

SPIRIT-PRO Checklist

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ANZGOG ASM 2019

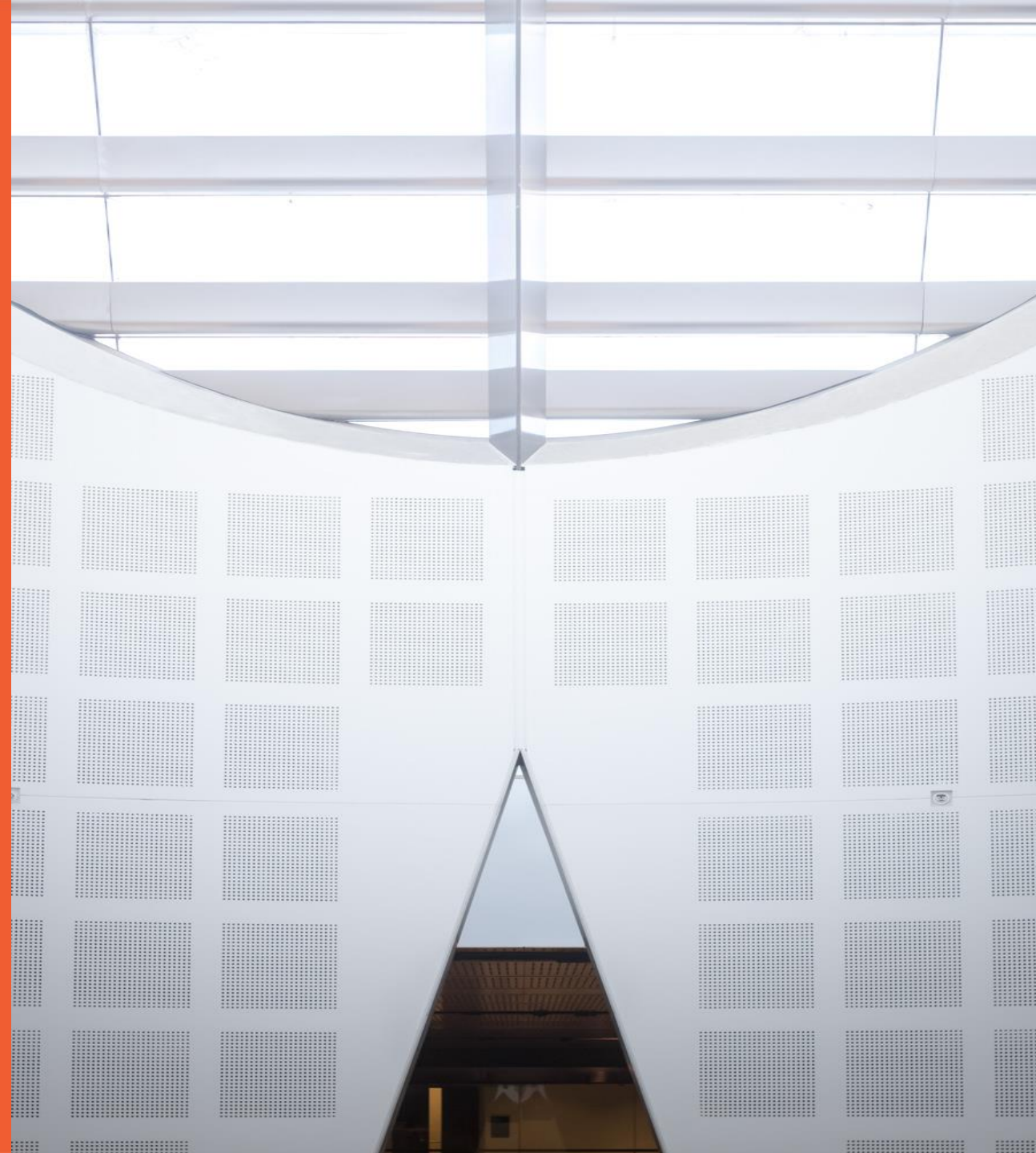


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CA QOL Technical Services @ University of Sydney QOL Office



