Transparent Reporting of Observational Studies Emulating a Target Trial: The TARGET Statement

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ABSTRACT

IMPORTANCE

When randomized trials are unavailable or not feasible, observational studies can be used, if assumptions hold, to answer causal questions about the comparative effects of interventions by emulating a hypothetical pragmatic randomized trial (target trial). Published guidance to aid reporting of these studies is not available.

OBJECTIVE

To develop consensus-based guidance for reporting observational studies performed to estimate causal effects by explicitly emulating a target trial.

DESIGN, SETTING AND PARTICIPANTS

The TARGET (TrAnsparent ReportinG of observational studies Emulating a Target trial) guideline was developed using the Enhancing the Quality and Transparency of Health Research (EQUATOR) framework. The development included (1) a systematic review of reporting practices in published studies that had explicitly aimed to emulate a target trial; (2) a 2-round online survey (August 2023 to March 2024; 18 expert participants from 6 countries) to assess the importance of candidate items selected from previous research and to identify additional items; (3) a three-day expert consensus meeting (June 2024; 18 panellists) to refine the scope of the guideline and draft the checklist; and (4) pilot of the draft checklist with stakeholders (n=108; September 2024 to February 2025). The checklist was further refined based on feedback on successive drafts.

FINDINGS

The 21-item TARGET checklist is organized into six sections (abstract, introduction, methods, results, discussion, other information). TARGET provides guidance for reporting observational studies of interventions explicitly emulating a parallel group, individually randomized target trial, with adjustment for baseline confounders. Key recommendations are to (1) identify the study as an observational emulation of a target trial; (2) summarize the causal question, and reason for emulating a target trial, (3) clearly specify the target trial protocol (i.e., the causal estimand, identifying assumptions, data analysis plan) and how it

was mapped to the observational data, and (4) report the estimate obtained for each causal estimand, its precision, and findings from additional analyses to assess the sensitivity of the estimates to assumptions, and design and analysis choices.

CONCLUSIONS AND RELEVANCE

Application of the TARGET guideline recommendations aims to improve reporting transparency and peer review, and help researchers, clinicians, and other readers interpret and apply the results.

When randomized trials are unavailable or not feasible, observational (non-randomized) data can be used in an attempt to emulate a hypothetical pragmatic randomized trial—the target trial.[1–4] The target trial framework has two steps: 1) specifying the causal questions in the form of the target trial protocol defining the causal effect of interest (causal estimand), the key assumptions, and the data analysis plan, and 2) describing how each component of the target trial protocol is mapped to the observational data. When followed correctly, the framework should eliminate some biases that are due to an incorrect use of the observational data (e.g. selection bias due to inclusion of individuals after initiation of treatment or other biases that generate 'immortal time'[5,6]), so that investigators can focus on other sources of bias due to limitations of the observational data (e.g., confounding, measurement error and missing data).[1]

The target trial framework aims to improve the conduct of comparative effectiveness studies that use observational data by providing a structured approach to study design, data analysis, reporting, and assessing risk of bias.[7] The framework's value is increasingly recognized by investigators,[8,9] regulators,[10,11] research organisations[12] and journals.[2] However, published studies using the target trial framework have been inconsistently reported; often not reporting key aspects of the target trial protocol.[13,14] Guidelines for observational studies such as STROBE,[15] RECORD[16] and their extensions do not capture some key nuances of target trial emulations, and there is no specific guidance for the reporting of studies emulating a target trial.[14]

The TARGET (TrAnsparent ReportinG of observational studies Emulating a Target trial) guideline was developed for reporting analyses of observational data that explicitly aim to estimate causal effects by emulating a target trial. It consists of a checklist to be used when writing or reading research reports, which is presented in this Special Communication alongside additional information for items. A glossary of terms used in this article and in the checklist appears in Table 1.

