SHORT COMMUNICATION

How to effectively analyze scientific evidence in clinical practice? Rationale behind and design of an observational analytical model

Mariusz Gąsior[1], Piotr Desperak[1], Daniel Cieśla[2], Jacek Niedziela[1], Łukasz Pyka[1], Michał Skrzypek[2], Michał Zembala[3], Wojciech Wojakowski[4]

1 3rd Department of Cardiology, Silesian Center for Heart Diseases, Faculty of Medicine in Zabrze, Medical University of Silesia, Zabrze, Poland
2 Department of Science, Training and New Medical Technologies, Silesian Center for Heart Diseases, Zabrze, Poland
3 Department of Cardiac Surgery and Transplantology, Silesian Center for Heart Diseases, Faculty of Medicine in Zabrze, Medical University of Silesia, Zabrze, Poland
4 Department of Cardiology and Structural Heart Diseases, 3rd Division of Cardiology, Medical University of Silesia, Katowice, Poland

Introduction Scientific societies stress the need for obtaining evidence from observational studies reflecting daily clinical practice.[1] Therefore, it seems important to search for observational analytical models based on dedicated methods and tools that would allow a combination of experimental (randomized controlled trials [RCTs]) and observational (databases) findings. In this report, we propose a model that uses large registries of healthcare system data to investigate the potential impact of different RCT interventions on the outcomes of patients in everyday clinical practice.

Methods **Characteristics of databases** To meet the study objective, a large clinical database should be available that contains detailed information on clinical characteristics, therapeutic procedures, pharmacologic therapy, and the incidence of adverse cardiovascular events in a long-term follow-up.

In the planned real-world evaluation of RCTs, data from the following databases will be used: SILCARD (Silesian Cardiovascular Database),[2] TERCET (Therapy in Tertiary Cardiological Center),[3] PRESAGE (Prospective Registry of Stable Angina Management and Treatment),[4] COMMIT-HF (Contemporary Modalities In Treatment of Heart Failure),[5] Zabrze-ACS Registry,[6] Ochojec Angioplasty Registry, and Zabrze Cardiac Surgery Registry.

The study was approved by institutional review boards and complies with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. Owing to the retrospective design of the planned studies, no additional patient consent is required.

Statistical analysis The statistical tests will be selected individually for each analysis to compare the population and long-term outcomes from a given RCT to the population from the registries.

Results and discussion Below we present a practical systematic approach based on an analytical model taking into consideration the setting of RCT and daily clinical practice. The analytical model presents the principles underlying an attempt to translate evidence from an RCT of a new drug or procedure (RCT-X) to the real-world setting of patients with a given disease. The main objective of the analytical model is to determine the target population and assess the potential impact of a new drug or procedure on improving the patient's prognosis. Additionally, in selected subgroups, the model will assess whether patients treated by different drugs or methods in daily clinical practice derive similar benefits to those shown by RCTs.

The design of the analytical model is presented in FIGURE 1. The necessary methodological conditions and subsequent stages of the model are listed below:

1 Study patients should be enrolled based on strict inclusion and exclusion criteria for the RCT-X.

Correspondence to:
Prof. Mariusz Gąsior, MD, PhD, 3rd Department of Cardiology, Silesian Center for Heart Diseases, Faculty of Medicine in Zabrze, Medical University of Silesia, ul. Skłodowskiej-Curie 9, 41-800 Zabrze, Poland, phone: +48 32 373 38 60, email: kardiologiazabrze@sum.edu.pl
Received: December 12, 2019.
Revision accepted: March 27, 2020.
Published online: March 31, 2020.
Kardiol Pol. 2020; 78 (6): 577-580
doi:10.33963/KP.15268

