McMaster University

Family Medicine

David Braley Primary Care Research Collaborative

@McMasterFamMed

Accountability, Transparency, Rigour, and Reproducibility: How & Why to Use ClinicalTrials.gov and Research Reporting Guidelines

Watch a recording of the session here

Dee Mangin, Larkin Lamarche, Jessica Gaber

May 23rd, 2018

Michael G. DeGroote SCHOOL OF MEDICINE

McMaster University

Family Medicine

Accountability, Transparency, Rigour, and Reproducibility: How & Why to Use ClinicalTrials.gov and Research Reporting Guidelines

Wednesday May 23, 2018

Jessica Gaber, Dee Mangin, Larkin Lamarche

@McMasterFamMed

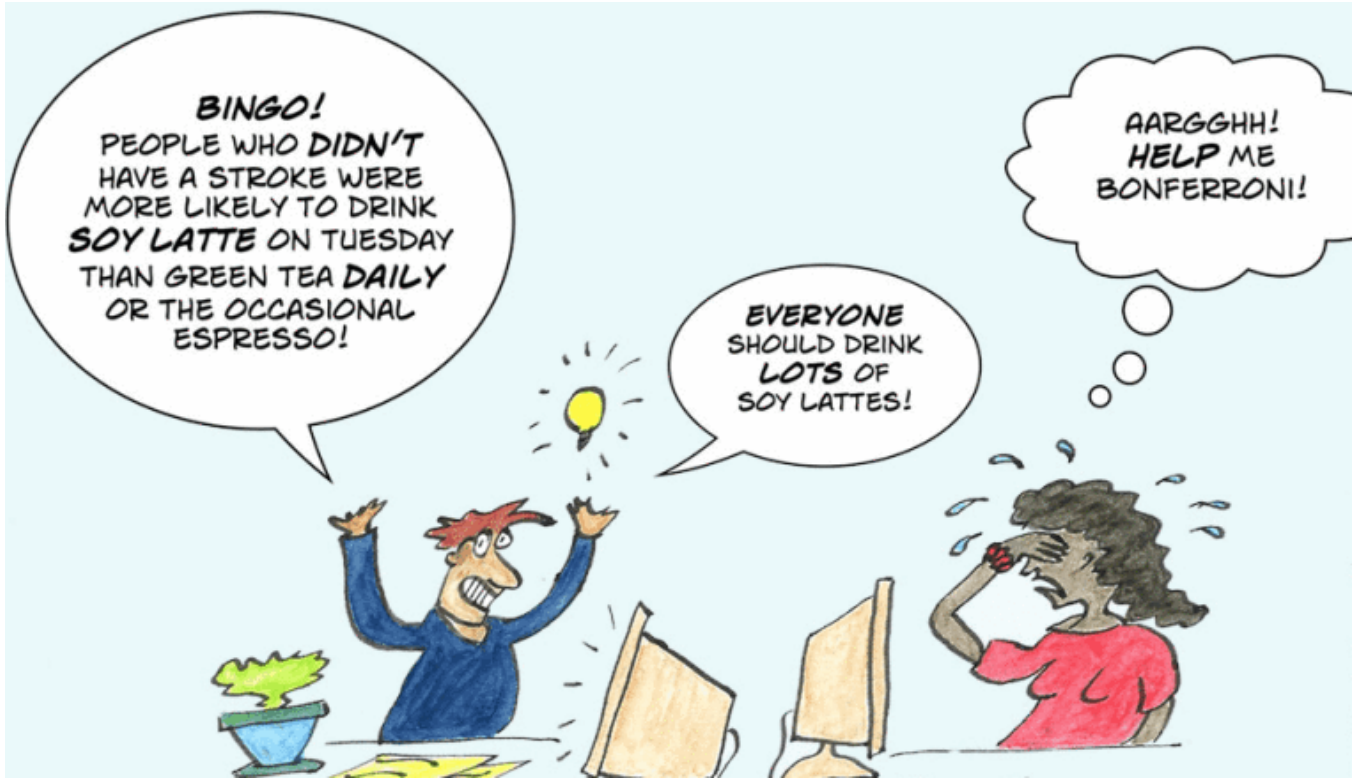
Michael G. DeGroote SCHOOL OF MEDICINE

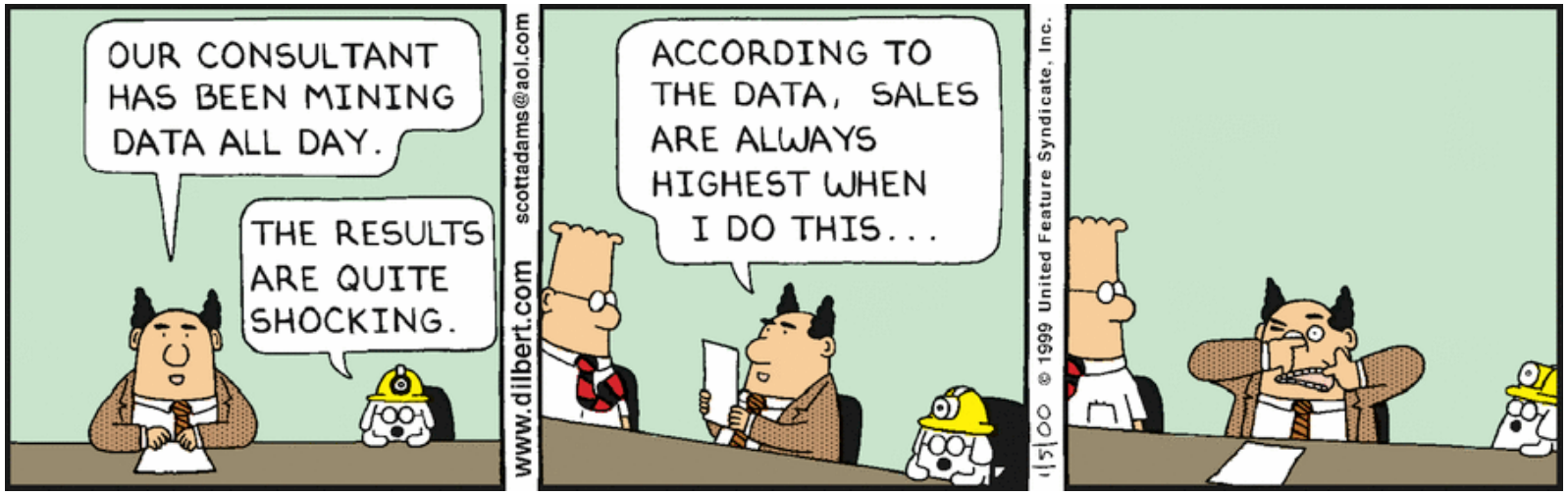
Agenda

- **Purpose of this Session**
- **Timelines of Registration & Reporting**
- **Accountability, Transparency, Reproducibility, Rigour, & Quality**
- **ClinicalTrials.gov**
  - What is it and what studies should register?
  - Registering a study on ClinicalTrials.gov
  - Navigating the site, and some tips & tricks
- **Guidelines for Reporting Research**
  - The EQUATOR Network
  - Common guidelines and their associated checklists
  - Practice

Learning Objectives

- To understand timelines, and why they matter
- To learn about accountability, transparency and rigour in research and why they matter
- To gain skills in registering a study at ClinicalTrials.gov
- To find and use appropriate guidelines and their checklists for research reporting


BINGO! PEOPLE WHO DIDN'T HAVE A STROKE WERE MORE LIKELY TO DRINK SOY LATTE ON TUESDAY THAN GREEN TEA DAILY OR THE OCCASIONAL ESPRESSO!
EVERYONE SHOULD DRINK LOTS OF SOY LATTES!
AARGGHH! HELP ME BONFERRONI!


OUR CONSULTANT HAS BEEN MINING DATA ALL DAY.
THE RESULTS ARE QUITE SHOCKING.
www.dilbert.com scottadams@aol.com
ACCORDING TO THE DATA, SALES ARE ALWAYS HIGHEST WHEN I DO THIS...
1|5|00 © 1999 United Feature Syndicate, Inc.