DEVELOPMENT OF TARGET

The TARGET guideline was developed according to the Enhancing Quality and Transparency of Health Research (EQUATOR) guidelines.[17] A detailed description of the methods is

provided in our published protocol.[18] First, we conducted a systematic review to investigate the reporting of published studies that explicitly aimed to emulate a target trial and identify available reporting guidance.[14] Second, we performed a 2-round online survey from August 2023 to March 2024, which involved 18 expert participants from 6 countries, to reach agreement on the importance of candidate items selected from previous research and to identify additional items. Third, a three-day expert consensus meeting involving 18 panellists was held in June 2024 to establish the final checklist; panellists included methodologists, statisticians, clinical trialists, epidemiologists, clinical researchers, clinicians, evidence synthesis experts, representatives from industry, and journal editors. Fourth, internal (n=13) and external (n=95) piloting was conducted with potential guideline users from September 2024 to February 2025 to ensure acceptability and appropriateness of the draft checklist and accompanying descriptions. Checklist item wording was finalized following consolidation of the piloting feedback and through iterative discussions.

The TARGET guideline is intended as a standalone reporting guideline for studies emulating a target trial. The international consensus process produced the 21-item TARGET reporting checklist (Table 2). eFigure 1 presents the flow of items through the 4 stages of checklist development. Briefly, the systematic review identified 44 items for reporting observational analyses emulating a target trial, which were evaluated in the online survey. Following the consensus meeting and internal and external pilot, modifications were made to the wording, presentation and grouping of the items to produce the 21-item checklist.

TARGET CHECKLIST

We present the TARGET checklist alongside additional information for items. Details on the rationale for and interpretation of each item, and examples of reporting, will be provided in a separate "explanation and elaboration" document.

Checklist items are grouped according to the typical structure of original investigations reporting research results: abstract (Item 1), introduction (Items 2-4), methods (Items 5-7), results (Items 8-14), discussion (Items 15-16) and other information (Items 17-21). Subitems contain related information within the same topic.

The checklist is organised with two items presented side by side: the target trial specification (items 6a-g) which outline the causal estimand, and emulation of the target trial (items 7a-g), describing how the causal estimand was mapped to the observational data.

When using the checklist, all items and subitems should be reported in sufficient detail and clarity in the manuscript or supplementary materials. Although the checklist provides one natural order in a report, the specific placement and sequence of items may depend on author preferences and journal style.

Abstract

Item 1a. Identify that the study attempts to emulate a target trial using observational data. State the study objectives and briefly summarize the specified target trial.

Readers should be able to identify from the abstract that the study used observational data to emulate a target trial, which supports easy identification and appropriate indexing of the study design. Avoid terminology such as 'emulated trial,' 'emulated randomized/clinical trial' which may lead readers to mistake the study for a randomized trial. Include a clear statement of the study objectives and causal questions through a summary of the target trial such as its eligibility criteria, treatment strategies, end of follow-up, outcomes, and causal contrasts.

Item 1b. Report the data sources used for emulation.

Knowledge of the data sources used to emulate the target trial provides context for assessing robustness and generalizability of the study findings and feasibility of emulation. State that the analysis used observational data and that individuals were not randomly allocated to the treatment strategies of interest.

Item 1c. Summarize key assumptions, statistical methods, findings and conclusions.

Provide a concise summary of the approaches used to identify and estimate the causal effects, including key assumptions made due to absence of randomisation (e.g. no unmeasured confounding) or other potential sources of bias (including measurement error and missing data, e.g., due to loss to follow-up), methods used to adjust for confounding, findings (e.g., descriptive results and point estimates with corresponding measures of precision for treatment effects) and conclusions.

Introduction

Background

Item 2. Describe the scientific background of the study and the gap in knowledge.

Report the relevant scientific background and rationale for the study, including prior research, to illustrate the knowledge gap addressed.

Causal question

Item 3. Summarize the causal question.

Summarize the causal question specified by the target trial protocol including the target population (eligibility criteria), treatment strategies compared, end of follow-up, and outcomes. The acronym PICO (Population, Intervention, Comparator, Outcome) has been used to summarize some of these components.[19]

Rationale

Item 4. Describe the rationale for emulating a target trial with the available data. Cite randomized trials informing the design of the target trial if applicable.

