Methodological Gaps in the Assessment of the Utility and Burden of Risk Minimisation Interventions

A. Bergamasco1, M. Salib2,3, A. Yousif2,4, N. Thurin2,4, Y. Moride1,2,3

1. YOLARX Consultants, Paris, France; 2. Faculty of Pharmacy, University of Montreal, Montreal, Canada; 3. YOLARX Consultants Inc., Montreal, Canada; 4. Université de Bordeaux, Bordeaux, France

BACKGROUND

• Risk minimisation interventions (RMIs) aim at optimizing the benefits-risks of medicines with important identified safety concerns.
• In some situations, stringent RMIs (e.g., restricted distribution programs or mandatory prescription certification) are required. However, these measures could be costly, time-consuming, and/or challenging to implement in the real-life clinical practice setting.
• Although regulatory authorities recommend an evaluation of the burden associated with such measures, there are currently no methodological guidance available.

OBJECTIVES

• To identify methodologies used to evaluate the utility and burden associated with RMIs.
• To define the methodological challenges and gaps regarding these evaluations.

METHODS

A non-systematic literature review was conducted using three complementary data sources:

1. Electronic Bibliographical Databases (EMBASE, Medline)
2. Web Search Engines (Google, Google Scholar)
3. Regulatory Agencies Websites (FDA, EMA, ...)

RESULTS

Literature review

• A total of 362 publications on usefulness and/or burden of RMIs were identified through electronic bibliographical databases.
• Snowballing and pragmatic searches yielded 10 additional relevant publications.
• After abstract screening, 17 articles were retained for in-depth review. However, only 10 publications mentioned the methods used to evaluate the burden associated with RMIs and were therefore included in the study.

Figure 1: Quorum Chart for Literature Search

Assessment Methodologies

• A variety of methods are used to assess the effectiveness of RMIs. However, few publications considered the burden associated with these interventions.
• Among methodologies used to evaluate the burden of RMIs, surveys and focus groups represented the most frequently cited approaches (n=8, 80%).
• However, mixed-method assessments considering the multi-factorial aspects of RMIs appeared to be of growing usage over the recent years. Indeed, these methods allow both a qualitative and quantitative assessment of outcomes of interest for various stakeholders such as the resources (time, costs, personnel, ...) needed to implement RMIs or the impact of such measures on the patient’s quality of life.
• The three major methodologies retrieved in the literature, for the assessment of the burden of RMIs are presented thereafter:

1. Cross-sectional surveys
   • Healthcare professionals (HCPs) are most frequently targeted.
   • Gather participants’ opinions on specific aspects of the RMIs.
   • Allow the identification of potential barriers and/or challenges related to the implementation of RMIs in the real-life clinical practice setting (i.e. additional time, cost or staff required).
   
   Main limitation:
   – Low response rates leading to small sample sizes and problems with representativity.

2. Focus Groups
   • Allow participants to share opinions.
   • Provide a better understanding of the perceived burden of RMIs according to different perspectives compared to surveys.
   • Provide suggestions and recommendations regarding the optimization of RMIs considering the expectations and needs of the different stakeholders interviewed.
   
   Main limitations:
   – Risk of group effect (participants’ opinions influenced by others).
   – Time-consuming and costly.

3. Mixed-Method Approaches
   • Combination of research methodologies providing both a qualitative and a quantitative assessments of the burden associated with RMIs.
   • Usually collect HCPs opinions through surveys or focus groups and document several aspects of the burden such as the costs or time required to comply with specific requirements of RMIs.
   • Support the development of targeted strategies aiming to improve the implementation of RMIs and enhance their outcomes.
   
   Main limitations:
   – Time- and resource- consuming

Methodological Challenges and Gaps

• Currently, there is no gold standard or guidance regarding the methodologies to be employed for the assessment of the burden associated with RMIs.
• A proper evaluation should consider several aspects of interventions:
  - Perceptions of HCPs and patients regarding RMIs
  - Challenges related to the implementation of RMIs in the real life clinical practice setting (i.e. additional time, personnel or cost)
  - Economic impact of such measures
• Regular re-assessments should be considered to evaluate the impact of potential adjustments or modifications of RMIs.
• Variety of interventions and lack of homogenization in RMIs explain the actual need for a case-by-case analysis aiming to select appropriate metrics and methodologies to evaluate the burden associated with specific RMIs.
• Future opportunities can relate on the standardization of RMIs and the use of new technologies such as online surveys to optimize response rates.
• In addition, according to results from a FDA public meeting, observational time-motion studies or, computer-simulated modeling exercises should also be considered as alternate methods to evaluate the burden associated with RMIs even if these have not yet been implemented in practice.

CONCLUSION

Several methodological gaps have been identified in the methods used to evaluate the burden associated with RMIs. Development of guidance regarding this aspect of RMIs is currently under consideration by several health authorities and should consider innovative approaches such as online survey and modeling strategies.