Finnish Institute of Occupational Health

Non-randomised studies in Cochrane Reviews

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Non-randomised studies (NRS)

- RCT gold standard for evaluating interventions
- Not always possible, thus need for including non-randomised studies (adverse effects, legislation)
- NRS = all intervention studies that did not randomise
- Non-randomised studies problematic
  - more difficult to find, no standardized naming, greater risk of bias, risk of bias more difficult to assess
- Handbook chapter 13: NRS
- Objective: What is usual in including NRS in Cochrane Reviews? Can we infer guidance for authors?

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What did we do?

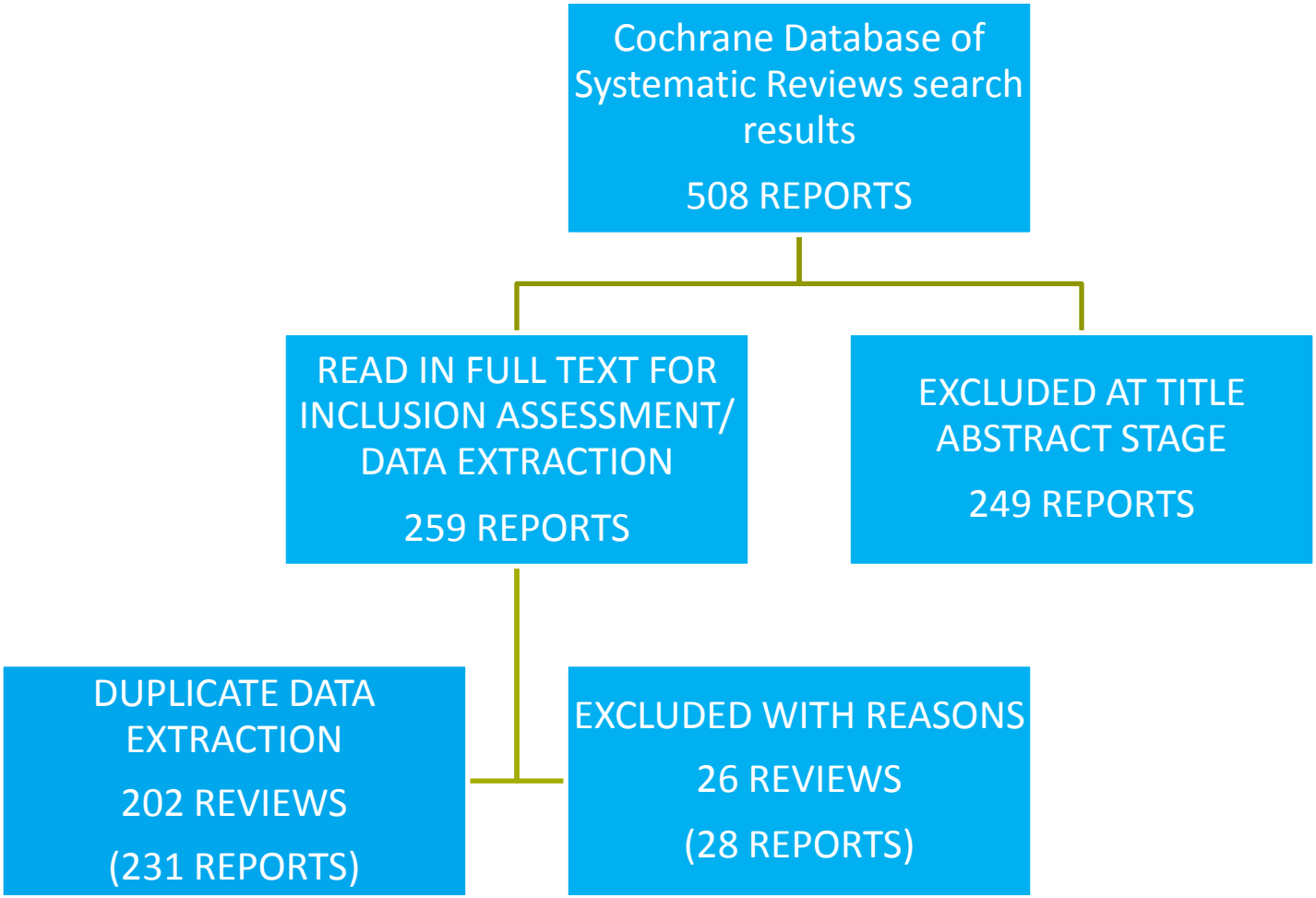
- Searched Cochrane Library up to May 2012
  - Included all reviews that included NRS
  - But not if only quasi-RCTs

- Extracted Review Content in duplicate:
  - Cochrane Review Group publishing the review
  - reasons for including non-randomised studies
  - inclusion criteria for PICO S
  - names and definitions of the non-randomised studies
  - risk of bias assessment method(s)
  - if non-randomised studies are included in conclusions

What did we do?

