Designing and planning research to assess causality in complex interventions

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SPAN workshop

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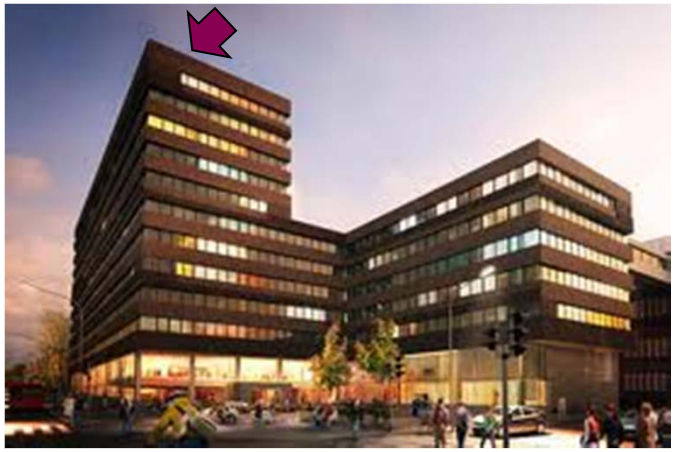


This seminar

- Definition of complex intervention
- Principles for assessing causal relations
- What does intervention complexity imply for causal inference?
  - Non-linear (non-deterministic) relations
  - Interactions

This seminar

What can be done to:

→ Enhance plausibility

→ Minimize bias

→ Specify level of inference

→ Enhance consistency

What is a complex intervention?*

- Multiple components
  - Inter-independence
  - Interaction
- Multiple populations/target groups
- Multiple deliverers
- Multiple behaviors/skills

- Multiple outcomes
- Length of the causal chain to outcome

* Developing and evaluating complex interventions: new guidance. Medical Research Council, 2006

Strengthening Families Programme (SFP10-14)*

Spoth R et al. Psychol Addict Behav 2005;19 (4):372-381

Components	Deliverers/ media	Behaviours/ skills	Target groups
Youth sessions (7)	Facilitators Discussions, instructional videotapes, games, practical activities	Goal setting, stress management, refusal skills, social bonding	Youths
Parental sessions (7)		Interactions, limit setting, supporting attitudes	Parents
Joint sessions (7)		Respectful listening, appropriate interactions	Dyads

Strengthening Families Programme (SFP10-14)*

Spoth R et al. Psychol Addict Behav 2005;19 (4):372-381

Outcomes	Latency
Substance use initiation Alcohol Cigarettes Marijuana	<1 year?
Regular alcohol use	1-2 years?
Weekly drunkenness?	2-3 years?

Causal relations (Bradford Hill, *Proc R Soc Med 1965;*58:295-300.)

- Temporal relations
- Strength
- Dose-response
- Alteration (manipulation)

- Consistency (place, population and time)
- Specificity

- Plausibility (explainable with previous knowledge)
- Coherence (doesn't contradict established knowledge)
- Analogy (with previous causal relations)

The notion of ”counterfactuality”

- Let I denote an individual
  - A child (John) in the group receiving SFP 10-14
- Let X denote the intervention, i.e. SFP 10-14
  - X=1 the intervention is present
  - X=0 the intervention is absent
- Let Y_i be an event concerning John’s behaviour, for instance alcohol initiation
  - Yi=0 means John doesn’t initiate
  - Yi=1 means John initiates
  - And also: Y_{i1}=event under intervention condition;
    Y_{i0}=event in absence of intervention

The notion of ”counterfactuality”

- What we would like to know is:
  - $Y_{i1} - Y_{i0}$

  → What would happen to John in absence of intervention?

- And we would conclude that the intervention is (causally) protective if

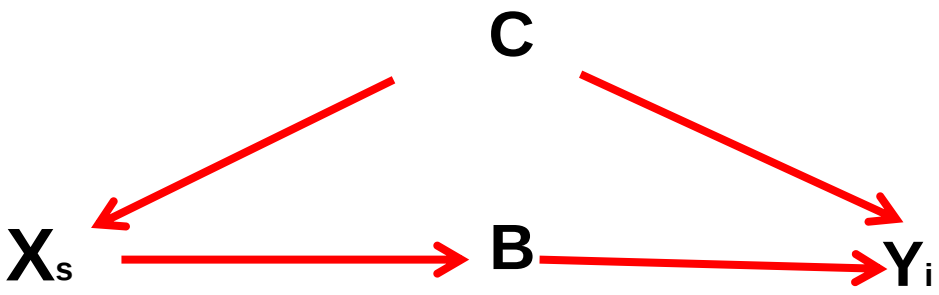
$$Y_{i1} - Y_{i0} = \mathbf{-1}$$

But we cannot….

