# SPIRIT-PRO Checklist

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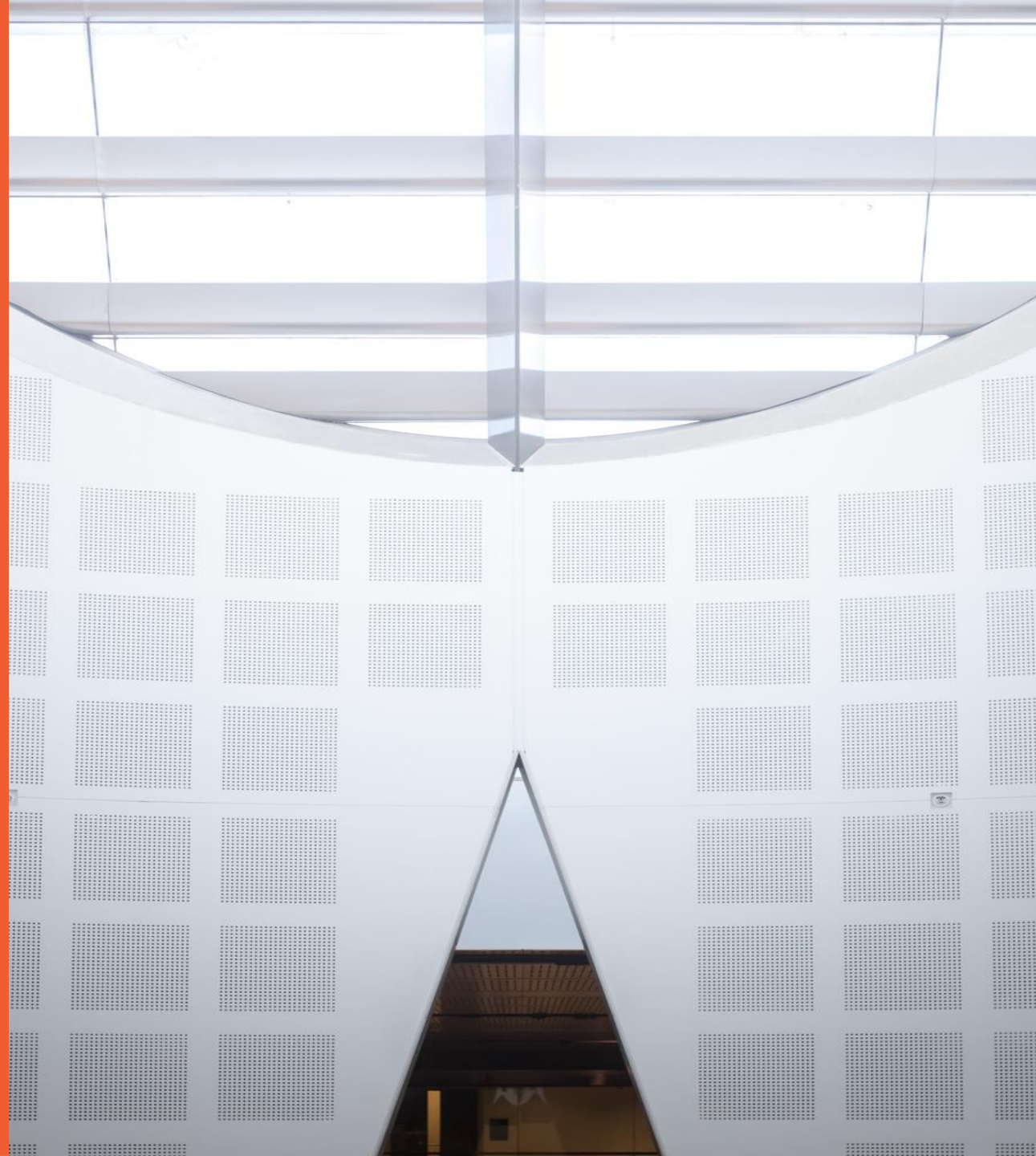
ANZGOG ASM 2019

