Efficacy, effectiveness and the “efficacy-to-effectiveness gap”: Review of the current state of play and perspectives

First results from the IMI GetReal Consortium

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Context

Decision-makers need to know the extent to which a drug does more good than harm. Under controlled conditions, such as in RCTs, this is termed efficacy while in real life conditions this is termed effectiveness. It is critical for regulators to understand the efficacy without any confounding factors and most trial data at launch is focussed on providing such information. However, payers and physicians are more concerned with effectiveness at the population level and payers are more concerned with cost-effectiveness at the patient level respectively and there is an emerging concept of an efficacy-effectiveness gap (EEG) in the evidence about new drugs.

Objectives

Work Package 2 of the IMI GetReal consortium has conducted a review of the origins of the concept of EEG:
1. On which historical background has it emerged?
2. How has the EEG been conceptualized and which solutions have been suggested to narrow the gap?
The purpose of the review was to inform development of a framework to identify which contextual factors have a meaningful impact on the effect of a drug

1950’s
1960’s
1970’s
1980’s
1990’s
2000’s

Paradigm 1

• In this paradigm, the EEG is understood as an issue of measure: different study designs (RCTs vs. effectiveness studies) to assess the impact of drugs, provide different results
• On one hand, the underlying assumption of the concept of evidence-based medicine and hierarchy of evidence is that: efficacy is the real effect of the drug whereas effectiveness is a distorted one, derived from “biased” real-life observational studies
• On the other hand, the concept of “pragmatism” suggests that RCTs are lacking external validity and generalizability
• It has been suggested that RCTs can be modified to include elements of real world data

Paradigm 2

• In this paradigm, the “ideal” drug’s effect is thought to be distorted by real-life factors: the behaviour of carers and patients’ adherence to treatment
• To narrow the EEG, it has been suggested to bring up real-life care to: promotion of knowledge dissemination, medical guidelines, adherence-enhancement strategies, etc.

Paradigm 3

• Another paradigm is emerging: the difference between the effects of a drug as measured in an experimental setting or in routine practice is the result of the interaction of multiple “real-life” characteristics on the biological effect of the drug

About IMI GetReal & funding

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