We have to estimate Yi0 under this unobserved (counterfactual=contrary to facts) condition

Representation of causal relations: DAGs

http://www.hsph.harvard.edu/miguel-hernan/causal-inference-book/



Directed= arrows link nodes (variables) and indicate causal relations

Acyclic= no backward arrows

Graphs= visual, intuitive representation

Representation of causal relations: DAGs

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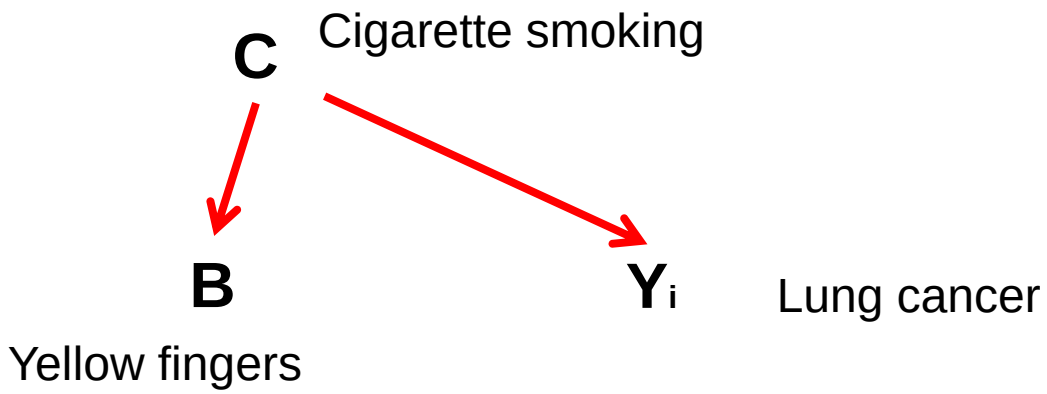
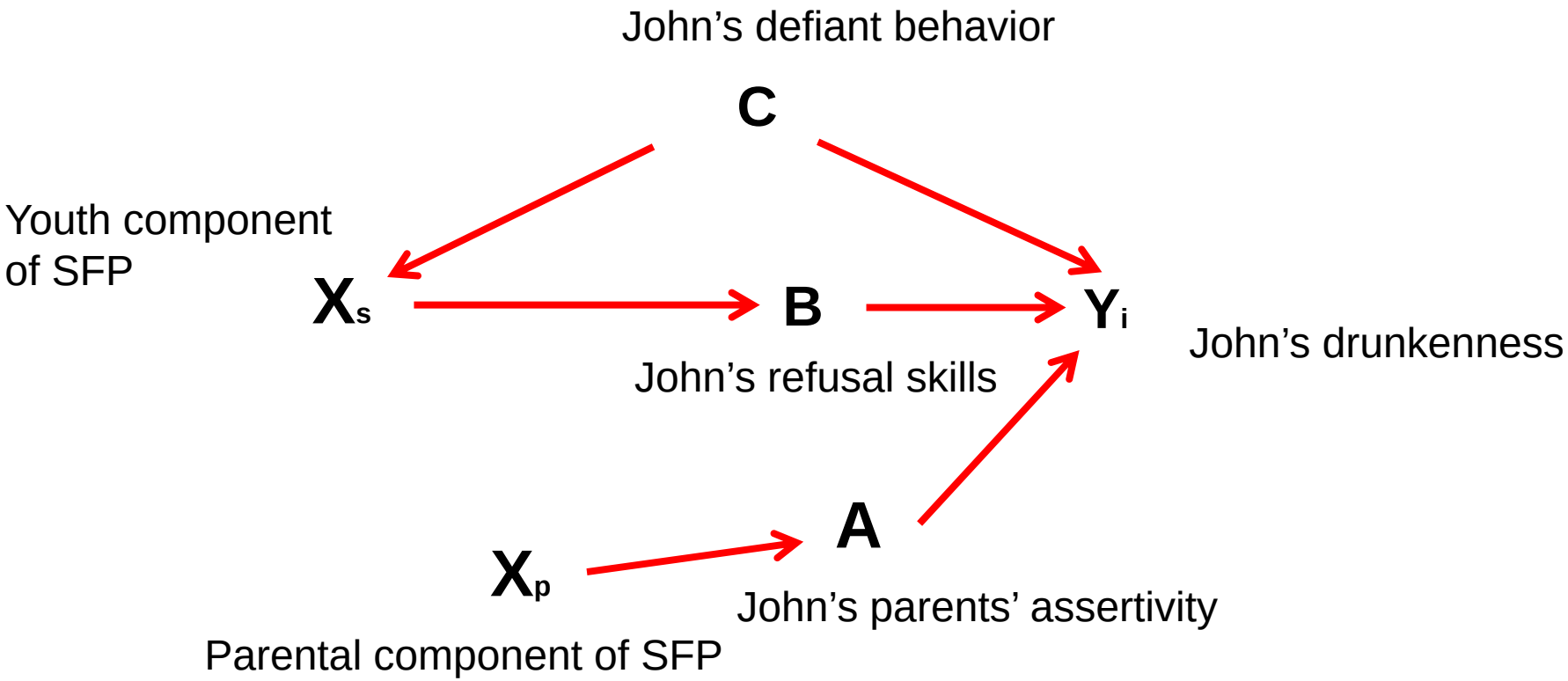


