Can RCTs always be done?

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Content

- Randomisation and ethics
  - What is unethical?
- Examples from CHARM topics
  - Traumatic Brain Injury (x2)
  - Huntington's disease
  - Elderly care
  - Children with cerebral palsy
  - Stroke
- General applicability

Messages

- RCTs are:
  - Ethically required if there is insufficient evidence
  - Practically possible in most circumstances
- And they are the best way to:
  - Change actual clinical practice
  - Change organisation
  - Obtain funding
- *Example – UK TBI project 1992*

Research

- A systematic approach to collecting and analysing data, to test a hypothesis
  - Population > sample(s)
  - Sample(s) > data
  - Data > analysis
- Essential to consider
  - Representative data-set ((random) selection)
  - Counter bias (randomisation, masking)
  - Account for variability (sample size)

RCTs – unethical?

- It is only unethical to randomise if there is unequivocal evidence that one choice is:
  - Superior in terms of
    - Benefit
    - Harm
  - And is approximately equivalent in cost
- Every other situation randomisation is morally sound

RCTs – unethical not to do!

- Failure to undertake RCTs risks:
  - Using harmful treatments
    - harming the 'treated' patient
  - Wasting resource on useless treatment
    - Harming other patients
  - Denying future patients effective treatment
    - Lack of evidence will reduce funding/use
  - Undermining Trust in healthcare
    - If/when ineffectiveness/harm proven

‘Ethics’ & practicality

- Some clinicians do not accept (lack of) evidence
  - Allow to randomise when personally uncertain
- Some patients have strong beliefs
  - Use patient preference design
    - *BMJ* 2008; 337 doi: http://dx.doi.org/10.1136/bmj.a1864

Apparent practical difficulties

- If it is a rare problem
  - The **disease** may be rare, but the problem often is not
- If it is a complex intervention
  - Define it in a way that can be replicated
- If collaboration in study is at risk
  - Explain carefully and openly
  - Look for and accept improvements
  - Patient involvement from outset

TBI – trajectories

- Unstated assumptions/hypotheses are:
  - Current care is disorganised/chaotic
  - This leads to/causes less good outcomes
  - Organised care would lead to:
    - Better outcome, at
    - Lest cost (to society)
- Method = observation and correlations
  - Cannot attribute cause/effect
  - Does not test the second & third hypotheses

‘Rehabilitation Prescription’

- Set of standards concerning ‘transfers of care’ (trajectory, pathway, care chain)
  - Every transfer must:
    - Start with documentation of state and need
    - Identify next service and person
    - Record unmet need **and** a plan to ameliorate that
  - Flexible set of documents, tailored to clinical situation

TBI – trajectories

- Assuming that there are some (inco-ordinated) services actually available
- RCT to compare:
  - Current 'pathway'
  - Coordination/better transfers using 'Rehabilitation Prescription'
- Randomise individual patients
  - **All** admitted to hospital for 24+ hours

TBI – neuropsychology

- Unstated assumptions/hypotheses are:
  - Cognitive losses determine specific treatment needs (= ability to **benefit** from intervention)
  - Outcome depends upon:
    - Specific interventions identified by impairment
    - 'Intensity' of rehabilitation (neither are defined)
- Method = observations

Possible trials

- Hypothesis one:
  - Treatments targeted on identified losses improves outcome (compared with chaos)
- Hypothesis two:
  - Treatments targeted on identified losses is worse than generic 'task-related' (functional) treatment based on strategies to practice wanted activities
    - Could include "both better than chaos" (3 arms)

TBI - neuropsychology

- An RCT to compare:
  - Treatment(s) to alleviate any identified losses
    - All patients have psychological assessment first
  - Strategies to reduce activity limitations
    - All patients have task analysis/goal identification
- Randomise individual patients
  - All who have activity limitations
    - Provided not totally due to other losses