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- ***Our mission:*** to facilitate the inclusion of health related quality of life (HRQOL) and patient reported outcome (PRO) measures/ sub-studies into cancer clinical trials developed by the CTGs
- Provide specialist advice and training to CTGs
 - HRQOL/PRO study design + collection, analysis, interpretation and reporting of HRQOL/PRO data
 - world-class best practice in PRO research from protocols to papers
- QOL Office – ad hoc advice, online resources, education, mentoring

SPIRIT-PRO Checklist

Standardised Protocol Items for
Randomised Intervention Trials –
Patient-Reported Outcomes

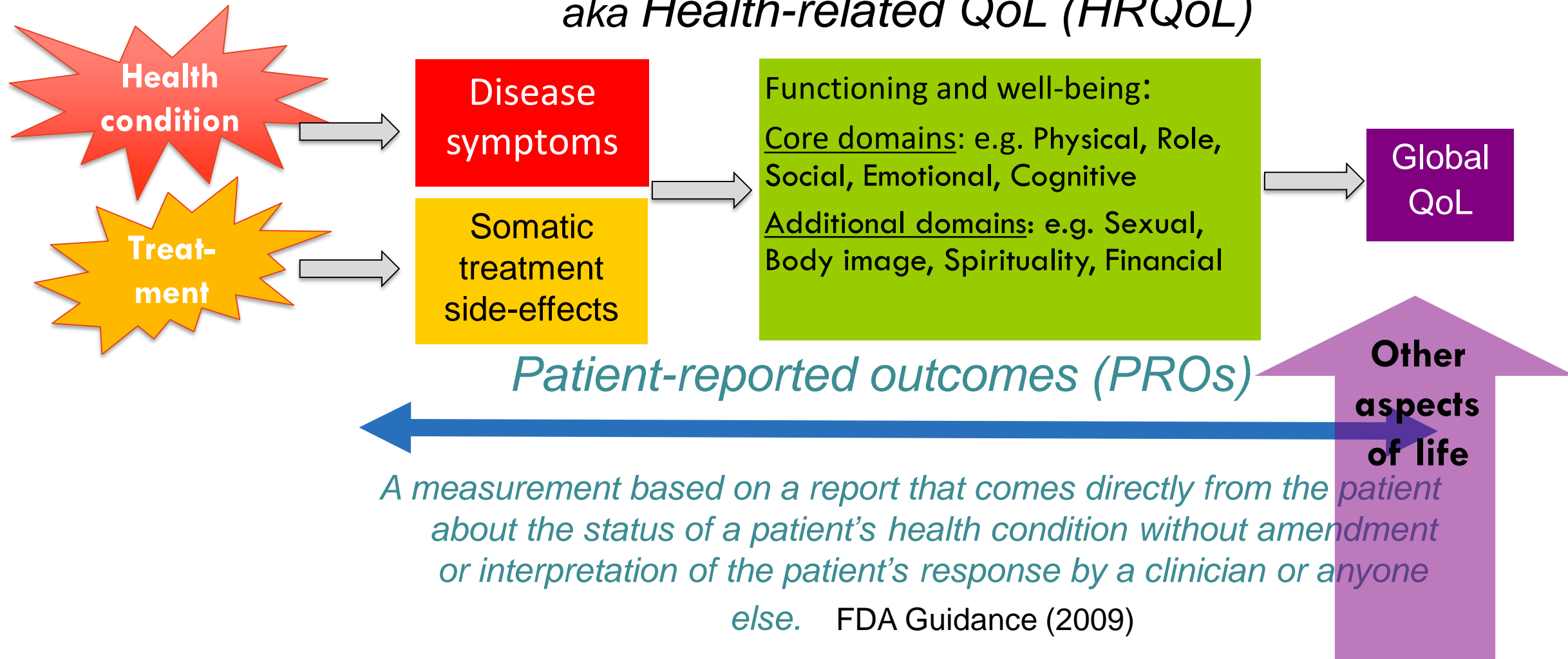
Outline

- Terminology: HRQOL v PROs
- Importance of the protocol
- Why we need guidance - what to include about PROs
- SPIRIT-PRO