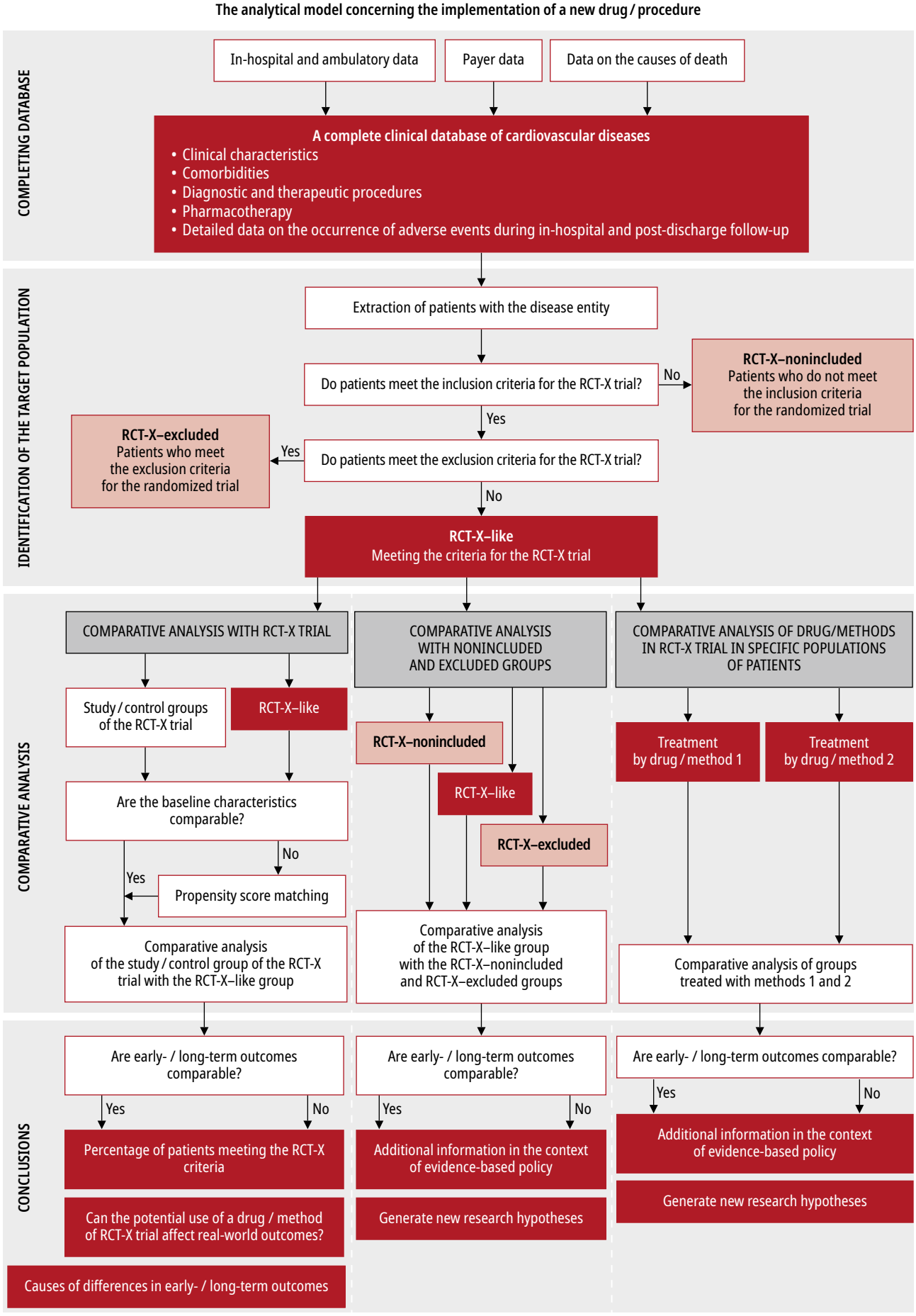

FIGURE 1 Design of the analytical model

Abbreviations: RCT-X, randomized clinical trial testing a given drug or procedure

2 Furthermore, the percentage ratio of selected patients to the initial study group should be determined. These patients will constitute the potential population in which a new drug or procedure might be applied.

3 Baseline characteristics, management, and treatment of the study group should be compared with those of the control group in the RCT-X. The results will show whether the selected population is clinically similar to the population of the RCT-X. This condition has to be fulfilled at this stage in order to draw proper conclusions from further analysis.

4 In the case of imbalance in baseline characteristics, a propensity score–matching analysis should be performed to balance analyzed groups (a sufficiently large study group of patients is required).

5 Subsequently, the frequency of adverse events during follow-up (primary and secondary endpoints of the RTC-X) should be determined and compared with that of the control group of the RCT-X. This analysis will show whether the study group has similar, better, or worse prognosis. Based on the obtained results, it will be possible to determine whether the potential use of a given drug or procedure tested in the RCT-X affects the treatment outcomes of the study population.

6 If the results are different, we should always search for the possible reasons (regardless of the direction of the difference). Considering that the baseline characteristics of the groups are similar (or similar when balanced), this problem may be due to the quality of treatment, healthcare after hospital discharge, patient compliance, and others. Identifying the reasons for these differences may be a key to legitimizing the introduction of a new drug or procedure into the healthcare system.

7 The next stage of the analytical model should be a comparative analysis of patients who do not meet the inclusion criteria and who meet the exclusion criteria in relation to the study group. This is valuable information that complements the analysis and can provide additional value for evidence-based policy.

8 The summary should contain the analysis of evidence obtained from a large clinical database with economic assessment as well as its use for evidence-based policy purposes with the participation of leading experts.

