Causal inference approaches using IPTW for multi-level treatments in medical studies: a systematic review.

F. Bettega[1], C. Leyrat[2] S. Bailly[1]

[1] Université Grenoble Alpes, Inserm, CHU Grenoble Alpes, HP2, [2] Department of Medical Statistics, LSHTM Londres

Introduction

Causal inference methods based on observational data represent an alternative to randomised controlled trials (RCT) when RCTs are not feasible, and they contribute to the development of real-world evidence. Inverse-probability-of-treatment weighting (IPTW) is one of the most popular marginal approaches to account for confounding. In medical research, IPTW is mainly applied to estimate the average causal effect of binary treatments, even when the treatment has multiple levels, despite the availability of IPTW estimators in that setting. This raises questions about the appropriateness of the use of IPTW in practice.

Aims

- How often, in which medical fields and for what types of interventions is multinomial IPTW used ?
- What are the characteristics of the studies using multinomial IPTW ?
- How are these methods implemented in practice ?
- What is the current quality of the reporting of studies using multinomial IPTW regarding the assessment of the validity of causal inference assumptions ?

Description of the included studies

- IPTW with more than two treatment levels in 17 different medical specialities.
- Most articles justify the use of causal inference methods 84 (92.3%)
- Number of groups varied between 3 (56 %) and 11.