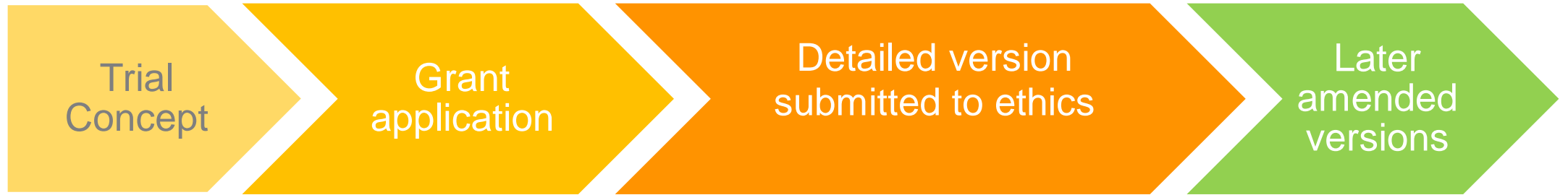
What are we talking about? QoL v HRQoL v PROs

All of these things together = Quality of Life (QoL)

aka Health-related QoL (HRQoL)



Evolution from trial concept to full protocol



+ other trial documents: participant information sheets/consent forms, site manuals, Standard Operating Procedures (SOPs), statistical analysis plan (SAP)

ANZGOG's Concept Development Form thankyou Paul Cohen ☺

Sections

- Background & significance
 - Summary (incl hypotheses, objective & endpoints)
 - Subject Population
 - Study Procedures
 - Statistical Considerations
 - Feasibility
 - Biospecimen Collection /Translational Research
- ## Quality of Life Assessment
- Health Economics
 - Funding
 - Drugs and sponsorship
 - Lay summary for consumer review (250 words)
 - List of other collaborative trial groups involved
 - Protocol (Y/N, ANZGOG assistance required?)
 - ANZGOG involvement requested?
 - Study chair, investigators, institutions

Concept Development Form

Please ensure that your concept addresses the majority of points noted in the Concept Development Form below. A checklist is provided below to aid investigators in preparing their concept for submission to ANZGOG.

Concepts are reviewed by the Research Advisory Committee, consumers and our collaborative partners, NHMRC CTC.

Email to: concepts@anzgog.org.au

Date of submission:

January 14th 2019



Concept Title	Getting the MOST out of follow-up: a randomised controlled trial to compare three-monthly nurse-led telephone follow-up, including monitoring serum CA125 and patient reported outcomes using the MOST (Measure of Ovarian Symptoms and Treatment concerns) with routine clinic-based follow-up, following completion of first-line chemotherapy in patients with advanced epithelial ovarian cancer. <i>Short Title: The MOST questionnaire in Ovarian cancer Survivors undergoing nurse-led Telephone follow-up</i>
Study Phase	<input type="checkbox"/> Phase I <input checked="" type="checkbox"/> Phase II <input type="checkbox"/> Phase III <input type="checkbox"/> Other
Cancer Type	<input checked="" type="checkbox"/> Ovarian <input type="checkbox"/> Cervical <input type="checkbox"/> Endometrial <input type="checkbox"/> Other
Background and Significance	<p>In 2018 an estimated 1613 women in Australia will be diagnosed with ovarian cancer (OC) and less than half will survive 5 years.¹ Almost 4000 Australian women are living with OC, 29% of whom live in regional and remote locations and 40% of whom are greater than 70 years of age.²</p> <p>Most patients are diagnosed with advanced disease and the majority will recur within 24 months following completion of 1st line treatment. Routine OC follow-up comprises 3 monthly clinic visits in oncology and gynaecology clinics and involves a blood test to measure serum CA125, and a history and physical examination by a doctor. On average the consultation takes 10-15 minutes and a different doctor may see patients at each</p>

13 pages

Example protocol: OUTBACK PI Linda Mileschkin

ANZGOG 0902: A Phase III trial of adjuvant chemotherapy following chemoradiation as primary treatment for locally advanced cervical cancer compared to chemoradiation alone

- Protocol 77 pages
- 4 pages about PROs (secondary endpoints)

A Phase III trial of adjuvant chemotherapy following chemoradiation as primary treatment for locally advanced cervical cancer compared to chemoradiation alone: THE OUTBACK TRIAL (ANZGOG 0902)

Version 3.0, dated 27 September 2010

Principal Investigator: Dr Linda Mileschkin
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Lead Radiation Oncologist: Associate Professor Kailash Narayan
Peter MacCallum Cancer Centre (as above)

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Study Statistician: Professor Val Gebski
NHMRC Clinical Trials Centre
Locked Bag 77
Camperdown NSW 1450, Australia

Lead Collaborative Group: ANZGOG: This is an independent multi-centre investigator-initiated study conducted under the auspices of ANZGOG.