Complete DAGS include all variables of relevance for a given causal pathway, i.e. all variables that are common causes for a given pair of variables

DAG of causal relations in SFP

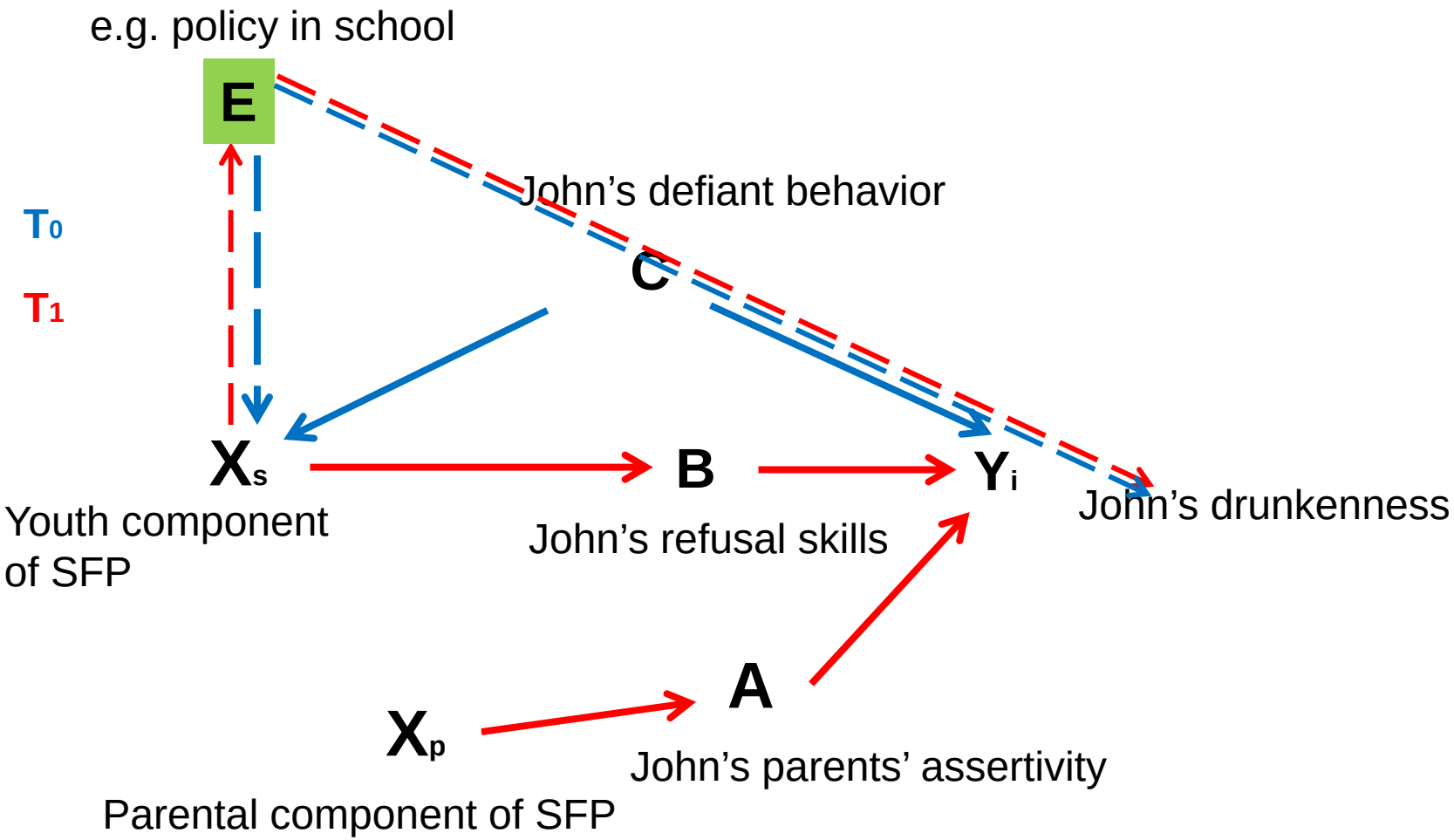


Pair discussion

- Could you further complicate (complete) this set of causal relations?

- How would this more complete explanatory model impact on causal inference?

More complete DAG of causal relations in SFP



What does complexity imply for causal inference?

- No direct manipulation of outcome
  - Length of chain
  - Competing causes
  - Synergy effects between components: necessary cause?
- Influence systems beyond the target
- No linearity of effects
- Difficult dose measurement
- High likelihood of inconsistency between studies

Effects of complexity is indifferent to design

- All of the above pose problems in any kind of design!
  - RCT no remedy
  - Observational studies may even be better

Possible ways to go

1. Enhance the plausibility of causal effects

- Use theories to make predictions
- Incorporate prior empirical evidence in middle-range theoretical models

- Segmentation- ”proof of concept”

  → Test of single components

  → Test of interactions

- Multiple design/control groups

  → Combination of different designs in the same evaluation (e.g. RCT and cohort)

Pair discussion: test of intervention components and in SFP 10-14

- Would you test for the effects of Xs and of Xp separately?
- Would you test for interaction Xs*Xp?
- Would you test for interaction E*Xs,p?
