Inferring incidence rate ratios (IRR) from cross-sectional odds ratios (OR)

using individual-based modelling

applied to major depression & harmful drinking

[B4.1] CSEB Conference
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[1] Imperial College London
[2] McGill University
[3] University of Bristol

Jesse Knight [1]
James Stannah [2]
Michael Pickles [1]
Jack Stone [3]
Peter Vickerman [3]
Marie-Claude Boily [1]

Background & Motivation

Major depression

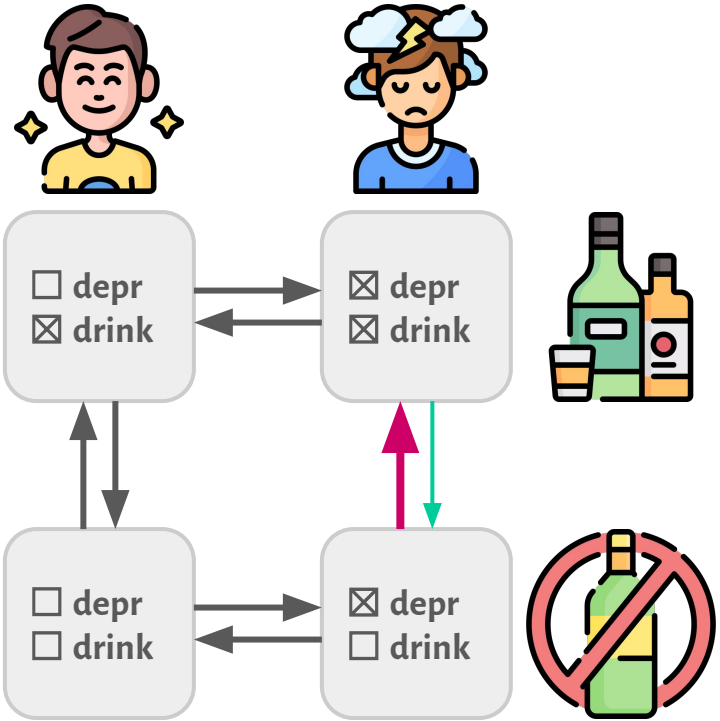
- prevalence: ~ 1 – 10% overall typically [1–3]

Harmful drinking

- prevalence ~ 2 – 20% overall typically [3–5]

ORs for depression & drinking: 1.0 – 4.2 [6]

- if depression "causes" drinking, could have:
  - ↑ **drinking onset** while depressed $IRR_O > 1$
  - ↓ **drinking recovery** while depressed $IRR_R < 1$
- How do prevalence OR relate to these IRR?



OR: odds ratio; IRR: incidence rate ratio

Research Question & Objectives

What can ORs tell us about onset & recovery IRRs (in this context) **?**

Objectives:

{1} **Reference case:** Characterize the relationship between **ORs** and:

- **{a}** $IRR_O > 1$ of drinking **onset** while depressed
- **{b}** $IRR_R < 1$ of drinking **recovery** while depressed

{2} **Sensitivity analysis:** Determine **if / how {1.a} depends on:**

- **{a}** **base rates of depression** (exposure) onset / recovery
- **{b}** **base rates of drinking** (outcome) onset / recovery

OR: odds ratio; IRR: incidence rate ratio

Methods: Individual-Based Simulation Model

Open population:

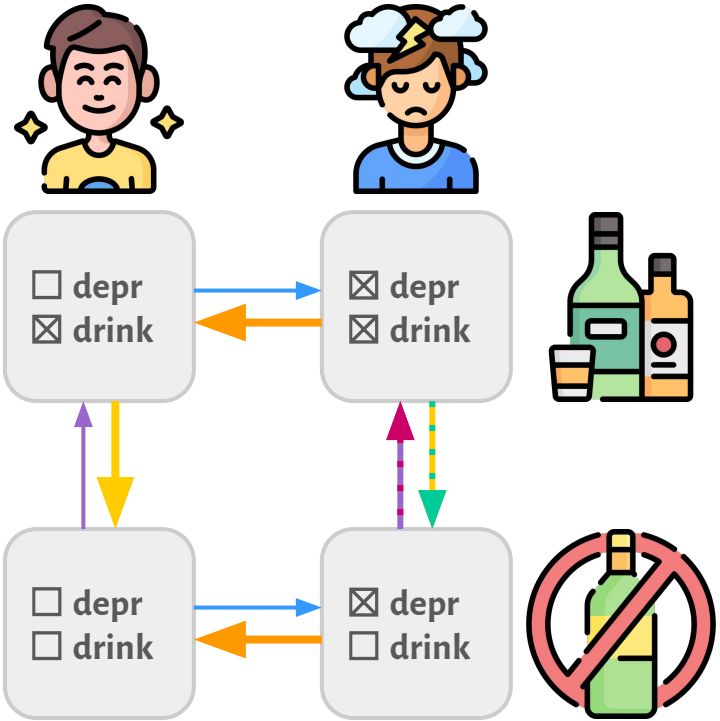
- ages [10, 60)
- enter depression / drinking-naive

