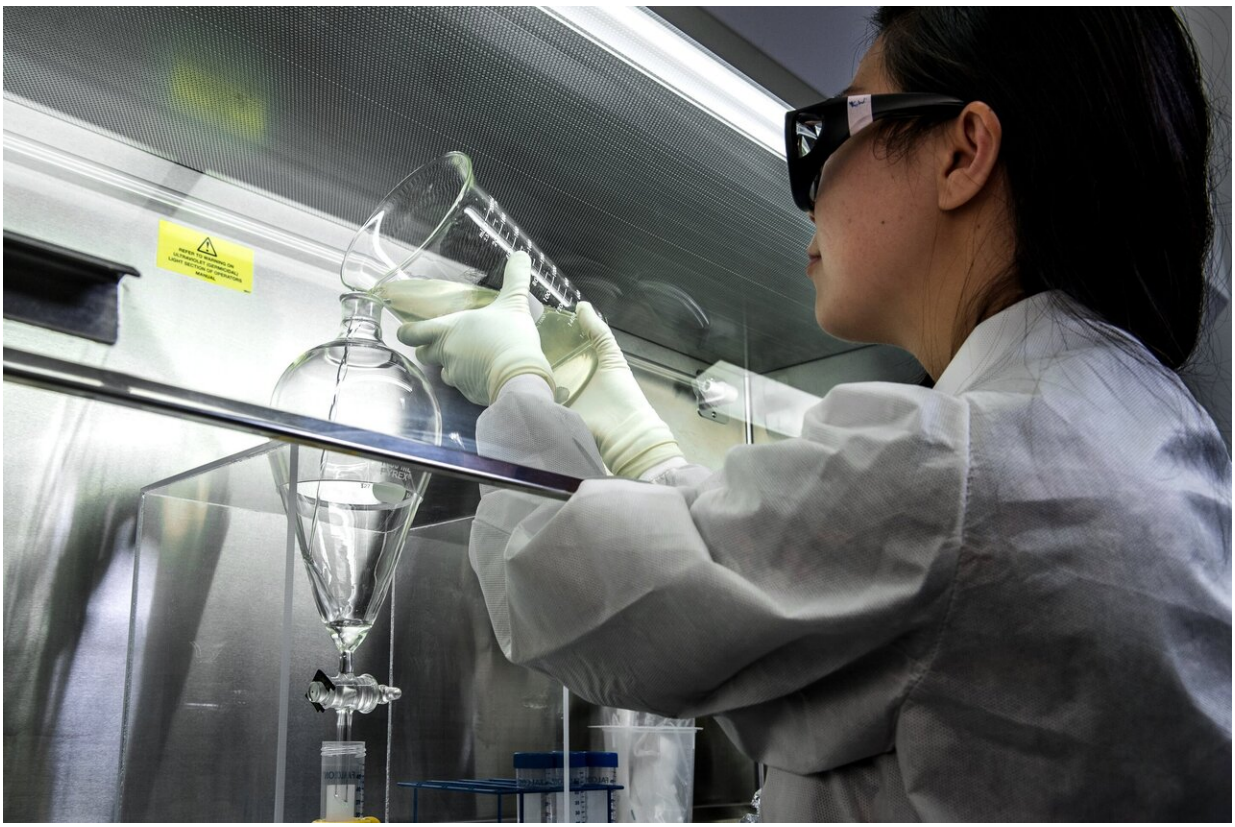
Personalized medicine: To optimize treatment for individual patients, physicians should employ experimental designs

March 3 2021, by Ellen Goldbaum



Credit: Unsplash/CC0 Public Domain

Randomized clinical trials are the undisputed gold standard for determining whether a treatment protocol is effective for a specific

disease or condition.

But while seen as the best way to determine how effective a drug or vaccine is, RCTs, as they are known, aren't designed to capture the nuances that distinguish how individual patients respond.

A recent paper in *JAMA Pediatrics* recommends that pediatricians and other providers explore the concept of single case, or N-of-1 experimental designs, as they are also known, the purpose of which is to apply experimental methods to caring for individual patients in challenging cases.

