N-of-1 Trials for Personalized Healthcare

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Course Description: Personalized (N-of-1) trials hold great promise for broadening the clinical knowledge production enterprise to engage individuals in trial design, creation and use of personal data, and decision making. N-of-1 trials use a multi-crossover design in which each individual receives two or more treatments multiple times in a randomized order. In contrast to traditional clinical trial designs, N-of-1 designs can measure individual treatment efficacy to create personalized knowledge. While frequently used to assess treatments for chronic conditions or lifestyle choices, these designs are also uniquely positioned to provide information about the efficacy of treatments for rare diseases and clinical conditions for which recruitment of large numbers of participants is impractical or which may need a personalized treatment protocol. N-of-1 trials may be deployed in a variety of ways. Individuals may create unique, personal designs focused on treatments and outcomes of interest carried out in a manner best suited to them. Or, when practical, trials may be coordinated to have similar protocols facilitating the sharing and combining of information to learn about groups of individuals as well. Such designs may better inform individuals too through borrowing of strength from the findings of exchangeable group members. Such group designs may be particularly valuable in clinical settings such as healthcare organizations that provide personalized care to groups of individuals. By combining individual trials in a multilevel structure, it is also possible to describe average treatment effects in populations and subgroups and measure treatment effect heterogeneity to create generalizable knowledge. We discuss the promise and challenges of N-of-1 trials, including the use of software to design and analyze trials, the use of mobile apps to facilitate participation, retain interest, collect data and provide interpreted results to participants, and some of the research barriers that need to be overcome, particularly the challenges of accommodating personalized protocols. These issues are illustrated by several of our recent projects each involving many N-of-1 trials in which we combined mobile device applications with server-driven statistical analytics using an R package to return results to individuals. We discuss defining treatments and sequences of treatments, synthesizing treatment networks, incorporating patient-specific prior information, automating the choice of appropriate statistical models and assessment of model assumptions, and automating graphical displays and text to facilitate appropriate interpretation by non-technical users.