Background on ISPOR Prospective Observational Clinical Studies Good Research Practices Task Force continued...

To enhance the credibility and reputation of prospective observational clinical studies for comparative effectiveness, researchers from academia, industry, and research organizations must be exemplary in execution and transparent in communication when performing and reporting scientific investigations. They should adhere to the highest standards in conducting meaningful research. Individual researchers face a wide range of choices in how to do such studies. Thus, although guidelines and recommendations for observational studies exist to one degree or another, this Task Force is specifically addressing prospective observational clinical studies. Some of the analytic challenges inherent in prospective observational studies could be addressed by employing a randomized naturalistic effectiveness study design – what has been called a "pragmatic" or "practical" study or large simple trial. This Task Force will also consider the extent to which such a study may or may not address various analytic issues including confounding and bias.

The following are the topics to be addressed by the members of this Task Force:

1. When is the design and conduct of an observational study adequate to provide probabilistic inference about causality? More specifically, when does a study provide information robust enough to inform policy decisions regarding comparative effectiveness?

2. When is the design and conduct of an observational study "fit for purpose" to answer questions of comparative effectiveness?

3. Are there different issues involved when one is examining the comparative effectiveness of biologics, drugs, devices, procedures, or programs of care?

These questions will be answered in the context of the following:

- **Noninterventional nature of prospective observational clinical studies.** Observational research is characterized by non-intervention in assignment of treatment. This contrasts with pragmatic studies where treatment is randomly assigned. Many factors may influence the assignment of an intervention including evidence-based guidelines, provider formularies, health practitioner training, health practitioner recommendations, patient preferences and out-of-pocket costs. The contribution of these factors to patient outcomes and comparative effectiveness analyses needs to be addressed by a robust analytic plan. However, it is integral to observational studies that the assignment of treatment not be dictated by the protocol. While a protocol may require additional data collection beyond what would be routinely performed, it does not interfere with the normal decision-making process involved in therapeutic choice or subsequent clinical management. Protocols may limit enrollment to defined patient groups to meet study objectives according to its analysis plan. Given the breadth with which the term "observational study" is commonly applied (even with the qualifier of "prospective"), a clear taxonomy of study types and their distinguishing features (including strengths and limitations with regard to threats to validity) would in itself be a useful reference.

- **Safety reporting.** For phase IV studies, investigators need to consider specific requirements to collect safety information. Following the guidelines for randomized clinical studies may not always be necessary or appropriate, and may confound the real-world behavior of practitioners and patients. Eliciting adverse events may itself be considered an intervention. Should safety issues be allowed to emerge in a naturalistic fashion and dealt with as a real-world circumstance? [8]

- **Reporting and publication.** Publication bias is a major factor to consider in observational research; hence, investigators may need to disclose analysis plans early and publish protocols creating visibility and transparency. The prior retrospective database taskforce made recommendations regarding reporting and publication. These will be revisited and recommendations regarding how they might apply or be adapted to prospective observational studies.
observational clinical studies will be made.

- **Appropriate remuneration for researchers and for subjects/participants.** As for any clinical study, investigators should be paid only for study-specific time and expenses incurred to conduct the research. What are, if any, appropriate incentives for patient participation in a study? Are there reasonable levels of remuneration for participants that do not skew their assessment of risk in deciding to participate? Also "types" of remuneration can be important (cash vs. gift card vs. something "material" vs. you name it).

**REFERENCES**

9. European Federation of Pharmaceutical Industries and Associations. EFPIA code on the promotion of prescription-only medicines to, and interactions with healthcare professionals 2007