4. Efficacy, effectiveness, and efficiency

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Although these terms may be considered synonymous by the lay public, they have different meanings for specialists in clinical research. Aware that these differences are not always well assimilated in basic pharmacology, we present here definitions that we hope will be clarifying. It should be noted that confusion may be exacerbated by the fact that the same terminology can have different meanings in basic and clinical research, as is the case with the term "efficacy".

In **basic research**, *efficacy* of a drug often refers to its maximal capacity to produce an effect; that is, the term is frequently used as a synonym for *intrinsic activity* (as termed by Ariëns in 1954) or *maximal agonist effect*, as currently recommended by the IUPHAR (Neubig et al., 2003), which is readily measured at the plateau of the concentration- or dose-response curve. This maximal effect is best expressed as a fraction (α) of the effect produced by a full agonist of the same type, acting through the same receptors, under the same experimental conditions. A full agonist has $\alpha=1$, a neutral antagonist has $\alpha=0$, and a partial agonist has $0<\alpha<1$.

More restrictively, and difficult to assess in practice, the term *intrinsic efficacy* (ε), introduced by Furchgott in 1966, is currently reserved to represent the stimulus produced by the interaction of a single drug molecule with a single receptor (this parameter is a property of the drug for a given receptor and does not depend on the signal transduction system present in the cell). Confusion may be further increased by consideration of a third parameter, τ (the "transduction ratio"), proposed to evaluate agonist efficacy in a given system in the operational model of Black and Leff (1983).

By contrast, in **clinical research**, *efficacy* refers to the ability of a medicine, at the recommended dose, to produce beneficial effects under ideal circumstances, such as those of randomized clinical trials (Marley, 2000). Efficacy is therefore measured by evaluating the clinical and statistical outcomes of the trial. However, patients studied in such controlled trials are generally young, male, white, affected by a single disease, and receiving a single treatment*. Most patients in routine medical practice do not fit this description.

Accordingly, the term **effectiveness** has a different meaning and is used to measure the effect of a medicine in therapeutic practice, that is, under *real-world* conditions in the population as a whole, as opposed to the conditions assessed in controlled clinical trials, where patients are rigorously selected. Thus, poor patient adherence (non-adherence) to treatment, due to adverse effects or the complexity of the therapeutic regimen, can influence effectiveness, as can the presence of comorbidities absent in patients included in controlled trials. Effectiveness can be assessed in observational studies in routine medical practice.

The third term, **efficiency**, is used when evaluating the cost–effectiveness relationship of a treatment for the patient or for society (Marley, 2000), and is of fundamental importance to the field of pharmacoeconomics and as one of the criteria for the selection of essential medicines, such as in the Brazilian National List of Essential Medicines-**RENAME** (Hoefler and Maluf, 2010).

**It should be noted, however, that there is a trend in phase III studies to test medicines in increasingly larger population samples, including patients with comorbidities and even those using multiple concomitant medications, in order to allow extrapolation of the data to the population that will use the product once it is available on the market.*

References

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