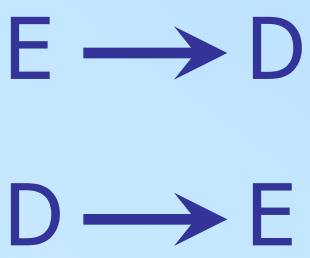
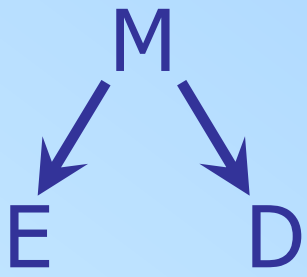
CLASSIFICATION OF BIAS

Apart from random variations, 3 basic causal structures (and more complex ones) can explain an association between an exposure (E) and a disease (D):

Cause and effect

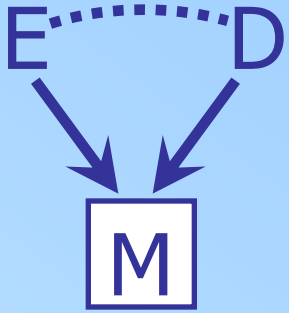


Common cause



Confounding bias: there is a common cause of E and D

Common effect



Selection bias (collider bias): conditional association within strata of a common effect

Hernán. A structural approach to selection bias. Epidemiology 2004.

APPLICATION of DAGs in N'HOOD & HEALTH RESEARCH

1. Identifying variables that need to be adjusted for in estimating n'hood health effects
2. Why adjusting for a mediator does not necessarily estimate the direct n'hood effect?
3. Why sample selection results in spurious associations between n'hoods and health?

Glymour 2006
Fleisher 2008

ADJUSTMENT OF N'HOOD EFFECTS (1)

Aim: identify the set S of variables that needs to be adjusted for to estimate the (total) causal effect

"Backdoor test for sufficiency":

S is sufficient for adjustment…

- if no variable in S is a descendant of the exposure (to avoid overadjustment) or the outcome
- if every unblocked backdoor path between the exposure and the outcome is intercepted by a variable in S

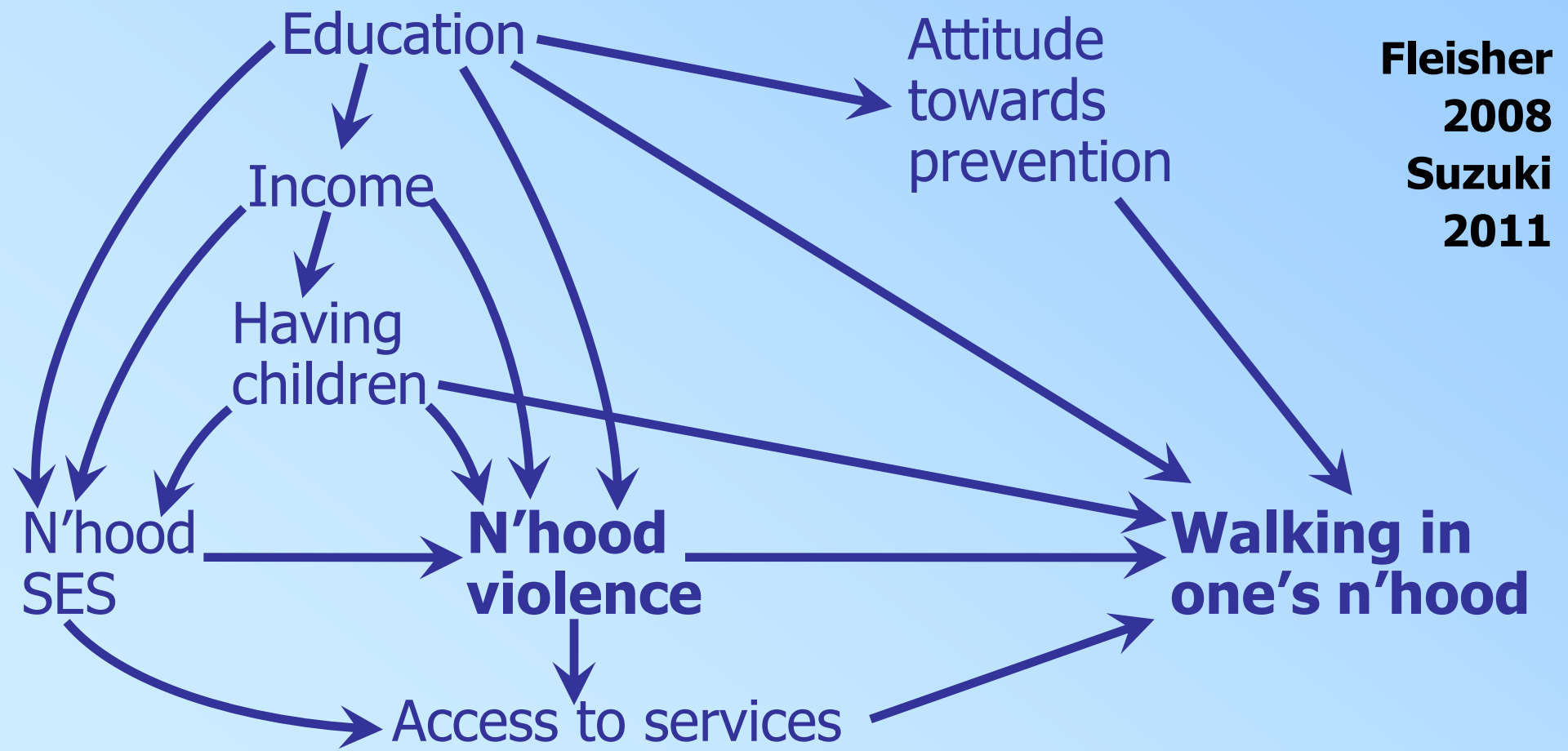
If there is a collider on a exposure-outcome path:

- we must not condition either on the collider or on any of its descendants
- **or** every unblocked path induced by adjustment for the collider must be intercepted by a variable in S

Greenland 1999. Glymour 2006. Fleisher 2008.

ADJUSTMENT OF N'HOOD EFFECTS (2)

Steps to determine the set of covariates S:



Fleisher 2008
Suzuki 2011

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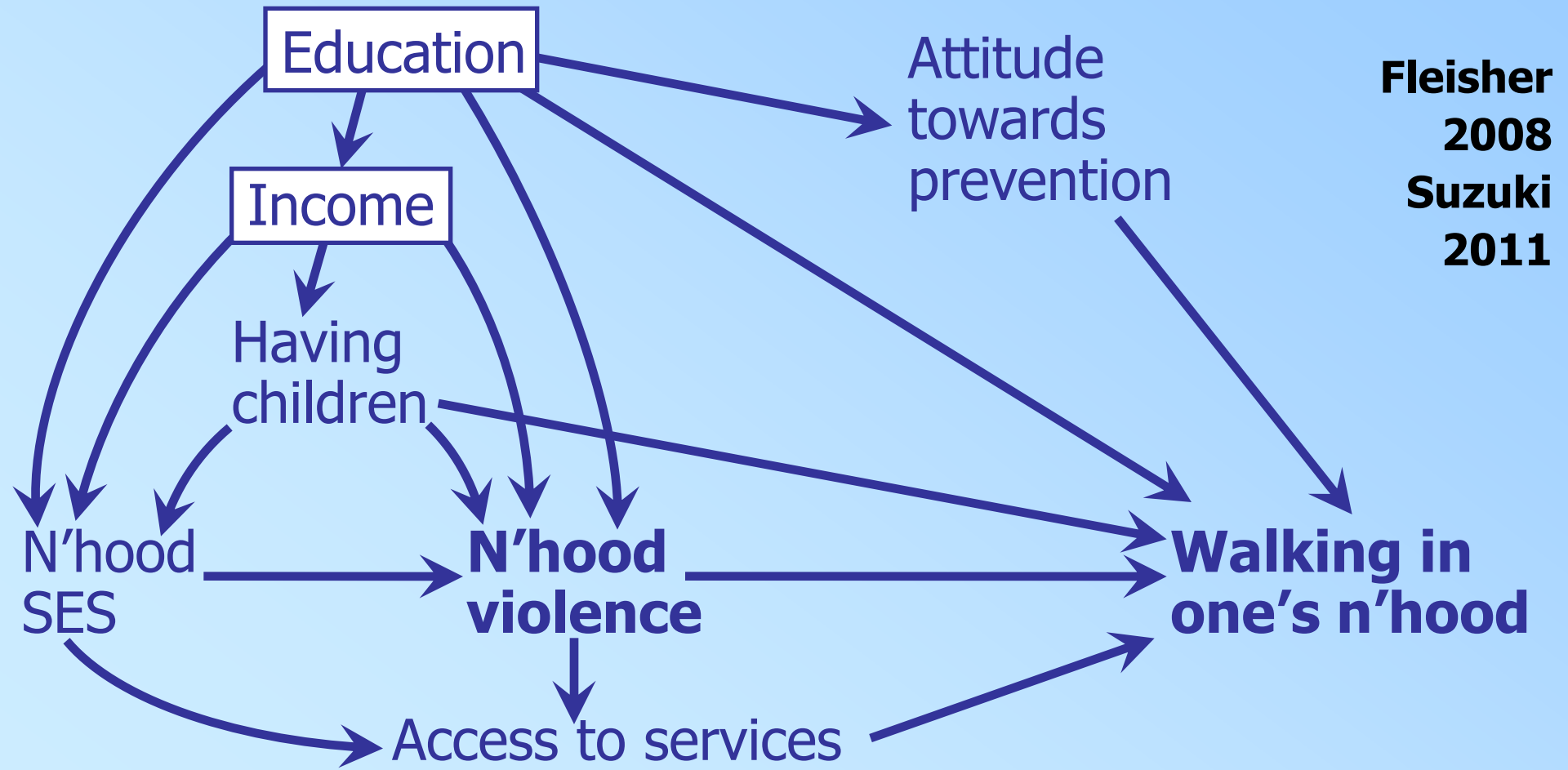

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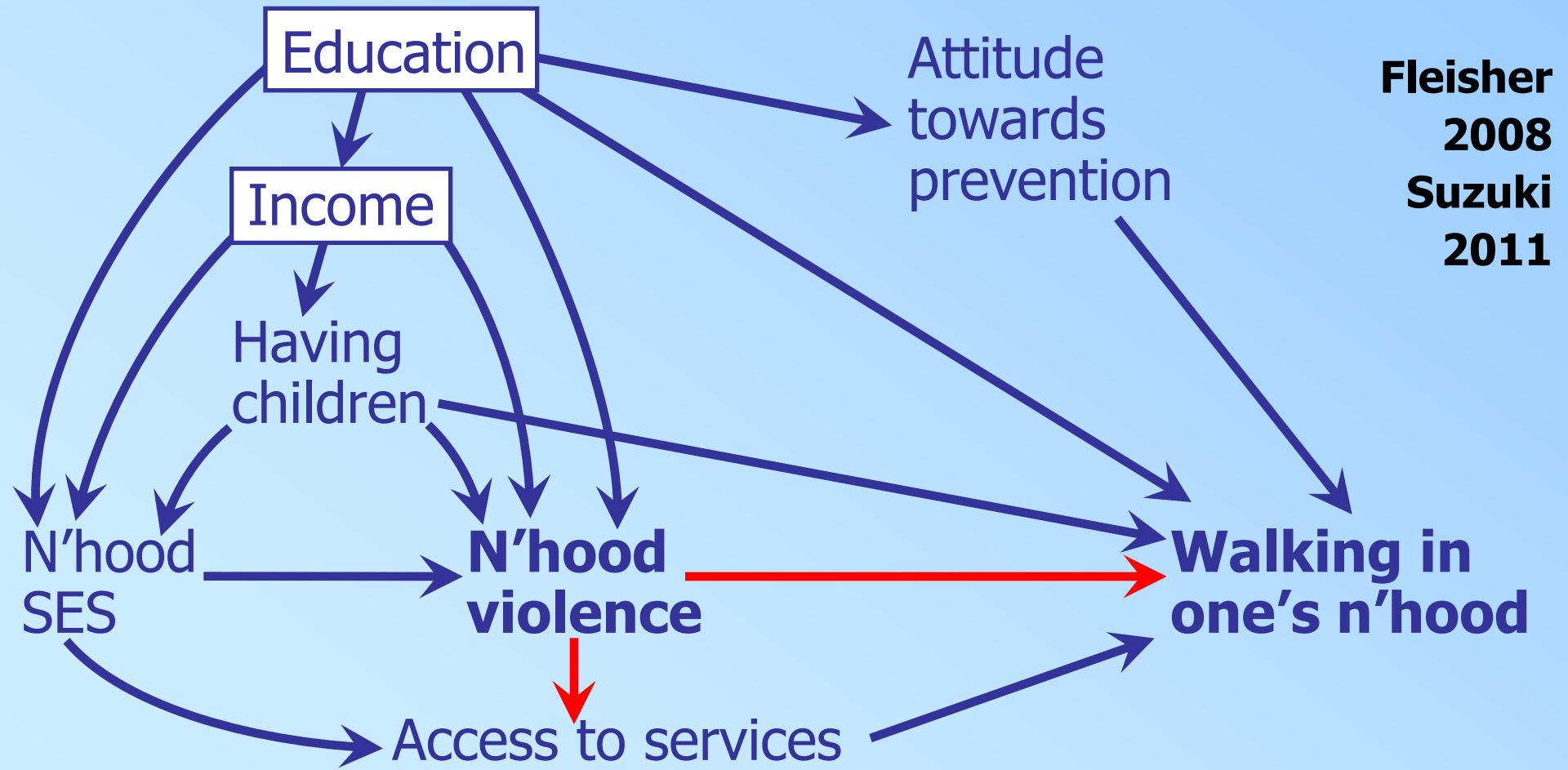
Suzuki 2011

ADJUSTMENT OF N'HOOD EFFECTS (2)

Steps to determine the set of covariates S:

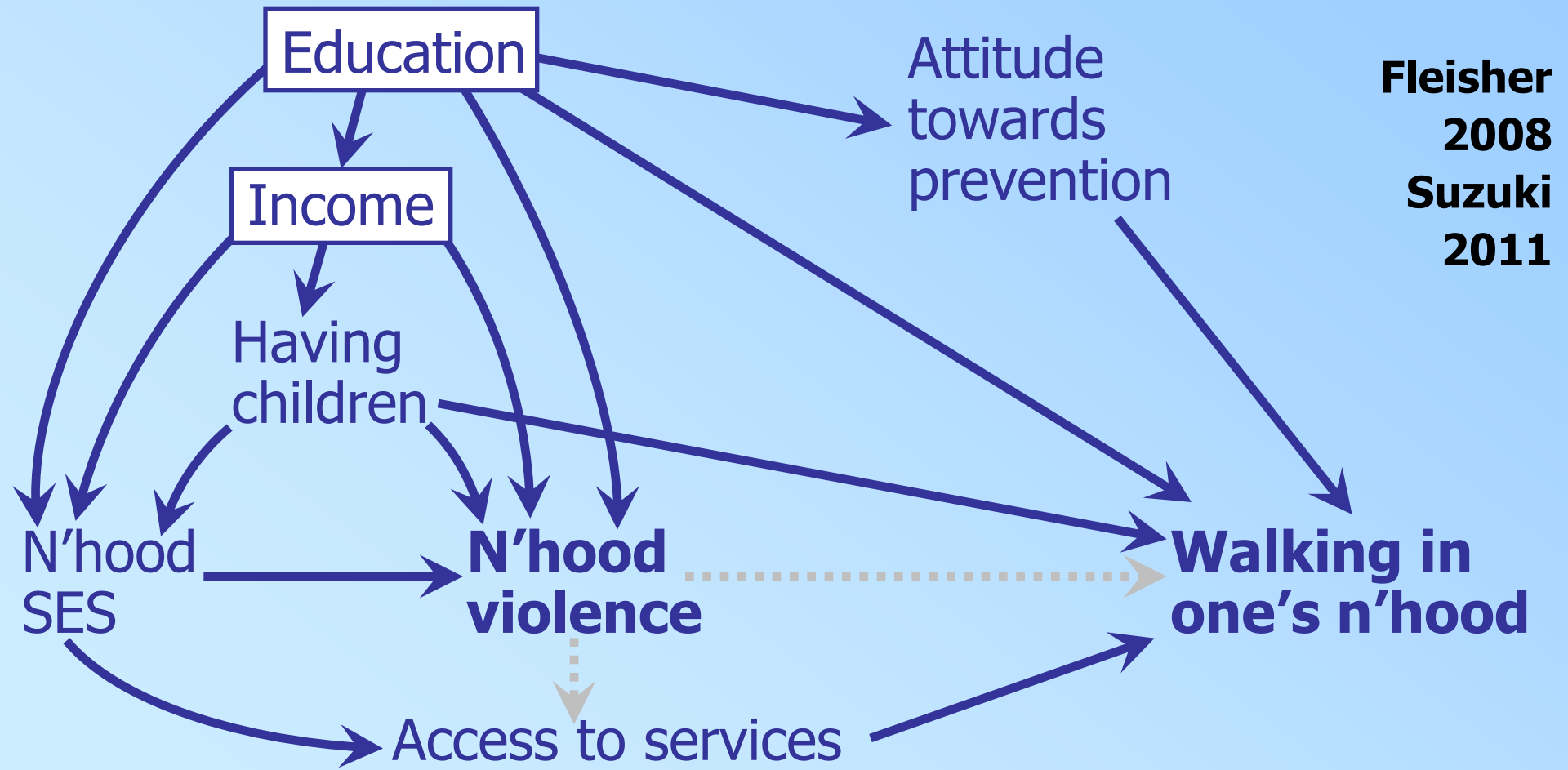
1) Delete all arrows emanating from the exposure



ADJUSTMENT OF N'HOOD EFFECTS (2)

Steps to determine the set of covariates S:

2) Draw undirected arcs to connect every variable that share a child or a descendent in S



Fleisher 2008
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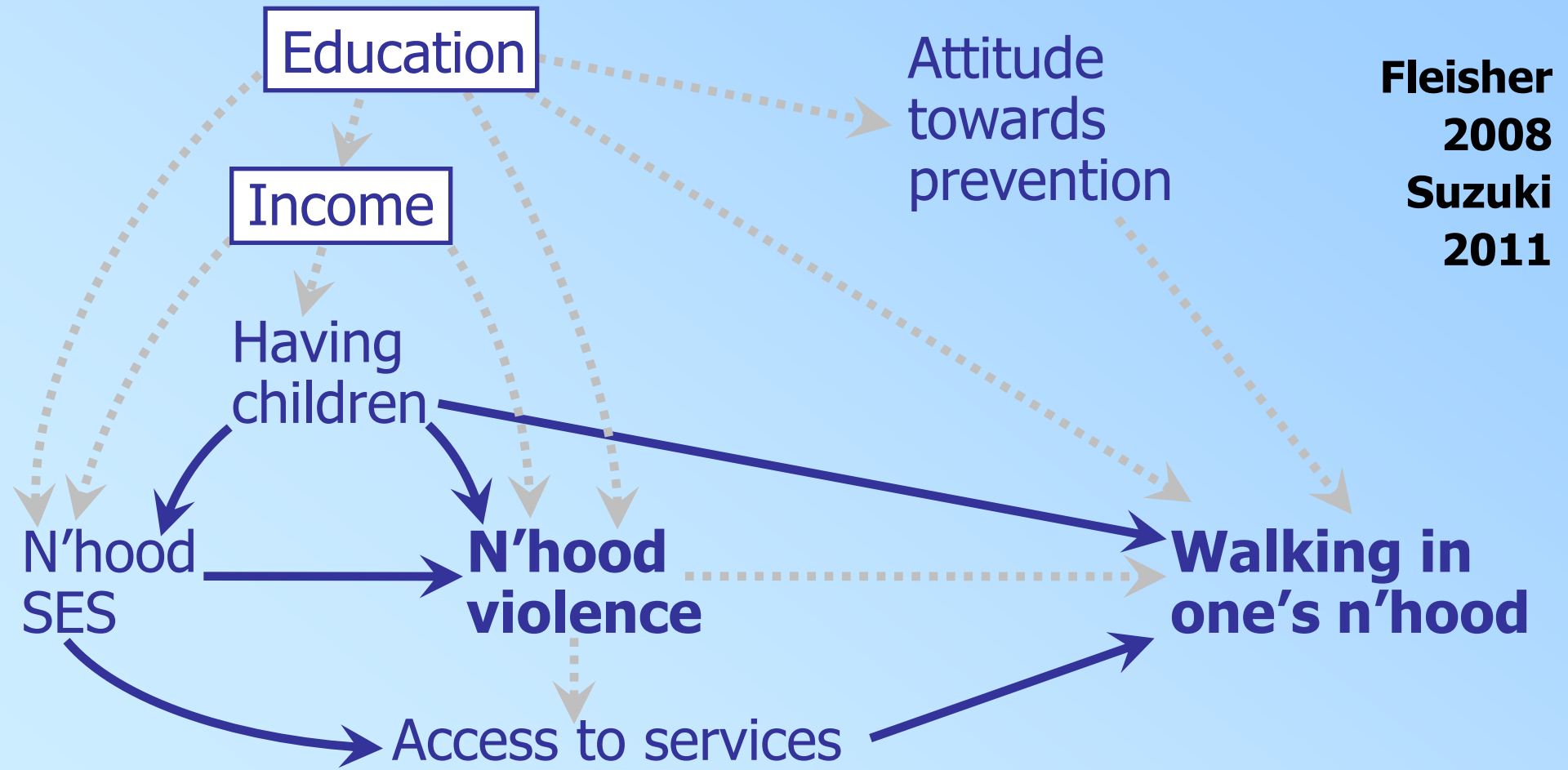
ADJUSTMENT OF N'HOOD EFFECTS (2)