Describe why the specific gap in knowledge (causal question) may be addressed by emulating a target trial (study design) with the available data. Where the target trial was designed based on a completed or ongoing randomized trial, cite the trial publication and/or its registration and protocol to provide readers with additional context for the causal question.

Methods

Data sources

Item 5. Cite the data sources used for the analyses and for each one describe the following: original purpose, type, the geographic locations, setting and time-period. If relevant, describe how the data were linked or pooled.

A detailed description of the data sources usually should include the original purpose (e.g., research, routine clinical practice), type (e.g., electronic health records, claims, registry), the geographic locations where the data were collected (e.g., countries, regions), setting (e.g., hospitals, primary care, general population), time period, and if applicable, how multiple

data sources were linked or otherwise combined. Where available, describe quality metrics (e.g., reliability and validity of data elements) for the data sources used.

Item 6. Target trial specification

Items 6a-h describe the target trial protocol. Specifically, Items 6a-6f clarify the causal question (see Item 3) by specifying elements of the causal estimand. Item 6g describes the assumptions made to identify the causal estimand, and Item 6h describes the data analysis plan (estimator). The target trial specification outlines the hypothetical pragmatic randomized trial that could be emulated given the constraints of the observed data.

Eligibility criteria

Item 6a. Describe the eligibility criteria.

The eligibility criteria indicate the specific population to which the results apply (target population). Describe the criteria and conditions for recruitment into the target trial (e.g., demographic characteristics, diagnostic criteria, disease stage, treatment history).

Treatment strategies

Item 6b. Describe the treatment strategies that would be compared.

The treatment strategies compared in the target trial should be described in sufficient detail to allow their implementation. This may include information on treatments or interventions, dosage or intensity, method of administration, frequency, duration, decision rules for initiation and discontinuation (including any grace period after baseline within which interventions must be started and allowable reasons for discontinuation), allowed concomitant treatments, and monitoring rules. If a treatment strategy is defined as 'usual care' or 'non-initiation', describe what that would constitute.

Assignment procedures

Item 6c. Report that eligible individuals would be randomly assigned to treatment strategies and may be aware of their treatment allocation.

The target trial, by definition, is a trial where individuals are randomly assigned to one of two or more treatment strategies to answer a causal question of interest,[1] and are generally aware of the treatment strategies they receive.[20]

Follow-up

Item 6d. Clarify that follow-up would start at time of assignment to the treatment strategies. Specify when follow-up would end.

In randomized trials, the commencement of follow-up typically aligns with the time an individual meets the study eligibility criteria and is randomly assigned to a treatment strategy (time zero). Confirm that follow-up would start at the time of assignment to the treatment strategies and describe when the follow-up period would end for each outcome as well as the possible reasons, such as the end of the study, loss to follow-up, death, or other events.

Outcomes

Item 6e. Describe the outcomes.

A description of the outcomes includes how and when they would be measured or assessed in the target trial. If relevant, indicate which outcome would be considered the main outcome of interest.

Causal contrasts

Item 6f. Describe the causal contrasts of interest, including effect measures.

Typical causal contrasts of interest are the effect of assignment to the treatment strategy (intention-to-treat effect) and the effect of receiving the treatment strategy under full adherence to the protocol (per-protocol effect). When relevant, indicate how competing events were defined and incorporated into the causal contrasts.[21] When applicable, quantify causal contrasts via both relative effect measures such as the risk ratio and absolute effect measures such as the risk or mean difference.

Identifying assumptions

Item 6g. Describe assumptions that would be made to identify each causal estimand. Describe the variables, if any, related to these assumptions.

If there are no losses to follow-up, the effect of assignment (intention-to-treat effect) can be validly estimated under assumptions that are expected to hold due to the randomized assignment. However, additional assumptions are required when there are losses to follow-

up (and, for some estimands,[22,23] when there are competing events). Correctly estimating a per-protocol effect requires additional assumptions such as the absence of unmeasured baseline or time-varying confounding.[24]

Data analysis plan

Item 6h. For each causal estimand, describe the data analysis procedures and any associated statistical modelling assumptions, including approaches for handling missing data.

