Please see below for a link to the webinar recording for the Trials Methodology Research Partnership:

SPIRIT-ROUTINE

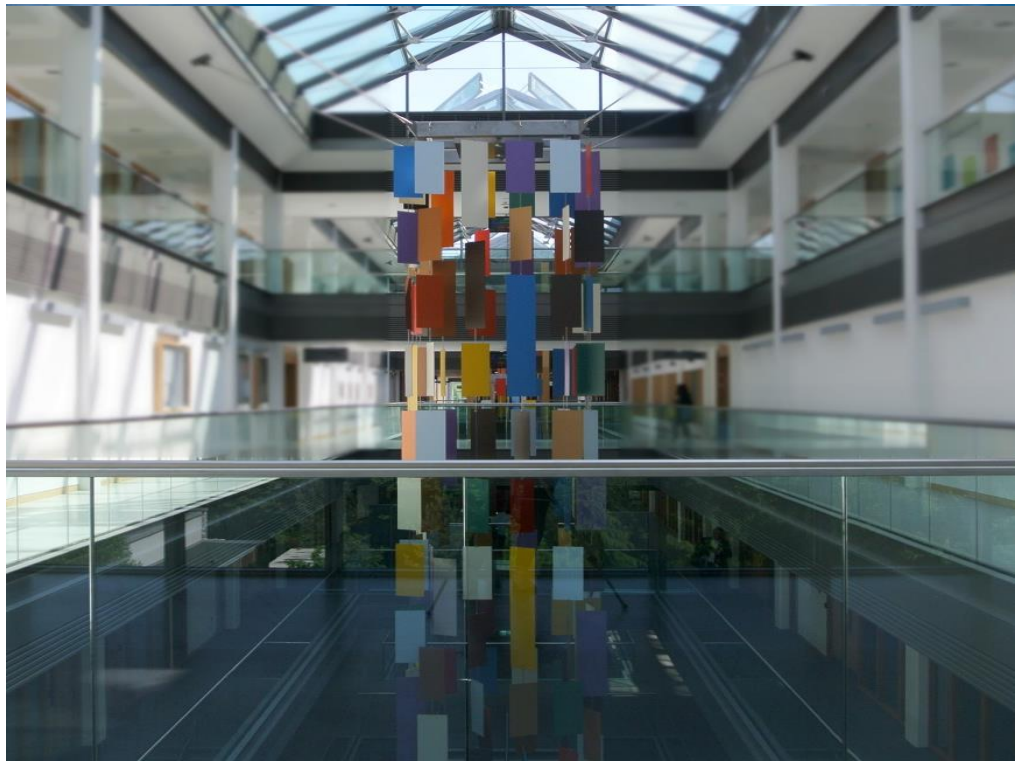
Patricia Kearney (University College Cork)

8 September 2021

On behalf of the HRB Trials Methodology Research Network

For any queries, please contact uktmn@nottingham.ac.uk

https://www.youtube.com/watch?v=KZbdAyTq_dI



SPIRIT-ROUTINE: Developing a SPIRIT extension for trials conducted using cohorts and routinely collected data

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A TRADITION OF INDEPENDENT THINKING

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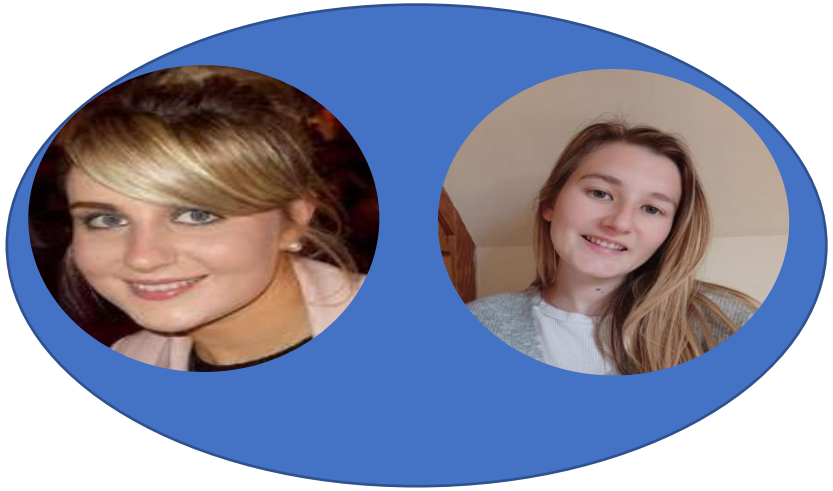
SPIRIT-ROUTINE Team
















