PHARMACOEPIDEMIOLOGY AND DRUG SAFETY 2016; **25**: 2–10
Published online 5 November 2015 in Wiley Online Library (wileyonlinelibrary.com) **DOI**: 10.1002/pds.3891

COMMENTARY

Guidelines for good pharmacoepidemiology practice (GPP)

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INTRODUCTION

Pharmacoepidemiologic studies provide valuable information about the health effects of healthcare products. The ISPE Guidelines for Good Pharmacoepidemiology Practice (GPP) are intended to assist investigators with issues pertaining to the planning, conduct, and interpretation of pharmacoepidemiologic research. This paper represents the fourth version and supersedes previous versions. While the overall structure and nature of the GPP has been preserved in the current revision, new sections have been added, and the text has been updated to reflect current practice.

Pharmacoepidemiology is being used increasingly to evaluate health care systems, interventions, and health-related behaviors. Pharmacoepidemiology is the scientific backbone of therapeutic risk management—the process of assessing a product's benefits and risks, and developing, implementing, and evaluating strategies to enhance the overall balance of such benefits and risks. Pharmacoepidemiology is also the scientific backbone of comparative effectiveness research (CER). These guidelines are intended to address these activities and other pharmacoepidemiologic studies.

The GPP addresses the following areas:

- protocol development,
- responsibilities, personnel, facilities, resource commitment, and contractors,
- study conduct,
- communication,
- adverse event reporting, and
- archiving

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Goals

The GPP propose essential practices and procedures that should be considered to help ensure the quality and integrity of pharmacoepidemiologic research and to provide adequate documentation of research methods and results. The GPP do not prescribe specific research methods nor will adherence to guidelines guarantee valid research.

The GPP have the following specific goals:

(1) to assist researchers in adhering to good pharmacoepidemiologic research principles, including the use of pharmacoepidemiologic studies for risk management activities and CER;
(2) to promote sound pharmacoepidemiologic research by encouraging rigorous data collection, analysis, and reporting;
(3) to provide a framework for conducting and evaluating pharmacoepidemiologic studies;
(4) to facilitate the appropriate utilization of technical resources by promoting careful study design and planning of study conduct; and
(5) to facilitate transparency and ethical integrity in research conduct.

Scope and application

The GPP are intended to apply broadly to all types of pharmacoepidemiologic research, including feasibility assessments, validation studies, descriptive studies, and etiologic investigations, and all of their related activities from design through publication.

Therapeutic risk management activities provide a formal framework in which medicine, pharmacoepidemiology, and public health are integrated in the development and life-cycle management of healthcare products. Pharmacoepidemiology is the core science of risk assessment and the evaluation of the effectiveness of risk minimization interventions. Therefore, the GPP also support risk management activities.

In a similar fashion, pharmacoepidemiology is the core discipline of CER. Such activities are based on problems from clinical medicine, by using rigorous methods to compare the outcomes of two or more therapeutic alternatives. Thereby, comparative effectiveness activities are defined by their research questions rather than by their methods.

PROTOCOL DEVELOPMENT

Each study should have a written protocol. A protocol should be drafted as one of the first steps in any research project, and the protocol should be amended or updated as needed throughout the course of the study. Some jurisdictions, such as the European Union, through EMA and ENCePP, provide guidance on the content and format of the protocol for post-authorisation safety or effectiveness studies. For studies where no such guidance is applicable, the protocol should include the following elements:

(A) a descriptive title (e.g., indicating study design and population) and version identifier (e.g., date); if applicable, the registration number (clintrials.gov or ENCePP register) should be indicated.
(B) the names, titles, degrees, addresses, and affiliations of all responsible parties, including the principal investigator, co-investigators, and a list of all collaborating primary institutions and other relevant study sites;
(C) the name and address of each sponsor;
(D) a synopsis of the protocol;
(E) the proposed study tasks, milestones, and timeline;
(F) a statement of research objectives, specific aims, and rationale;
Research objectives describe the knowledge or information to be gained from the study. Specific aims list key exposures and outcomes of interest, and any hypotheses to be evaluated. The protocol should distinguish between a limited number of a priori research hypotheses and hypotheses that are generated based on knowledge of the source data. The rationale explains how achievement of the specific aims will further the research objectives. The research question
relevant animal and human experiments, clinical studies, vital statistics, and previous epidemiologic studies. The literature review should also cite the findings of similar studies, and the expected contribution of the current study.
(H) a description of the research methods, including the following:

(1) the overall research design and reasons for choosing the proposed study design;
Research designs include, for example, case–control, cohort, cross-sectional, nested case–control, self-controlled, randomized trials or hybrid designs. Any feasibility or pilot work that informed the choice of design should be described here.
(2) the population or sample to be studied;
The population is defined in terms of persons, place, time period, and selection criteria. The rationale for the inclusion and exclusion criteria and their impact on the number of subjects available for analysis should be described, if known. If any sampling from a defined population is undertaken, description of the population and details of sampling methods should be provided. Some justification should be given to support that the necessary study size is actually attainable from the given data source or design. This could be data from informal queries or pilot studies. Considerations of generalizability from the study population to those actually receiving the drug may be voiced here.
(3) the strategies and data sources for determining exposures, health outcomes, and all other variables relevant to the study objectives, such as potential confounding variables and effect measure modifiers;
Data sources might include, for example, questionnaires, hospital discharge files, abstracts of primary clinical records, clinical databases, electronic medical records, ad hoc data collection, administrative records such as eligibility files, prescription drug