



Other issues

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Revisiting the consistency assumption

– consistency continuum

Consistency means that the observed outcome of a treated/untreated individual is the same with the counterfactual outcome, had he/she been treated or untreated

In other words, treatment should correspond to a **well-defined intervention**

Different treatment strategies that are pooled together

- May have different effect on the outcome
- May have different confounders
- May induce positivity problems (less often)

Revisiting the consistency assumption

Well-defined interventions

Ill-defined interventions



never feasible (Hernan 2016)

There is always room to go into more detail, e.g. statins and cancer

- What time do the patients receive the drug? How many times per day? How many mg? From which pharma company? Etc

In practice, usually there are only prescription data on drugs every month/two months...

Continuum of the consistency assumption

Well-defined interventions

Ill-defined interventions



never feasible (Hernan 2016)



that's what we aim for

In practice, usually there are only prescription data on drugs every month/two months...

Revisiting the consistency assumption

Well-defined interventions



Ill-defined interventions



e.g. people with obesity becoming normal weight vs remaining with obesity

There is some room for improvement for some ill-defined interventions

Revisiting the consistency assumption

Well-defined interventions



Ill-defined interventions



 Less ill-defined intervention

e.g. people with obesity → arm I: weight loss 5%-15% per year

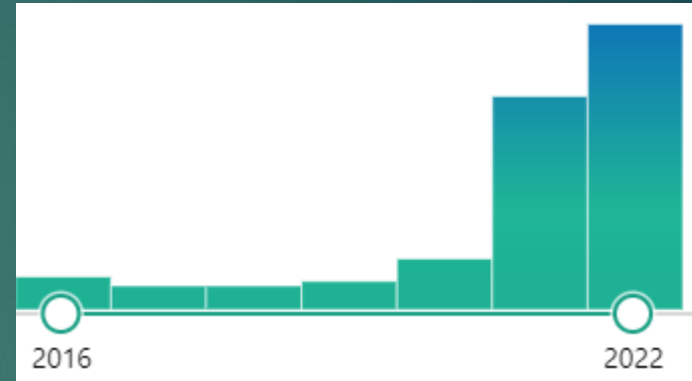
arm II: weight maintenance (-5 to 5% weight change)

Also, we can consider only healthy weight change and not weight change due to illness

There is some room for improvement for the ill-defined interventions (Katsoulis 2021)

Explosion of TTE studies

Over the last years, we have experienced an increase of target trial emulation studies (from 6 in 2016 to 62 in 2022)



Especially during the COVID era, TTE studies have helped us to evaluate

- ▶ the effectiveness of the vaccines [Dickerman 2022, Hulme 2022],
 - ▶ treatment strategies in hospitalised patients [Martinez-Ales G 2022],
 - ▶ policy evaluation with group level data [Ben-Michael E 2021]
- etc.

Future: Potential

- ▶ In the era of Big data, there is a great opportunity to emulating a hypothetical trial using EHR in a transparent, reproducible and principled manner to improve medical guidelines when the corresponding RCTs do not exist
- ▶ It is very likely that TTE studies will further increase in the future
- ▶ These studies can be very useful to provide an indication of what works to improve human health and inform the clinical guidelines adequately

Future: Challenges

- ▶ The performance of TTE studies is not straightforward; requires good understanding of the causal inference principles
- ▶ Data wrangling and analysis is demanding. Extensive sensitivity analysis is needed to evaluate any source of bias (e.g. using positive and negative controls)
- ▶ It is likely that TTE studies from a specific eHealth database cannot answer some research questions. We should never forget the usual problems of the observational studies (unmeasured confounding, missing data etc)

References

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Thanks!

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