Development of a SPIRIT (Standard Protocol Items: Recommendations for Interventional Trials) Extension for N-of-1 trial protocols: SPENT

Interest in N-of-1 trials, defined as an ABAB multiple cross-over design with a single participant, is well established (1-4). N-of-1 trials have long been included in research design textbooks (5) and recommended since the mid-1980s for personalizing treatment (6,7). N-of-1 trials are a good fit with the current emphasis on personalized care such as recommended by U.S. Patient-Centered Research Institute (PCORI) and the Canadian Strategy for Patient-Oriented Research (SPOR) (3). N-of-trials are especially important when parallel group randomized controlled trials (RCTs) cannot be done, such as for rare disease. They also facilitate the development of rigorous evidence in populations often overlooked by RCTs, such as patients with co-morbid conditions and/or multiple concurrent treatments (8-12). The N-of-1 trial design has very specific design requirements in addition to that of a parallel group randomized controlled trial (RCT). Currently, no authoritative protocol guideline exists for N-of-1 trials, though a number of articles clearly describe protocol recommendations (1,13-19).

The need for and the resulting development of protocol reporting guidelines, the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) Statement, has been well established (20). As with protocols for randomized group trials, a similar publication guideline for protocols for N-of-1 trials—both single trials and N-of-1 trial series—can play an essential role in study planning, guiding conduct, and detailing plans from study inception (including plans for ethics review) to study implementation and results dissemination. A systematic review (SR) of N-of-1 trials (Punja, manuscript in process) used in developing reporting guidelines for N-of-1 trials, the Consolidated Standards of Reporting Trials (CONSORT) Extension for N-of-1 Trials (CENT) (9), highlights significant variability in reporting. The SPIRIT and CENT guidelines therefore provide a strong basis and guidance for undertaking this extension development, for the purpose of developing a SPIRIT extension for N-of-1 trial protocols. The guideline development will follow published recommendations (21): a systematic review, Delphi consultation on items development, publication of statement and "explanation and elaboration" articles, and knowledge translation activities.

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