Base rates per 100 person-years:

- depression: **onset:** 4 [2,3,7,8] **recovery:** 100 [9,10]
- drinking: **onset:** 2 [3–5] **recovery:** 33 [5,11,12]

Effects while depressed:

- faster drinking **onset: $IRR_O > 1$**
- slower drinking **recovery: $IRR_R < 1$**



Methods: Scenarios & Odds Ratios

Reference case: Objective {1}

- default base rates as above
- vary **onset IRR_O** ~ [1, 8], **recovery IRR_R** ~ [1, ⅛]

→ prevalence (IRRs = 1):

- 3.8% depressed
- 5.4% drinking
- 0.2% both

Sensitivity analysis: Objective {2}

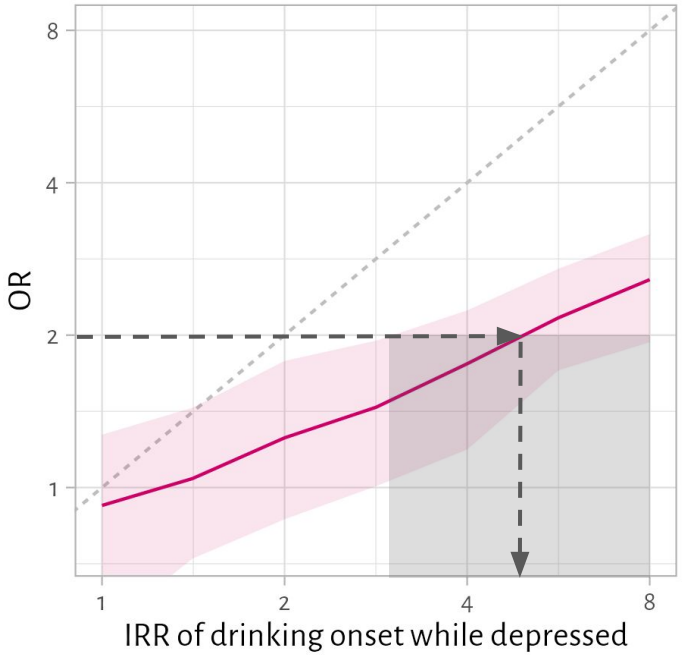
- vary **base rates** of onset/recovery **x [0.5, 1.0, 1.5]** for depression & drinking

Calculating ORs:

- analytic sample: entire population aged [10,60) at equilibrium (N ≈ 10,000)
- report mean (95% CI) outputs across 41 stochastic model runs (seeds)

Results {1}: Reference Case

Result {1.a} OR underestimates onset IRR by factor of 4+



Summary:

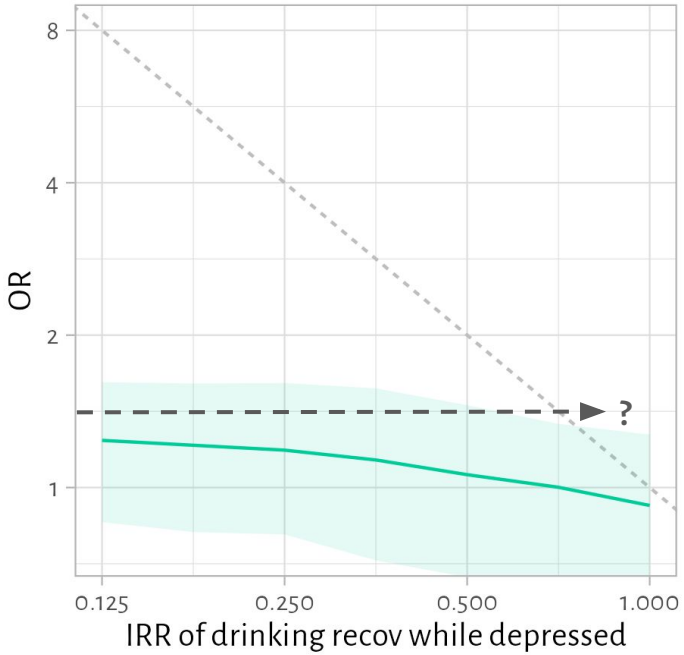
- **OR ≈ 1 + ¼ (IRR_O − 1)**
  - e.g. OR = 2 → $IRR_O \approx 5$

Implication:

- onset effect can be ~4x what OR implies (in this context)

base rates (per 100 PY)	depression	onset: 4	recovery: 100	
	drinking	onset: 2	recovery: 33	recovery $IRR_R = 1$

Result {1.b} OR hardly influenced by recovery IRR



Summary:

- **OR < 1.5** with recovery IRR_R alone

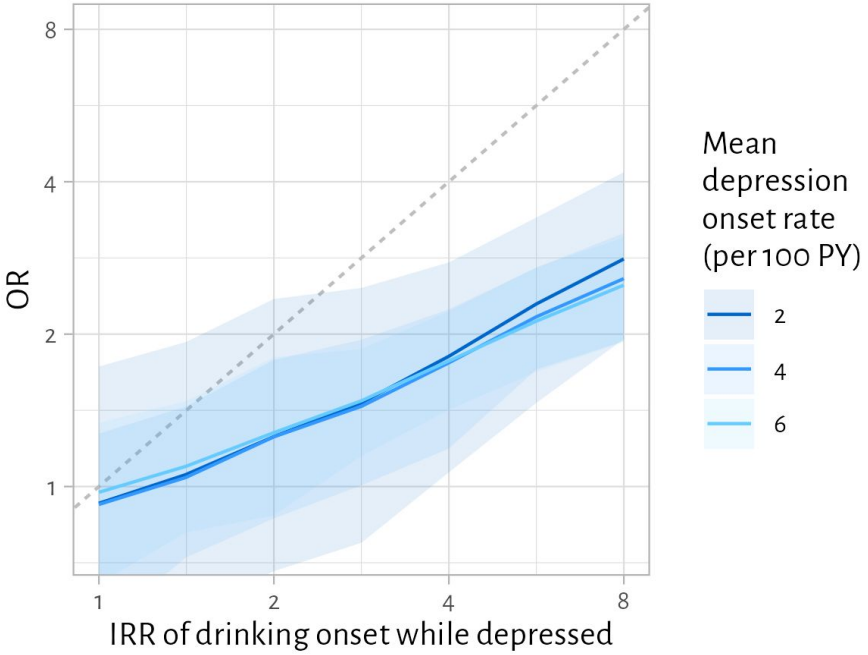
Implication:

- recovery IRR_R hard to identify from OR (in this context)
- if OR > 1.5 → onset IRR_O > 1

base rates (per 100 PY)	depression	onset: 4	recovery: 100	
	drinking	onset: 2	recovery: 33	onet $IRR_O = 1$

Results {2}: Sensitivity Analyses

Result {2.a} Bias ~ with faster depression (exposure) onset

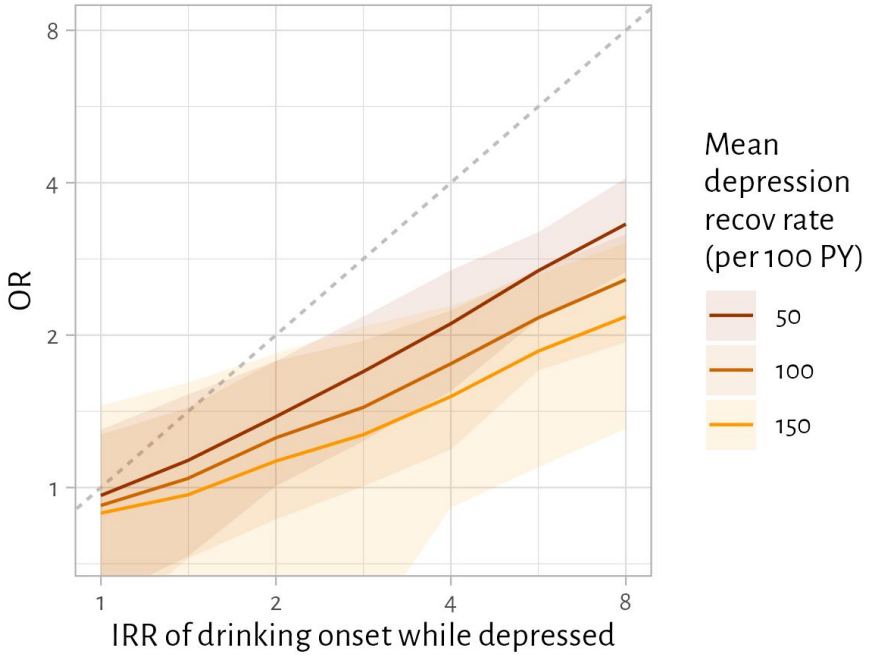


Summary:

- ↑ depression onset rate: ~ bias

base rates (per 100 PY)	depression	onset: …	recovery: 100	recovery $IRR_R = 1$
	drinking	onset: 2	recovery: 33	

Result {2.a} Bias ↑ with faster depression (exposure) recovery



Summary:

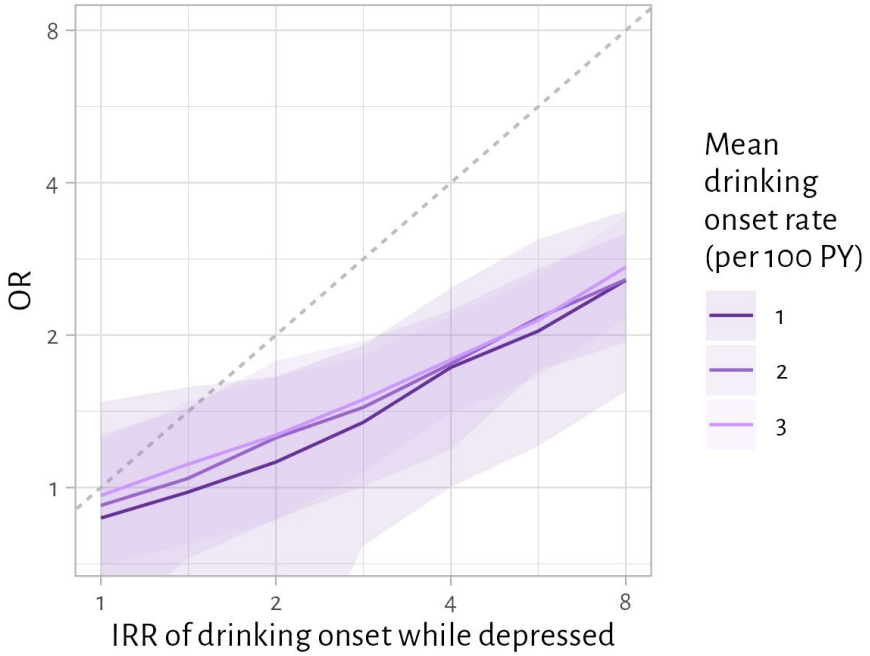
- ↑ depression onset rate: ~ bias
- ↑ depression recovery rate: ↑ bias

Implication:

- OR better approximates IRR_O when depression **(exposure) episodes are long**

base rates (per 100 PY)	depression	onset: 4	recovery: …	
	drinking	onset: 2	recovery: 33	recovery $IRR_R = 1$

Result {2.b} Bias ~ with faster drinking (outcome) onset

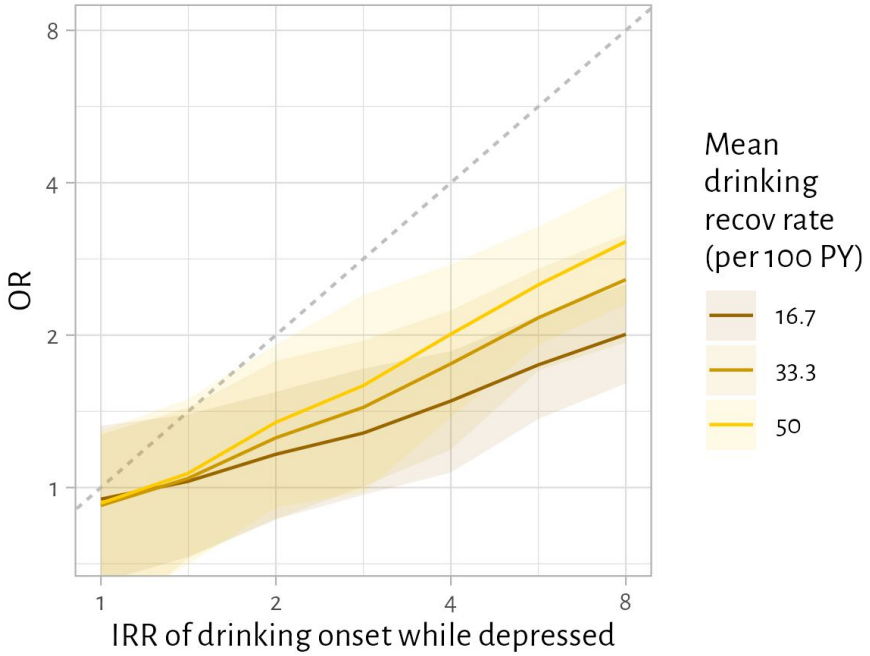


Summary:

- ↑ drinking onset rate: ~ bias

base rates (per 100 PY)	depression	onset: 4	recovery: 100	recovery $IRR_R = 1$
	drinking	onset: …	recovery: 33	

Result {2.b} Bias ↓ with faster drinking (outcome) recovery



Summary:

- ↑ drinking onset rate: ~ bias
- ↑ drinking recovery rate: ↓ bias

Implication:

- OR better approximates IRR_O when drinking **(outcome) episodes are short**

base rates (per 100 PY)	depression	onset: 4	recovery: 100	
	drinking	onset: 2	recovery: …	recovery $IRR_R = 1$

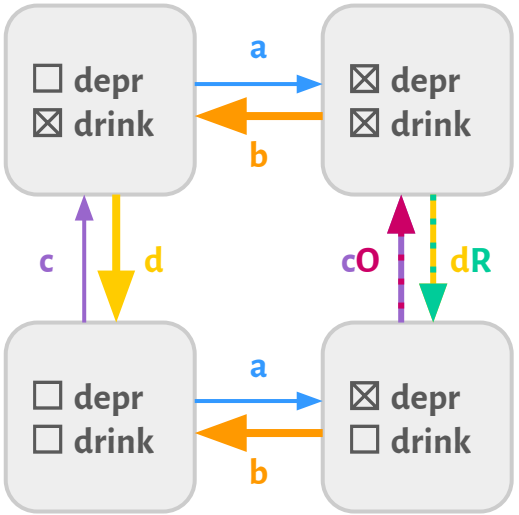
Why do recovery rates influence OR more than onset rates?