Steps to determine the set of covariates S:

3) Mentally remove backdoor paths that are blocked by a variable in S

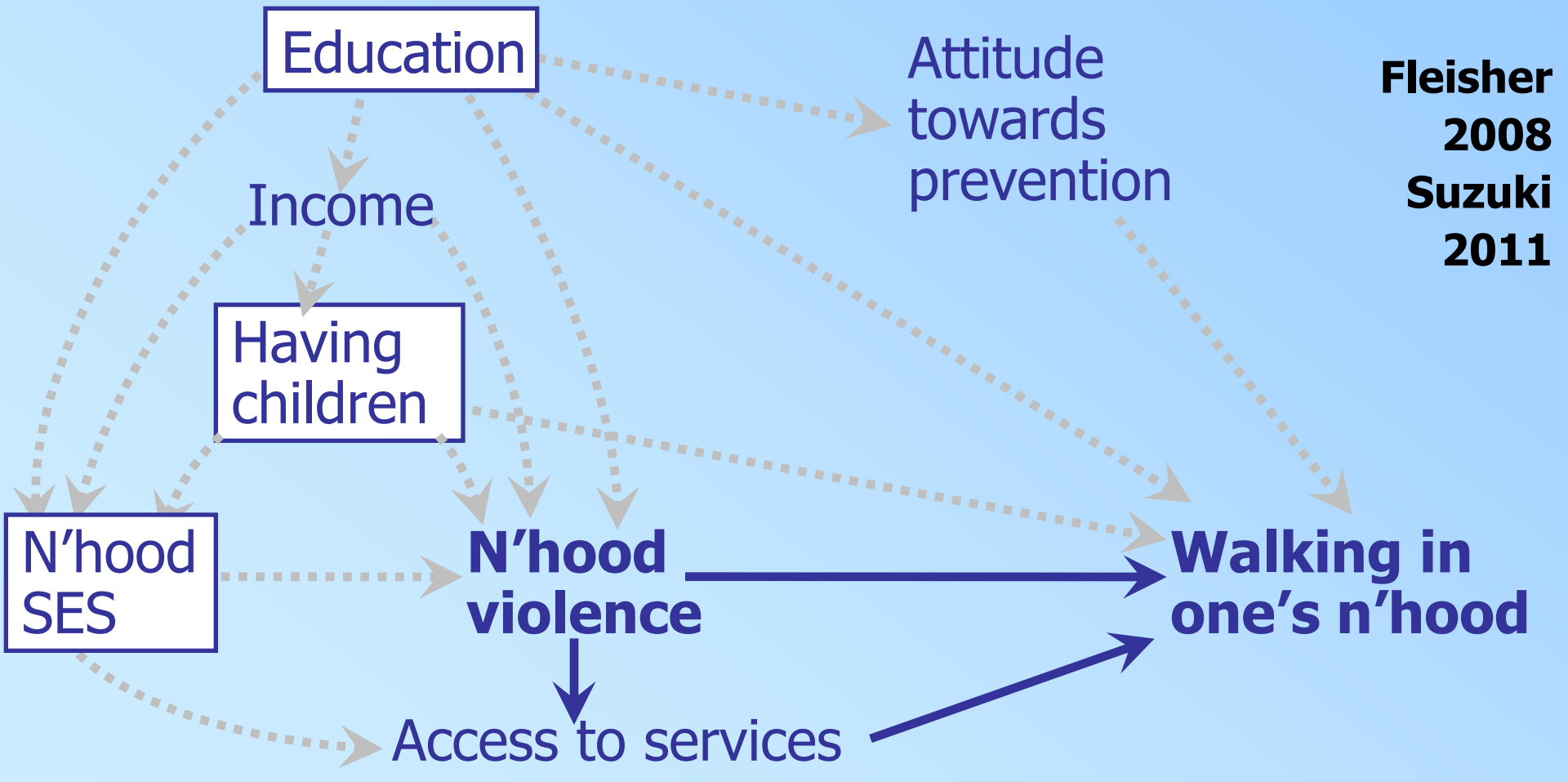


Fleisher 2008
Suzuki 2011

ADJUSTMENT OF N'HOOD EFFECTS (2)

Steps to determine the set of covariates S:

4) Redefine the adjustment set and identify the "minimally sufficient adjustment set"



Fleisher 2008
Suzuki 2011

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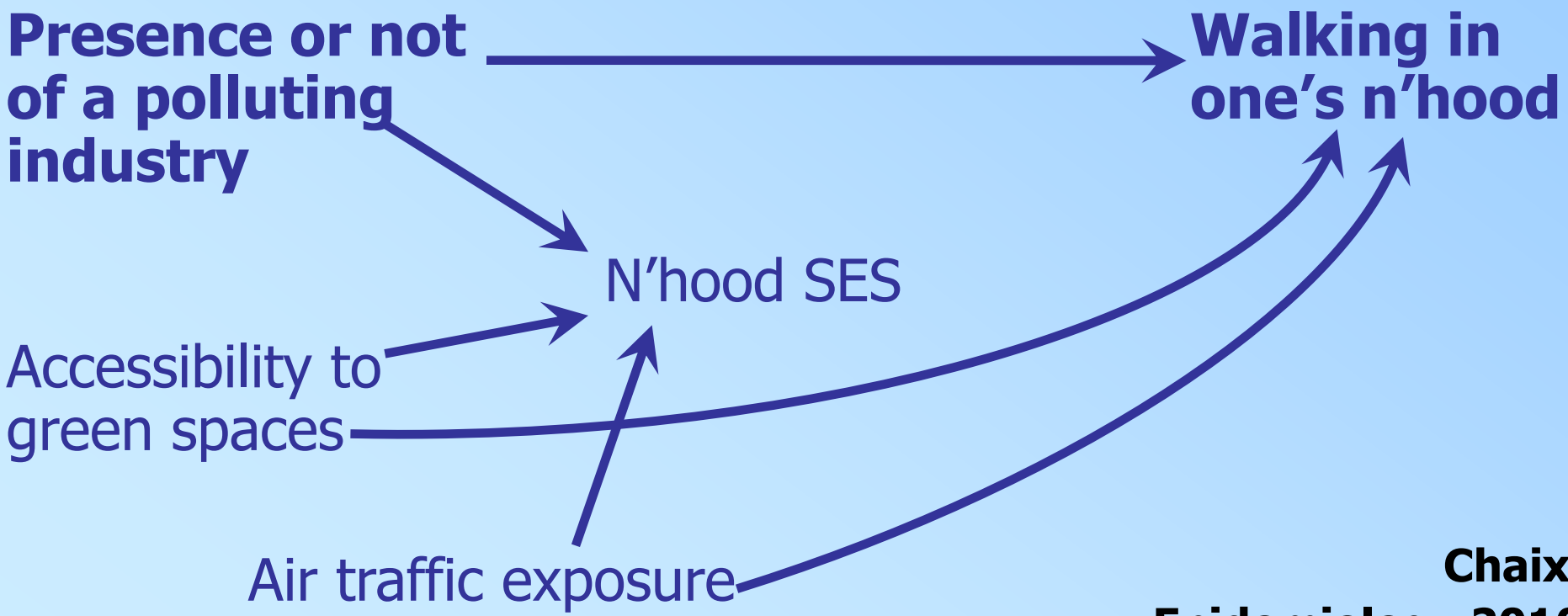