Elderly

- Stated assumptions/hypotheses
  - Structured assessment by nurses **and**
  - Better communication with/involvement of GPs
  - *Will lead to*
  - Better outcome for frail elderly patients

Identified problem

- Difficult to get system to change

- Solution offered
  - In depth analysis of process and qualitative factors

Actual problem

- Lack of sound evidence that change is worthwhile
  - Difficult for research team to be firm
  - Difficult for organisations to support change
- Cochrane reviews
  - None support model
    - Assessment without MDT input ineffective

Better solution

- Identify better system through RCT(s)
- RCT to compare, in frail elderly at home:
  - Current system
  - Visit by a trained person **supported by** a full multi-disciplinary team **including** social care services etc
  - Cost-consequences analysis essential

Huntington's disease

- Has a clear hypothesis
- Using an RCT to test it

- **Comment**
  - Might increase numbers **and** usefulness by including people with similar problems from other causes (e.g. TBI, cerebrovascular disease etc)

Cerebral palsy and dexterity

- No stated hypotheses/assumptions
- Difficult to guess hypotheses:
  - ?association between brain injury and dexterity
  - ?association between intervention and dexterity
- States that therapy ‘has been shown to be effective’ in unilateral cerebral palsy

Cerebral palsy RCT

- Hypothesis: current treatments also benefit children with bilateral problems
- Compare:
  - Therapy focused on worse arm, with
  - Therapy focused on both arms
- Looking at two outcomes:
  - Function of the worse arm alone
  - Performance on bimanual tasks

Work & participation

- Unstated hypothesis/assumptions
  - Nature of discussion on goals has an influence upon return to work in people on sick leave
- Method:
  - Uncertain
    - Restricted to low back pain?
    - Qualitative study on actual interviews?
    - Interviews with professionals?

RCT

- Hypothesis: rate of return to work (both time off and actual percentage returning) is influenced by approach of professional.
- Compare two techniques such as:
  - Motivational interviewing
  - Self-directed goal setting, or
  - Negotiated externally-directed goal setting, or
  - Graded exercise therapy, or
  - Cognitive behavioural therapy

Stroke Psychosocial outcome

- Has hypothesis
- Using RCT

- **Comment:**
  - Good as includes all patients **and** (I think) involves nurses
  - Will need an out-patient version later

Randomisation in research

- Two or more similar populations provide
  - Opportunity to contrast interventions
  - Counter to bias
- Can be done to investigate
  - Assessment
  - Goal setting
  - Treatment and care
  - Evaluation (outcome assessment)

Patient-centred interventions

- Specific external aids/drugs such as:
  - AFO, botulinum toxin
- Specific patient techniques such as:
  - CBT, walking practice, CIMT
- Clinical management strategies, such as
  - Structured programme (e.g. follow-up after acute anoxia), memory strategies, task-specific practice

Contextual interventions

- Physical, localised such as:
  - Flooring, view from window
- Social/physical such as:
  - Training carers/family, setting family expectations
- Personal such as
  - Setting expectations, altering confidence
- Temporal such as
  - Structuring days, routines

Cluster RCTs for:

- Ward-based and team-based changes
  - Nursing input, lay-out of ward
  - Goal-setting approach
- Locality approaches
  - Altering attitudes to sickness

Conclusions

- RCTs are:
  - Almost always **possible**
  - Morally superior (not ethically dubious)
  - More likely to generate practically useful knowledge
  - Able to test hypotheses rather than just generating them

Conclusion - 2

- Focus on developing specific hypotheses
- Always assume that using an RCT is the best research strategy to test a hypothesis
  - If not using or working towards and RCT, ask "Why am I not using an RCT?"
- **Note**: there are already too many descriptive studies looking at selected samples and associations, generating hypotheses

Conclusions - 3

- Develop and describe in practical terms the intervention – Why (goal)? Who to? Who by? Where? When? How long? Etc
- Consider carefully the contrasting intervention ('control')
- Randomise patients or teams or environments

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