Simulation-based studies related to the G-computation for causal inference: an overview of recent results

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methodS in Patient-centered outcomes & HEalth ResEarch

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Average causal effect

- Let A denote the binary treatment ($A = 1$ for treatment and 0 otherwise).
- Let Y denote the binary outcome ($Y = 1$ for event and 0 otherwise).
- Let $Z = (Z_1, Z_2, ..., Z_k)$ denote the set of the k baseline covariates.
- Let $Y(1)$ and $Y(0)$ be the two potential outcomes under the treatment and the control, respectively.
- The average causal effect is :

$$ACE = E[Y(1) - Y(0)]$$

- It represents the mean difference between the outcomes of individuals if they had been treated or untreated.

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Three categories of methods for estimating the ACE

- The regression of the treatment allocation to obtain propensity scores (PS) :
  - Inverse Probabiliy Weighting (**IPW**)
  - Full matching (**FM**)
  - Etc.
- The regression of the outcome for G-computation (**GC**)
- The targeted maximum likelihood estimator (**TMLE**) as a doubly robust estimation which combines the outcome and treatment regressions
- Etc.

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Literature related to GC is less prolific compared to PS-based methods

- Suppose (Y_i, A_i, Z_i) a dataset of n independent realisations of (Y, A, Z).
- The first step of GC is to fit $f(Y|A, Z)$
- This outcome model is frequently referred to the Q-model.
- The second step consists in predicting the two potential outcomes for each individual i : $\hat{Y}_i(1) = \hat{f}(Y|1, Z_i)$ and $\hat{Y}_i(0) = \hat{f}(Y|0, Z_i)$
- The average causal effect is then estimated by

$$A\hat{C}E = n^{-1} \sum_i \left[\hat{Y}_i(1) - \hat{Y}_i(0) \right]$$

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Three simulation-based were performed in the context of binary outcome and binary treatment

1. Which covariates should be considered in GC (true confounders, those causing the outcome, etc.) ?
2. What is the robustness of GC to a near-violation of the positivity assumption ?
3. What are the performances of GC associated with machine learning (ML) ?

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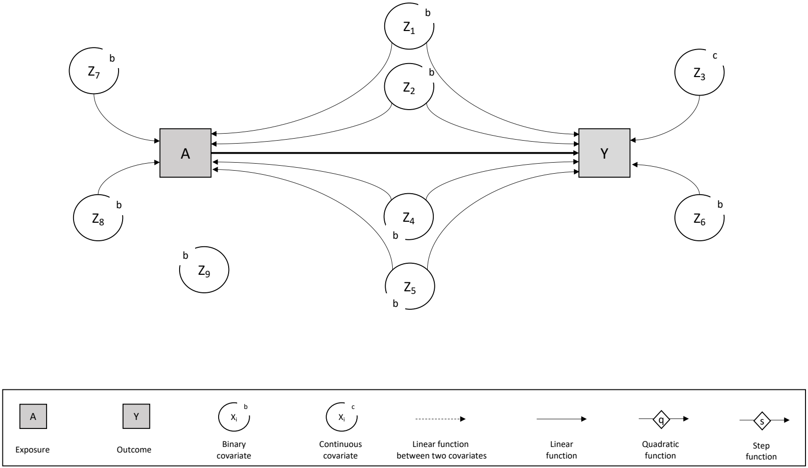
Simulated data



- 4 sample sizes ($n = 100, 300, 500, 2000$)
- 2 treatment effect (H_1 versus H_0)

Compared methods

We compared several methods (all based on logistic regression) :

- GC : variance obtained by parametric simulations.
- IPTW : stabilized weights and robust sandwich-type variance estimator.
- FM : robust sandwich-type variance estimator.
- TMLE : variance obtained by efficient influence curve.

We compared different sets of covariates :

- those causing outcome $(Z_1, Z_2, Z_3, Z_4, Z_5, Z_6)$.
- those causing treatment $(Z_1, Z_2, Z_4, Z_5, Z_7, Z_8)$.
- those causing outcome and treatment (true confounders : Z_1, Z_2, Z_4, Z_5).
- all the covariates.

