Transporting treatment effects with incomplete attributes

Application to critical care management

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- Randomized Controlled Trials (RCT): gold standard to estimate a treatment effect.

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- Indeed, an RCT yields an unbiased estimate (high *internal validity*), but this property may be of limited practical value (low *external validity*).

🤔 *How can we use several data sources to gain information about a target population treatment efficacy?*

Motivating application

Real data gathered: Effect of tranexamic acid (TXA) on brain-injured related (TBI) deaths

Randomized Controlled Trial
CRASH-2

- 40 different countries
- 3727 patients

Concludes on positive effect of TXA for traumatic brain injury with severe extracranial hemorrhage (Shakur-Still et al., 2009)

Real World data
Traumabase ≡ target population

- 23 French Trauma centers
- 8270 patients

Concludes on no significant effect of TXA for traumatic brain injury (Mayer et al., 2020)

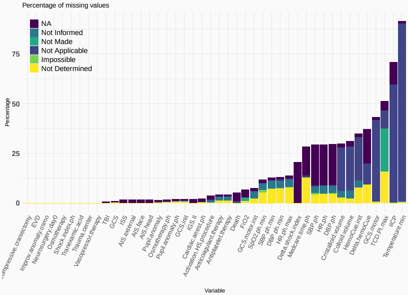
🤔 *Could the generalization help solving/understanding the apparent difference?*

Yes, but ...

📖 See our review article summarizing the different available estimators in the **complete data case**: ▸ arXiv:2011.08047

🧰 **Real data in practice**: It's all about the missingness! 🧩

- ▷ Missing data in the Traumabase, leading to a biased estimation of transported effect?
- ▷ Missing a key covariate in one of the data set, breaking the identifiability?



NA (not available), but also *not informed*, *not made*, *not applicable*, *impossible*.

Impact of NA on identifiability and estimation

🥥 Identifiability in the complete data case in a nutshell:

Everyone has a non-zero chance to be eligible and that conditionally on attributes, the treatment effect is stable across populations.

🔧 Two approaches to maintain the identifiability from the complete data case:

- ▷ Conditionally independent selection (CIS)
  - $\rightarrow$ eligibility and selection depend on the missingness pattern
- ▷ S-ignorability + classical missingness assumptions
  - $\rightarrow$ missing values don't alter selection or outcome models

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Estimation: multiple imputation (MI)

Well explored for single data source. But in case of multiple data sources, less straightforward. Parallels with MI in *meta-analysis*.

We explored several strategies with different imputation models

The best performing: multilevel MI on the joint dataset, with data source indicator.

Conclusion and perspectives

Contributions

- Leverage RCTs **and** observational data →*internal* vs. *external validity*

  👉 See our review paper: Colnet et al. (2020) (arXiv:2011.08047) 📖
- Deal with missing covariate values

  for identifiability → solutions with or without informative NA

  for estimation → multilevel multiple imputation solution

  👉 See our preprint: Mayer et al. (2021) (arXiv:2104.12639) 📖

Perspectives

- Systematically missing values (Colnet et al., 2021).
- Different missing values mechanisms in RCT and obs. data.
- ML for transporting effects? Have a look at the recorded talks from our virtual workshop on *Leveraging Observational Data with Machine Learning*: `https://files.inria.fr/leveraging2021/` 🎬

🤔 Motivation

Transportability of treatment effects is increasingly relevant due to increasing availability of rich obs. data. But **missing values** flaw these data and their impact on methodologies should be made explicit to guarantee that we are working on **well-defined problems and methods despite missingness**.

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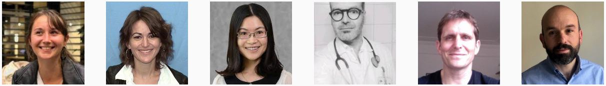
- Medical experts (AP–HP, CHU Vaudois): F.-X. Ageron, T. Gauss, J.-D. Moyer.



❓💡 Questions / remarks / discussions / ideas are very welcome:

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