- Coded reasons for inclusion in a iterative process
- We reached consensus on what we deemed good or bad reasons
- Compared reasons to Chapter 13 Handbook
  - ***Good*** *justifications for including NRS:*
    1. *making a case for RCTs*
    2. *intervention cannot be randomized*
    3. *long-term, rare outcomes*
  - ***Poor*** *justifications for including NRS*
    1. *patients not recruited to RCTs such as pregnant women*
    2. *to supplement RCTs*
    3. *large intervention effect*

Results



202 reviews with 38 CRGs

Reviews with non-randomised studies per Review Group	# of reviews	Review Groups
61 to 10 Reviews	61	Effective Practice and Organisation of Care Group
	25	Injuries Group
	11	HIV/AIDS Group
	10	Musculoskeletal Group
9 to 7 Reviews	9	Consumers and Communication Group
	8	Gynaecological Cancer Group
	7	Airways Group; Metabolic and Endocrine Disorders Group
Less than 5 Reviews	4	Ear, Nose and Throat Disorders Group; Heart Group; Infectious Diseases Group; Neuromuscular Disease Group; Pain, Palliative and Supportive Care Group
	3	Epilepsy Group; Hepato-Biliary Group; Occupational Safety and Health Group; Public Health Group
	2	Back Group; Colorectal Cancer Group; Dementia and Cognitive Improvement Group; Developmental, Psychosocial and Learning Problems Group; Eyes and Vision Group; Inflammatory Bowel Disease and Functional Bowel Disorders Group; Menstrual Disorders and Subfertility Group; Multiple Sclerosis and Rare Diseases of the Central Nervous System Group; Oral Health Group; Stroke Group; Tobacco Addiction Group
	1	Breast Cancer Group; Childhood Cancer Group; Drugs and Alcohol Group; Depression, Anxiety and Neurosis Group; Fertility Regulation Group; Hypertension Group; Incontinence Group; Pregnancy and Childbirth Group; Skin Group; Wounds Group

NRS Designs

Non-randomised studies	in % (n) of reviews
Controlled Before After Study	60.3 (122)
Interrupted Time- Series	52.0 (105)
Cohort Studies	36.6 (74)
Case-control	26.2 (53)
Other designs	34.1 (69)

Randomised and quasi-randomised designs	
RCT	99.5 (201)
Quasi-RCT	45.1 (91)
Controlled Clinical Trial	55.0 (111)

Reasons for including NRS

RCTs wanted (N=81)	RCTs wanted but not possible	Randomisation not feasible	47 (53 %)
		Randomization not ethical	5 (6 %)
	RCTs wanted but missing	Lack of RCTs	33 (38 %)
	NRS additional to RCTs	To include all data and maximize evidence	13 (15 %)
		Compare with RCT evidence	6 (7 %)
RCTs not necessary (N=7)	NRS as good as RCTs	NRS evidence equivalent value	7 (8 %)
No reason given			114 (56%)

Randomisation not feasible

- Too few units/participants for randomization (2)

- Intervention applied at group level (12)
- Complex Intervention (5)

- Adverse outcome (12)
- Small effect (1)
- Rare outcome (2)
- Long term effects (2)

- Setting makes randomization difficult (3)

- Unspecified (13)

Lack of RCTs

- We anticipated lack, Pilot test showed lack (20)
- NRS will be included when RCTs or quasi-RCTs are not available (6)
- Based on non-feasibility arguments (7)

To maximize evidence

- To include all available evidence (4)
- Because most data is from NRS (3)
- Because restriction to RCT is too dogmatic (2)
- To include NRS if no sufficient RCTs included (1)
- To increase power of analysis (2)
- To identify research needs (1)
- To further understand effect of intervention (2)
- To increase relevance of review (1)

NRS Equivalent

- No need for control groups (progression disease known) (1)

- CBAs and RCTs best for social/ public health interventions (1)
- Methods (NRS or RCT) deemed of similar quality (2)
- NRS deemed good because used or showed positive effects (3)

Our justification of NRS inclusion

- NRS are equivalent or better
  - unintended outcomes or the course of the disease does not vary
- Randomisation is unethical
  - no uncertainty about the treatment
- Compare NRS to RCTs
  - increase the uptake of RCT results, differences in participants included in RCTs
- Randomisation is difficult and unlikely to be done
  - few units available or intervention at the group level, complex interventions or a setting, for rare outcomes, outcomes which occur at very long-term follow-up, treatment has been firmly established

NRS Risk of Bias

- EPOC 38%
- NewCastle Ottawa (NOS) 8%
- Downs and Black 5%
- MINORS 2%
- CRD checklist 2%
- Review Group 2%
- Self-defined 13%
- None mentioned 5%
- Other 30%

NRS synthesis / in conclusions

- Narrative reporting NRS 52%
- Statistical pooling NRS 25%
- No clear synthesis 23%

- NRS in conclusions 68%

Conclusions

- Varying practice of including NRS in CC

- When including NRS:
  - Give arguments for inclusion
  - Define what you mean with NRS
  - Use validated tool for RoB in NRS
  - Be specific about synthesis and use in conclusions

- Better guidance and better implementation of guidance needed