Short Answer: recovery rates (**b**,**d**) >> onset rates (**a**,**c**) (in this context)

Mathematically: (ignoring age effects)

$$OR = \frac{(aR+b+cO+dR)(aO+b+cO+dO)}{(aR+b+cR+dR)(aO+b+cO+dR)} \approx \frac{(b+dO)}{(b+dR)}$$

Notation: **a:** depr onset rate **c:** drink onset rate **O:** onset IRR_O
b: depr recovery rate **d:** drink recovery rate **R:** recovery IRR_R



- if recovery rate depression **(b)** >> drinking **(d)**: **OR → 1** "biased towards null"
- if recovery rate depression **(b)** << drinking **(d)**: **OR → O / R** "unbiased"

Summary & Conclusions

- **OR > 1** may derive mechanistically from: **onset $IRR_O > 1$** and/or **recovery $IRR_R < 1$**
- **OR substantially underestimates IRRs**

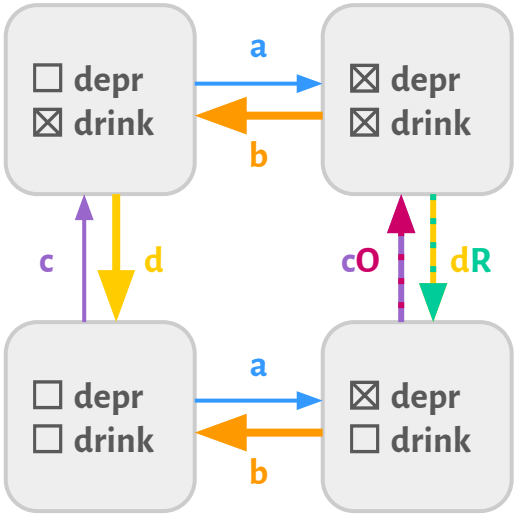
$$OR \approx \frac{(b+dO)}{(b+dR)}$$

OR is biased towards 1 by:

↑ **b** faster recovery from depression

↓ **d** slower recovery from drinking

+ similar results with heterogeneous rates (not shown)



- **implication:** assuming IRR ≈ OR would underestimate projected impact of depression intervention on drinking
- **limitations:** no age effects, no weighted sampling

References

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[6] Boden & Fergusson, **Alcohol and depression**, *Addiction* (2011)

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model & analysis code: `github.com/jessexknight/shift`

Thanks

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Instituts de recherche en santé du Canada