(SPIRIT) Standard Protocol Items: Recommendations for Clinical Trials guidelines

- Information in clinical trial protocols may be incomplete or inadequate

- In 2007, an international group of stakeholders (the SPIRIT Group) launched the SPIRIT initiative to help improve the completeness and quality of trial protocols

https://www.spirit-statement.org/

SPIRIT guidance has been instrumental in promoting transparent evaluation of new interventions

RESEARCH METHODS AND REPORTING

SPIRIT 2013 explanation and elaboration: guidance for protocols of clinical trials

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High quality protocols facilitate proper conduct, reporting, and external review of clinical trials. However, the completeness of trial protocols is often inadequate. To help improve the content and quality of protocols, an international group of stakeholders developed the SPIRIT 2013 Statement (Standard Protocol Items: Recommendations for Interventional Trials). The SPIRIT Statement provides guidance in the form of a checklist of recommended items to include in a clinical trial protocol.

This SPIRIT 2013 Explanation and Elaboration paper provides important information to promote full understanding of the checklist recommendations. For each checklist item, we provide a rationale and detailed description; a model example from an actual protocol; and relevant references supporting its importance. We strongly recommend that this explanatory paper be used in conjunction with the SPIRIT Statement. A website of resources is also available (www.spirit-statement.org).

The SPIRIT 2013 Explanation and Elaboration paper, together with the Statement, should help with the drafting of trial protocols. Complete documentation of key trial elements can facilitate transparency and protocol review for the benefit of all stakeholders.

Every clinical trial should be based on a protocol—a document that details the study rationale, proposed methods, organisation, and ethical considerations.[1] Trial investigators and staff use protocols to document plans for study conduct at all stages from participant recruitment to results dissemination. Funding agencies, research ethics committees/institutional review boards, regulatory agencies, medical journals, systematic reviewers, and other groups rely on protocols to appraise the conduct and reporting of clinical trials.

To meet the needs of these diverse stakeholders, protocols should adequately address key trial elements. However, protocols often lack information on important concepts relating to study design and dissemination plans.[2-12] Guidelines for writing protocols can help improve their completeness, but existing guidelines vary extensively in their content and have limitations, including non-systematic methods of development, limited stakeholder involvement, and lack of citation of empirical evidence to support their recommendations.[13] As a result, there is also variation in the precise definition and scope of a trial protocol, particularly in terms of its relation to other documents such as procedure manuals.[14]

Given the importance of trial protocols, an international group of stakeholders launched the SPIRIT (Standard Protocol Items: Recommendations for Interventional Trials) Initiative in 2007 with the primary aim of improving the content of trial protocols. The main outputs are the SPIRIT 2013 Statement,[14] consisting of a 33 item checklist of minimum recommended protocol items (table 1) plus a diagram (fig 1); and this accompanying Explanation and Elaboration (E&E) paper. Additional information and resources are also available on the SPIRIT website (www.spirit-statement.org).

The SPIRIT 2013 Statement and E&E paper reflect the collaboration and input of 115 contributors, including trial investigators, healthcare professionals, methodologists, statisticians, trial coordinators, journal editors, as well as representatives from research ethics committees, industry and non-industry funders, and regulatory agencies. Details of the scope and methods have been published elsewhere.[13-15] Briefly, three complementary methods were specified beforehand, in line with current recommendations for development of reporting guidelines[16]: 1) a Delphi consensus survey[15]; 2) two systematic reviews to identify existing protocol guidelines and empirical evidence supporting the importance of specific checklist items; and 3) two face-to-face consensus meetings to finalise the SPIRIT 2013 checklist. Furthermore, the checklist was pilot tested by graduate course students, and an implementation strategy was developed at a stakeholder meeting.

