Trial Fidelity and Quality Control Strategies

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Faculty Disclosures

1. Relevant financial relationships with a commercial interest:

No relevant commercial interests.

"I, along with some of the other doctors, now charge $800 an hour. If that don't motivate people to eat right and exercise, then nothing will."

Objectives

1. RCT pharma and non pharmacological
2. Review
   2.1 Trial fidelity problems/challenges
   - using examples
   2.2 Quality control strategies
   - using examples
3. Conclusions

Trial “RCT”: best design to show the efficacy of an intervention

Fundamental principles:

- Prospective study
- Control group
- Randomized allocation

Claiming you have done a RCT
doesn’t insure the quality of the results
(poor quality can lead to biases and inaccuracies) !

Trial fidelity :
Set up standards of high quality !

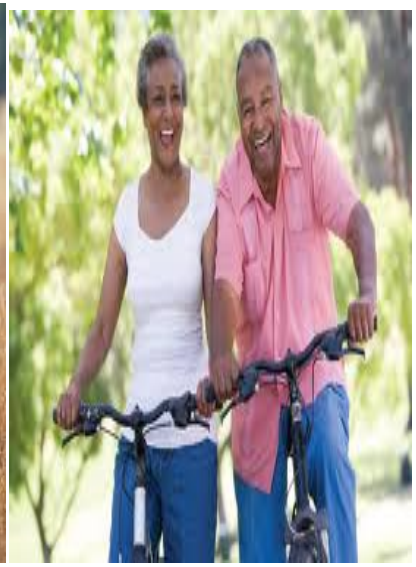
CONSORT (Consolidated Standards of Reporting Trials)

- Parallel-group control RCT
- List of 22 items
- Diagram of the study

- *Moher D, Schulz KF, Altman DG. The CONSORT statement: revised recommendations for improving the quality of reports of parallel-group randomised trials. Lancet. 2001;357:1191-4.*
- *Altman et al.; CONSORT GROUP (Consolidated Standards of Reporting Trials). The revised CONSORT statement for reporting randomized trials: explanation and elaboration. Ann Intern Med. 2001;134:663-94.*

Trials of non pharmacological interventions: Additional challenges

Complexity on many aspects of the design, implementation and interpretation compared to drug trials



Importance of monitoring and assessing protocol fidelity

Any discrepancies between the intervention planned and that actually administered should be recorded

- Participative interventions that involve contacts between patients and HCP require particularly careful attention

Without this knowledge, it is impossible to interpret the trial results

- Negative results: Mask whether study findings are due to an ineffective treatment or infidelity to an intervention protocol
- Positive results: Cannot insure replication and improve the results

Extension of the CONSORT for the non pharmacological trials

Main recommendations:

- 11 items need modifications
- **1 new item**
- Diagram of modify flow

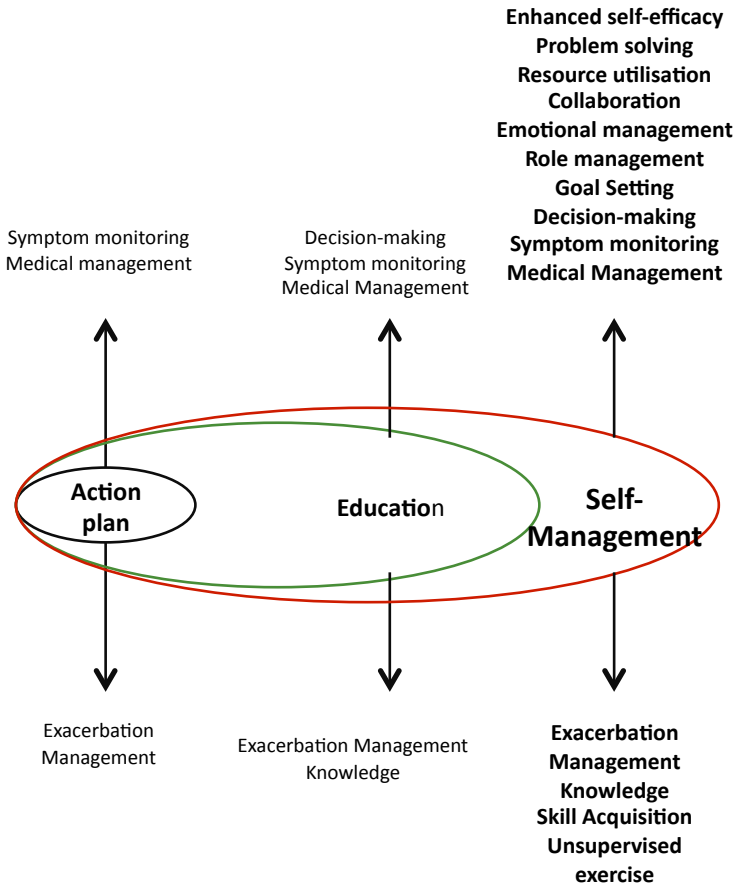
Intervention, randomization, sample size, blinding, etc