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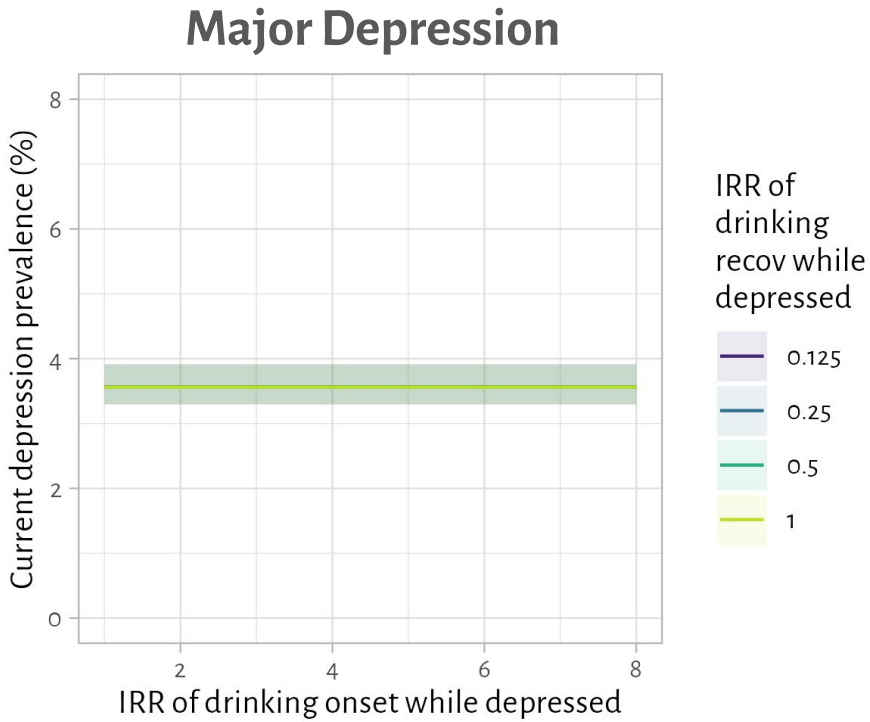
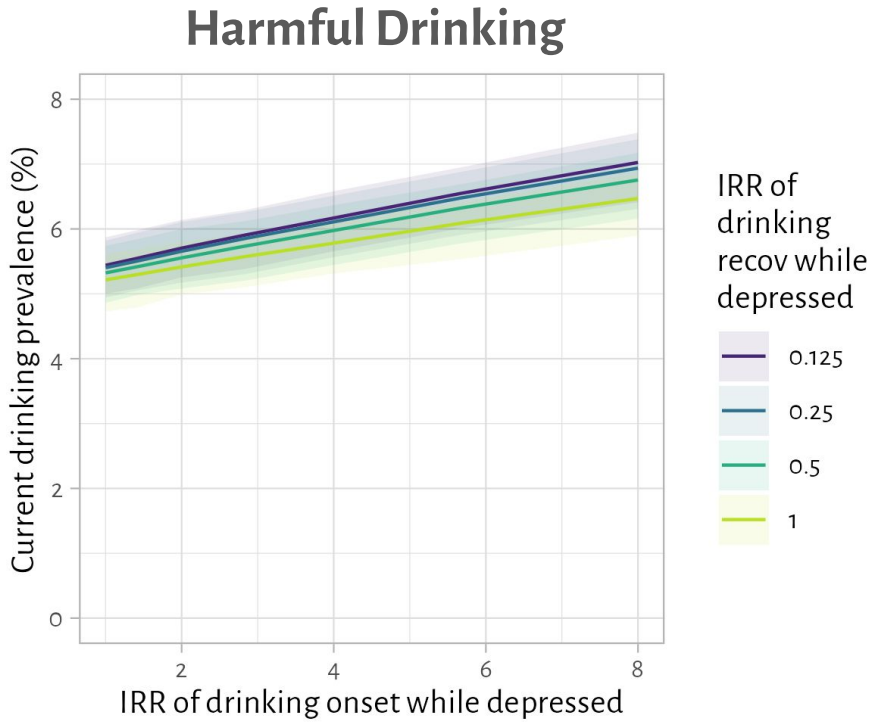
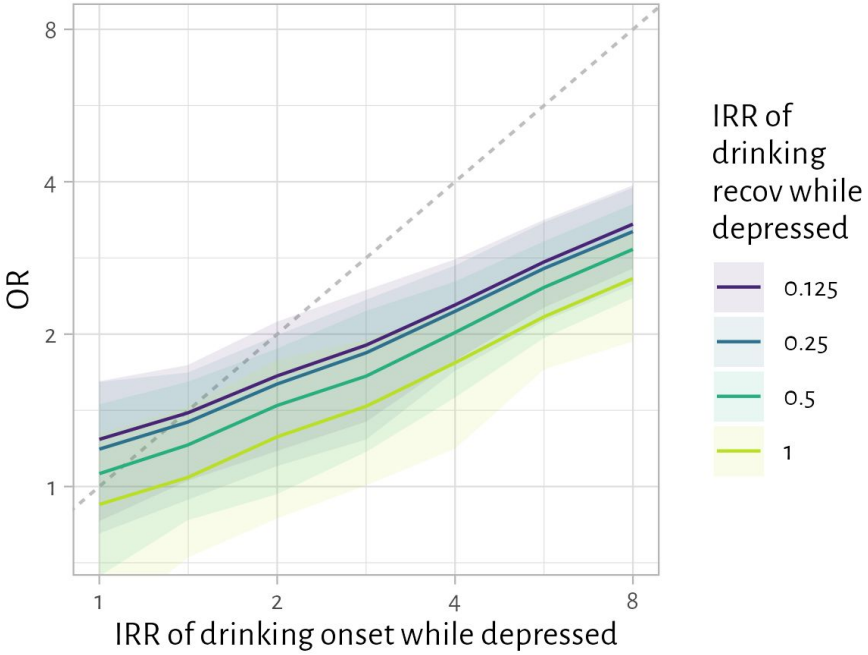
Result {x.1}: Current prevalence of depression & drinking





base rates (per 100 PY)	depression	onset: 4	recovery: 100
	drinking	onset: 2	recovery: 33

Result {x.2}: OR jointly determined by onset & recovery IRRs



Summary:

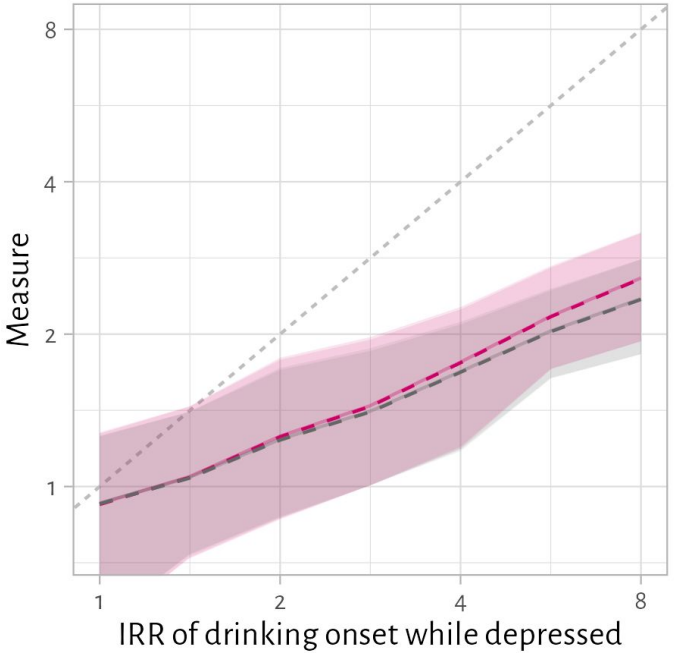
- Both IRRs jointly determine OR
  - OR more sensitive to onset IRR_O vs recovery IRR_R