Coordinating Centre: NHMRC Clinical Trials Centre
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Participating Collaborative Groups: GOG (USA), RTOG (USA), NCIC CTG (Canada), GEICO (Spain) NSGO (Norway, Sweden, Finland, Denmark)

Other participating countries: India, Romania, Brazil

The OUTBACK Trial

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The OUTBACK Trial

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Version 3.0, 27 September 2010

The OUTBACK Trial

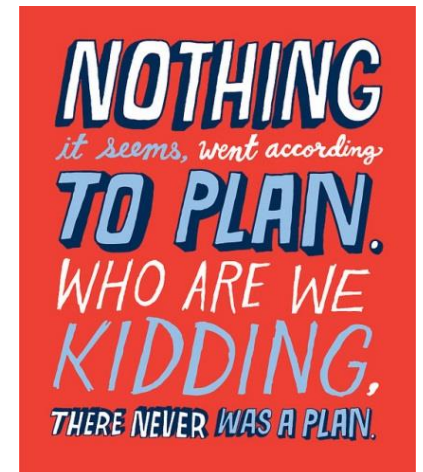
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Importance of the protocol

- Procedures for good conduct of the trial
 - sufficient detail to enable scientific/ethics committees & peers to appraise the trial's scientific, methodological and ethical rigor and for the research team to deliver a high quality study
 - all relevant requirements so the study can be implemented uniformly by all sites and staff
 - success or failure of a trial may depend on how well the protocol was designed and written
 - detailed and clearly worded
- These general points apply just as much to PRO assessment to any other aspect of a trial

Chan et al., 2013 – SPIRIT
Gotay et al., 1992



Guidance for protocol writers

RESEARCH AND REPORTING METHODS

Annals of Internal Medicine

SPIRIT 2013 Statement: Defining Standard Protocol Items for Clinical Trials

An-Wen Chan, MD, DPhil; Jennifer M. Tetzlaff, MSc; Douglas G. Altman, DSc; Andre Karmela Krleža-Jerić, MD, DSc; Asbjørn Hróbjartsson, PhD; Howard Mann, MD; Kay I Caroline J. Doré, BSc; Wendy R. Parulekar, MD; William S.M. Summerskill, MBBS; Tri Harold C. Sox, MD; Frank W. Rockhold, PhD; Drummond Rennie, MD; and David Mo