Results for $n = 100$ under H_1

n	method	selection strategy	mean bias π_0	mean bias π_1	mean bias $\Delta\pi$	mean bias log OR	log OR MSE	log OR MSE*	log OR VEB (%)	log OR coverage (%)	log OR power (%)
100	GC	outcome	0.000	−0.001	−0.001	0.012	0.526	0.716	−6.2	94.1	17.7
		treatment	0.002	−0.001	−0.003	0.006	0.580	0.786	−5.7	94.1	14.0
		common	0.002	−0.001	−0.003	0.006	0.552	0.735	−4.2	94.8	15.1
		entire	−0.001	−0.001	−0.001	0.013	0.558	0.768	−8.8	93.3	16.9
	IPTW	outcome	0.000	−0.001	−0.001	0.008	0.578	0.727	10.8	97.3	7.8
		treatment	−0.000	−0.001	−0.001	0.000	0.716	0.837	−1.2	95.1	9.8
		common	0.002	−0.001	−0.003	0.003	0.587	0.743	6.6	96.8	8.8
		entire	−0.003	−0.001	0.002	0.005	0.741	0.838	−1.5	95.2	9.6
	TMLE	outcome	−0.001	−0.001	0.000	0.002	0.694	0.794	30.0	95.7	5.8
		treatment	0.000	−0.001	−0.001	−0.020	0.876	0.955	183.3	98.8	1.0
		common	−0.000	−0.001	−0.001	−0.001	0.702	0.794	10.4	95.3	7.3
		entire	−0.003	−0.001	0.001	−0.013	0.886	0.953	412.2	98.8	0.5
	FM	outcome	−0.004	−0.001	0.003	0.022	0.665	0.787	−16.7	90.1	18.9
		treatment	−0.006	−0.001	0.004	0.017	0.822	0.911	−32.3	81.3	25.2
		common	−0.001	−0.001	−0.000	0.010	0.653	0.795	−15.3	91.0	17.5
		entire	−0.008	−0.001	0.006	0.022	0.842	0.921	−33.8	80.3	26.7

- No bias for GC, IPTW, TMLE.
- The highest power was for GC with the covariates causing outcome.

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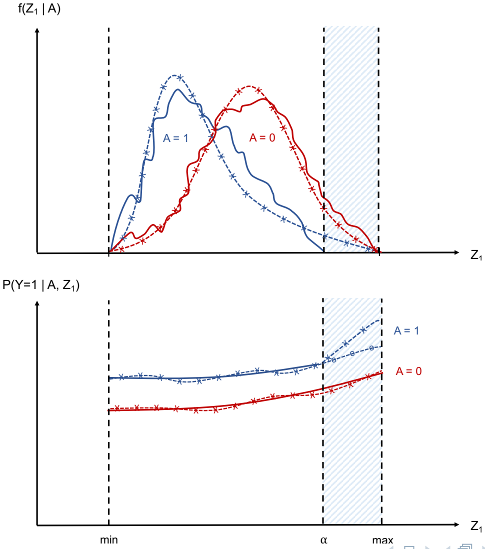
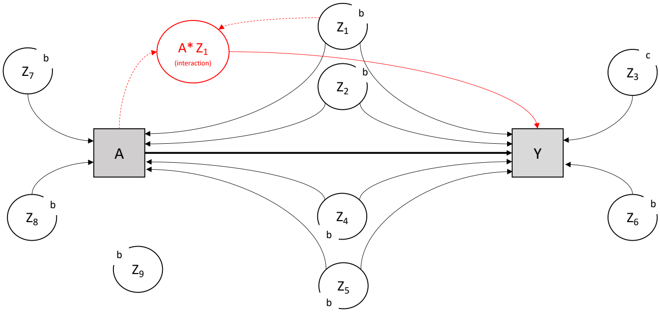
Extrapolation issue from the Q-model

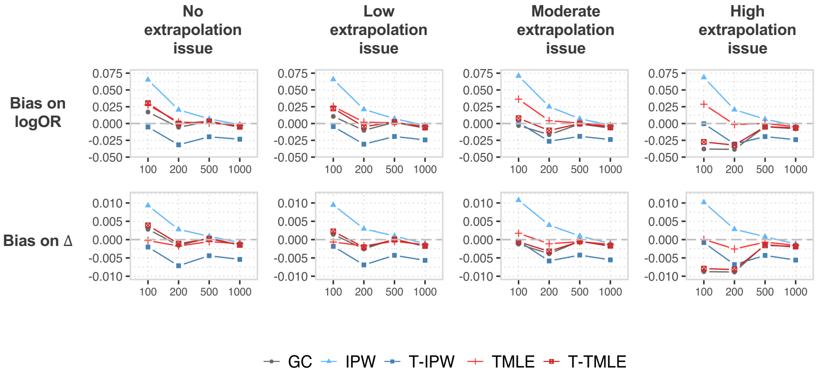


Simulated data



- Z_1 was generated with a 10% prevalence. The near-violation concerned :
  - 0% of the datasets for $n \geq 500$.
  - 1.3% for $n = 200$ subjects.
  - 14.1% for $n = 100$ subjects.
- The extrapolation issue was proportional to the interaction level.

Results



- T-IPW and T-TMLE are the truncated IPW and TMLE with bounds at the 10th and 90th percentiles.
- GC and TMLE were the most robust methods
  - only high extrapolation issue lead to substantial bias.