Describe the data analysis procedures for the target trial including methods to address potential selection bias arising from loss to follow-up or other types of missing data. When estimating a per-protocol effect, describe any methods to adjust for confounders. When using statistical models, describe the modelling approach and the functional form of variables in models (e.g., variable transformations, use of product or "interaction" terms). Describe any subgroup or sensitivity analyses. The data analysis plan for each causal estimand should be reported separately.

Item 7. Target trial emulation

Items 7a-h describe how the components of the target trial were mapped to the observational data (Item 5), including how all variables were measured or ascertained.

Eligibility criteria

Item 7a. Describe how the eligibility criteria were operationalized with the data.

A description of how the eligibility criteria were ascertained in the available data sources (e.g., using codes from the International Classification of Diseases). Describe any imperfections in the mapping of eligibility criteria of the target trial due to data limitations.

Treatment strategies

Item 7b. Describe how the treatment strategies were operationalized with the data.

A description of how the components of the treatment strategies were ascertained or defined using the data. This may include specifying any treatment codes or dictionaries used (e.g. the Anatomical Therapeutic Chemical classification) and any information used to determine adherence to the treatment strategies.

Assignment procedures

Item 7c. Describe how assignment to treatment strategies was operationalized with the data.

The concept of an individual's 'assignment' to a treatment strategy in the target trial (Item 6c) is operationalized as their classification by the investigators into a treatment strategy using the observational data. Describe how individuals were assigned (i.e., classified) to each treatment strategy (e.g., based on a new prescription of a medicine) at the start of follow-up. The assumption that random assignment might be emulated through adjustment of baseline confounders is described in 7g. For treatment strategies that cannot be distinguished at the start of follow-up, report the approach used for classification into treatment strategies (e.g., cloning[6,25]).

Follow-up

Item 7d. Clarify that follow-up starts at the time individuals were assigned to the treatment strategies. Describe how the end of follow-up was operationalized with the data.

Starting the follow-up (time zero) when each eligible individual is assigned (i.e., classified) to a treatment strategy can avoid design-related biases in observational analyses.[5] Describe how the follow-up period of the target trial was operationalized in the observational data, including how the reasons for the end of follow-up were ascertained in the data (e.g. ascertaining deaths through a mortality registry). For studies that compare treatment to no action (e.g., usual care), report when the start of follow-up was operationalized for individuals in each group (e.g., all, the first or a random time eligible).[5]

Outcomes

Item 7e. Describe how the outcomes were operationalized with the data.

A description of how the outcomes were ascertained with the observational data including any differences to the target trial. This may include detailing the codes or algorithms used to identify the outcomes, highlighting whether any validation activities have been conducted or referencing previous validation activities.

Causal contrasts

Item 7f. Describe how the causal contrasts were operationalized with the data, including effect measures.

A description of the observational analogs of the causal contrasts (Item 6f). The effect of assignment can be operationalized as the comparison of groups classified into different treatment strategies at time zero, regardless of whether they follow those strategies afterwards (e.g., the effect of initial medication prescription, regardless of adherence). Per-protocol effects can then be defined equivalently to those in the target trial (e.g., the effect of initial medication prescription and continuation as specified in the protocol). When relevant, describe how competing events were ascertained and clarify that they are incorporated into the contrasts as in the target trial.[21]

Identifying assumptions

Item 7g (i) For each causal estimand, describe assumptions made to identify it, including assumptions regarding baseline confounding due to lack of randomization.

Due to the lack of randomized assignment, the identification of causal effects likely requires the assumption of exchangeability (comparability) conditional on baseline variables (i.e., the assumption that there is no unmeasured confounding conditional on those variables). Describe and justify the choice of baseline variables, if any.

Like in the target trial with randomized assignment, the identification of causal effects may require additional conditional exchangeability assumptions to handle loss to follow-up, non-adherence (for per-protocol effects), and competing events. Describe the corresponding choice of variables proposed for conditional exchangeability.