- Pick up one question. Whether you answered yes or no, which kind of assumption did you make?

Possible ways to go

2. Enhance counterfactual thinking

- Minimization of bias (confounding in particular)
  - →RCT in our heart….
  - →What about restriction?
- Consider levels of inference*
  - →**Adequacy**: are we meeting the expectations?
  - →**Plausibility:** effect present when other explanations are reasonably excluded?
  - →**Probability:** is the effects observed with a known probability of error?

* Habicht JP et al. International Journal of Epidemiology, 1999; 28:10-18

Possible ways to go

3. Enhance consistency (comparability)*

- Guide to replication
  - → create typologies
  - → document changes in protocol
  - →use of ”grey” and qualitative data
- Mediation
- Effect modification

* Shepperd et al. PLoS Medicine 2009; 6(8)

SFP 10-14 -Replications

	Spoth et al, 2005	Brody et al, 2006	Skärstrand et al, 2013	Ökulickz et al., 2013
Country	USA	USA , A-A families	Sweden	Poland
Comparator	SFP+LST vs. Control© vs. LST only	SFP vs. Control © information leaflet	SFP vs Control © usual conditions	SFP vs. Control © information leaflet
Alcohol (substance use) initiation	SFP+LST more effective than C	SFP more effective than C	Substance use, No effects	NA
Drunkenness	Borderline/mixed effect	--	No effect	NA
Regular alcohol use	No effect	SFP more effective than C	--	NA

Pair discussion: consistency of SFP 10-14 evaluations and causal inference

- Assuming that the effects are really heterogeneous, does this speak against an overall causal effect of the intervention on alcohol use/misuse?