Implementation of the intervention

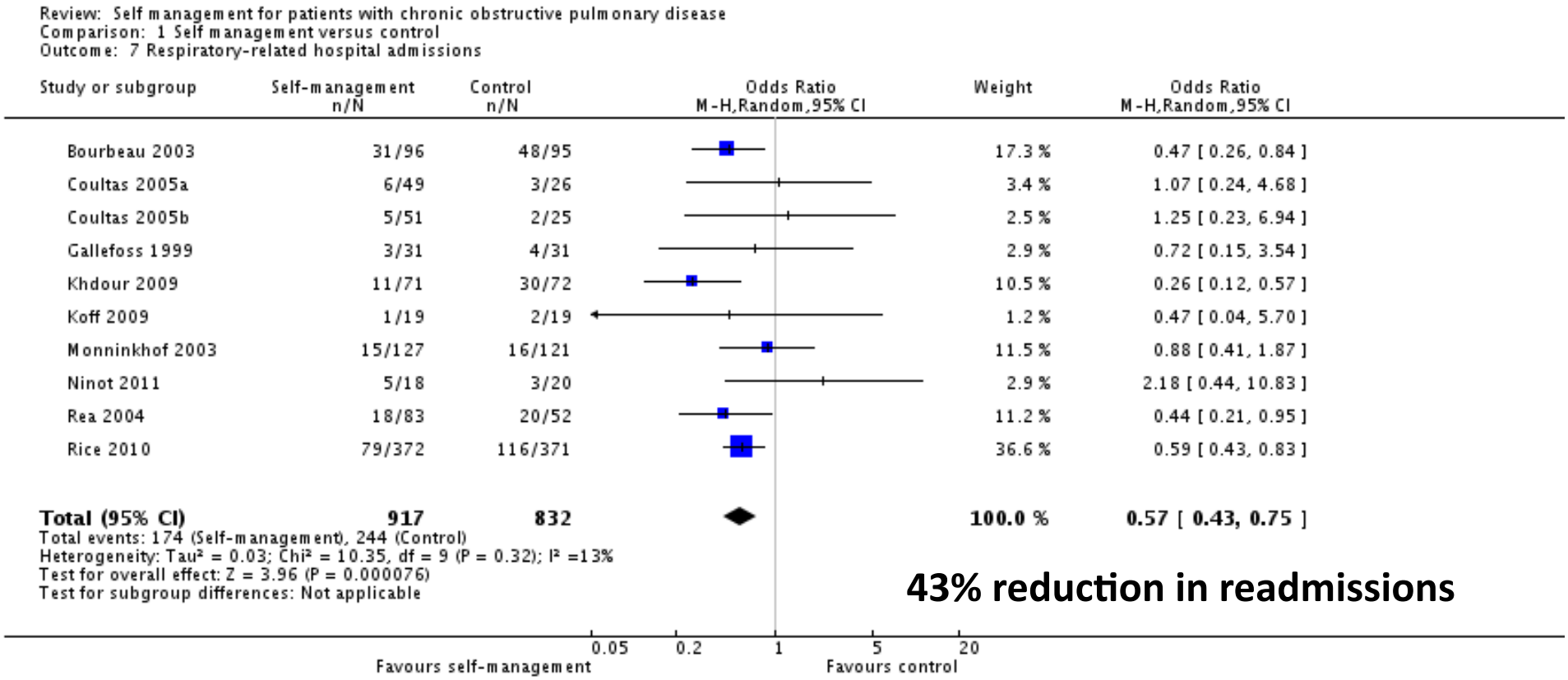
Boutron I, Moher D, Altman DG, Schulz KF, Ravaud P; for the CONSORT Group. Methods and processes of the CONSORT group: example of an extension for trials assessing nonpharmacologic treatments. Ann Intern Med. 2008;148:W-60-6

There are problems/challenges
Let give some examples ?