Item 7g (ii). Describe how the variables related to these assumptions were operationalized with the data.

The variables may include those that relate to baseline confounding, and those necessary to handle loss to follow-up, non-adherence or competing events. Include a description of how the variables were defined and ascertained from the observational data.

Data analysis plan

Item 7h (i). For each causal estimand, describe the data analysis procedures and any associated statistical modelling assumptions, including approaches for handling missing data.

Describe modifications to the data analysis methods of the target trial needed by the emulation using observational data. This may include modifications to adjust for confounding due to lack of randomization, to accommodate eligibility at multiple times (e.g., emulation of sequential trials[5,26]), and to handle treatment strategies that are not distinguishable at time zero (e.g., cloning[25,27]). All models used should be described.[5,25,27] Reporting the statistical software (name, version, any specific packages) used is useful for reproducing analyses.

Item 7h (ii). For each causal estimand, describe any additional analyses conducted to assess the sensitivity of the results to the choice of operationalizations, assumptions and analysis.

Report all additional analyses conducted to assess the sensitivity of the results to the choice of operationalization of the components of the target trial, identifying assumptions, and data analysis. Providing a rationale for the specific biases investigated can help readers understand how the potential threats to study validity have been addressed. Sensitivity analyses may include outcome or population controls,[28] and quantitative bias analysis.[29]

Results

Participant Selection

Item 8. Report numbers of individuals assessed for eligibility, eligible, and assigned to each treatment strategy. A flow diagram is strongly recommended.

Knowledge of the number of people assessed for eligibility and the number of individuals excluded (and with reasons provided) gives useful insights into the degree and type of selection. A flow diagram (e.g., as described in the CONSORT (CONsolidated Standards Of Reporting Trials)[30] guideline) helps visualize participant selection and classification into treatment strategies. When individuals contribute to multiple trials (e.g. sequential trials)[5] or treatment strategies (e.g. cloning),[25,27] provide the number of unique individuals and the total analyzed in the flow diagram. Terms such as 'person-trials' or 'clones' can be helpful to differentiate numbers analyzed from unique individuals.

Baseline data

Item 9. Describe the distribution of characteristics of individuals at baseline, by treatment strategy.

Describe the distribution of relevant characteristics of individuals (e.g., demographic, clinical) by treatment strategy at baseline. When appropriate, reporting baseline characteristics before and after adjustment for confounding (e.g., when using standardization, inverse probability weights or matching) can help readers assess the comparability of groups based on the measured characteristics. When cloning is used,[25,27] characteristics can be reported for all individuals combined at baseline (because characteristics will be identical between treatment strategies) and by treatment strategy at the first time during follow-up when the treatment strategies become distinguishable.

Follow-up

Item 10. Summarize length of follow-up and describe reasons for end of follow-up for each treatment strategy and causal contrast.

Describe the duration of follow-up for each treatment strategy and causal contrast. For analyses that include censoring, report the number of individuals who were censored for each reason (e.g., loss to follow up, non-adherence) by treatment strategy. It can be helpful to report the evolution of individuals at relevant times during the follow-up in the flow diagram (Item 8), including censoring events, competing events, and outcome events.

Missing data

Item 11. Describe the frequency of missing data in all variables, by treatment strategy when applicable.

Report the extent of missing data, if any, in all variables used to operationalize the target trial protocol (e.g., variables used to adjust for confounding, outcomes, and any other relevant variables).

Outcomes

Item 12. Describe the frequency or distribution of each outcome, by treatment strategy.

For time-to-event outcomes, report number of individuals with the outcome, and estimated absolute risks over time, with measures of precision. For other outcomes, report relevant measures such as proportions, median and interquartile range, mean and standard deviation.

Effect estimates

Item 13. Report the effect estimates for each causal contrast with corresponding measures of precision, including both absolute and relative measures of effect when applicable.

Estimates of relative and absolute effect measures need to be accompanied by measures of precision.

