◆ EVIDENCE SECTION

The Future of Clinical Trials

Walter Masson 🆔

Chief of Cardiovascular Prevention, Hospital Italiano.
Ciudad Autónoma de Buenos Aires, Argentina.

Clinical trials represent the highest level of evidence for medical decision-making, as indicated in clinical guidelines under the class I recommendation. However, these studies present limitations, such as the time and costs required, difficulty obtaining samples from some populations, and ethical barriers. A clear definition of prognostic or predictive biomarkers and well-established endpoints are essential to accelerate the development of new drugs. In addition, personnel limitations can hinder the progress of clinical trials.

For this reason, and with the advance of new methodologies, the digitalization of information and artificial intelligence (AI) will favor a change in the structure of the design of clinical trials, as well as in their generalization. The world of clinical trials is in full transformation, both in the conduct of studies and in the development of different treatments.

The Future of Design and Methodology

Innovative research strategies are required to increase patient engagement and produce the highest quality evidence, enabling rapid translation of diagnostics and therapies from research to clinical settings to improve population health. Coronavirus disease 2019 (COVID-19) has accelerated the development of next-generation clinical trials, forcing trials to become more patient-centered.

Future studies will rely on AI, machine learning and deep neural networks to improve drug discovery, image interpretation, streamlining electronic medical record data and improving trial workflow. These studies will also accommodate recent advances in immunology and precision medicine. Master protocols, comprising sub-studies such as general studies, basket studies, platform studies and master observational trials, will be used to improve clinical trial design.

Future clinical trials will be more decentralized and virtualized and will comprise digitized endpoints for more realistic and standardized monitoring of real-world patient experiences. Pragmatic trials are one step towards this approach and will enable remote monitoring.

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Correspondence: *Walter Masson*
Mail: walter.masson@hospitalitaliano.org.ar

Another feature of future trials is the ability to answer multiple research questions using advanced techniques such as big data and AI. Currently, endpoints can be multidimensional, spanning metabolic, cardiovascular and renal outcomes in a single study, and combined with patient-centered outcomes using techniques such as win ratio. It is therefore important to use new designs that allow integration with public health registries, using randomized studies based on reliable registry and electronic clinical record data.

Endpoints including well-being, quality of life, and length of hospital stay may provide substantial information beyond morbidity and mortality, improving patient care, especially in those with a short life expectancy, where quality is more important than quantity.

Another point to consider is the advancement of biomarkers and imaging studies associated with AI, where this information will improve the inclusion of patients in studies and the focus on specific subgroups that would benefit from a particular therapeutics or research target. That is, we will move from "single organ" study designs to a multi-organ approach, with cross-linking of information from different systems. An example of this is metabolic syndrome, where the heart, kidney, microbiome, liver and brain interact.

On the other hand, the advance of sensors and portable devices allows data collection and remote monitoring, which represents another point of improvement in the efficiency of studies in the future. All these considerations on the advancement of technology must have a fundamental basis: the reliability and quality of the available data. Otherwise, inclusion bias will persist, and the results and their generalization will be seriously affected.

In conclusion, the advance of technology, which will favor a less restrictive inclusion of the population, a patient-centered approach, more pragmatic designs and the identification of subgroups as research targets, will improve the quality of evidence with greater efficiency in generalization and in the management of populations yet excluded from clinical trials.

The focal points of the future of clinical trials could be summarized as:
- Patient-centered.
- Use of technology and decentralized studies to reduce and simplify the workload.
- Improved data accuracy by incorporating the most parameterized and reliable electronic databases.
- Increased availability and quality of real-world data.
- Emphasis on patient experience.
- Streamlining, adapting and making study design more flexible (hybrid designs) to adapt to changing contexts.
- Increased efficiency in clinical research infrastructure, including telemedicine, electronic data capture and remote monitoring.

References

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