The SPIRIT recommendations are intended as a guide for those preparing the full protocol for a clinical trial. A clinical trial is a prospective study in which one or more

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ESPRIT Evidence to Support Prevention Implementation & Translation

SPIRIT Extensions

SPIRIT-PRO: Calvert M, Kyte D, Mercieca-Bebber R, Slade A, Chan A-W, King MT; and the SPIRIT-PRO Group. Guidelines for Inclusion of **Patient-Reported Outcomes** in Clinical Trial Protocols: The **SPIRIT-PRO** Extension. JAMA. 2018;319(5):483-494.

SPIRIT-TCM: Dai L, Cheng CW, Tian R, Zhong LL, Li YP, Lyu AP, Chan AW, Shang HC, Bian ZX. Standard Protocol Items for Clinical Trials with **Traditional Chinese Medicine** 2018: Recommendations, Explanation and Elaboration (**SPIRIT-TCM** Extension 2018). Chin J Integr Med. 2019;25(1):71-79. PMID: 30484022

SPENT 2019: Porcino AJ, Shamseer L, Chan A-W, Kravitz RL, Orkin A, Punja S, Ravaud P, Schmid CH, Vohra S; on behalf of the SPENT group. SPIRIT extension and elaboration for **n-of-1 trials**: **SPENT 2019** checklist. BMJ 2020; 368.

SPIRIT-AI: Rivera SC, Liu X, Chan A-W, Denniston AK, Calvert MJ; on behalf of the SPIRIT-AI and CONSORT-AI Working Group. Guidelines for clinical trial protocols for **interventions involving artificial intelligence**: the **SPIRIT-AI** Extension. BMJ. 2020;370:m3210. PMID: 32907797 Nat Med. 2020;26(9):1351–1363. PMID: 32908284 Lancet Digital Health. 2020;2(10):e549-e560. PMID: 33328049

SPIRIT - Routine

- Trials are expensive and complex
  - Increasing interest in use of Routinely Collected Data (RCD) in trials
    - ✓ Improve participant recruitment
    - ✓ Improve generalisability of findings
    - ✓ Simplify assessment of outcome measures

Aim

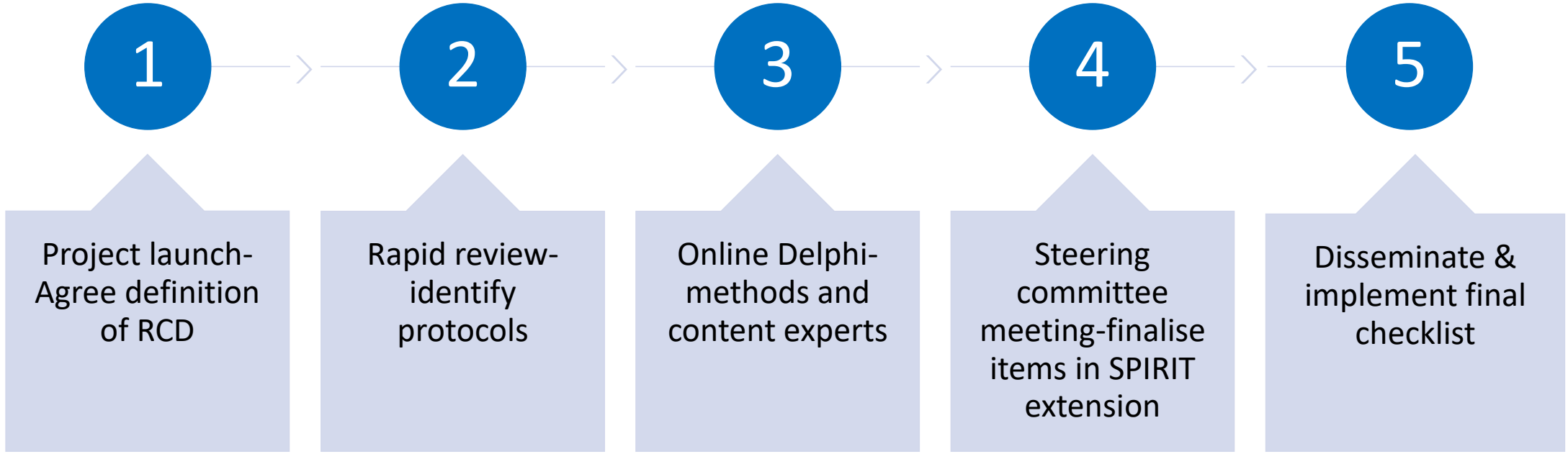
- Develop, test, and disseminate an extension of the SPIRIT reporting guidelines for the minimum content of clinical trial protocols for trials using Routinely Collected Data