"It has been known for some time that there is considerable heterogeneity of treatment effects in randomized trials, with the trial capturing the average benefit, which cannot always be generalized to the individual patient," said Leonard H. Epstein, Ph.D., a co-author and SUNY Distinguished Professor in the Jacobs School of Medicine and Biomedical Sciences at the University at Buffalo.

"With the emphasis on personalized or precision medicine, different designs are needed to identify the optimal treatment approach for that particular person," said Epstein, also chief of the Division of Behavioral Medicine in the Department of Pediatrics at the Jacobs School.

First author on the paper is Karina W. Davidson, Ph.D., of the Center for Personalized Health of Northwell Health and of Hofstra University.

The paper notes that RCTs typically depend on the enrollment of hundreds of patients, usually at multiple sites, in order to have "enough statistical power" to determine if an intervention is effective. Patients must be enrolled according to strict eligibility criteria, such as age and gender, and those with certain comorbidities often are disqualified.

RCTs are also expensive to undertake and "take an extraordinary amount of time," Epstein says, which can significantly delay the transfer of that benefit to the patient.

Single case experimental design, by contrast, can be especially useful with patients with rare diseases or who have comorbidities that would exclude them from being eligible for RCTs. These single case studies may be appropriate when implementing combination interventions, such as a behavioral and a pharmaceutical protocol. They can also be an optimal way to individualize preventive measures; for example, early signs of hypertension or prediabetes.

Benefit to the patient

Epstein explained how experimental design in personalized medicine differs from standard medical care.

"Many health care professionals attempt to take individual characteristics of their patients into account when developing a treatment plan, and they adapt the plan based on patient response to the treatment," he said. "However, they seldom do it using experimental designs to increase confidence that the change in patient symptoms was, in fact, due to the change in the treatment plan. A personalized trial differs from a case study in the use of experimental versus observational methods."

The paper points out that personalized trials have not yet "found a home in pediatrics" but that pediatric care could benefit from their expanded use. A hypothetical example of a combined drug and behavioral approach to attention-deficit/hyperactivity disorder (ADHD) is used to demonstrate how experimental design could potentially optimize treatment in pediatrics.

"Time well spent'

Personalized trials can require more of a clinician's time and resources, Epstein noted. It can also require that a practice has the ability to properly collect and organize the data involved.

"As an experimental approach, a personalized trial is more complicated than just normal treatment of a patient, as repeated measures of symptoms are needed, and treatments need to be introduced according to a plan," he explained.

"Visual inspection of graphs and statistical analysis are used to ensure the changes were in fact due to the treatment, and the changes represent a significant improvement in the person's condition," he said. "It is hard to know how much more time it takes, but for a difficult case it is time well spent."

Key distinctions between RCTs and personalized trials are that in RCTs people are randomized to a treatment or control group and a small number of measurements are made for each person. In a single case design, Epstein explained, experimental conditions are manipulated within the same person and many measurements are collected on that individual.

He added that results from several personalized trials can be incorporated into a meta-analysis to strengthen confidence in the effects of a given intervention across several patients.

Personalized trials also are being used as proof-of-concept studies that then lead to the establishment of RCTs, serving as "important steps in translating basic science into new clinical interventions," according to the paper.

Epstein is an internationally recognized authority in the fields of childhood weight control, physical activity and family intervention who has spent 40 years conducting research relevant to the prevention and treatment of childhood obesity, including mechanisms that regulate intake and energy expenditure in children. He has been using personalized trials or single case experimental designs since he started doing research in graduate school decades ago.

Epstein has a complementary paper on use of single case designs for translational research in press at Health Psychology. He is conducting ongoing studies on using single case experimental designs to evaluate the use of weight loss interventions and continuous glucose monitors to improve glucose regulation and reduce blood glucose variability. He also has a paper in review on using single case experimental designs to improve medication adherence in people with prediabetes.

More information: Karina W. Davidson et al. Experimental Designs to Optimize Treatments for Individuals, *JAMA Pediatrics* (2021). DOI: 10.1001/jamapediatrics.2020.5801

Provided by University at Buffalo