Randomised controlled trials and real-life studies: two answers for one question

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Real-life studies have a place alongside randomised controlled trials http://ow.ly/7S5Q30lCiYN

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Real-life studies have become increasingly important in the scientific world in recent years. Although they have numerous limitations, they have the advantage of better representing the population with which we normally have to deal in our everyday clinical practice. Randomised controlled trials (RCTs) remain the most effective form of evaluation of the efficacy of a therapeutic intervention to date, but their selection criteria limit the recruitment of patients in upper or lower age ranges or suffering from multiple comorbidities. These are individuals who are suffering from severe medical conditions and take several different medications, and these are the subjects we meet and we take care of when taking charge of the general population. This is so true that in some RCTs the screening failure rate has exceeded 70% of patients [1]. Therefore, integrating RCTs with real-life studies is increasingly important, as is deepening the discussion of the selection criteria used in the registration studies, so that they better reflect the true situation of our patients. Moving from the ideal world to the real world may represent a hazardous shock that in the past has caused both surprises and bitter disappointments [2].

Recently, an article in *Nature* highlighted these problems, noting that: "Nearly 20% of publicly funded cancer clinical trials in the United States fail because investigators are unable to enrol enough participants" [3]. The author, quoting some American researchers, recalls HIV as an example of questionable selection criteria: "People with HIV, for example, were once excluded from trials because of their poor prognosis. Now, with treatment, they often live as long as people without the virus and should be included in many cancer trials". The same source also questions the age for participation in clinical trials: is the age of 18 years an appropriate limit, even though the metabolism of drugs is already mature long before this time? The same could apply to upper age limits. This article also indicates that: "A joint project by the FDA [US Food and Drug Administration], the American Society of Clinical Oncology (ASCO) in Alexandria, Virginia, and the advocacy group Friends of Cancer Research in Washington DC has found that five common criteria for cancer-trial eligibility often could be amended without harming participants or the integrity of the trial" [4].

These are all legitimate questions that can be used to encourage a debate, which today has not yet yielded precise answers but which should be further explored, without prejudice to the fundamental role of the RCTs. Real-life studies have several limitations and should be interpreted cautiously, although they can fill

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the important gap between efficacy and effectiveness: efficacy meaning proof in a carefully controlled trial, and effectiveness meaning success in the circumstances of everyday life [2]. However, even today, these studies are considered by the scientific community to be of lesser dignity, while the possibility of their being published in prestigious journals remains very limited; and yet, effectiveness is what interests us the most.

Conflict of interest: S. Harari has relationships with drug companies. In addition to being investigator in trials involving these companies, relationships include lectures and membership of scientific advisory boards.

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