Innovative Designs, Extrapolation, Simulation Methods and Evidence-Tools for Rare Disease

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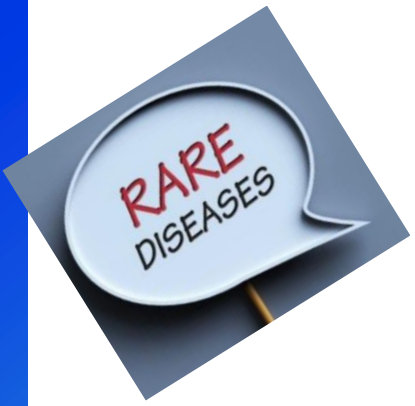
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RARE DISEASE: A disease is rare when it affects only a small group of people: In the European Union, a prevalence threshold of no more than 5 affected persons per 10,000 (equivalent to 1 in 2,000 people).

Innovative Study Designs

Instead of playing a video game in the same way every time (standard study design), scientists create a new set of rules (**innovative** study designs) to win (find the right treatment) even with **few players**.



Adaptive Trials: Allow changes to the study protocol on interim results

Basket Trials: Test a single targeted therapy across different disease groups that share the same genetic mutation or biomarker

Bayesian Designs: Use prior data and probability models to guide decisions like dose escalation or treatment allocation

Platform Trials: Test multiple treatments under a single master protocol in an ongoing manner

Umbrella Trials: Test multiple targeted therapies within a single disease population

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Extrapolation

Extrapolation methods in clinical research refer to the practice of inferring unknown efficacy, safety, or long-term outcomes for a target population by extending known data from a studied source group or short-term observation.



Imagine you are playing *Super Mario*. You build a staircase using three blocks going up. Even if you stop building, you can easily guess what the 4th, 5th, and 6th blocks will look like. They will keep going up in the same pattern!

Scientists might not know how a rare disease affects pediatric patients, but if they know how it affects adults, or how a similar common disease works, they use that information to guess the best way to treat the young patients: taking what we already know about how a drug works in adults (the "source" population) and using it to predict how it will work in children (the "target" population).

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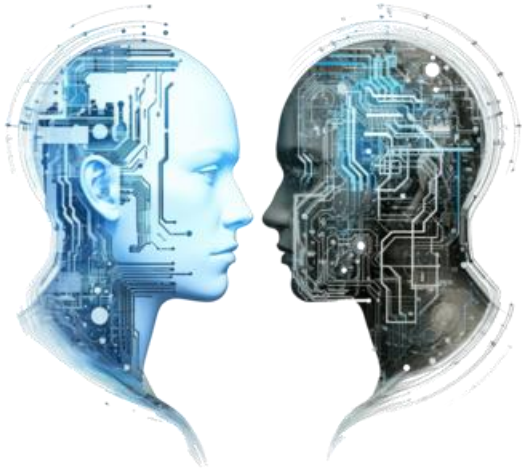
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Simulation Methods

Simulation methods in clinical research use mathematical, or statistical models to mimic real-world clinical trials, or patient responses, before they happen.

Imagine you are playing *EA Sports FC*. Instead of playing the game yourself, you set both teams to be controlled by the computer (CPU vs. CPU) and watch them. You can speed up the game to see who wins 1,000 times in just a few minutes!





Testing a rare disease treatment in real life can take years. Instead of waiting, scientists build a "**digital twin**" of a human body inside a powerful computer. They feed the computer all the rules of how blood, bones, and cells work. Then, they press "Play" to let the computer simulate what happens when the drug hits the disease. The computer can run thousands of pretend tests in seconds!

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Evidence-Tools

Evidence tools in clinical research are digital platforms, software, and methodological frameworks used to find, appraise, synthesize, and manage medical data to guide patient care and study design.



Think of the quest log in *Fortnite*. To prove you are a Master Trainer, the game looks at your evidence: Do you have the gym badges? The game uses these built-in trackers to look at your data and officially say, "Quest Complete!"

Because rare diseases are so rare, a scientist might only see one patient who has it. If a scientist tries a new treatment and it helps that one patient, how do they prove to the world that it works? They use **Evidence-Tools**. These are smart digital checklists and global databases. Scientists from America, Japan, and Europe can all log into the same system and type in their data. When all the tiny bits of proof are combined, the tool shows undeniable evidence that the dug works.

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Thank you

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