Additional analyses

Item 14. Report results of all analyses to assess the sensitivity of the estimates to choices in operationalization, assumptions and analysis.

Reporting and comparing results obtained from sensitivity and other additional analyses (outlined in Item 7h) helps readers assess the robustness of findings and appropriately interpret the study findings.

Discussion

Interpretation

Item 15. Provide an interpretation of the key findings.

The key findings with respect to the causal questions should be concisely summarized. Interpret the key effect estimates in the context of their precision, under the identifying assumptions (Item 7g) warranted for causal interpretation.

Limitations

Item 16. Discuss the limitations of the study considering differences between the target trial and its emulation and the plausibility of assumptions, including assumptions regarding baseline confounding due to lack of randomization.

Discuss difficulties that stem from the use of the available observational data to operationalize the target trial protocol components (i.e., eligibility criteria, treatment strategies, start of follow-up, or outcomes), including components that could not be well

mapped to the data and the reasons for the incomplete mapping (e.g., quality, validity or coverage of the data). Address the plausibility of assumptions, including no unmeasured baseline confounding due to lack of randomization, and incorporate considerations regarding the sensitivity analyses (Item 14).

Other Information

Items 17-21 describe additional information required across health and medical research: ethical approval (Item 17), study registration (Item 18), sharing of study data, analytic code and other materials (Item 19), funding sources (Item 20), and conflicts of interest (Item 21).

DISCUSSION

The TARGET guideline provides consensus-based recommendations on the minimum items that should be reported in observational studies that aim to estimate causal effects by explicitly emulating a target trial. This guideline is intended to provide authors with a tool to help them report essential information so that readers, peer reviewers, and editors can more easily evaluate the validity and usefulness of their work. The target trial framework[1] was used alongside the CONSORT[30] and STROBE (STrengthening the Reporting of OBservational studies in Epidemiology)[15] checklists as a point of departure to create specific reporting guidance for studies that explicitly emulate target trials.[17] Through this process, the guidance was informed by empirical evidence,[14] expert consensus, and consultation with a large group of individuals representing relevant stakeholders and end users. To improve accessibility, the TARGET checklist will be made publicly available online (*target-guideline.org*) and indexed in the EQUATOR Network website.

The application of the target trial framework[1] to analyses of observational data is rapidly expanding across study designs,[31] settings[32] and methods.[33] The scope of TARGET covers observational studies of interventions explicitly emulating a parallel group, individually randomized target trial, with adjustment for baseline confounders due to lack of randomized assignment. It is anticipated that as the target trial framework continues to be used and applied to different settings, the guidance will be updated and extensions developed to accommodate changes.

The purpose of TARGET is to improve the transparency, completeness and accuracy of reporting. *It should not be interpreted as an attempt to prescribe reporting of studies emulating a target trial in a rigid format restricting the choice of methods or the style of exposition*. The checklist items should be addressed in enough detail and clarity in an article (including supplementary material), but the order and format for presenting information will depend on author preferences and journal style. For example, the target trial specification and emulation could be concisely formatted reported in a table (templates available at target-guideline.org) but are not required to be. The TARGET guideline was not designed to be used as a tool to assess the risk of bias or quality of a target trial, however, improved reporting of necessary information can facilitate systematic reviewers applying various assessment tools (e.g., ROBINS-I to assess risk of bias)[7]. Also, although not the explicit intention, the TARGET guideline may help to improve the methods and conduct of observational analyses explicitly emulating a target trial by further serving as an educational tool and clarifying the issues that should be addressed.[34]

Limitations

The guideline attempts to support comprehensive and clear reporting of analyses of observational data that explicitly emulate a target trial, but does not describe all settings, methods and assumptions that may be required in this evolving field. The guideline focused on the most common applications of the target trial framework,[14] emulation of a parallel-group trial with adjustment for confounders, providing the minimum essential items to be reported for these studies. The TARGET guideline does not, for example, specifically intend to guide the reporting of target trial emulations that use instrumental variable estimation or other methods for confounder control which require additional information.