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Method : a super learner (SL) applicable in practice with small sample size and computation time

- The SL consists in averaging the predictions obtained from the four approaches :
  - **Lasso logistic regression.** A was forced. All the possible interactions between A and covariates Z were tested. B-splines for the quantitative covariates Z.
  - **Elasticnet logistic regression** with similar assumptions.
  - **Neural network** with one hidden layer.
  - **Support vector machine** with a radial basis function kernel.
- The tunning parameters and the weights were obtained by maximizing the average AUC of a ten-fold cross-validation.
- The variance was obtained by bootstrap cross validation.
- The tuning parameters being estimated once on the entire sample.

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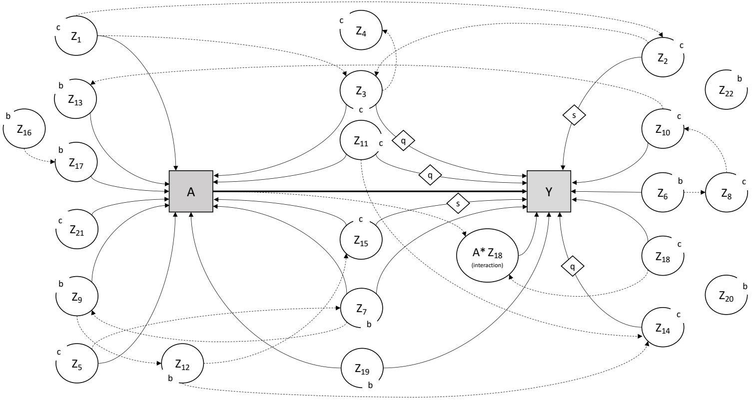
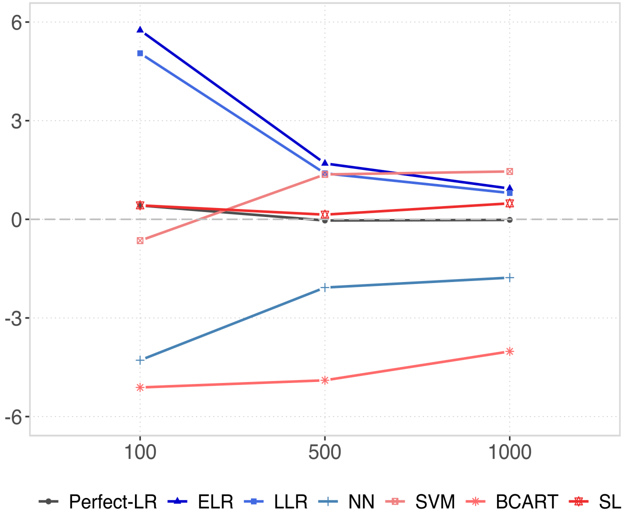
Simulated data



Results in terms of Mean Bias (MB).



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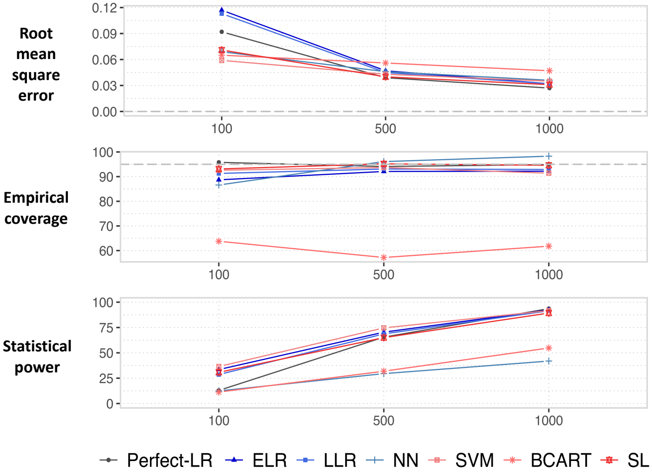
Results in terms of power



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1. Introduction
2. Covariates to consider in GC
3. GG with positivity near-violation
4. GC with Machine Learning
5. Conclusions

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Conclusions

The main advantages of the GC :

- The GC is simple to implement.
- The GC is a powerful method, especially when considering the covariates causing the outcome.
- The GC is quite robust to the positivity near violation, except for high extrapolation issues.
- The proposed SL allows to prevent the Q-model misspecification.
- The automatic algorithm allows bootstrapping the entire estimation procedure, including the Q-model construction, in the variance estimation.

The main limitation of the GC :

- It does not constitute a doubly robust estimator.

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References

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2. G-computation and machine learning for estimating the causal effects of binary exposure statuses on binary outcomes. **Le Borgne** et al. Sci Rep. 2021

3. Causal inference in case of near-violation of positivity : comparison of methods. **Léger** et al. In revision.

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