Timelines

- **Trial registration**: needs to be finalized *before first participant recruited*
  - Major journals will **require** reporting of everything registered; will **only** allow reporting of registered outcomes
  - Anything else? Minor reporting; “post hoc”/hypothesis generating only anything else is relegated to minor reporting and clearly labelled “post hoc” / for hypothesis generation only
    - Any new outcomes/analyses should be added ASAP to registration

- **Protocol publication:** needs to be accepted *before data collection has finished*
  - Use SPIRIT Guidelines

McMaster University

Family Medicine

Accountability, Transparency, Reproducibility, Rigour & Quality

Accountability in Research

Accountability: “The ***obligations the researcher has*** to the various stakeholders in the research process such as the research participants, the funding body, and the researcher's employing organization”[1]

1. Ballinger, C. (2012). Accountability. In L. M. Given (Ed.) *The SAGE Encyclopedia of Qualitative Research Methods* (p.4). Thousand Oaks: SAGE Publications, Inc.

Transparency in Research

"Published articles should provide clearly written, transparent descriptions of how the research was conducted, results were obtained, and conclusions were reached based on appropriate uses of analytical tools. Reporting of research should be truthful, free of bias, and provide enough information about how the work was performed to allow others to replicate the work and to be useful for further analyses. In the case of medical research, **the information (especially from clinical trials) influences decisions regarding patient care and health policy**."[1]

1. Baskin, P. K & Gross, R. A. (2015). Transparency in research and reporting: Expanding the effort through new tools for authors and editors. *Author Resource Review.* Retrieved from https://www.editage.com/insights/transparency-in-research-and-reporting-expanding-the-effort-through-new-tools-for-authors-and-editors.

Is There a Reproducibility Crisis in Science?

(TED-Ed video)

In the News: Problems with Replicability & Reliability in Research

- Wall Street Journal (2011) – Scientists' Elusive Goal: Reproducing Study Results
- NY Times (2012) – A Sharp Rise in Retractions Prompts Calls for Reform
- FiveThirtyEight (2015) - Science Isn't Broken, on p-hacking

Being Accountable & Transparent in Research

1. Prior to the study, **make your methods known**. For example, through:
   - Publishing or publically posting a protocol
   - **Registering your study with ClinicalTrials.gov**
   - Ethics approval
     - *"Every research study involving human subjects must be registered in a publicly accessible database before recruitment of the first subject."* – Declaration of Helsinki, 2003

Being Accountable & Transparent in Research

2. In publications, **explain your methods** to show rigoir in mitigating bias and with enough detail that it would be replicable. For example, through:

- Following the methods you publically set out to follow
- **Using guidelines and checklists for research reporting**
  - Also a great tool for rigour at the protocol development and design stage

McMaster University

Family Medicine

ClinicalTrials.gov

ClinicalTrials.gov

- An online database of studies
- Register to ‘set your methods in stone’
- All clinical trials, interventional studies should be registered; can also register other types of studies
- To register: https://register.clinicaltrials.gov/
  - Organization: McMaster_University
  - Username/Password: should be under the study PI

Registering for Clinical Trials: Timeline

- Register *as you apply* for ethics
  - For true clinical trials, you won't get final ethics approval without it
- Register *before* you begin recruiting patients, publish a protocol, or collect data
- Steps: a) You create and write in the project
  - b) Our McMaster contact reviews and approves it
  - c) Clinical Trials reviews and approves it
  - d) It goes public, journals will hold you to whatever original says

Tips & Tricks

- The website is dated and not that user-friendly – just follow along with where it takes you
- Watch for RED
- Understand that the definitions they give tend to be aimed at medical/clinical trials, so extrapolate what they mean
- Clearly split all items, e.g. outcomes, for ease of review
- Don’t use first-person language
- Have one person in the team designated to deal with changes – someone a PI can quickly forward any emails to

McMaster University

Family Medicine

Guidelines and Checklists for Reporting Research

The EQUATOR Network

- Enhancing the QUAlity and Transparency Of health Research
- “Promoting transparent and accurate reporting, and wider use of robust reporting guidelines”
- A one-stop shop for checklists to help guide your reporting
  - Varied methods and fields

http://www.equator-network.org/

Common Checklists

SPIRIT

STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description
Administrative information		
Title	1	Descriptive title identifying the study design, 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 identifier
Funding	4	Sources and types of financial, material, and other support
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention
	6b	Explanation for choice of comparators
Objectives	7	Specific objectives or hypotheses
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)