CONCLUSION

TARGET provides guidance for reporting analyses of observational data that aim to estimate causal effects by explicitly emulating a target trial.

Author contributions: Drs Cashin, McAuley and Mr Hansford had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Dr Cashin and Mr Hansford contributed equally.

Concept and design: Cashin, Hansford, Swanson, Jones, Lee, Hernán, McAuley.

Acquisition, analysis, or interpretation of data: All authors

Drafting of the manuscript: Cashin, Hansford, Swanson, Jones, Hernán, McAuley.

Critical review of the manuscript for important intellectual content: All authors

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MAH is an advisor to ProPublica and Adigens Health, a company of which he owns equity, and a member of ADIALab's Advisory Board. IJD is a consultant to Moderna on work related to target trial emulation. SS is participating in investigator-initiated grants to the Brigham and Women's Hospital from Boehringer Ingelheim, Takeda, and UCB unrelated to the topic of this study. He is advisor to and owns equity in Aetion Inc., a software manufacturer. He is an advisor to Temedica GmbH, a patient-oriented data generation company.

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Table 1. Glossary of Terms Commonly Used in Studies Emulating a Target Trial[a]

Term	Explanation
Causal contrast	The comparison of the outcome distributions under two different treatment strategies. Examples of causal contrasts are being assigned to one vs. another treatment strategy, irrespective of whether people actually receive the treatment assigned (the intention-to-treat effect), and the effect of fully adhering to one vs. another treatment strategy as specified by the protocol (the per-protocol effect).
Causal estimand	The causal effect that would be estimated to answer a causal question of interest. Key components of the causal estimand are the target population (eligibility criteria), the treatment strategies, the outcome, the timing of follow-up, and the causal contrast (see above).
Confounding	Confounding occurs when groups receiving different treatment strategies differ in their distribution of prognostic factors at time zero.[35] When there is confounding, differences in the outcome distribution between treatment groups may be explained by differences in prognostic factors rather than differences in treatment. A key concern for target trial emulation is whether some confounding bias remains after adjustment for measured confounders.
Design-related biases	Design-related biases refer to those that arise from decisions made by investigators' when designing their analyses of observational data,[1,5] rather than biases associated with the observational study design (e.g., confounding, measurement error). Common design-related biases include selection and misclassification which may produce periods of time in the analysis when an individual cannot develop an outcome of interest (immortal time). These biases are due to misalignment of the start of follow-up (time zero) with the time an individual becomes eligible and is classified into a treatment strategy; selection bias may arise

	when eligibility occurs after assignment to a treatment strategy (selection depends on the outcome) and misclassification bias may arise when assignment occurs after eligibility (classification depends on the outcome).[6,36]
Identifying assumptions	Informally, assumptions that link the causal estimand to the observed data. Some examples of identifying assumptions for the per-protocol effect are[37] 1) Within levels of the adjustment variables, groups receiving each treatment strategy at each time have the same counterfactual risk of the outcome (conditional exchangeability). 2) For every combination of the adjustment variables, there is a non-zero (i.e., positive) probability of receiving each treatment strategy at each time. 3) The treatment strategies are sufficiently well-defined.
Target trial framework	A methodological framework for causal inference from observational data which applies the design principles of randomized trials. This involves designing observational analyses to explicitly emulate a hypothetical pragmatic randomized trial that would answer the question at hand: the target trial. The framework has two components, specification of the target trial, and mapping that target trial to the data (emulation).

[a] Explanations adapted from Hernán et al. 2020[37] & 2025[1]

Table 2. TARGET Checklist of Recommended Items to Address in Reports of Studies Emulating a Target Trial[a]