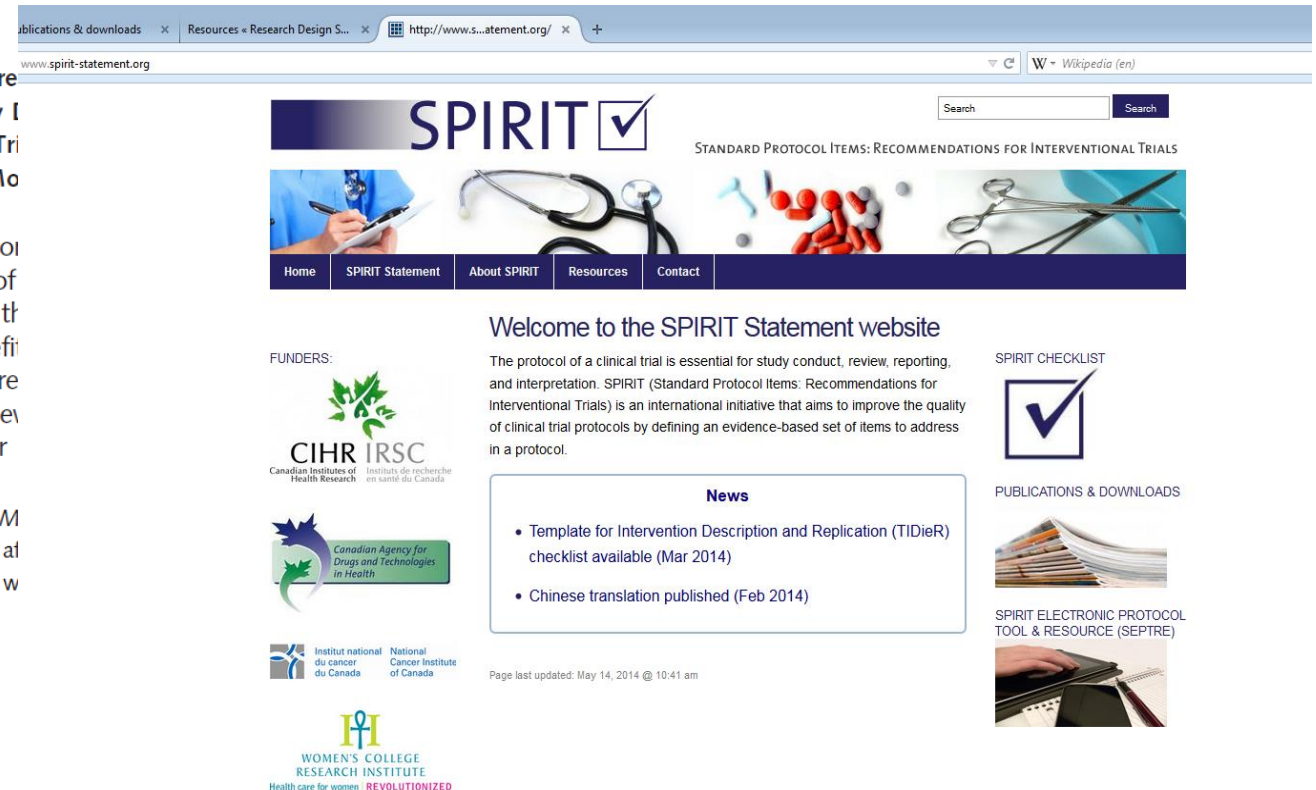
The protocol of a clinical trial serves as the foundation for study planning, conduct, reporting, and appraisal. However, trial protocols and existing protocol guidelines vary greatly in content and quality. This article describes the systematic development and scope of SPIRIT (Standard Protocol Items: Recommendations for Interventional Trials) 2013, a guideline for the minimum content of a clinical trial protocol.

The 33-item SPIRIT checklist applies to protocols for all clinical trials and focuses on content rather than format. The checklist recommends a full description of what is planned; it does not prescribe how to design or conduct a trial. By providing guidance

for key components of drafting of protocols to enhance the benefit to trial funders, researchers, peer reviewers, and other

Ann Intern Med
For author information
This article was

<http://www.spirit-statement.org/>



The screenshot shows the SPIRIT Statement website. At the top, there's a navigation bar with links for 'Publications & downloads', 'Resources', and 'Research Design'. The main header features the SPIRIT logo with a checkmark and the tagline 'STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS'. Below the header is a navigation menu with links for 'Home', 'SPIRIT Statement', 'About SPIRIT', 'Resources', and 'Contact'. The main content area includes a 'Welcome to the SPIRIT Statement website' section, a 'FUNDERS' section listing CIHR IRSC, the Canadian Agency for Drugs and Technologies in Health, and the National Cancer Institute of Canada, and a 'News' section with two items: 'Template for Intervention Description and Replication (TIDieR) checklist available (Mar 2014)' and 'Chinese translation published (Feb 2014)'. On the right side, there's a 'SPIRIT CHECKLIST' section with a checkmark icon and a 'PUBLICATIONS & DOWNLOADS' section with a stack of papers icon. The footer includes the 'WOMEN'S COLLEGE RESEARCH INSTITUTE' logo and the text 'Health care for women | REVOLUTIONIZED'.

Why do we need a SPIRIT-PRO Extension?

