Underrepresentation – Researcher and Clinician experience

Clinical Trial design and development

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It’s the wrong trousers…

• Failing to reach underrepresented groups means…

  – Trials don’t enrol the people we need to study
  – Trials don’t test interventions that are relevant to a wide range of groups
  – So the evidence doesn’t apply to the people who need it
  – And clinicians can’t use the evidence to have conversations with people that we see
  – Which means that we end up guessing…
  – …. and we aren’t always right!
  – It also means that we as clinicians ignore the evidence as we don’t think it applies to the people we see – which might be denying people effective treatment
The example of heart failure

- ACE inhibitors – tested in younger people; unclear whether tolerated in older people
- Underused for years in older people
- Probably good for older people

- Spironolactone – tested in younger people with relatively little comorbidity
- Low rates of side effects (1-2% kidney injury / hyperkalemia)
- High rates of side effects in real-world patients (older, CKD, multimorbid): 20-25% kidney injury / hyperkalemia

Pitt B et al. NEJM 1999;341:709-17
Despite decades of trials, we still don’t know whether treating high blood pressure in the very old is of net benefit. Still don’t know whether people with frailty benefit. No idea whether it’s of net benefit for people with dementia. So we end up guessing for large number of patients. And we have no basis on which to base conversations with patients...
Life-cycle approach to trials

- Dissemination
- Guideline development
- Driving uptake by health services

- Real-world evaluation
- Systematic reviews

- Trial design and funding

- Trial delivery, recruitment, retention

- Intervention development

- Recruiting

- Implementing

- Evaluating

- Selecting

- Developing
Design and co-design

• Understand what the barriers and motivators are for a group
• Study interventions that patients want us to study – i.e. not drugs…
• Involve representatives in trial design
• E.g. for older people:
  – Transport is a major issue – so pay for taxi transport to study visits
  – Studying people with mobility issues? Offer study visits in their own home
  – Fatigue – shorter study visits, fewer outcomes
  – High dropout – use routinely collected data
Recruitment and retention

• Value of pilot trials to test recruitment and retention strategies
• Ask the target group for help (e.g. marketing messages, info sheets)
• Engage with clinical colleagues; they hold great sway in the decision-making process (and probably more so for rare diseases)

More work needed on:

Who recruits (age, sex, background)
How they recruit (language, process)
Crafting trial brands and marketing messages
Building brand loyalty
Dissemination, feedback and long-term relationships

• Clinical studies shouldn’t be a one-night stand…
• Big cohort studies are good at this; we need to learn from them
• Building long-term relationships with a target group starts with dissemination:
  – Tea parties and other face to face events – not just a side of A4
  – Engage members of the target group in designing the dissemination plan
  – Put as much effort into non-academic dissemination as you do in academic dissemination
Institutional barriers

Some recent quotes from funders and R+D depts…

- “Visits take too long with older people”
- “Home visits aren’t convenient for our research nurses”
- “Cut costs – its too expensive” (every funder, including NIHR!)
- “This trial is too difficult. We’ve got easier trials to recruit to and we are going to prioritise those”

Wider issue about doing research where the patients are – and where the clinicians are too; not where the researchers or research capacity is
Engaging with underrepresented communities – some examples

- South Asian women vitamin D trial

- Vitamin D levels are very low in the south Asian community esp in Scotland – skin colour, dress, northern latitude

- Reaching South Asian women presents a greater challenge than reaching men

- Small trial of vitamin D vs placebo for a few weeks; effects on cardiometabolic parameters

- Worked with South Asian community to recruit.

  - South Asian PI and South Asian research fellow (who was female)
  - Early engagement with community leaders (incl at mosque)
  - Sign up sessions at community events
  - Recruits encouraged to spread the word to their friends
  - Modification of study outcome procedures to preserve modesty

FFIT (Football Fans In Training)

- Interventions to improve lifestyle (esp diet) are often targeted at women
- In this context, men are an underrepresented group
- FFIT partnered with football clubs to host lifestyle improvement intervention for overweight/obese men
- Focus on weight loss, activity, healthy eating
- Recruited via football clubs (Scottish Premier League)
- Intervention delivered by football clubs – mostly male coaches
- Delivered at the stadium. Included football activities; delivered to groups of men

Hunt K et al. Lancet 2014;383:1211-21
CFS/ME

- Similar trial to South Asian women vitamin D trial
- Vitamin D vs placebo for people with chronic fatigue syndrome
- Effects on fatigue, vascular function, oxidative stress
  - Early engagement with the CFS community
  - Representatives from CFS community involved in trial design
  - Funded by a CFS charity (ME Research UK)
  - Used the charity to publicise
  - Deliberately limited length of visits
  - Provided transport to those who needed it

Home Oxygen Therapy for heart failure

- Multicentre RCT of home oxygen therapy vs usual care
- People with severe heart failure and breathlessness
- Originally aimed to recruit 450
- Actually recruited 114
- Potential contributors:
  - Lot of trial visits; burdensome outcome measures including overnight oxygen saturation measurements
  - Difficult intervention – concentrator; issues of paying for electricity; logistics of delivery
  - Trusts not always willing to pay for excess treatment costs; de-investing in home oxygen for COPD
  - Structures not always in place at sites to find potential participants
  - Adherence to oxygen in the trial was poor; therapy is burdensome
  - Some participants viewed oxygen therapy as a prelude to death, not a long-term therapy

BUT: Those recruited did have severe heart failure and poor exercise tolerance
Still got useful information from the trial

Clark A et al. HTA 2015;19:75
Summary

- Success starts with engagement and ends with engagement
- The right design is key
- Need to find better ways of sharing successful practice and failures
- Need to remove disincentives (e.g. underfunding, reward structures)
- Learn from marketing colleagues

- We need more research on to how to do research