1

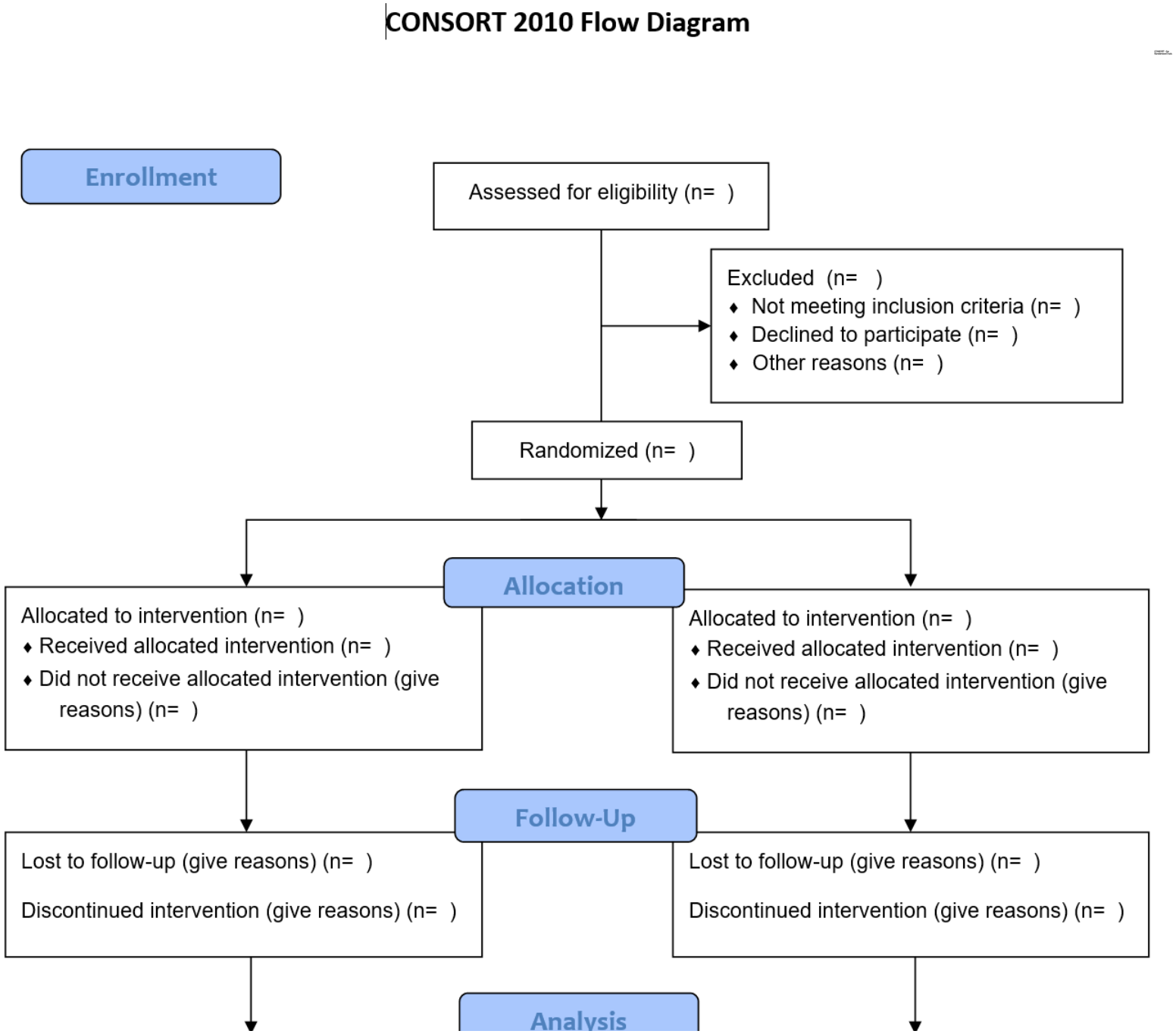
Methods: Participants, interventions, and outcomes		
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return,

SPIRIT – for protocols

STROBE – for observational studies

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
Methods		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect



CONSORT – for Randomized Trials

Example included: the patient recruitment tracking from CONSORT

(see also CONSORT Extension for Pilot & Feasibility Trials)