- Protocols can lack key PRO content (Kyte et al 2013, Mercieca-Bebber et al 2016a)
 - PRO data quality may be affected
- Reporting is suboptimal viz CONSORT-PRO (e.g. Mercieca-Bebber 2016b, Mercieca-Bebber 2017a, Mercieca-Bebber 2017b, Brundage 2011, Bylicki 2014, Efficace 2015, Efficace 2014, Joly 2007, Mack 2018)
 - Hinders/prevents uptake in clinical practice
- SPIRIT 2013 does not provide PRO-specific guidance

Inclusion of PROs in a protocol

What to include

- Why and how PROs will be assessed
 - Mixture of science and logistics

Why to include

- How well the PRO assessment methods are planned and described in the protocol will be a major determinant of the quality of PRO data, and the evidence/papers arising
- Recruiting staff & sites will be convinced PROs are important, worth the effort

SPIRIT-PRO Checklist

editable version available on QOL Office Website

<http://www.pocog.org.au/qoloffice>

JAMA | Special Communication

Guidelines for Inclusion of Patient-Reported Outcomes in Clinical Trial Protocols The SPIRIT-PRO Extension

Melanie Calvert, PhD; Derek Kyte, PhD; Rebecca Mercieca-Bebber, PhD; Anita Slade, PhD;
An-Wen Chan, MD, DPhil; Madeleine T. King, PhD; and the SPIRIT-PRO Group

Calvert et al, JAMA 2018

SPIRIT-PRO Checklist, 16 items

Minimum standards, whether PROs are primary or secondary endpoints

ADMIN

1. Person responsible for the PRO content of the trial protocol

INTRO

2. Background and rationale - summarize PRO findings in relevant studies
3. State specific PRO objectives or hypotheses (including relevant PRO concepts/domains)

METHODS

4. Eligibility criteria – for PRO substudy, e.g. language
5. Outcomes
 - Specify the PRO concepts/domains used to evaluate the intervention
e.g. overall HRQOL, specific domain(s), specific symptom(s)
 - analysis metric (eg, change from baseline, final value, time to event)
 - principal time point or period of interest.

SPIRIT-PRO Checklist, 16 items

Minimum standards, whether PROs are primary or secondary endpoints

METHODS (cont.)

6. Schedule of PRO assessments, rationale for the time points

7. Sample size

8. PRO questionnaires

- Justify choice
- Describe domains, number of items, recall period
- Scoring: range & direction of scores, e.g. high score = good/poor outcome
- Evidence of validity, reliability, interpretation guidelines
- Patient acceptability/burden
- Will q'aire be used in accordance with any user manual? If not, specify & justify planned deviations

9. data collection plan

- mode(s) of administration: paper, telephone, electronic, other
- setting: clinic, home, other

SPIRIT-PRO Checklist, 16 items

Minimum standards, whether PROs are primary or secondary endpoints

METHODS (cont.)

10. Language versions / translations
11. Proxy needed? If yes, justify & provide validity evidence
12. Data collection & management strategies to **minimise missing data**
13. Participants who discontinue or deviate from their assigned intervention protocol

STATISTICAL METHODS (outline, details in SAP)

14. plans for addressing multiplicity/type 1 (α) error
15. how will missing be described, methods for handling missing items, e.g. imputation, sensitivity analyses

MONITORING

16. Will PRO data be monitored during the study to inform the clinical care of individual trial participants?
 - how this will be managed in a standardized way?
 - how will this be explained to participants, eg, in the participant information sheet and consent form.

Workshops/Webinars on May 17th (at Syd Uni)

Two half-day workshops:

Workshop 1: Developing your protocol: what to include about PROs (including QOL) and why, how to use the **SPIRIT-PRO Checklist**

Intended for protocol developers (clinician researchers or TROG staff).

Workshop 2: Trial Conduct: Guidelines for PRO administration to optimise PRO data quality and avoid missing data.

Intended for clinical trials coordinators or TROG staff.



Ca Aust QOL Technical Services

University of Sydney QOL Office Resources

**Assistance with questionnaire
selection & protocol
development**

Educational Workshops

**QLQ v FACT
content
comparison
spreadsheets**

for each
cancer site
(available on
request)

**Statistical
analysis
position
paper**

FAQs
Various QOL
topics



Searchable database of 350+ Patient
Reported Outcome Measures (PROMs)

**Checklists: SPIRIT-PRO, Administration
of PRO Measures, CONSORT-PRO**

CoMiDa form

Form to record PRO form completion
rates & reasons for missing data

Suggested reading lists & useful links

Contact Us

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Website: <http://www.pocog.org.au/qoloffice>

Online queries: <https://goo.gl/wVyGRt>



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Dr. Rachel Campbell