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Systems medicine, a new paradigm for drug discovery and development, from an academic perspective

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The sample size computation has become a must in designing clinical trials. This is the best simple illustration of how modeling approaches improves drug development. In that example, using appropriately rather simple mathematical equations helps in formally addressing a question, defining principal hypothesis and trial objective, and sizing the population to be recruited in order to minimize the risk of trial failure, i.e. false positive or negative conclusions.

For marketing rather that public health and scientific purposes, drug access to the market is based on oversimplified models e.g. in terms of dosage of drugs required for the whole populations of individuals supposed to be treated. For a while, pharmacologists have described the drug journey within human body through mathematical equations of pharmacokinetic (PK) models, and the impact of drug on human body through pharmacodynamics (PD) models. The possibility to adjust the drug dosage on a lot of variability factors, playing at the PK and / or PD level, has been illustrated in therapeutic drug monitoring when the range between efficacy and safety dosages is narrow. Few trials have attempted to demonstrate the added value of this approach compared to simpler adjustment procedures. But the variability of PK models parameters, and of the inter-individual drug responses, becomes more and more obvious, as well as the logic of specific individual adjustment, leading to use population approaches and setting up virtual (more or less realistic / representative) population to capture this variability.

More complex approaches, converging towards the systems biology paradigm, begin to be used at various stages of drug development, from discovery to public health impact estimation. Several examples will be taken to illustrate how improving the realism of mathematical models, in introducing physiology in PK, systems regulation and dysregulation in PD, and experimental constraints in drug trial design, illustrate how the rapidly improving models will change the landscape of drug making and using.