The conclusions should include:

1 precise determination of the percentage of patients in the study population who meet the inclusion and exclusion criteria for the RCT-X;

2 comparison with other similar analyses and identification of potential differences in relation to the selected population;

3 determination of whether the study group has comparable baseline characteristics, implemented treatment, and prognosis in relation to the results of the RCT-X;

4 assessment of patients who do not meet the inclusion criteria and who meet the exclusion criteria in comparison with the selected study group.

The specific nature of RCTs requires that inclusion criteria are precisely defined, which automatically excludes part of the population with a given disease or undergoing a given procedure.[7,8] Similarly, strict exclusion criteria are justifiable, considering patient safety, especially when implementing new therapies. This usually results in the lack of good representativeness of the population enrolled in RCTs.[9]

The presented analytical model provides the basis for a series of comprehensive analyses that will allow a verification of scientific evidence from RCTs and guidelines in real-world populations. In addition to assessing the implementation of guidelines in everyday clinical practice, the outcomes of the analyses may also result in the generation of new hypotheses.

The analytical model is the next step in connecting evidence-based medicine with evidence-based policy. A methodological analysis using large databases is extremely important from the perspective of the real-world population. The analysis should primarily focus on treatment strategies that cannot be tested in an RCT for ethical or financial reasons but also when the results of RCTs are inconclusive and when there is a high suspicion that the population, practice, or other factors in a given treatment strategy differ from those applied in the RCT.

We are aware that the presented analytical model has some limitations. In addition to the typical advantages associated with the registry design of the study, the main limitation is potential selection bias, even after using multivariable analysis and propensity score matching.

The availability of scientific evidence from RCTs has started a new era in medicine. It is difficult to imagine modern medicine without scientific evidence from clinical trials. Without reliable RCTs and meta-analyses, progress seems virtually impossible. Therefore, an increasing number of therapies are tested in RCTs. On the other hand, the assessment and verification of scientific evidence in the real-world population become not only a necessity but also a duty.[10] In the context of the country's healthcare policy, large observational studies will allow a more favorable adjustment of cost valuations and access to health services for patients. Therefore, the presented analytical model could facilitate verification of scientific evidence in the real-world setting.

ARTICLE INFORMATION

CONFLICT OF INTEREST None declared.

HOW TO CITE Gąsior M, Desperak P, Cieśla D, et al. How to effectively analyze scientific evidence in clinical practice? Rationale behind and design of an observational analytical model. Kardiol Pol. 2020; 78: 577-580. doi:10.33963/KP.15268

REFERENCES

1 European Society of Cardiology. Clinical Practice Guidelines. https://www.escardio.org/Guidelines/Clinical-Practice-Guidelines. Accessed March 1, 2020.

2 Gąsior M, Pres D, Wojakowski W, et al. Causes of hospitalization and prognosis in patients with cardiovascular diseases. Secular trends in the years 2006-2014 according to the SILesian CARDiovascular (SILCARD) database. Pol Arch Intern Med. 2016; 126: 754-762.

3 Desperak P, Hudzik B, Gąsior M. Assessment of patients with coronary artery disease who may benefit from the use of rivaroxaban in the real world: implementation of the COMPASS trial criteria in the TERCET registry population. Pol Arch Intern Med. 2019; 129: 460-468.

4 Trzeciak P, Desperak P, Ciślak A, et al. Clinical characteristics, and in-hospital and long-term outcomes of stable angina treatment in patients below and over 40 years of age (from the PRESAGE registry). Kardiol Pol. 2018; 76: 186-194.

5 Gąsior M, Pyka Ł, Gorol J, et al. COnteMporary Modalities In Treatment of Heart Failure: a report from the COMMIT-HF registry. Kardiol Pol. 2016; 74: 523-528.

6 Gąsior M, Gierlotka M, Pres D, et al. Effects of direct stenting on epicardial and myocardial perfusion in patients with acute ST segment elevation myocardial infarction. Kardiol Pol. 2007; 65: 503-514.

7 Jha P, Deboer D, Sykora K, Naylor CD. Characteristics and mortality outcomes of thrombolysis trial participants and nonparticipants: a population-based comparison. J Am Coll Cardiol. 1996; 27: 1335-1342.

8 Steg PG, Lopez-Sendon J, Lopez de Sa E, et al. External validity of clinical trials in acute myocardial infarction. Arch Intern Med. 2007; 167: 68-73.

9 Van Spall HG, Toren A, Kiss A, Fowler RA. Eligibility criteria of randomized controlled trials published in high-impact general medical journals: a systematic sampling review. JAMA. 2007; 297: 1233-1240.

10 Cohen A, Goto S, Schreiber K, et al. Why do we need observational studies of everyday patients in the real-life setting? Eur Heart J Suppl. 2015; 17 (suppl D): D2-D8.