Chaix, Epidemiology 2010

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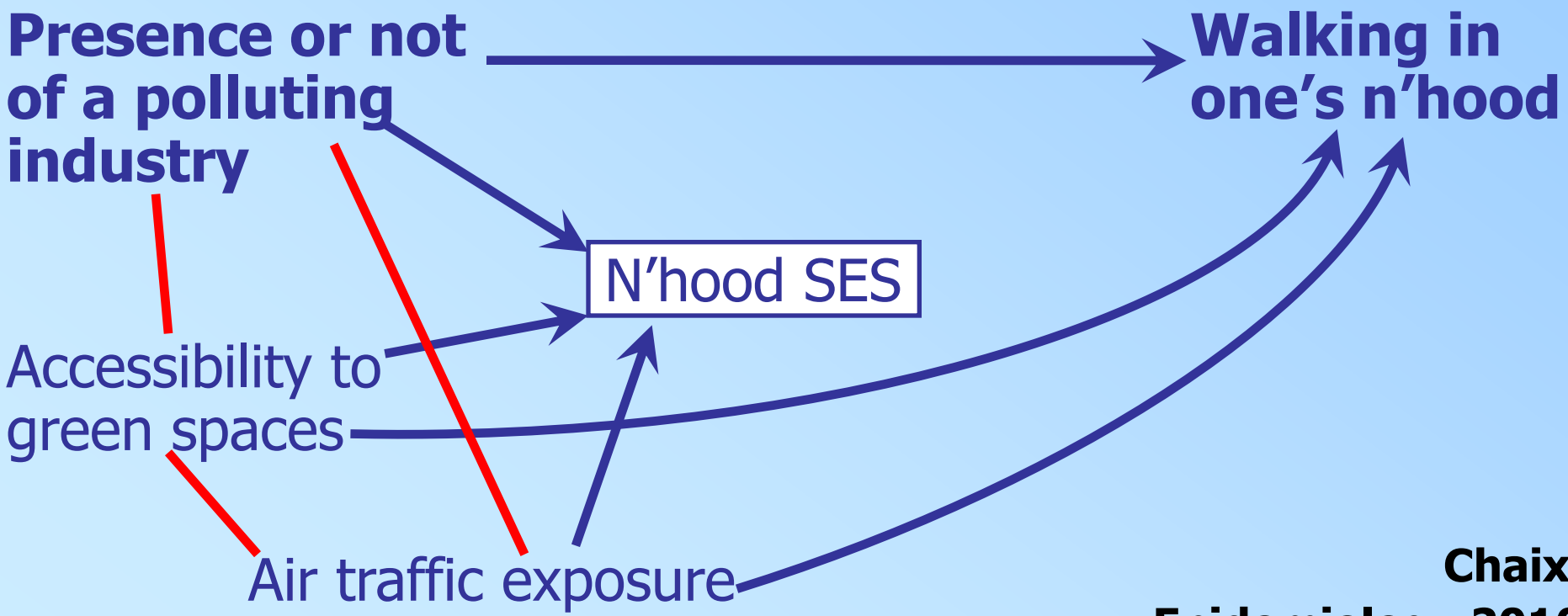
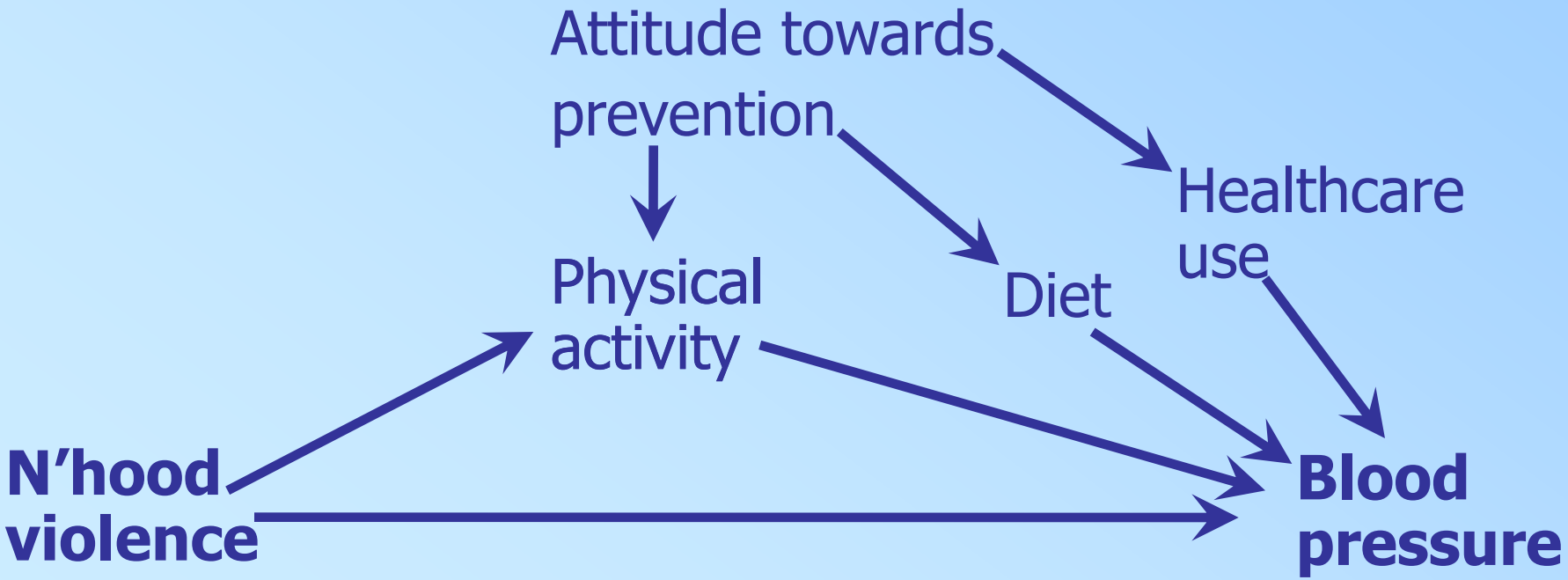


Chaix, Epidemiology 2010

Estimating a direct effect by conditioning on a mediator

- The total effect is not confounded.
- In case of confounding between the mediator and the outcome, adjusting for the mediator (as a collider) will induce a spurious association between the exposure and outcome.