THE UNIVERSITY OF SYDNEY

Australian Government

Cancer Australia



# CA QOL Technical Services @ University of Sydney QOL Office

- ***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

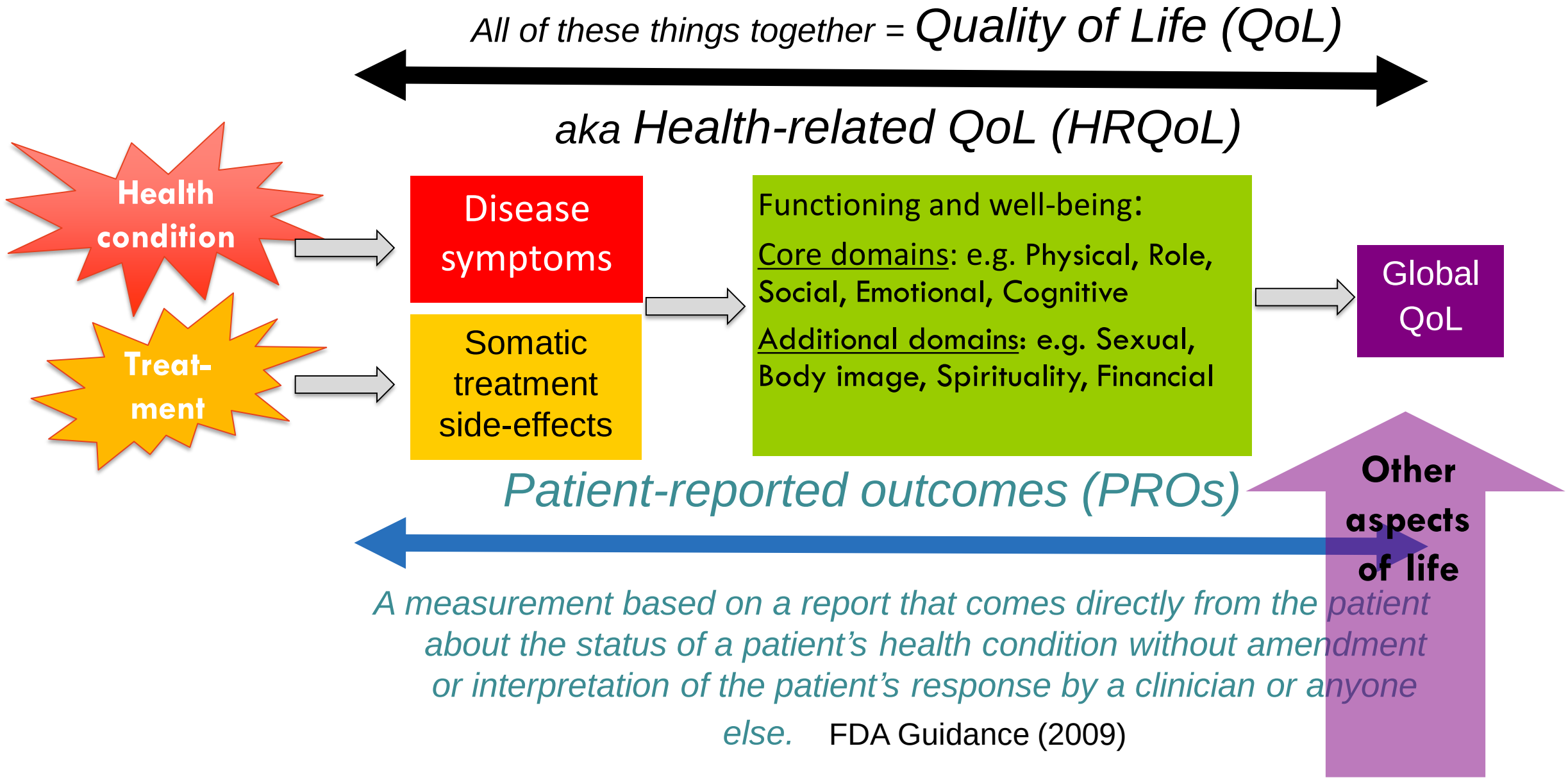
SPIRIT-PRO Checklist

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




*A measurement based on a report that comes directly from the patient about the status of a patient's health condition without amendment or interpretation of the patient's response by a clinician or anyone else.* FDA Guidance (2009)