This project is complete, well described and proposed appropriate methods to achieve research goal.

but we deplore the absence of PPI, as it was requested.

No early career individuals specified which is a shame as developing guidance is a great skill for an ECR to adopt.

SPIRIT – Routine Process



Project Launch

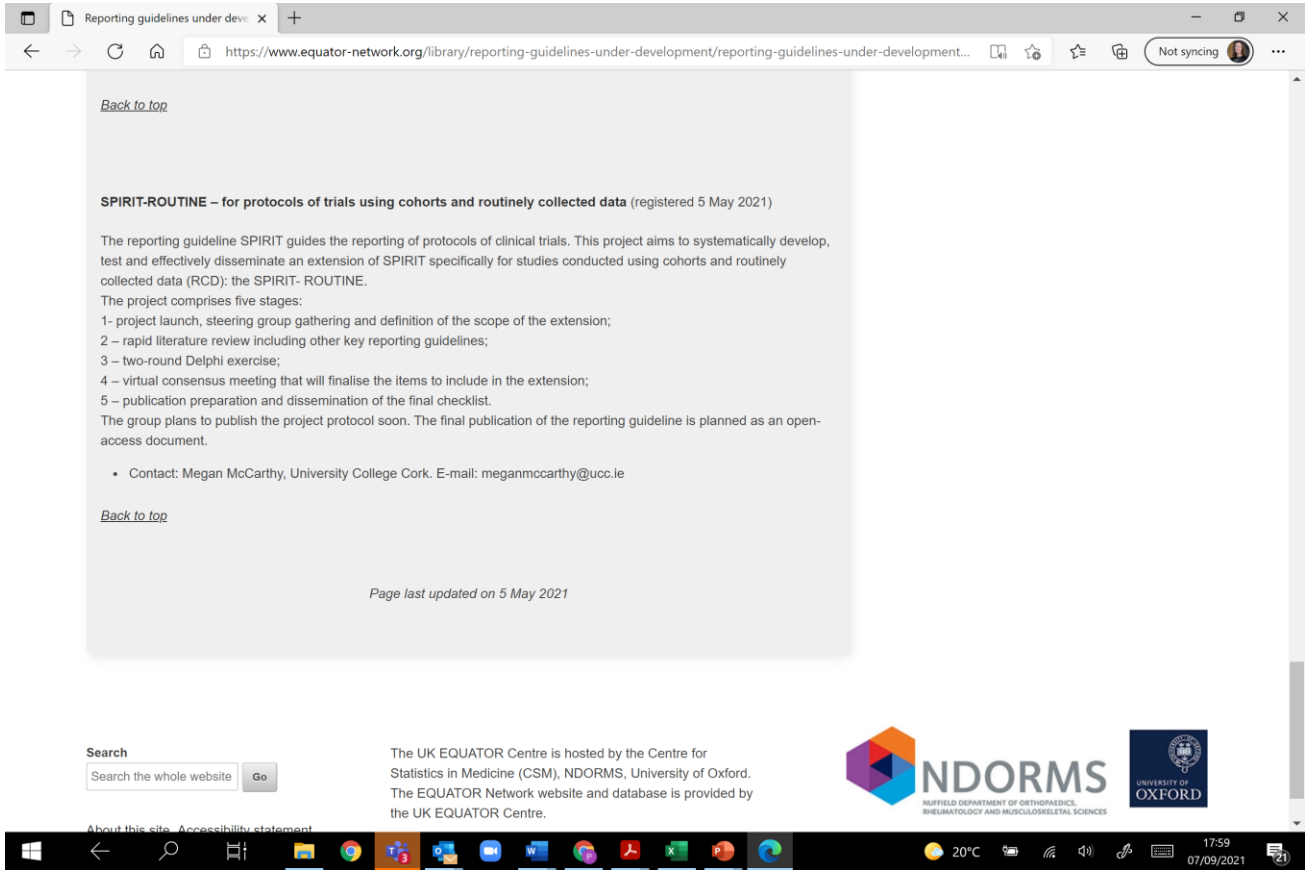
- A project operational team and a study steering committee was established to deliver the project aims