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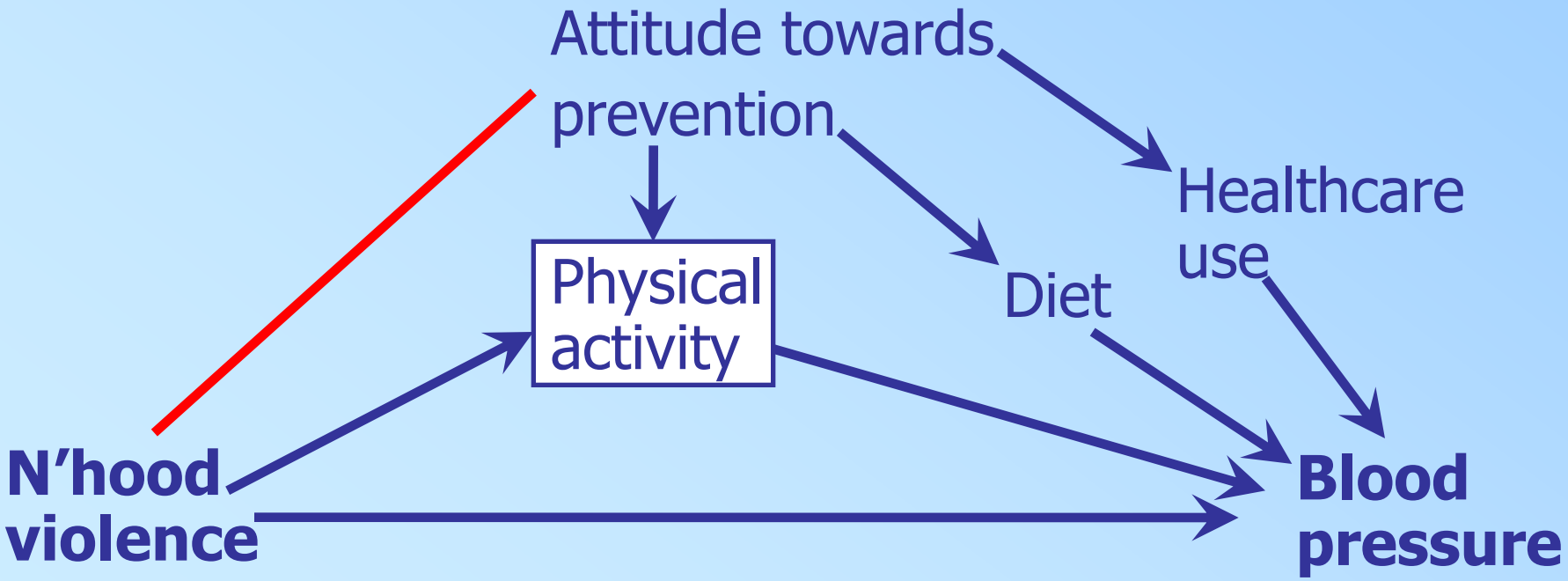
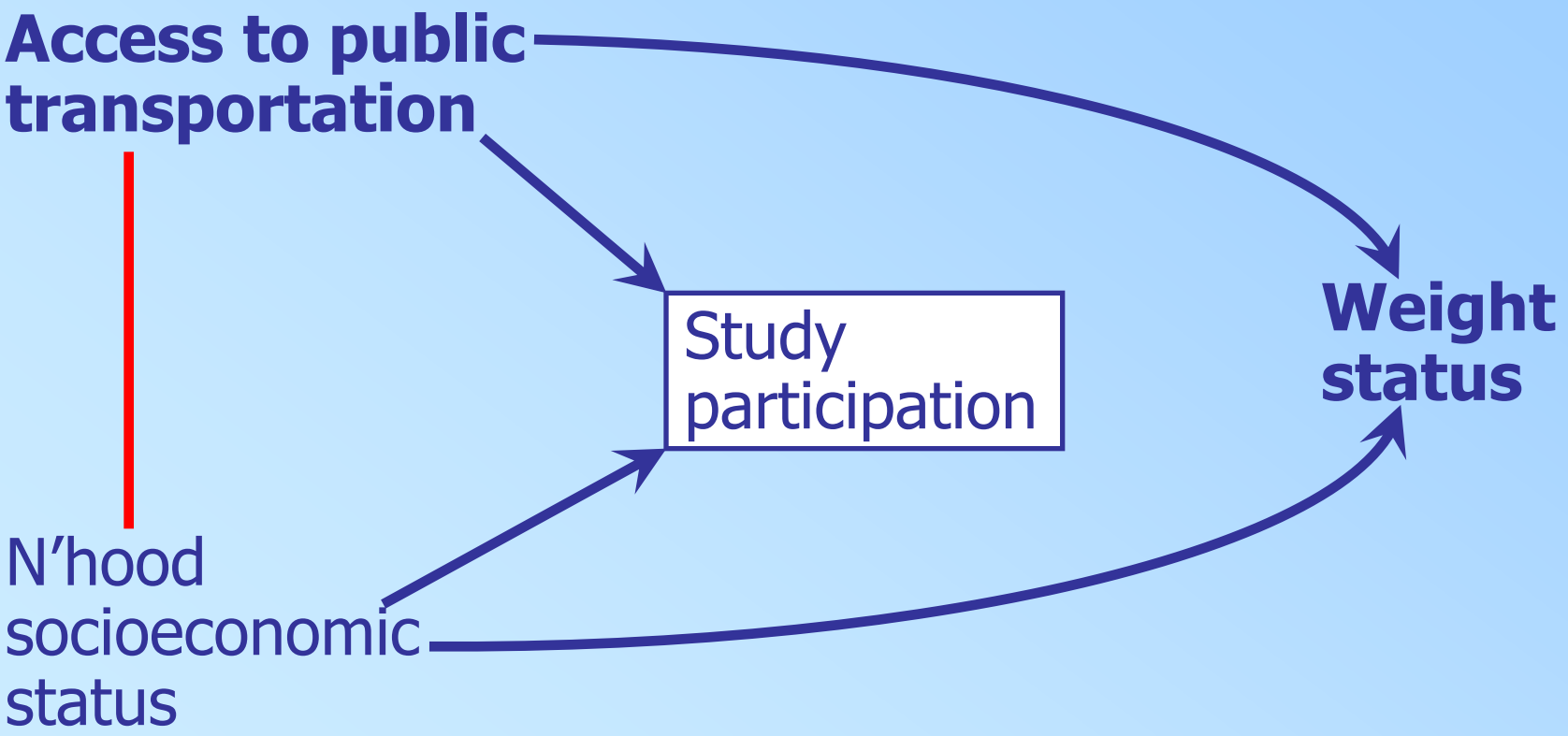


Fleisher 2008

SAMPLE SELECTION BIAS

Sample selection bias may occur if study participation depends on both the exposure and the outcome or their causes.



