Virtual patients for therapeutic drug trials

Using modelling, different doses of drugs can be given to 'patients' to test effectiveness

VITAL PATIENTS: Modelling and simulation allow clinicians to be reassigned for individualised therapy, while maximising therapeutic benefits and minimising risks. Organ size, tissue blood flow and organ function are just a few of the many known physiological variables defining an individual. Differences among individuals arise because these variables are altered across different ethnic groups, life stages or disease states. With a growing understanding of how these parameters are altered, various virtual patient populations can be created.

Physiologically based pharmacokinetic (PBPK) modelling uses mathematical representations of the physiological system to quantify how such variability in health and disease affects drug exposure in the human body and its associated therapeutic outcome.

Ensuring that drug levels fall within a safe and efficacious range is one of the primary goals of treatment. Using PBPK modelling, our laboratory at the National University of Singapore (NUS) has recently looked at the complex drug-drug interactions between ciclosporin and amidine, two medications which are frequently co-administered in patients with atrial fibrillation – a condition characterised by an irregular and often rapid heart rate, that can increase the risk of stroke, heart failure and other heart-related complications.

Based on the simulation results, dosage adjustments of ciclosporin are recommended to mitigate its bleeding risk while preserving its anti-coagulation effect in patients with both atrial fibrillation and renal impairment. Our recommendation was published in the journal Of The American College Of Cardiology.

PBPK MODELLING COMES OF AGE

In recent years, the emergence of user-friendly software platforms which allow the integration of human population databases and drug attributes have greatly facilitated the widespread adoption of PBPK modelling by academia, the pharmaceutical industry and regulatory agencies. The regulatory endorsement has been emphatic as the United States Food and Drug Administration (FDA), the European Medicines Agency and the Japanese Pharmaceuticals and Medical Devices Agency have emphasised the necessity of this shift towards precision dosing based on modelling.

In the real world, we envision a landscape where healthcare and technology will converge in perfect synergy to direct and inform precision medicine – not just for subsets of patients, but for individual patients. Each person will have a virtual self, based on their genes and characteristics, who can participate in virtual clinical trials on behalf of the real person.

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About the writers