Self-management in COPD: Multi component intervention



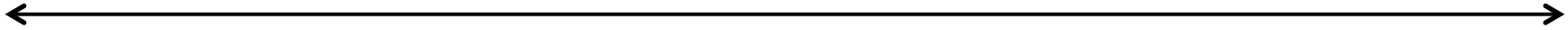
Example 1
Self management interventions in COPD



43% reduction in readmissions

Zwerink M. Cochrane Database Syst Rev. 2014 Mar 19;3:CD002990

Difficult to formulate clear recommendations



on the most effective **form and content**

of a self-management intervention in COPD

considering the …

- range of heterogeneity across studies, and
- lack of precise definitions of self-management components (e.g., skills taught and targeted behaviors) and fidelity measures.

Zwerink M. Cochrane Database Syst Rev. 2014 Mar 19;3:CD002990

Self-management intervention (concept)

- A **COPD self-management intervention** is structured but personalised, and often multi-component, with goals of motivating, engaging, and supporting the patients to positively adapt their health behaviour(s) and develop skills to better manage their disease.

Tanja E., Vercoulan Jan H., Bourbeau J., et al. Definition of a COPD self-management intervention: International Expert Group consensus. Eur Respir J 2016.

Self-management intervention (concept)

The process

- **More important,** it is the process of supporting self-management, which refers to the strategies, techniques and skills used by healthcare providers <case manager> to instrument patients with the knowledge, motivation, confidence and skills required to effectively self-manage their disease.

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Self-management intervention (concept)

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The behaviors to change

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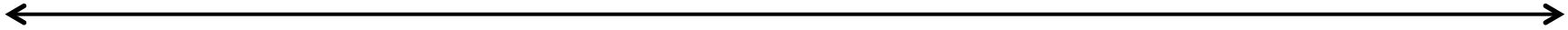
Example 2
Why some RCT succeed and others failed?

	Patient factors	Intervention factors		
	Eligibility Criteria	**Self-management Education**	**Action Plan**	**Case management**
CSP #560	COPD hosp	4 individual sessions with 1 group session	Yes	Monthly calls x 3, then every 3 months
Bourbeau	COPD hosp	7-8 Individual sessions at home	Yes	Monthly
Rice	COPD hosp. or Home O2 or Prior course Pred/Abx	1 group session by an RT	Yes	Monthly

Bourbeau et al. Arch Intern Med 2004
Rice et al. Am J Respir Crit Care Med 2010
Fan et al. Ann Intern Med 2012

Due to an ineffective treatment or infidelity to an intervention protocol



In Fan study, it appears that **SM intervention was implemented/delivered** according to protocol:

- 87% of patients **completed all 4 individual sessions**
- 77-89% of the **education items were covered** by the CM
- 89% of the **tel follow up were made** by the CM

Closer look at how the SM program was **received by the patients:**

- Fan study- patients failed to use the SM skill taught, e.g., using promptly antibio/prednisone (no difference) and calling CM (4.5%)
- Bourbeau study- 48% of patients called the CM

Bourbeau et al. Arch Intern Med 2004
Fan et al. Ann Intern Med 2012

Example 3

RCT **health coaching (MI) in hosp. COPD** with exacerbation decreases the risk of readmission up to 6 months (not at 1 yr)

- study does not allow to determine if the reduction in hospital admissions is a consequence of
  - patients gaining knowledge, confidence and skills or
  - frequent telephone calls (rescuing the patient) …from weekly to monthly phone calls

- also unknown which behavior the coaching program intended to change to decrease hospital admissions
  - the use of antibiotics and/or prednisone was not different between groups.