Linda O'Keeffe
Megan McCarthy
Matthew Sydes
Paula Williamson
Amanda Farrin
An-Wen Chan
Fiona Lugg-Widger
Brett Thombs
Gwyneth Davies
Linda Kwakkenbos

David Moher
Kerry Avery
Alan Watkins
Lars Hemkens
Chris Gale
Merrick Zwarenstein
Sinead Langan
Edmund Juszczak
Lehana Thabane

EQUATOR Registration

- Registration of SPIRIT-ROUTINE with Enhancing the QUAlity and Transparency Of health Research (EQUATOR) library of reporting guidelines



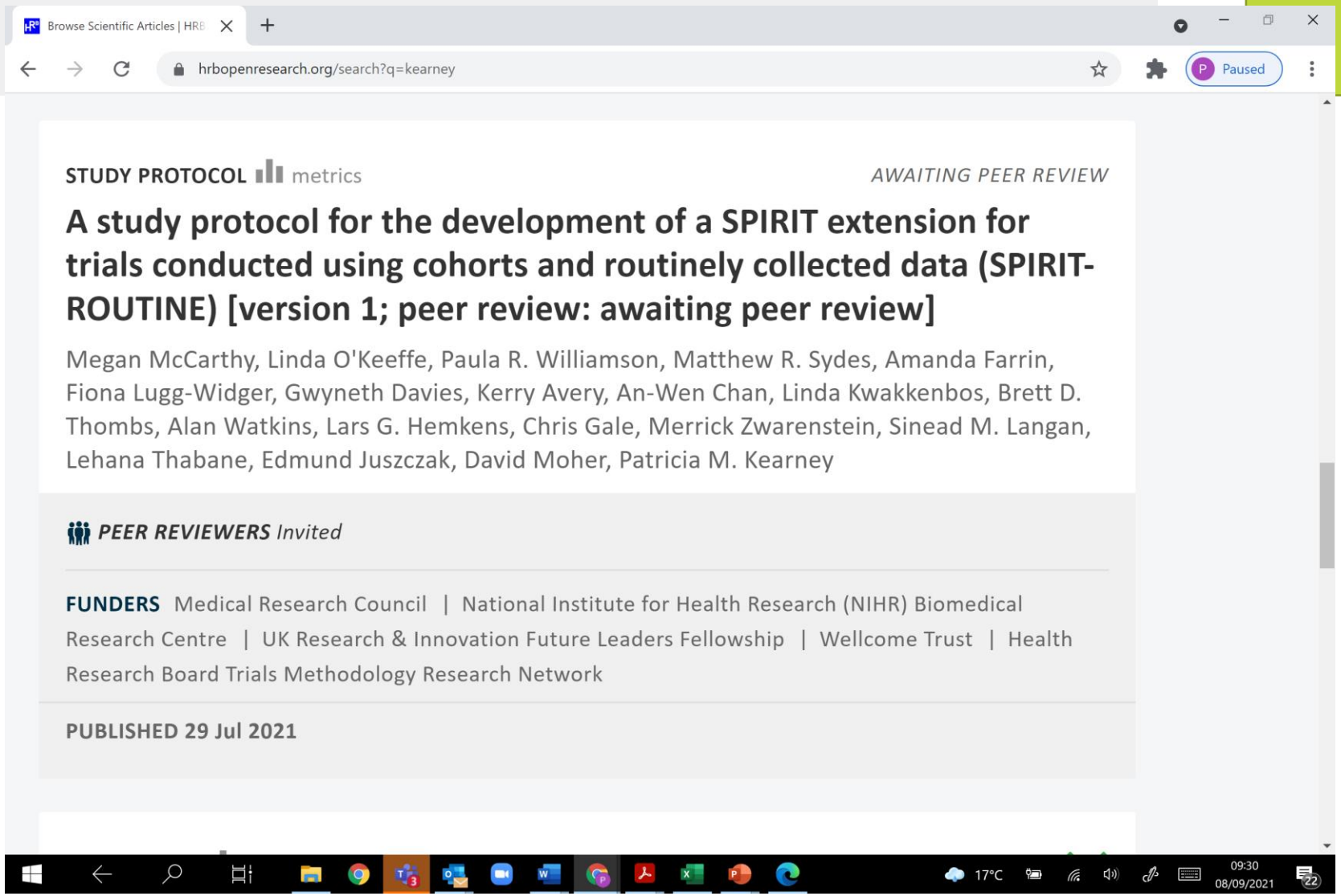
Agreement on Scope of the Extension

- Specified and agreed consensus definition of Routinely Collected Data in trials:

Routinely collected data (RCD) refers to data collected for purposes other than research

Stage 1

