Fourth meeting of the CIOMS Working Group XV:

Harnessing the Potential of Pharmacoepidemiology for Public Health (PEPH)

Virtual, 21 October 2024

Participants

CIOMS: Hervé le Louet (HL) (President); Lembit Rägo (LR) (Secretary-General).

Academia: Bernard Bégaud (BB) (University of Bordeaux, France); Kate Gillespie (Institute for Health Metrics and Evaluation (IHME) at the University of Washington).

Industry: Ana Sofia Afonso (AA) (Eli Lilly, The Netherlands); Selin Cooper (AbbVie, UK); Alicia Gayle (AG) (Chiesi, UK); Karin de Haart (IQVIA, The Netherlands); Véronique Kugener (VK) (Takeda, USA); Marie-Laure Kurzinger (MLK) (Sanofi, France); Patricia Saddier (PS) (MSD, USA); Montse Soriano-Gabarro (MSG) (Bayer, Germany); Muhamad Younus (Pfizer, USA).

Intergovernmental organization: Noha Iessa (WHO, Switzerland).

Regulatory: Takashi Ando (Pharmaceuticals and Medical Devices Agency, Japan); Craig Allen (CA)(MHRA, UK); Hui-Lee Wong (HW) (Food and Drug Administration, USA).

Hervé le Louet (HL) opened the meeting. The meeting agenda was confirmed, and HL and Bernard Bégaud (BB) agreed to co-chair.

HL requested the working group (WG) participants to provide some feedback on their activities since the Paris (Gentilly) meeting in May 2024.

Patricia Sadier (PS) reported on her efforts to secure a site that the WG could use, rather than Google Drive1, to share information and work collaboratively (and securely) on the planned report. Unfortunately, Merck decommissioned the site that it had been using for external collaboration and has not yet installed the new site. It is likely that the new site will use Microsoft Teams. The domain of each of the participants will have to be vetted. Hui-Lee Wong (HW) mentioned that FDA has a SharePoint that can be used for external collaboration. But for the moment, PS will continue with her efforts to ensure that the new site hosted by Merck can be used by all WG members.

Alicia Gayle (AG) reported on the annual meeting of the International Society for Pharmacoepidemiology (ISPE), held in Berlin in August. It was attended by several WG members who took the opportunity to meet up. **The next annual ISPE meeting (in 2025) will be held in Washington DC. AG suggested that a formal WG meeting be organized during this event to facilitate some further work, in person, on the report.**

In addition, Montse Soriano-Gabarro (MSG) suggested that the Washington DC meeting be used to present the topic of this WG and to stimulate interest in it among the

[1]Available at: https://docs.google.com/document/d/1E6LoENI5k3i2QtmA9EuPUrQsPtpDAs3eQOE329Cs3EM/edit?usp=sharing

pharmacoepidemiology (PE) community. The deadline for submission of abstracts to ISPE for the meeting is mid-February 2025.

HL commented that CIOMS already has an ISPE delegate and that since the WG remains in an early phase, it cannot communicate in detail about its progress. **Moreover, anything to be communicated about the work must be agreed upon by the WG, and the ISPE delegate kept informed. MSG responded that a workshop or symposium could be proposed: not to present the WG's work but rather to learn about the current priorities and efforts of ISPE's PE experts.** Ana-Sofia Afonso (AA) and Véronique Kugener (VK) both concurred that ISPE would provide a good opportunity for exchanging ideas. VK commented that Sub-group 2 has made reference to some ISPE guidelines on PE studies, specifically with respect to methodologies.

BB referred to the four groups that were created during the Paris meeting to focus on key issues:

- **How to perform (or use of) PE in different settings (led by VK).**
- **When not to conduct a PE study (led by BB).**
- **The use of PE in crises (led by AA).**
- **Interpreting the results of existing PE study data (led by PS).**

The topics were selected because they are topics of repeated discussion. BB requested an update from each group, presented below.

How to perform (or use of) PE in different settings

(Group members: Monique Falconer; Karin de Haart; Noha Iessa; VK; Miguel Ángel Maciá; Innocent Ngwa; HW; Muhamad Younus.)

VK reported that the group had met five times online and that all of its output has been incorporated in the Google Drive document. Within this document, the group has started cross-referencing (in yellow) its work with the work of the other three groups.

The group created three sub-sections:

- **Different scenarios and settings that justify application of PE as a tool in order to enhance public health (PH).** Covering available prevention treatment, comparative interventions, access to medicines, info-medics, and optimization of implementation of PE interventions.
- **Different health care systems.** To acknowledge that PE is highly dependent on health care systems. The concept of reliance was introduced since not all countries have the same level of resources and not all health systems are at the same level of maturity. This would be an important topic of discussion for a bigger group.
- **Benefit–risk strategy.** From a PH perspective, little guidance is available on this topic, which the group considers is not sufficiently visible in the proposed report framework. This would also be an important topic of discussion for a bigger group.