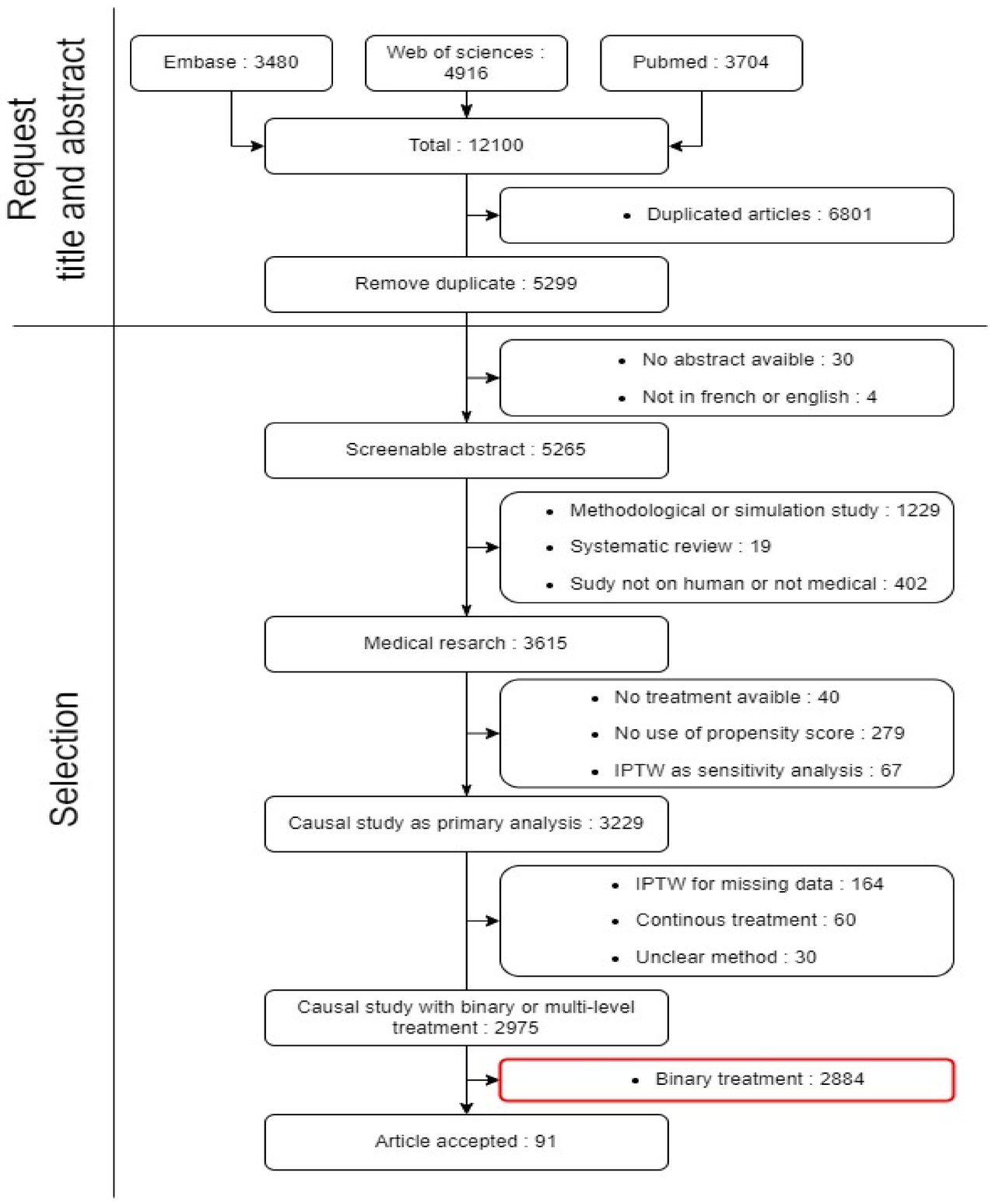
Outcome models

Outcome model	Outcome type	N (%)
Poisson	Count	7 (7.7 %)
Poisson	Time-to-event	1 (1.1 %)
Other	Other	4 (4.4 %)
Negative binomial	Binary	1 (1.1 %)
Multinomial	Categorical	4 (4.4 %)
Multinomial	Ordinal	1 (1.1 %)
Logistic	Binary	18 (19.8 %)
Linear	Continuous	4 (4.4 %)
Cox	Time-to-event	51 (56 %)

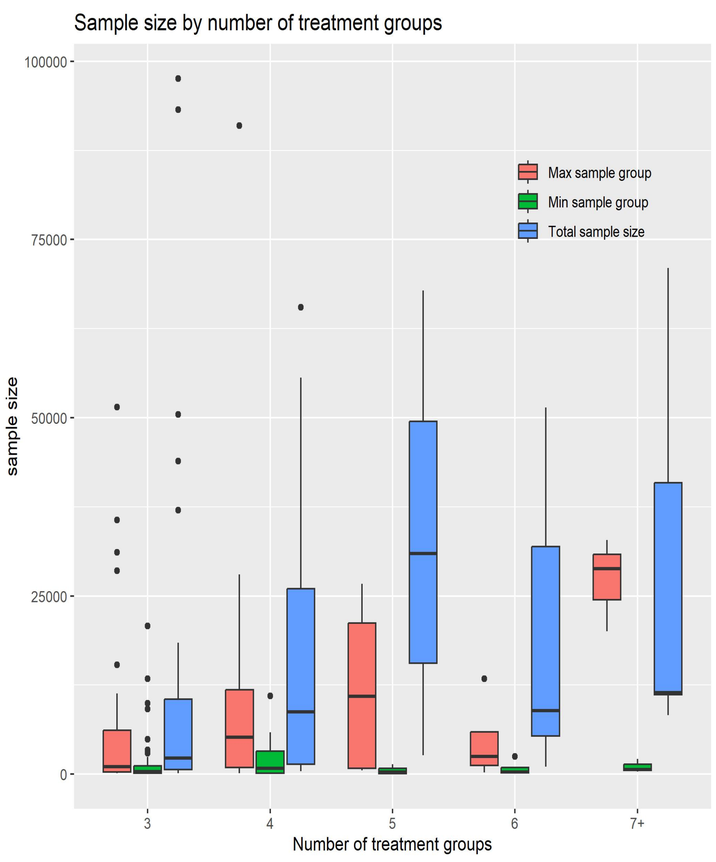
Assumptions

- Only 9 articles (9.8%) refer to the assumptions needed to obtain correct inferences.
- Only 3 articles (3.3%) present a DAG, which are very useful tools for presenting the causal structure of the data and relationships between measured and unobserved variables.

Flow chart



Sample size



[a]=8 articles not show in figures because of sample size greater than 100,000

Weighting models

- The variables included in the weight model 13 (14.3%) or the model used for propensity score estimation 4 (4.4 %) was even missing
- 59 (64.8%) used multinomial regression
- 26 (28.6%) used GBMs.

Assessing covariate balance

- 52 (57.1%) of the articles did not mention the evaluation of the balance of confounding factors after weighting.

Weighted estimator

- IPTW 72 (79.1 %)
- AIPTW 19 studies (20.9%)

Good research practice

- 1 (1.1%) study had previously registered a protocol.
- 3 (3.3%) make the code available
- 2 (2.2%) propose all or part of the data

Conclusion

IPTW estimators, for multi-level treatments, are tools to address certain medical issues. However, their reporting could be greatly improved in order to make the results of the analysis of observational studies using them more transparent and reproducible.