Guidance Document for Claims based on Non-Experimental (Observational) Studies

January 2013

Non-Experimental Claims Checklist

Item No	Checklist Item (clients can use this tool to help make decisions regarding use of observational study data in advertising claims)	√
What Must Appear in the Advertisement or Promotional System		
2	Study Design	
13	Outcome Data	
14	Main Results	
16	Funding	
What Must Appear in the Published Study for Claim Validation		
1	Objectives	
2	Study Design	
3	Settings	
4	Participants	
5	Variables	
6	Data sources/ measurement	
7	Bias	
8	Study size	
9	Quantitative variables	
10	Statistical Methods	
11	Participants	
12	Descriptive data	
13	Outcome Data	
14	Main Results	
15	Other Analyses	
16	Funding	

1. Key Benefits:

Claims based on observational evidence can provide additional information to aid HCPs in making appropriate therapeutic choices that may not be captured in claims based solely on experimental evidence, such as randomized trials. Observational research can reliably answer clinically relevant questions in a complimentary way. It can also provide important information for clinical decisions in an easier fashion than experimental research. Some important information for clinical decision-making cannot be reliably answered with experimental studies.

2. Key Pitfalls:

Claims of comparative effectiveness from observational studies rely on more elaborate techniques for measuring and analyzing data. Findings from observational research may be largely influenced by the scientific judgments of the researchers analyzing the data. There is no real consensus on what statistical adjustment techniques are most reliable. Although there is no compelling evidence that observational studies are consistently less reliable than those of experimental studies, the reliability of findings from a single observational study is much more suspect than that of a similarly sized randomized trial and requires sufficient details regarding the analytic approach to be properly scrutinized.

Managing pitfalls:

As a general principle, the degree of evidence must support the degree of claim. In general observational studies may be appropriate for claims relating to adherence, persistence, preference, and as additional support of efficacy/safety claims established by evidence based on randomized controlled trials. In general, the use of observational studies alone is <u>not</u> sufficient to support claims of efficacy and safety.

A consensus checklist has been developed for **S**trengthening **T**he **R**eporting of **OB**servational studies in **E**pidemiology (STROBE) that are intended to appear in biomedical journals. Most of the elements of the checklist are also relevant to allow scrutiny of claims based on observational data submitted to the PAAB.

The checklist should be used to guide industry and to assist the PAAB staff in determining whether findings from observational studies may appear within advertising/promotional systems (APS). The checklist relates to factors specific to the reporting of observational studies that attempt to make comparisons (i.e. causal claims). Before using the checklist, applicants should be sure the claim is consistent with the Health Canada approved Terms of Market Authorization (TMA). Observational studies cannot be used to support observations that contradict anything in the TMA (with respect to magnitude, direction, or duration of clinical effect).

Observational Claims Checklist (Adapted from the STROBE Checklist)

	Item No	Recommendation
Objectives	1	State specific objectives, including any prespecified hypotheses
Methods		
Study design	2	Present key elements of study design early in the paper
Setting	3	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	4	(a) Cohort study—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up Case-control study—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls Cross-sectional study—Give the eligibility criteria, and the sources and methods of selection of participants
		(b) Cohort study—For matched studies, give matching criteria and number of exposed and unexposed Case-control study—For matched studies, give matching criteria and the number of controls per case
Variables	5	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	6*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	7	Describe any efforts to address potential sources of bias
Study size	8	Explain how the study size was arrived at
Quantitative variables	9	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	10	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) Cohort study—If applicable, explain how loss to follow-up was

		addressed Case-control study—If applicable, explain how matching of cases and controls was addressed Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy
		(*e*) Describe any sensitivity analyses
Results		
Participants	11*	(a) Report numbers of individuals at each stage of study (i.e. numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analyzed)
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	12*	(a) Give characteristics of study participants (i.e. demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
		(c) Cohort study—Summarize follow-up time (i.e. average and total amount)
Outcome data	13*	Cohort study—Report numbers of outcome events or summary measures over time
		Case-control *study*—Report numbers in each exposure category, or summary measures of exposure
		Cross-sectional study—Report numbers of outcome events or summary measures
Main results	14	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (i.e. 95% confidence interval). Make clear which confounders were adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	15	Report other analyses done (i.e. analyses of subgroups and interactions, and sensitivity analyses)

Other information		
Funding	16	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Principles, Rationale and Application of Checklist Items

An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting.

This checklist is best used in conjunction with the article, freely available at

http://www.plosmedicine.org/article/info:doi/10.1371/journal.pmed.0040297

Information on the STROBE Initiative is available at www.strobe-statement.org .