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GENERAL INTEREST

79MO Developing international consensus-driven SPIRIT and CONSORT extensions for early phase dose-finding clinical trials: The DEFINE (DosE FIndiNg Extensions) study

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Background: Early phase dose-finding (EPDF) trials are crucial for the development of a new intervention and influence whether it can be investigated in further trials. Guidance exists for clinical trial protocols and trial reports in the SPIRIT and CONSORT guidelines, respectively. The features of EPDF trials are not well addressed in both guidelines and their extensions. Building on the SPIRIT and CONSORT checklists, the DEFINE study aims to develop international consensus-driven guidelines for EPDF trial protocols and reports.

Methods: The initial generation of candidate items was informed by reviewing published EPDF trial reports. The early draft items were further enriched via a review of the published and grey literature, real-world examples analysis, citation and reference searches and experts' recommendations. Following a 2-round modified Delphi process, an international consensus meeting was held. The resultant SPIRIT-DEFINE and the CONSORT-DEFINE checklists are then piloted prior to being finalised.

Results: Tailored to cover the specific features of EPDF trials, the Delphi survey included new or modified candidate items for SPIRIT (n = 36) and CONSORT (n = 44) extensions. 206 interdisciplinary stakeholders participated in Round 1 from 24 countries, and 151 stakeholders in Round 2. The Delphi results and a subsequent consensus meeting led to the recommendation of 31 and 36 candidate items for the SPIRIT-DEFINE and CONSORT-DEFINE checklists respectively. New items added include starting dose and dosing regimens with rationale, dose [de-]escalation strategies and decision criteria. International stakeholders are currently testing the checklists, and their feedback will be integrated into the final guidelines.

Conclusions: The SPIRIT-DEFINE and CONSORT-DEFINE guidelines will allow investigators to effectively address the essential items that should be present in EPDF trial protocols and their reporting of the results. These will promote transparency, completeness and reproducibility of methods and ultimately contribute to reducing research waste and enhancing patient care and safety.

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80MO Optimising participant flow diagrams for phase I clinical trials

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Background: CONSORT 2010 recommends the use of flow diagrams within Randomised Control Trials (RCTs). Phase I trial designs have dose-finding features not captured by flow diagrams for RCTs, yet there are currently no recommendations on diagrams for these trials. This project aims to: (1) assess the completeness of information in flow diagrams of phase I published trials based on CONSORT recommendations, and if additional features on dose (de-)escalation were presented; (2) propose new flow diagrams presenting how doses were (de-)escalated throughout the trial.

Methods: Flow diagrams were extracted from a random sample of 259 phase I papers across all diseases, published from 2011-2020 indexed in PubMed. Diagrams were scored out of 15 following CONSORT recommendations with an additional score for presence of (de-)escalation. New templates were proposed for features that were deficient and presented to 39 attendees at the 7th Early Phase Adaptive Workshop held in October 2022 and 11 members of the Drug Development Unit (DDU) team at the Institute of Cancer Research in December 2022.

Results: 98 (38%) papers included a flow diagram. Flow diagrams best reported the number of patients allocated to intervention (95%) and received allocated intervention (55%). Flow diagrams were most deficient in the reporting of reasons for lost to follow up (2%) and reasons for not receiving allocated intervention (14%). Few