Benzo et al Health Coaching and COPD Re-hospitalization: a Randomized Study. AJRCCM 2016


MIND THE GAP
Non pharmacological trial
improvement

COPD Patient Management European Trial (COMET)

COMET (345 patients; 33 centers; 4 European countries)

Main objective:

- to evaluate a multi-component home-based COPD self-management program LWWCOPD compared to usual care on unscheduled all-causes hospital days over 1 year follow-up in severe COPD patients

It is **hypothesized** that the COMET program helps patients with severe COPD learn and adopt behaviour needed to cope with their disease and consequently this will result in a reduction of hospitalisations

Bourbeau et al. An international randomised study of a home-based self-management program for severe COPD: the COPD Patient Management European Trial (COMET). International J COPD *2016.*

COPD Patient Management European Trial (COMET)

The **key interventions**

- involve patient self-management education and coaching by health care professionals, e.g., case managers;
- promote self-efficacy, adopt sustainable self-management skills and behaviors (early recognition and treatment of COPD exacerbations);
- close patient monitoring for early detection of symptom worsening (e health platform);
- healthcare coordination to reduce treatment delays and improve chronic disease management.

COPD Patient Management European Trial (COMET)

•Standardisation of the program/content:

•self-management program Living Well with COPD

•Case managers

•experience in taking care of home-based chronic patients;
•initial four-day training (+specific training MI);
•access given to 'reference guides' describing the objs, interventions, suggested questions, expected results and resources;
•trainings at each country level during the study for new comers, program refreshing and experience sharing.

•Monthly telephone contacts

•between the case managers and a pneumologist from the COMET study coordination center, in each country separately

Doing the right thing in our studies

1. Details of the non pharmacological intervention and comparaison
   - detailed enough that someone else could replicate the intervention
   - how the intervention is standardized
2. Details on adherences to intervention protocol
   - The deliverer : the way the implementation (content and process) was done by the “case manager or the coach” (audio taping with evaluation/feedback) and
   - The receiver: the way patient is adherent (attended sessions, follow up, etc)

Boutron I, Moher D, Altman DG, Schulz KF, Ravaud P; for the CONSORT Group. Methods and processes of the CONSORT group: example of an extension for trials assessing nonpharmacologic treatments. Ann Intern Med. 2008;148:W-60-6

PHYSACTO® study

PHYSACTO® : multicentre drug trial, 34 sites in 11 countries

Objectives:

- to assess the effect of a new COPD maintenance bronchodilator therapy and supervised exercise training on exercise capacity and physical activity

Challenges:

- to provide behavior-change self- management in all intervention arms in an optimal environment
- to ensure that delivery of the behaviour-change programme can be standardised across different locations/countries, while also ensuring that individual patient needs, preferences and personal goals inform the intervention.

Bourbeau J, Lavoie K, Sedeno M et al.. Behaviour-change intervention in a multicentre, randomised, placebo-controlled COPD study: methodological considerations and implementation B*MJ Open 2016.*

PHYSACTO® study

Methodological considerations integrating behaviour-change interventions into a multicentre study:

1. the Site Case Manager, with careful monitoring of programme
2. the patient, incorporating patient-/programme-evaluation measures to guide the Site Case Manager in the self-management intervention; and
3. the quality control strategies, to help identify and correct any problems or shortcomings in programme delivery and ensure the effectiveness of any corrective steps.

PHYSACTO® study

Our approach is designed to **effect changes in patient behaviour** by

1. building on the experience;
2. training and effectiveness of case managers;
3. standardising the content of the programme across sites;
4. helping case managers adjust the programme based on patient responses using a standardised feedback process;
5. and including quality control steps throughout the programme.