Implication:

- Impossible to infer from OR *both* IRR onset & recovery

base rates (per 100 PY)	depression	onset: 4	recovery: 100
	drinking	onset: 2	recovery: 33

Result {x.3}: No change with other measures of association



Summary:

- OR ≈ PR (prevalence ratio) with/out age adjustment

Implication:

- main results apply to PR too
- age adjustment won't help

base rates (per 100 PY)	depression	onset: 4	recovery: 100	
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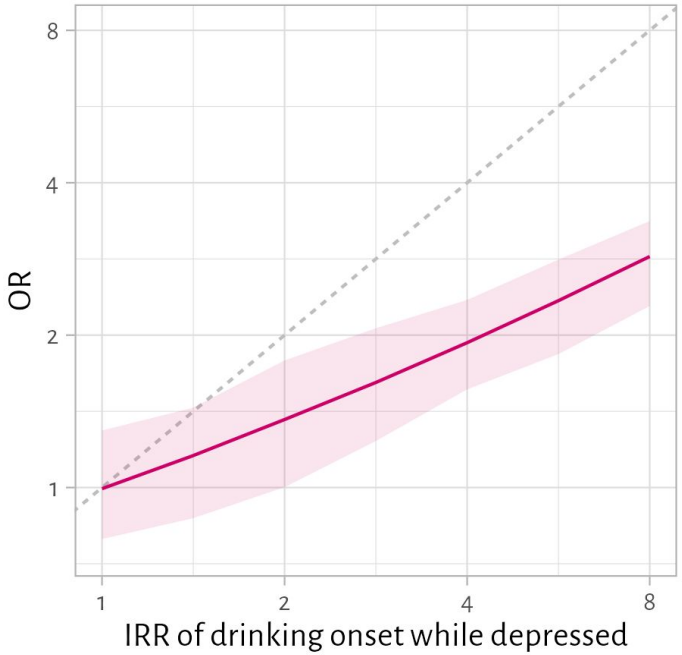
Result {x.4}: heterogeneous rates {1.a}



Methods:

- individual-specific base rates
  sampled from log-normal distribution
  - fixed CV (std. dev / mean) = 1

Summary:

- qualitatively same as homogeneous rates
- reduced influence of recovery rates

base rates (per 100 PY)	depression	onset: 4	recovery: 100	
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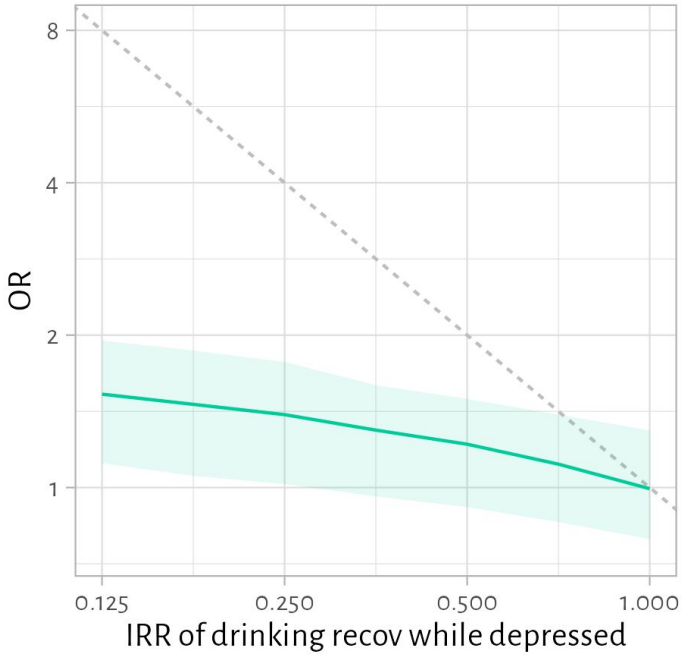
Result {x.4}: heterogeneous rates {1.b}