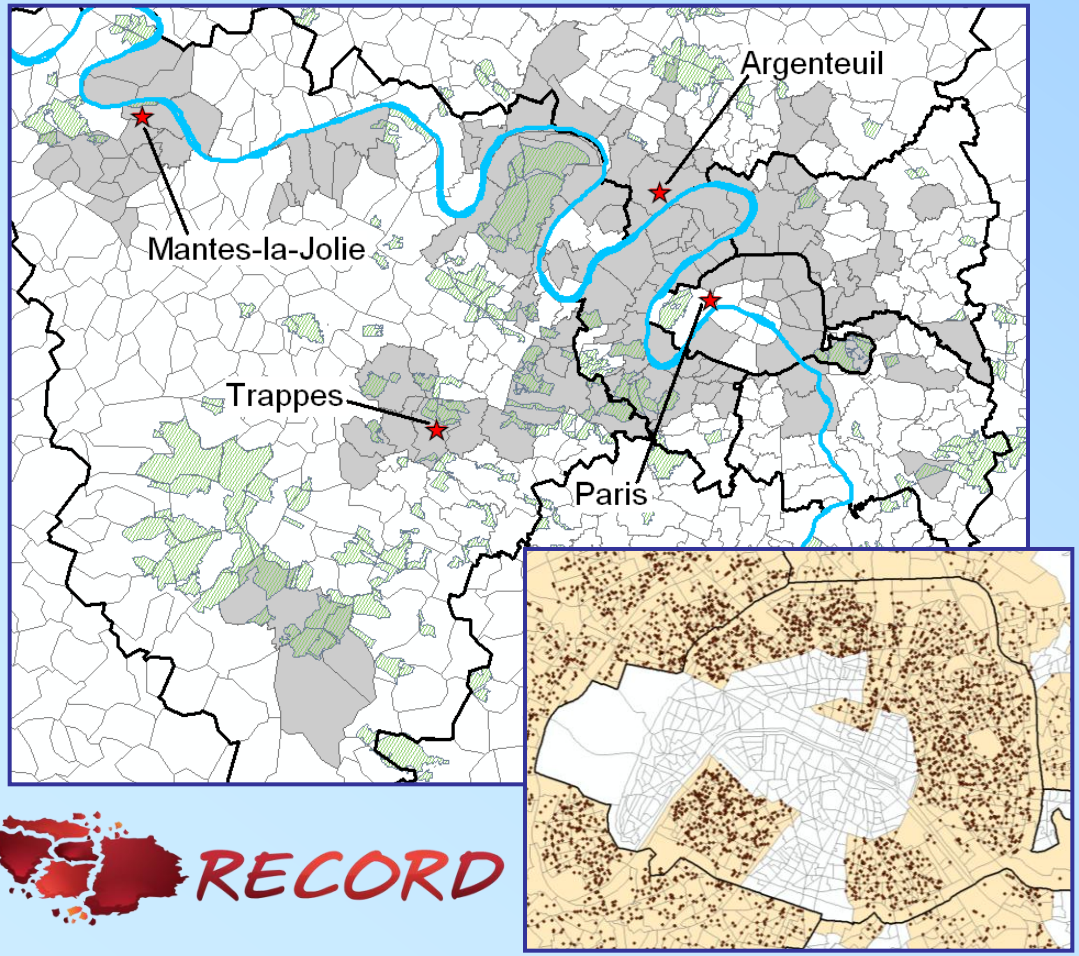
Chaix et al. Epidemiology 2011

APPLICATION: THE RECORD STUDY

Recruitment during health checkups

- **7290 participants (30–79 years)**

111 municipalities + 10 districts of Paris
= 1915 different neighborhoods



RECORD

RECORD Study, wave 1

- Biological data
- Paramedical examinations
- Medical questionnaires
- Address & contact info
- RECORD questionnaire

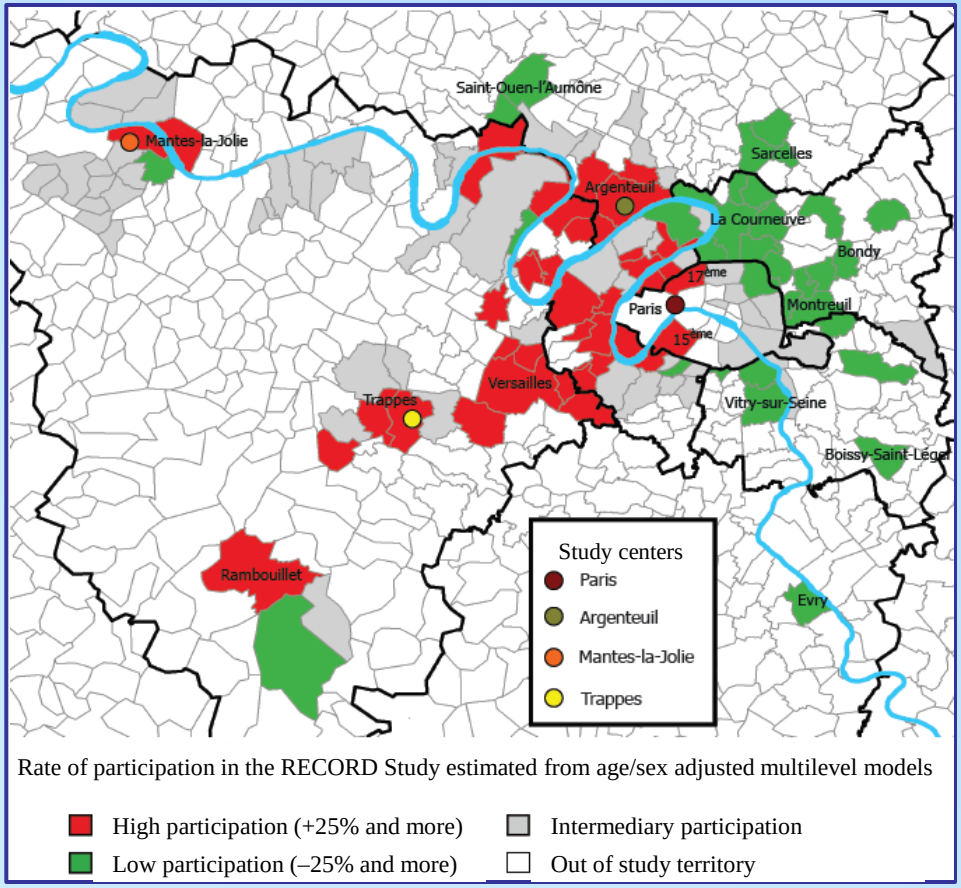
- Geocoding of participants
- Environmental data

- Healthcare use (SNIIR-AM)
- Hospitalizations (PMSI)
- Mortality (Insee, CepiDC)
- Professional career (CNAV)

MODELING OF STUDY PARTICIPATION

Multilevel Poisson model for participation of populations in the RECORD Cohort Study

Relatively large variance between neighborhoods



Rate of participation in the RECORD Study estimated from age/sex adjusted multilevel models

High participation (+25% and more)
Low participation (–25% and more)
Intermediary participation
Out of study territory

	PRR* (95% CI)
Individual education (vs. low)	
Medium	1.90 (1.74, 2.08)
High	4.25 (3.87, 4.67)
Distance to the center (vs. long)	
Medium-long	1.19 (1.09, 1.30)
Medium-short	1.45 (1.32, 1.58)
Short	1.75 (1.60, 1.91)
Median income (vs. low)	
Medium-low	1.20 (1.09, 1.32)
Medium-high	1.29 (1.14, 1.45)
High	1.39 (1.20, 1.60)
Mean real estate prices (vs. low)	
Medium-low	1.10 (1.00, 1.21)
Medium-high	1.11 (1.00, 1.24)
High	1.23 (1.09, 1.39)
% looking for work (vs. low)	
Medium-low	1.01 (0.93, 1.10)
Medium-high	1.18 (1.06, 1.31)
High	1.31 (1.15, 1.47)
% of area with buildings (vs. high)	
Medium-high	1.13 (1.03, 1.23)
Medium-low	1.26 (1.14, 1.39)
Low	1.37 (1.23, 1.51)
Building height (vs. high)	
Medium-high	1.11 (1.03, 1.21)
Medium-low	1.27 (1.16, 1.39)
Low	1.27 (1.15, 1.40)

Chaix et al. Epidemiology 2011.