A tutorial on pilot studies: the what, why and how

Lehana Thabane ✉, Jinhui Ma, Rong Chu, Ji Cheng, Afisi Ismaila, Lorena P Rios, Reid Robson, Marroon Thabane, Lora Giangregorio and Charles H Goldsmith

BMC Medical Research Methodology 2010 **10**:1
https://doi.org/10.1186/1471-2288-10-1 © Thabane et al; licensee BioMed Central Ltd. 2010
Received: 9 August 2009 | Accepted: 6 January 2010 | Published: 6 January 2010

Abstract

Pilot studies for phase III trials - which are comparative randomized trials designed to provide preliminary evidence on the clinical efficacy of a drug or intervention - are routinely performed in many clinical areas. Also commonly know as "feasibility" or "vanguard" studies, they are designed to assess the safety of treatment or interventions; to assess recruitment potential; to assess the feasibility of international collaboration or coordination for multicentre trials; to increase clinical experience with the study medication or intervention for the phase III trials. They are the best way to assess feasibility of a large, expensive full-scale study, and in fact are an almost essential pre-requisite. Conducting a pilot prior to the main study can enhance the likelihood of success of the main study and potentially help to avoid doomed main studies. The objective of this paper is to provide a detailed examination of the key aspects of pilot studies for phase III trials including: 1) the general reasons for conducting a pilot study; 2) the relationships between pilot studies, proof-of-concept studies, and adaptive designs; 3) the challenges of and misconceptions about pilot studies; 4) the criteria for evaluating the success of a pilot study; 5) frequently asked questions about pilot studies; 7) some ethical aspects related to pilot studies; and 8) some suggestions on how to report the results of pilot investigations using the CONSORT format.

For Pilot Studies
(includes a checklist)

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	

PRISMA – for Systematic Reviews

Consolidated criteria for reporting qualitative studies (COREQ): 32-item checklist

No	Item	Guide questions/description
Domain 1: Research team and reflexivity		
Personal Characteristics		
1.	Interviewer/facilitator	Which author/s conducted the interview or focus group?
2.	Credentials	What were the researcher's credentials? *E.g. PhD, MD*
3.	Occupation	What was their occupation at the time of the study?
4.	Gender	Was the researcher male or female?
5.	Experience and training	What experience or training did the researcher have?
Relationship with participants		
6.	Relationship established	Was a relationship established prior to study commencement?
7.	Participant knowledge of the interviewer	What did the participants know about the researcher? e.g. *personal goals, reasons for*

COREQ – for qualitative research (specifically focus groups & interviews)

TIDieR – for describing interventions

TIDieR
Template for Intervention Description and Replication

The TIDieR (Template for Intervention Description and Replication) Checklist*:

Information to include when describing an intervention and the location of the information

Item number	Item	Where located **	
		Primary paper (page or appendix number)	Other † (details)
	BRIEF NAME		
1.	Provide the name or a phrase that describes the intervention.	_____	_____
	WHY		
2.	Describe any rationale, theory, or goal of the elements essential to the intervention.	_____	_____
	WHAT		
3.	Materials: Describe any physical or informational materials used in the intervention, including those provided to participants or used in intervention delivery or in training of intervention providers. Provide information on where the materials can be accessed (e.g. online appendix, URL).	_____	_____
4.	Procedures: Describe each of the procedures, activities, and/or processes used in the intervention, including any enabling or support activities.	_____	_____
	WHO PROVIDED		
5.	For each category of intervention provider (e.g. psychologist, nursing assistant), describe their expertise, background and any specific training given.	_____	_____
	HOW		
6.	Describe the modes of delivery (e.g. face-to-face or by some other mechanism, such as internet or		

Practice with Checklists

Common Guidelines/Checklists

- SPIRIT – Protocols
- STROBE – Observational Studies
- CONSORT – Randomized Trials
- Lehana's for Pilot Studies ("A tutorial on pilot studies: the what, why and how")
- PRISMA – Systematic Reviews
- COREQ – Qualitative (focus groups & interviews)
- TIDieR – Describing Interventions

McMaster University

Family Medicine

Department of Family Medicine
Michael G. DeGroote School of Medicine
Faculty of Health Sciences

famedmcmaster.ca
@McMasterFamMed