Underrepresentation – Researcher and Clinician experience

Clinical Trial design and development

Professor Miles D Witham
Professor of Trials for Older People

Newcastle Biomedical Research Centre
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
The example of hypertension

- 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
- Intervention development
- Trial design and funding
- Trial delivery, recruitment, retention
- 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 especially 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