Quality control strategies

Evaluating whether the case manager intervention

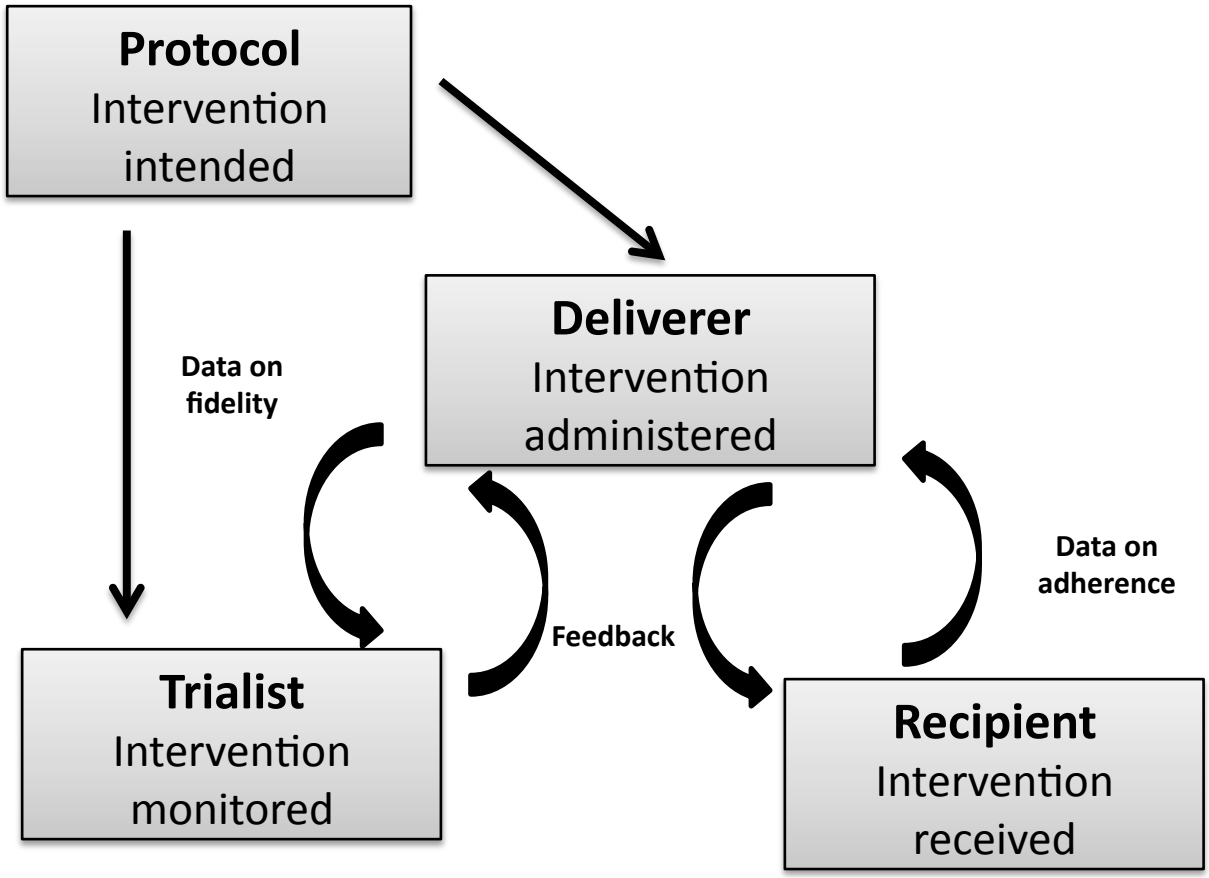
has been delivered as intended (using audio taping):

- Content: Where the intended education topics covered? If so, where they covered properly?
- Delivery style (coaching), using a MC (using open questions, asking for permission before providing information, etc.)
- Adjustment of the intervention to fit patient needs
  - Using specific measurement tools (Stage of change, Physical Activity Outcome Expectancies, and Motivation / Self-efficacy questionnaires)

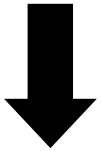
Bourbeau, Lavoie, Sedeno et al. Behaviour-change intervention in a multicentre, randomised, placebo-controlled COPD study: methodological considerations and implementation BMJ Open 2016

We have to **do the right thing**

Key points for monitoring of intervention fidelity and adherence during a trial



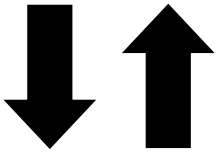
A recurrent clinical & quality problem



Evidence-Base Medicine

(Doing the right thing)

Formulate an answerable question
Find the best evidence
Critically appraise the evidence
Work to apply the evidence to individual and systems of care



Quality improvement Process

(Doing it right)

What are we trying to accomplish? (Aim)
How will we know a change is an improvement? (Measures)
What changes can we make? (Change management)

"Doing the right things right"
adapted from Glasziou, Ogrinc & Goodman (2011)

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Québec

Agence de la santé et des services sociaux de Montréal

Sponsors

- Non commercial: CIHR, FRQS, RI MUHC, RQAM
- Commercial: **BI**, GSK, Novartis, AZ

Most important: All the COPD patients