# 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 Researc

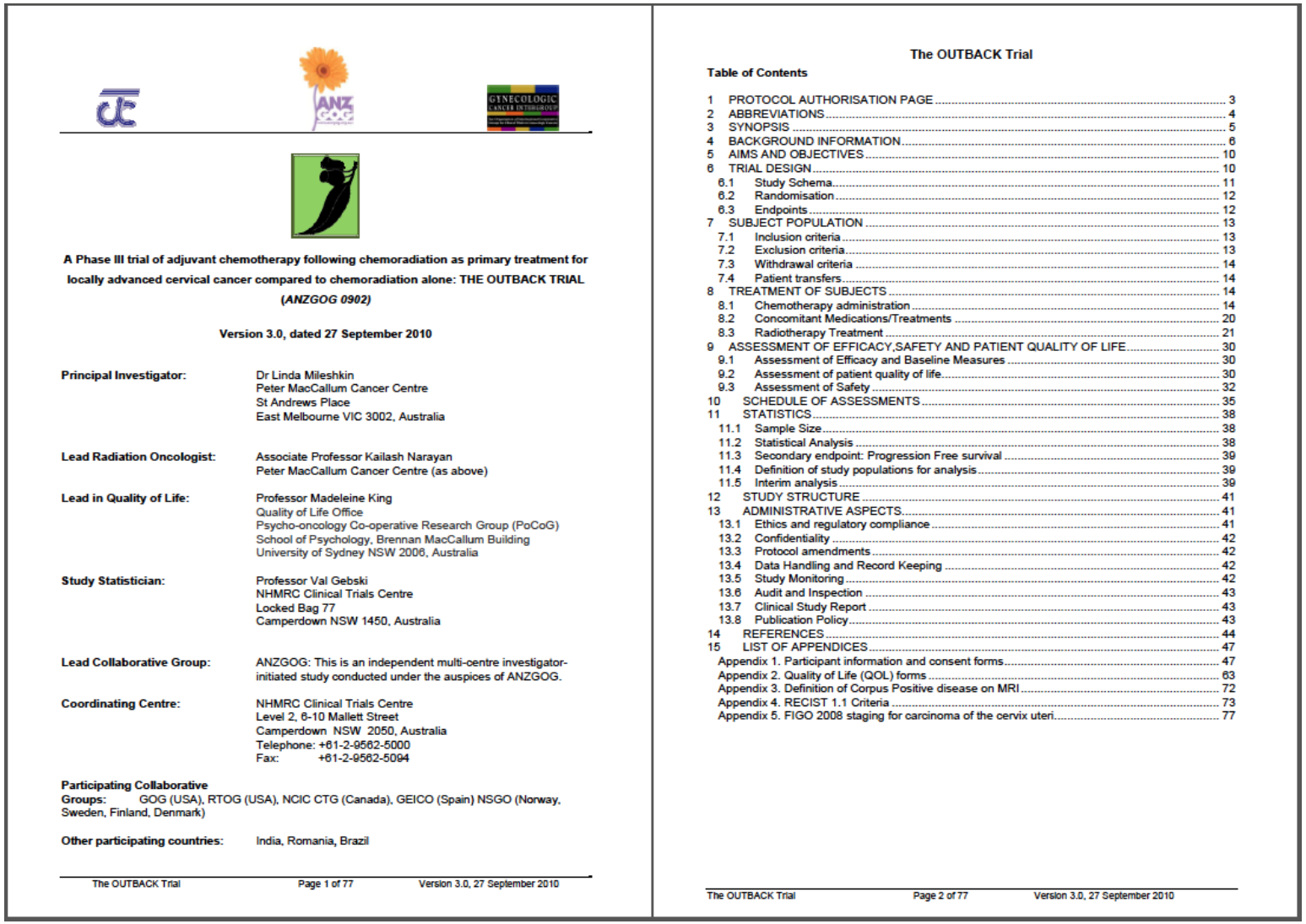
## Quality of Life Assessment

- 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

# *Example protocol:* OUTBACK PI Linda Mileshkin

**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 Mileshkin
Peter MacCallum Cancer Centre
St Andrews Place
East Melbourne VIC 3002, Australia

**Lead Radiation Oncologist:** Associate Professor Kailash Narayan
Peter MacCallum Cancer Centre (as above)

**Lead in Quality of Life:** Professor Madeleine King
Quality of Life Office
Psycho-oncology Co-operative Research Group (PoCoG)
School of Psychology, Brennan MacCallum Building
University of Sydney NSW 2006, Australia

**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
Level 2, 6-10 Mallett Street
Camperdown NSW 2050, Australia
Telephone: +61-2-9562-5000
Fax: +61-2-9562-5094

**Participating Collaborative Groups:** GOG (USA), RTOG (USA), NCIC CTG (Canada), GEICO (Spain) NSGO (Norway, Sweden, Finland, Denmark)