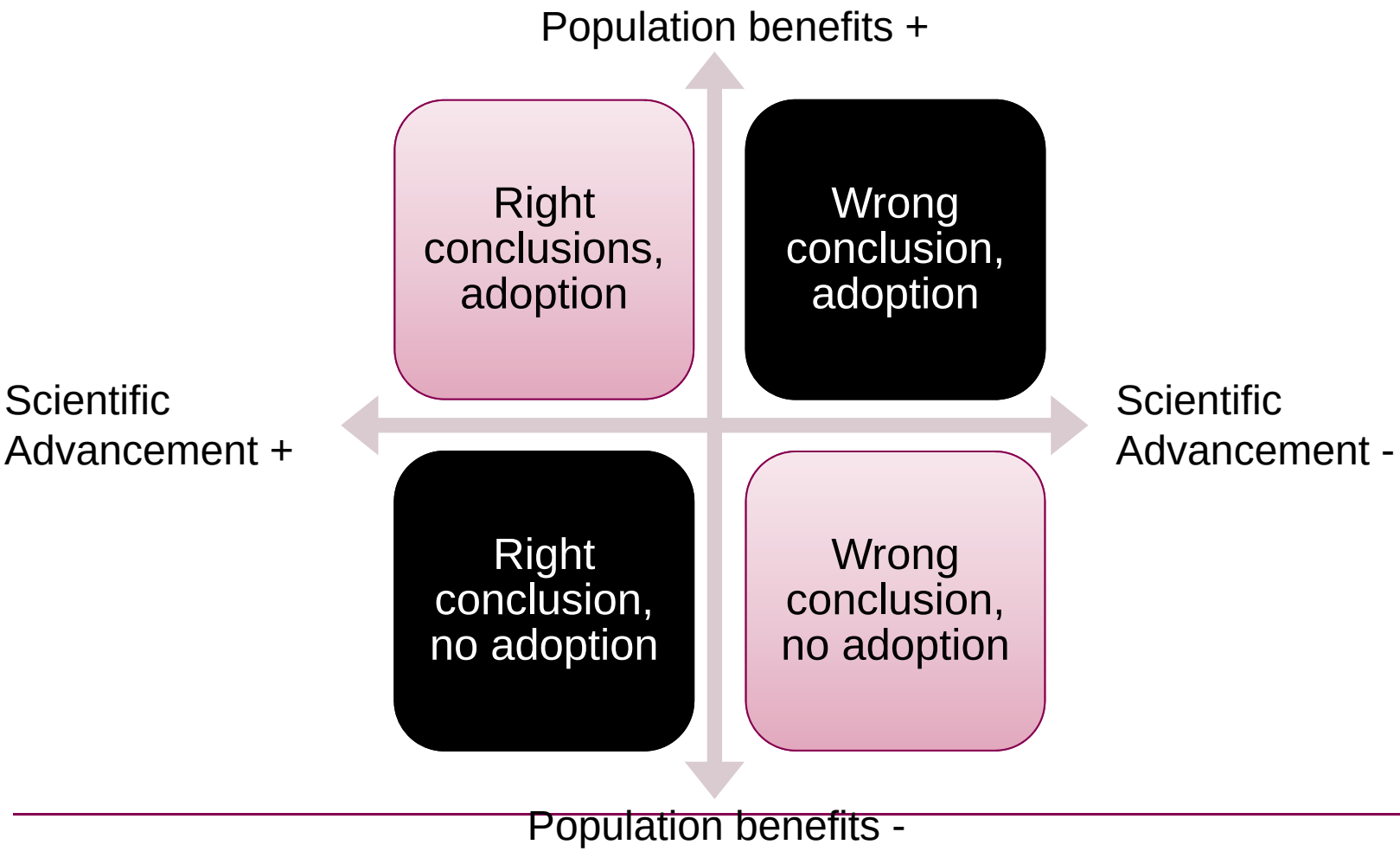
- What would you like to know/consider to improve causal inference?

Which amount of evidence for causal effect?

- Adverse consequences of a wrong conclusion
- Benefits of a right conclusion

Which amount of evidence for causal effect?

Truth= SFP10-14 is effective=causes decreased alcohol use



Thanks for listening!