Effect modification in epidemiologic studies – a template for analysis

Henrik Støvring

stovring@ph.au.dk

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What is effect modification?

- Knol & VanderWeele (2012) distinguishes between:
    - Effect modification:
      Causal effect of intervening on one factor in strata
    - Interaction
      Causal effect of intervening on two factors

- What would be examples of these two situations?

A recipe for analysis of effect modification

1. Identify cohort and outcome variable
2. Identify the variable inducing the effect (effect variable)
3. Estimate association between effect variable and outcome in the full cohort

4. Identify the effect modifier variable
5. Subdivide the cohort into strata based on effect modifier
6. Estimate effect in each strata (association between effect variable and outcome)
7. Compare effect estimates from different strata

8. Estimate full model with interaction between effect variable and effect modifier – report p-value for interaction term to test for presence of effect modification

Exercise (apply the recipe on previous slide)

- Open the dataset partic_data_dist.dta/xlsx (provided with email and github: https://github.com/steno-aarhus/epi-stats)
- Identify outcome variable, effect variable and effect modifier (see Jensen paper for relevant info: https://doi.org/10.1093/pubmed/fdt068)
- Estimate effect
- Estimate effect in relevant strata
- Estimate model with interaction between effect variable and effect modifier
- Is the effect modification statistically significant?
- Discuss which of your estimates you would report in a paper
- Compare with Table 2 in Jensen 2013 (see next slide)
  – would you report more or fewer numbers?

Table 2, Jensen 2013

Table 2 Crude, adjusted and stratified RRs with 95% confidence intervals for associations between distance in km and screening non-participation

	Unadjusted	Adjusted[a]	Stratified on access to vehicle[b]	
			Access	No access
Distance in km				
0–10	1 (ref.)	1 (ref.)	1 (ref.)	1 (ref.)
>10–15	0.89 (0.83–0.95)	1.04 (0.97–1.11)	1.05 (0.97–1.13)	0.99 (0.91–1.08)
>15–25	0.98 (0.92–1.04)	1.11 (1.05–1.17)	1.09 (1.03–1.16)	1.14 (1.07–1.21)
>25–35	1.01 (0.95–1.08)	1.16 (1.10–1.23)	1.14 (1.07–1.22)	1.23 (1.16–1.31)
>35–45	1.15 (1.06–1.25)	1.30 (1.21–1.40)	1.29 (1.19–1.40)	1.31 (1.21–1.41)
>45–55	1.21 (1.11–1.32)	1.35 (1.25–1.46)	1.35 (1.24–1.47)	1.32 (1.20–1.44)
>55–65	1.20 (1.11–1.30)	1.30 (1.21–1.41)	1.31 (1.20–1.43)	1.27 (1.17–1.38)
>65 max	1.24 (1.10–1.39)	1.36 (1.22–1.52)	1.32 (1.15–1.51)	1.46 (1.27–1.68)

[a]Adjusted for age, ethnicity, education, income, marital status and access to vehicle.
[b]Adjusted for age, ethnicity, education, income and marital status.

Thanks for your attention – questions welcome!