FROM RANDOMIZED CLINICAL TRIALS (RCTS) TO ARTIFICIAL INTELLIGENCE (AI) – HISTORY AND METHODOLOGICAL CHALLENGES

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Generating knowledge from studies or trials has been one of the key objectives of empirical research. This has been an essential issue in many research specialties with plenty examples during the last centuries, showing the movement towards increasingly more systematic approaches. A rich source of this development is the James Lind Library [1] evolved from a website called Controlled Trials from History. It's using material from history to illustrate the principles underlying fair tests of treatments and their development and application over time. Modern times have started in the late 1920 with the first publications describing the principles of randomization as a tool to minimize bias in the comparison of the effectiveness of interventions. This work was completed with the publication of the methodology and advantages of the design of trials in which groups were filled by the randomization procedure, by R. A. Fisher (The Founder of Modern Statistics) in 1929. Those designs were called experimental, in contrast to observational studies where the treatment allocation was not influenced but simply observed. The next decades saw a steady development of these principles in trial designs, their practical application and next steps of progress of these designs. Implicit in this progress was a permanent competition between experimental and observational studies, with permanent controversies, often very fierce. A significant event in the gradual evolvement was the first steps of a development which led, three decades later, to what is now known as Evidence-based Medicine (EBM), at the McMaster University in Hamilton, Canada, in 1969. This pioneering work was guided by Dave Sackett, a US doctor in internal medicine. Parallel to those early days the foundation of the methodology of systematic reviews was laid in the United Kingdom by Archie Cochrane with his legendary book "Effectiveness and Efficiency: Random Reflections on Health services". There he claimed that all medical interventions should show their effectiveness in RCTs. In this period the more theoretical principles of clinical trials and medical practice were merged into a shared model of both perspectives. However, the first two decades were not labelled as EBM but used Clinical Epidemiology as specialty name for that framework. The term Evidence-based was introduced 1991 and marked the starting of a remarkable era of major methodological developments. More than 35 years of Evidence-Based Medicine (EBM) have achieved major contributions to systematically integrating the results of clinical trials into decision making in health care. This progress has been enabled and supported by an enormous amount of methodological developments. The rigour of the methodological framework, in particular addressing quality assessment and quality issues in general, is a characteristic of EBM. However, considering 35 years as time for those achievements is misleading because that time period included the pandemic where in 4 years time many of the achievements were destroyed or lost. This can easily be seen by the role

quality issues played in all aspects of the planning, conduct, analysing the results of trials. From 1991 to 2020 a considerable number of quality devices (i. e. Equator [2] have been developed and implemented, for the quality of all steps of trials from planning to implementing the knowledge derived from results. This may sound as if it was an easy path but it was not. Quality is a value which is under permanent attack and has to be defended. Bias is a major aggressor, probably the most famous in that camp is the publication bias. Up to 50% of research results are not published, with a heavy bias of what is published and visible [3], accordingly with serious ethical impact [4]. In recent years a new era has been launched, starting 2008 with a provocative article claiming that enough data make the scientific method obsolete [5]. Big Data, artificial intelligence (AI) and personalized medicine (also called precision medicine) have generated a realm of visions and promises where the quality issue seems to have completely disappeared: Unlimited data guarantee any level of needed quality, without particular effort. Can this be expected, or where is the border between realistic expectations and marketing-driven promotion? We are observing a confrontation and a cultural clash between the "old", methods-driven world and the new "informatics-based" or "data-driven" world which is not receiving the attention it deserves in the current climate of enthusiasm and hype [6]. It is urgent to avoid misleading perspectives and return to strictly quality-driven research agendas and the implementation of these methods [7]. The presentation describes and illustrates these different methods worlds and their tensions and controversies.

References

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