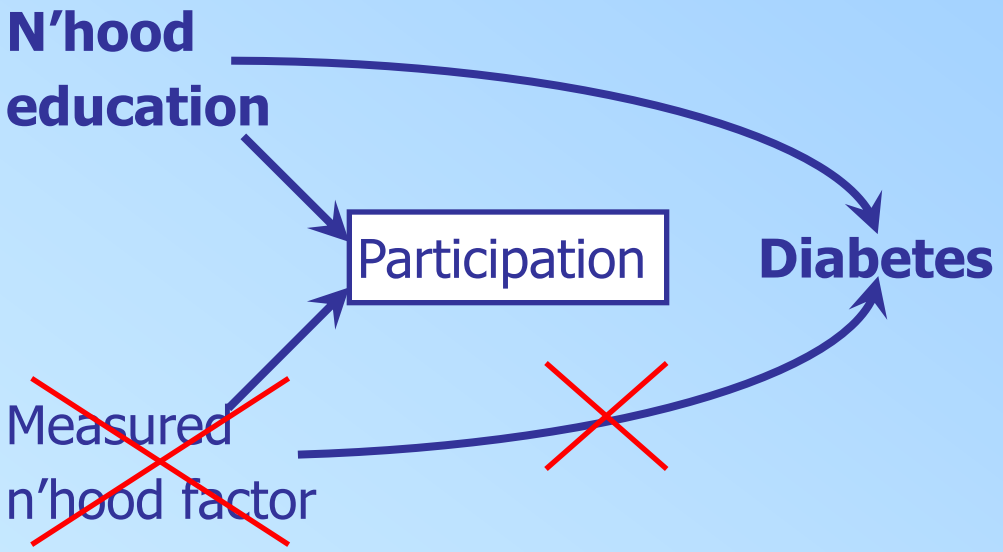
*PRR, Prevalence rate ratio

Neighborhood education and type 2 diabetes

- Weak association between neighborhood average education and prevalence of type 2 diabetes after adjustment for individual socioeconomic characteristics

Association between n'hood education and diabetes		
Neighborhood education (vs. high)	OR	(95% CrI)
Medium-high	1.05	(0.70 – 1.56)
Medium-low	1.19	(0.80 – 1.75)
Low	1.56	(1.06 – 2.31)

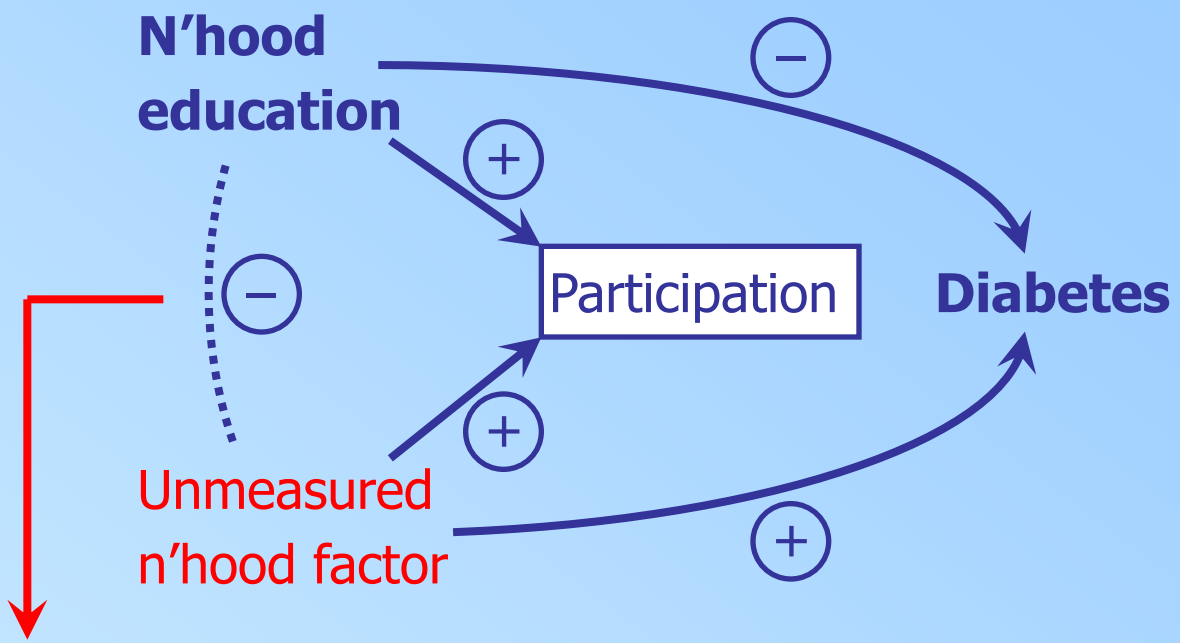
- None of the identified n'hood determinants of study participation biased the relationship of interest



Neighborhood education and type 2 diabetes

- Unmeasured n'hood determinants of participation could also bias the relationship between n'hood education and diabetes: positive association with diabetes

- Unmeasured n'hood determinants of participation were assessed with the **n'hood random effect** of the model for participation



- Correlation between n'hood education and the participation random effect:
  - in the population: r = –0.004 (–0.005, –0.002) [N = 3.1 m]
  - in the sample: r = –0.14 (–0.17, –0.12) [N = 7233]

Neighborhood education and type 2 diabetes

→ Adjust for the random effect reflecting variations in participation (a model-based value implying uncertainty)

Modeling inspired from: **Heckman JJ. Sample selection bias as a specification error. *Econometrica 1979;47:153-61.***

Joint estimation of the 2 models through MCMC:

Model for participation

$$\mathbf{Log}(\lambda_{ij}) = \beta_0 + \Sigma\, \beta_i \mathbf{X_i} + \mathbf{s_j}$$

Model for diabetes

$$\mathbf{Logit}(p_{ij}) = \beta'_0 + \Sigma\, \beta'_i \mathbf{X_i} + \gamma\, \mathbf{s_j} + \mathbf{u_j}$$

	Initial model		Model with correction	
Neighborhood education (vs. high)	OR	(95% CrI)	OR	(95% CrI)
Medium-high	1.05	(0.70 – 1.56)	1.01	(0.68 – 1.48)
Medium-low	1.19	(0.80 – 1.75)	1.15	(0.78 – 1.69)
Low	1.56	(1.06 – 2.31)	1.44	(0.98 – 2.13)

CONCLUSION

DAGs are useful because they challenge researchers:
- to formalize their research hypotheses
- to provide rationale for their analytic strategies
  (ex: avoid the "kitchen sink approach" to adjustment)

Relevant developments based on DAGs:

1) Standardized methods to explore the coherence between alternative DAGs and empirical data (e.g., c-equivalence, **Pearl 2008**) **(D. Evans, EHESP)**
2) DAGs cannot encode assumptions on the strengths of associations → It is important to develop methods to place bounds on the amount of bias likely to be present under different assumptions.
3) Integration of interactions in DAGs, etc.