- Publication of study protocol in HRB Open Research



Rapid Review

- A search of the US National Library of Medicine's clinical trial registry (ClinicalTrials.gov) was undertaken to find trial protocols using cohorts and RCD in Canada and the US (National Institute of Health (NIH) funded US trials)
- A similar search of the National Institutes of National Institutes of Health Research (NIHR) journals library in the UK was also undertaken
- *Inclusion criteria:*

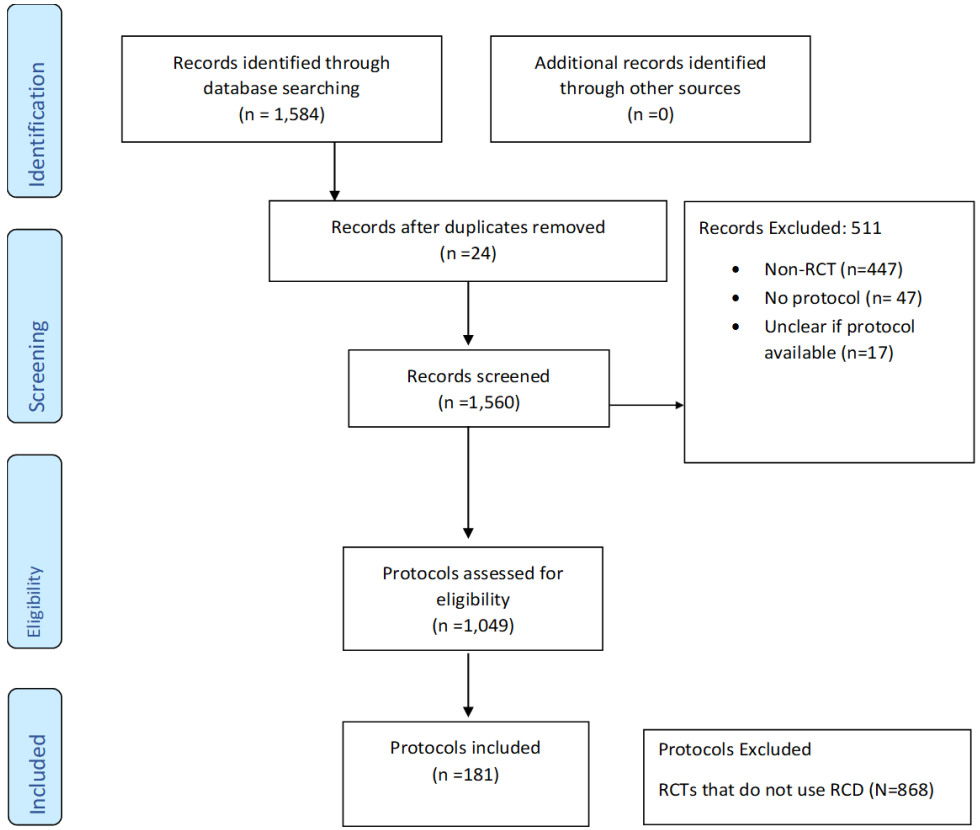
✓ RCT of any type

✓ use of cohorts and RCD; and

✓ availability of a protocol

- Search results were individually downloaded into the citation management database Mendeley, and duplicates were removed.