The group is aware that another CIOMS WG is dealing with benefit–risk and would like to cross-reference its work. More generally, guidance is needed on how this WG can refer to the work of other CIOMS WGs.

LR responded that the benefit–risk report of WG XII is mature enough to be released, but that this will probably not happen until the first quarter of next year. LR will ask WG XII if it would be willing to share its report ahead of publication.

When not to conduct a PE study

(Group members: BB, Marie-Laure Kurzinger; Yola Moride.)

BB stressed that points from this group probably need to be discussed in a plenary session since they are likely to generate some disagreement among WG members. He will write a statement paper for this group, to share its discussion and provide some examples of misuse of PE and where it would have been better not to have conducted a PE study. The group has collected many examples of when announcing the start of a PE study, or the results of a PE study, would risk complicating a PH situation and any associated decision-making. The paper will be shared on Google Drive so that other WG members can comment on it.

BB further commented that this topic will probably be the most difficult for external reviewers to consider. PE studies are conducted for many reasons, including in order to secure funding. So for some reviewers, recommendations when not to conduct a PE study, or an indication that PE studies could be dangerous, may be unwelcome. Therefore, it is very important that the WG reach agreement on how this topic is to be presented in the report. A virtual meeting could be organized once the statement paper becomes available.

HL responded that the trend is to apply PE everywhere. So **it would be helpful to draft "inclusion criteria" and "exclusion criteria".** A PE study can actually be deleterious for PH. He supported BB's decision to produce a statement paper for discussion by the WG.

The use of PE in crises

(Group members: AA; Alex Asiimwe; Karin de Haart; Jennifer Lund; Doris Oberle; MSG; Sabine Straus.)

AA reported that this group had held five virtual meetings and had distributed its work among smaller sub-groups:

- **Introduction,** including a definition of PH and some examples of how PE has been used during PE crises.
- An overview on **how to prepare and respond to a PE crisis.** This includes a table outlining the stages of a public health crisis, and PE study objectives and designs that are relevant to each stage.
- Examples of **uses of PE during PH crises** were drafted and include references.

What is needed now is critical review by the whole WG.

VK commented that her group appreciates the aforementioned table and will replicate its structure for presentation of some elements of its own discussions.

Interpreting the results of existing PE study data

(Group members: Craig Allen (CA); Selin Cooper; AG; Kate Gillespie; PS.)

PS reported that this group worked mainly off-line.

CA gave an overview of this group's work. It has been developing a work flow that PH practitioners follow when they are evaluating existing evidence. The first step is to clarify the overall PH issue and the key questions that should be developed, and for which engagement with relevant stakeholders such as patients, clinicians and patient advocates should be sought. Ideally, when reviewing the existing evidence, a small team of epidemiologists, statisticians, clinicians and health economists should be established. Librarian support should be considered since this can be very useful when developing search strategies for identifying relevant literature. Tools for critical appraisal and evaluation of existing data are available: for example, the GRADE and ROBINS-I and E tools. A critical appraisal tool also exists for gray literature. However, further expansion on these tools – including some description – is needed.

The group also considered situations for which data is lacking, or where there are gaps in knowledge, and whether the report should include recommendations about commissioning future research in order to overcome these.

A communications strategy may also be required to assist with communicating study results. In which case, communications specialists to draft public assessment reports or press releases should be recruited. Data visualization tools can be helpful in communicating key messages to the public.

Preparation of draft WG report

WG members should review and refine their sections ahead of the next in-person meeting (to be held 4 and 5 December 2024, in Geneva).

Lembit Rägo (LR) commented that after the Geneva meeting, a more mature draft of the report can be created which incorporates not only the outputs of the four small groups, but also those of Sub-groups 1 and 2.

BB requested that each of the four groups incorporate practical examples, including historical examples, in their drafts, to make it easier for readers to understand the issues under discussion and to ensure that the report is useful for PH and related decision-making, and not overly theoretical.

LR suggested that any lengthy examples could be included in an appendix.

Next steps

- BB to finalize statement paper of the *When not to conduct a study* group and upload it available on Google Drive (or the Merck (Teams) platform if it becomes available).
- WG members to refine the draft Google Drive document – including by adding examples – ahead of the next in-person meeting on 4 and 5 December, in Geneva.
- Not reviewed at this meeting but included on next steps of Paris meeting: WG members to review other relevant guidance that is being drafted by other organizations, such as ICH, to identify not only overlap but also gaps that this report could fill.