Item no.		Checklist item		
Abstract				
1	a	Identify that the study attempts to emulate a target trial using observational data. State the study objectives and briefly summarize the specified target trial.		
	b	Report the data sources used for emulation.		
	c	Summarize key assumptions, statistical methods, findings and conclusions.		
Introduction				
2	Background	Describe the scientific background of the study and the gap in knowledge.		
3	Causal question	Summarize the causal question.		
4	Rationale	Describe the rationale for emulating a target trial with the available data. Cite randomized trials informing the design of the target trial if applicable.		
Methods				
5	Data sources	Cite the data sources contributing to the analyses and for each one describe the following: original purpose, type, the geographic locations, setting and time-period. If relevant, describe how the data were linked or pooled.		
6	**Target trial specification**	Specify the components of the target trial protocol that would answer the causal question.	7	**Target trial emulation** Describe how the components of the target trial protocol were emulated with the observational data, including how all variables were measured or ascertained.
	Eligibility criteria			**Eligibility criteria**
	a	Describe the eligibility criteria.	a	Describe how the eligibility criteria were operationalized with the data.
	Treatment strategies			**Treatment strategies**
	b	Describe the treatment strategies that would be compared.	b	Describe how the treatment strategies were operationalized with the data.
	Assignment procedures			**Assignment procedures**
	c	Report that eligible individuals would be randomly assigned to treatment strategies and may be aware of their treatment allocation.	c	Describe how assignment to treatment strategies was operationalized with the data.
	Follow-up			**Follow-up**
	d	Clarify that follow-up would start at time of assignment to the treatment strategies. Specify when follow-up would end.	d	Clarify that follow-up starts at the time individuals were assigned to the treatment strategies. Describe how the end of follow-up was operationalized with the data.
	Outcomes			**Outcomes**
	e	Describe the outcomes.	e	Describe how the outcomes were operationalized with the data.
	Causal contrasts			**Causal contrasts**

	f	Describe the causal contrasts of interest, including effect measures.	f	Describe how the causal contrasts were operationalized with the data, including effect measures.
	Identifying assumptions		**Identifying assumptions**	
	g	Describe assumptions that would be made to identify each causal estimand. Describe the variables, if any, related to these assumptions.	g.i	For each causal estimand, describe assumptions made to identify it, including assumptions regarding baseline confounding due to lack of randomization.
			g.ii	Describe how the variables related to these assumptions were operationalized with the data
	Data analysis plan		**Data analysis plan**	
	h	For each causal estimand, describe the data analysis procedures and any associated statistical modelling assumptions, including approaches for handling missing data.	h.i	For each causal estimand, describe the data analysis procedures and any associated statistical modelling assumptions, including approaches for handling missing data.
			h.ii	For each causal estimand, describe any additional analyses conducted to assess the sensitivity of the results to the choice of operationalizations, assumptions and analysis.
Results				
8	Participant selection	Report numbers of individuals assessed for eligibility, eligible, and assigned to each treatment strategy. A flow diagram is strongly recommended.		
9	Baseline data	Describe the distribution of characteristics of individuals at baseline, by treatment strategy.		
10	Follow-up	Summarize length of follow-up and describe reasons for end of follow-up for each treatment strategy and causal contrast.		
11	Missing data	Describe the frequency of missing data in all variables, by treatment strategy when applicable.		
12	Outcomes	Describe the frequency or distribution of each outcome, by treatment strategy.		
13	Effect estimates	Report the effect estimates for each causal contrast with corresponding measures of precision, including both absolute and relative measures of effect, when applicable.		
14	Additional analyses	Report results of all analyses to assess the sensitivity of the estimates to choices in operationalizations, assumptions and analysis.		
Discussion				
15	Interpretation	Provide an interpretation of the key findings.		
16	Limitations	Discuss the limitations of the study considering differences between the target trial and its emulation and the plausibility of assumptions, including assumptions regarding baseline confounding due to lack of randomization.		
Other information				
17	Ethics	Provide the institutional research board or ethics committee that approved the study and approval numbers, if relevant.		
18	Registration	State whether, when and where the study protocol was registered.		
19	Sharing of study materials	Provide information on whether data, analytic code and/or other materials are accessible, and where and how they can be accessed.		
20	Funding sources	Provide the sources of funding and detail the role of the funders in the design, conduct and reporting of the study.		

21	Conflicts of interest	State any conflicts of interest and financial disclosures for all authors.

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