Rapid Review



Potential new items/modifications

- Trial protocols that described aspects of methods or reporting of trials conducted using cohorts or RCD, were examined
- Areas of trial design considered important to report identified
- Potential items applicable to trials using cohorts or RCD which clarified or altered an existing SPIRIT 2013 item (**modifications**)
- Preliminary 'long list' of possible **new reporting items** was also formulated based on review of the SPIRIT 2013 statement items and the CONSORT-ROUTINE items

Potential new items/modifications

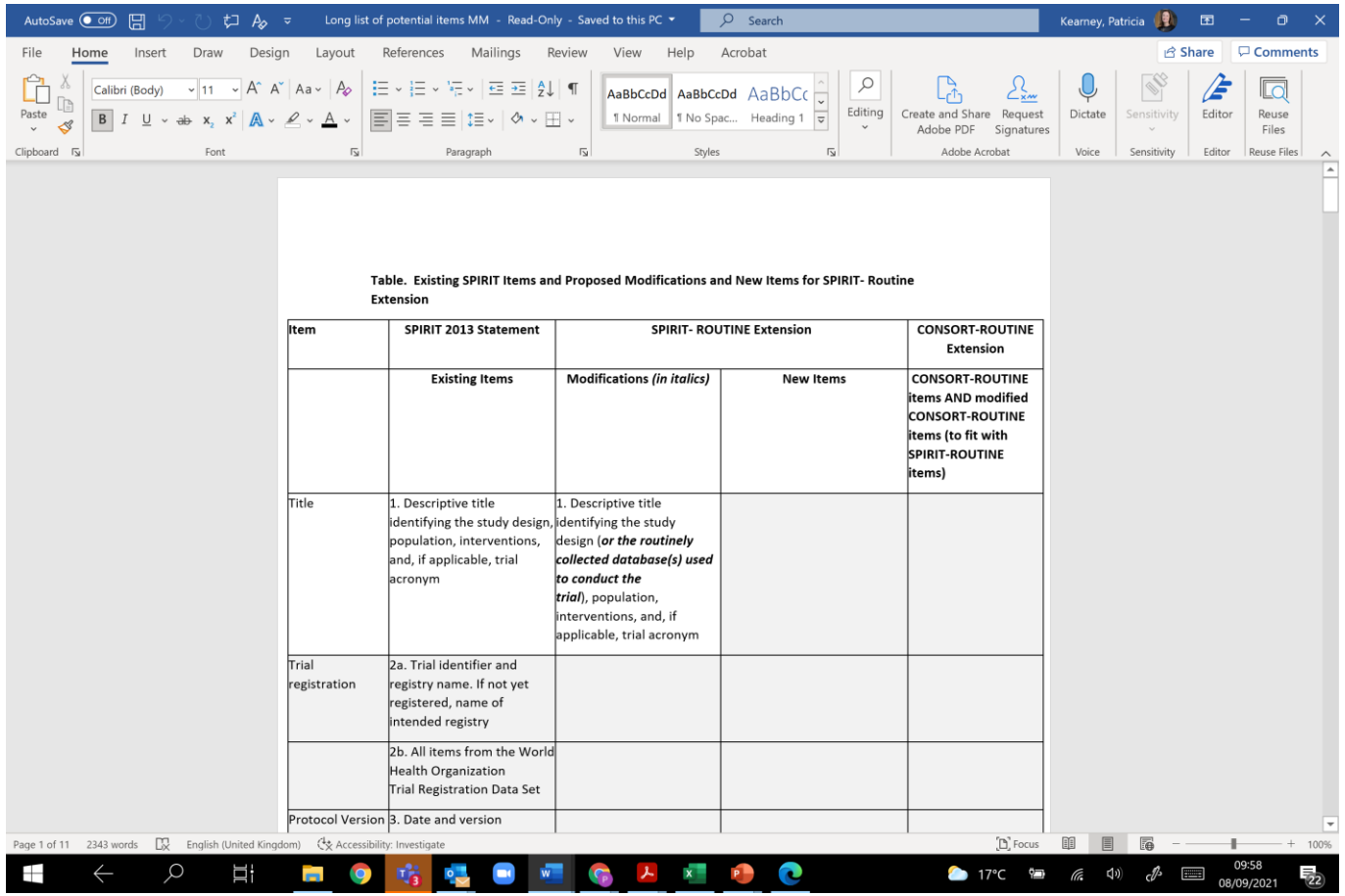


Table. Existing SPIRIT Items and Proposed Modifications and New Items for SPIRIT- Routine Extension

Item	SPIRIT 2013 Statement	SPIRIT- ROUTINE Extension		CONSORT-ROUTINE Extension
	Existing Items	Modifications *(in italics)*	New Items	CONSORT-ROUTINE items AND modified CONSORT-ROUTINE items (to fit with SPIRIT-ROUTINE items)
Title	1. Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1. Descriptive title identifying the study design (***or the routinely collected database(s) used to conduct the trial***), population, interventions, and, if applicable, trial acronym		
Trial registration	2a. Trial identifier and registry name. If not yet registered, name of intended registry			
	2b. All items from the World Health Organization Trial Registration Data Set			
Protocol Version	3. Date and version			

Delphi

- Evaluate the list of items for consideration to be included in the SPIRIT-ROUTINE extension
- Identify additional items that may not have been identified in the review

- COMET DelphiManager software
- Participants: clinical trialists, trial methodologists, guideline experts, TMRN members and PPI contributors
- Rate items based on how valuable they are for the reporting of trial protocols on a Likert scale of 1–9:
  - 1- 3= 'not critical' (items should not be part of the SPIRIT-ROUTINE extension checklist)
  - 4–6= 'no consensus' (items should be discussed)
  - 7–9 = 'critical to include' (item should be part of SPIRIT-ROUTINE extension checklist)

Consensus Meeting

- Presentation of items by individuals with expertise, followed by a discussion
- The items in the Delphi survey which reached consensus will be discussed, followed by any possible objections