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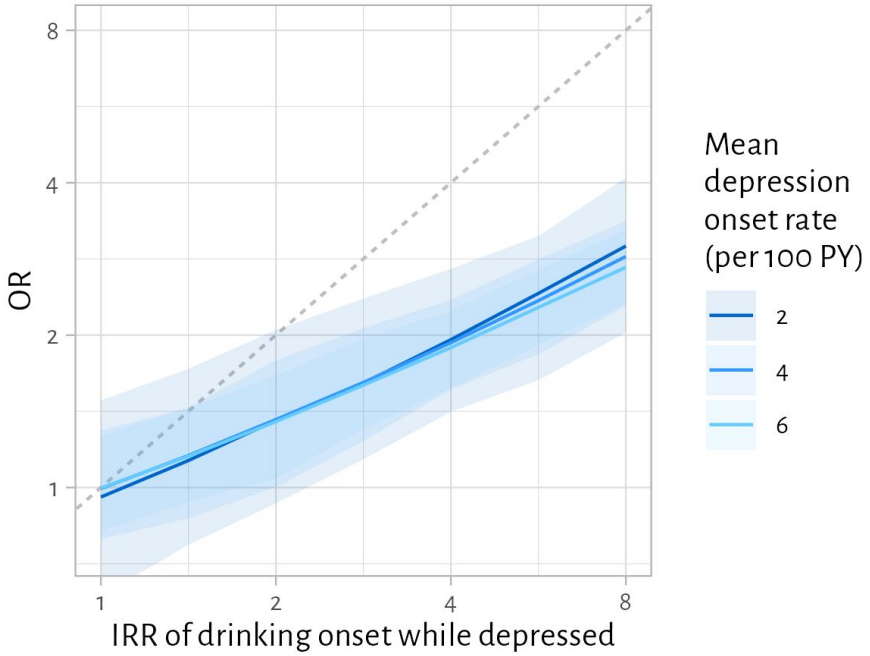
Result {x.4}: heterogeneous rates {2.a}



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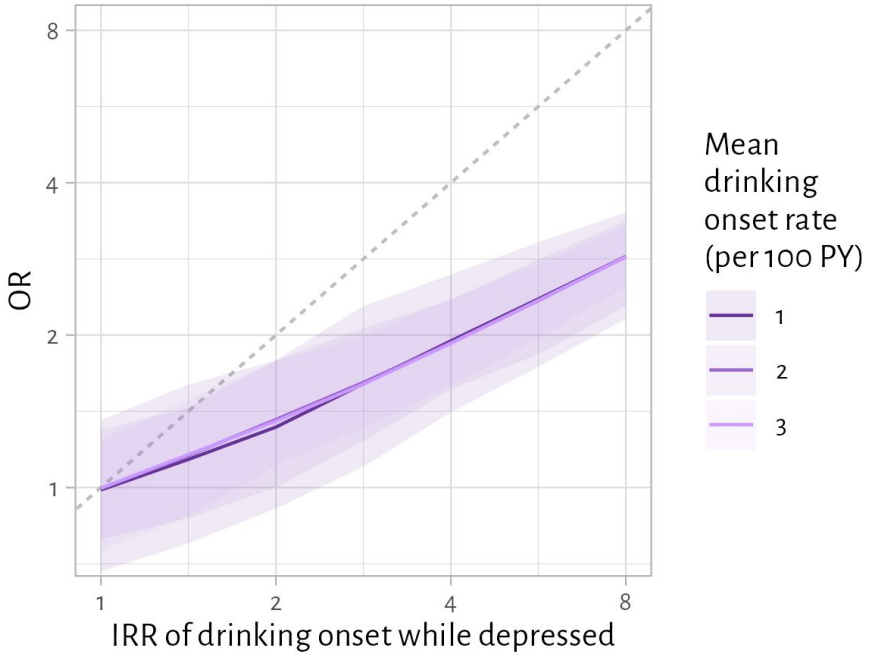

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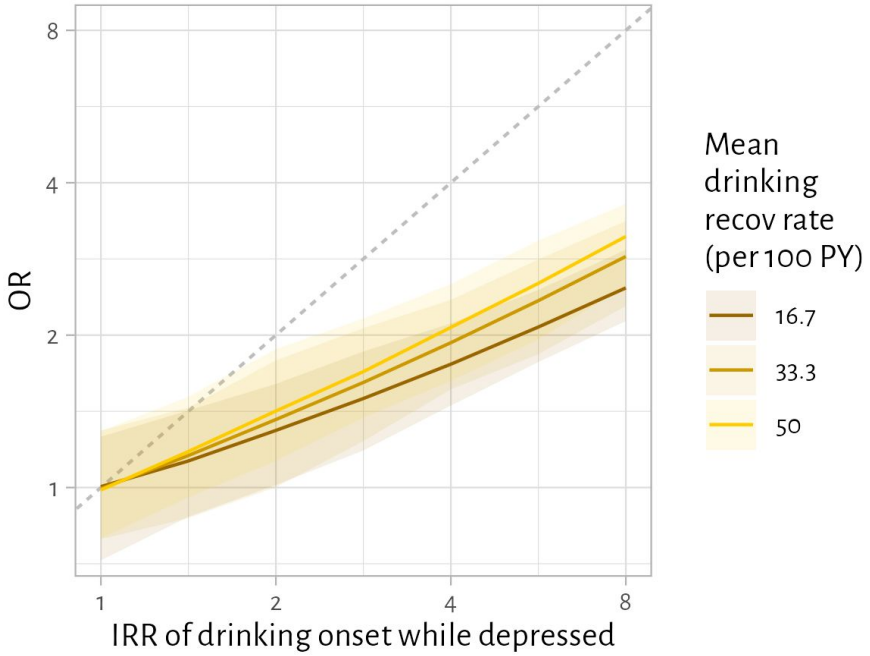

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