**Other participating countries:** India, Romania, Brazil



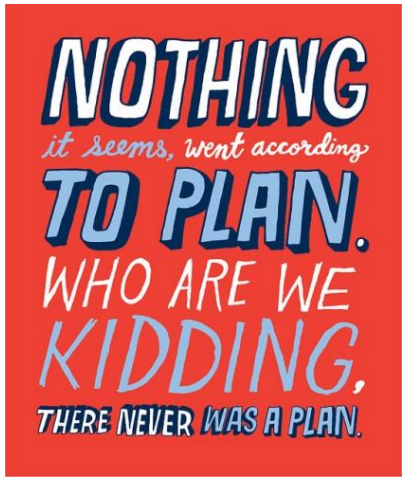
**The OUTBACK Trial**

**Table of Contents**

# 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 D
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 co
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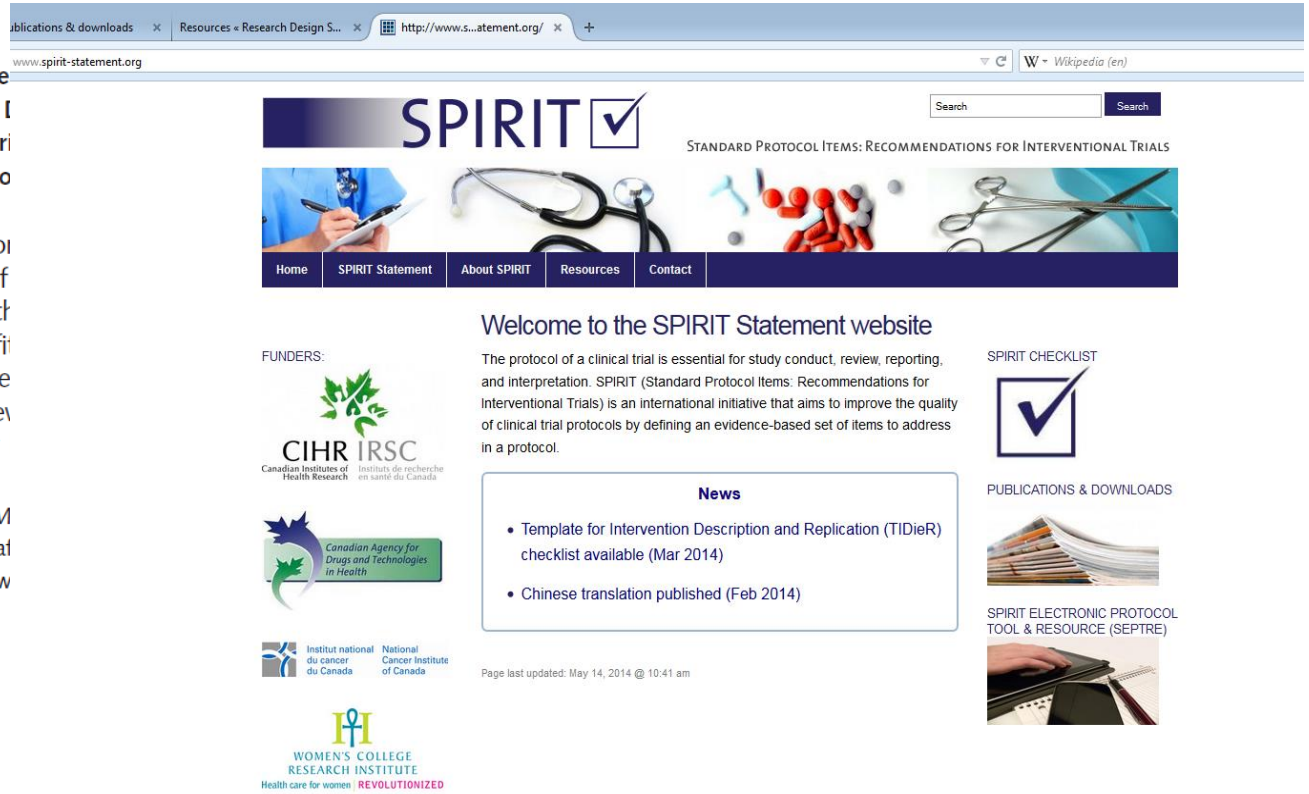


**http://www.spirit-statement.org/**

# 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

PoD
Psycho-oncology Outcomes Database

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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**Margaret Ann-Tait**

**Dr. Rachel Campbell**

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**Online queries:** https://goo.gl/wVyGRt