- Outstanding items will be examined, and meeting participants will be provided with the opportunity to discuss each item
- Participants will be provided with the opportunity to discuss any items excluded during the Delphi process and will be able to propose better explanations of any excluded items
- Items with >75% or more of voters voting for its inclusion will be retained.

Dissemination and Knowledge translation

Strategies for knowledge translation will include:

1. Publication of the SPIRIT-ROUTINE extension in journals
2. Dissemination via the SPIRIT group and EQUATOR network, including publication on their websites
3. Presentations at conferences (e.g. submission to ICTMC 2022) and focused workshops on trials embedded in existing data sources
4. Dissemination via the TMRN and TMRP with delivery of a Clinical Research Facility-Cork (CRF C/TMRN) webinar on the process of the development of a SPIRIT extension
5. Dissemination will include presentation at the HRB-TMRN webinar and through relevant social media channels such as Twitter and YouTube

SPIRIT Routine

- Valuable to researchers who are planning to design a study using RCD
- May optimize the use of RCD in clinical trials
- Standardise what is expected in protocols of clinical trials using RCD
- Improve access to trial data and efficiency of data access Help improve the transparency and quality of clinical trial protocols and reports of trials using RCD

SPIRIT Routine

- This SPIRIT-ROUTINE extension for trials conducted using cohorts and RCD aims to promote transparency and clarity and to reduce research waste due to inadequate reporting
- Consistent with the recently developed CONSORT extension for trials conducted using cohorts and RCD, this SPIRIT extension is being carried out with the long-term goal of improving the quality of reporting by establishing standards early in the process of uptake of these trial designs

References

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5. Benchimol EI, Smeeth L, Guttmann A, et al.: The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) statement. PLoS Med. 2015; **12**(10): e1001885

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Thank You!

Any Questions?

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