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Drug Research and Development for Adults Across the Older Age Span

Barriers to Conducting Clinical Trials that Include Older Adults: An Industry Approach

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Disclosure

Dr. Dawson is an employee of and holds stock in Biogen

The views and opinions presented today are my own and do not necessarily reflect the official policy or opinions of Biogen.

Objectives

- Understand the clinical development challenges posed by drug development and clinical research on the 65+ and 80+ population.
- Provide industry perspectives and insights on barriers to clinical trials that include older adults
- Share possible approaches to engage and ways to potentially optimize treatment and trials

Challenges that May Arise in Clinical Trials Involving Older Adults

Original Investigation | Global Health

Global Public Attitudes About Clinical Research and Patient Experiences With Clinical Trials

Annick Anderson, MBA; Deborah Borfitz, BS; Kenneth Getz, MBA

Center for Information and Study on Clinical Research 2017 Online Survey

- 12,427 responses, 68 countries (10% response)
- Mean age (SD) 55(15 yrs), 59% female,
- 29% ≥65 yrs, 17.7 % prior clinical research
- 84% believe clinical research is important
- 59% unable to name where studies were conducted
- 66% unable to name agency overseer,
- 39.2 % believe entire drug development process takes less than 5 yrs
- 45% rarely considered trials as an option with HCP
- Those with experience – 49% expressed that participation disrupted daily routine

Anderson et al, JAMA Network Open 2018

Table 4. Most Important Participation Factors

Participation Factor	No. (%) of Respondents Rating Very Important	
	2015 (n = 12 009)[a]	2017 (n = 12 427)[b]
Potential risks and benefits	9059 (75.4)	10 264 (82.6)
Purpose of the clinical research study	8263 (68.8)	9269 (74.6)
Types of medical procedures required[c]	6374 (53.1)	9063 (72.9)
If my confidentiality would be protected	6745 (56.2)	7783 (62.6)
Physical location of the research study center	6591 (54.9)	7429 (59.8)
Potential costs and reimbursements	5918 (49.3)	7106 (57.2)
Length of participation	5836 (48.6)	7019 (56.5)
Receiving a summary of the study results after my participation ended	6270 (52.2)	6979 (56.2)
Being provided with supporting information on the clinical research study	NA	6703 (53.9)
Provided with information on managing my health condition in general	NA	6580 (52.9)
Duration of each study visit	NA	6157 (49.5)
No. of study visits[c]	6374 (53.1)	5931 (47.7)
If I would have access to the study drug after my participation ended	5006 (41.7)	5817 (46.8)

Abbreviation: NA, not asked (in 2015 study).

Challenges that May Arise in Clinical Trials Involving Older Adults: Recruitment

- Knowledge gap
  - Misperceptions and unknowns
  - Lack of awareness
- Burden of clinical trial
  - Travel/transportation
  - Clinic visit and assessments
  - Length of trial
  - Protocol procedures
- Care partner and their burden
- Role of HCP/Study Staff

Attitudes of Older Adults to Their Participation in Clinical Trials: A Pilot Study

Frédéric Bloch · Nathalie Charasz

Table 1 Distribution of reasons given for refusal of elderly adults to participate in a clinical trial with personal benefit

Reason	%
I think I am too old for this type of experiment	24
I am afraid of taking an ineffective drug	21
I already use a lot of drugs	16
I am afraid for my well-being	16
It will only increase my worries	12
I'm afraid of being given a placebo	8
Others	3

- 44% would agree to participate in trial with personal benefit
- Only 21% willing if there was no benefit

Bloch F, Charasz N., Drugs Aging (2014) 31:373–377

Biogen, patient & caregiver advisory board/survey, data on file

Challenges that May Arise in Clinical Trials Involving Older Adults: Recruitment

Motivation for Participation

Trial participant and care partner

- Access to potential new treatment
- Access to study physician with high expertise
- Altruism

Headwinds for Participation

Trial participant

- Overwhelmed by complexity
- Misperceptions and unknowns
- Mistrust
- Protocol procedures
- Possibility of placebo

Care partner

- Concerns about safety
- Worry about side effects
- Lack of awareness of study

Challenges that May Arise in Clinical Trials Involving Older Adults: Retention

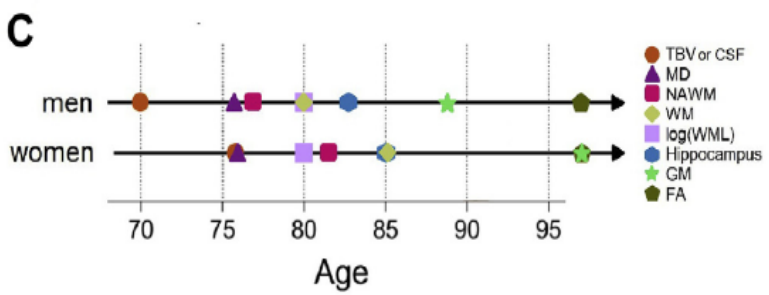
- Increases with longer studies
  - Drop out may be unrelated to trial outcomes
    - Transportation needs
    - Care partner burden over time
- Unrelated underlying health changes
  - Vision, hearing, balance, mobility, frailty, cognition
- Adherence to drug
  - Ease of use
  - Acceptance

Efficacy Challenges Can Increase with Aging: Treatment for Brain Edema after Large Vessel Stroke

Trajectories of imaging markers in brain aging: the Rotterdam Study

Elisabeth J. Vinke[a], Marius de Groot[a,b,c], Vikram Venkatraghavan[a,c], Stefan Klein[a,c], Wiro J. Niessen[a,c,e], M. Arfan Ikram[a,b,d,1], Meike W. Vernooij[a,b,*,1]

Sequence in which volumetric and microstructural MRI markers reach a 2SD change after age 45 years. First change seen was in total brain volume.



E.J. Vinke et al. / Neurobiology of Aging 71 (2018)

The effect of brain atrophy on outcome after a large cerebral infarction

Sang Hyung Lee [1] Chang Wan Oh [2] Jung Ho Han [2] Chae-Yong Kim [2] O-Ki Kwon [2] You

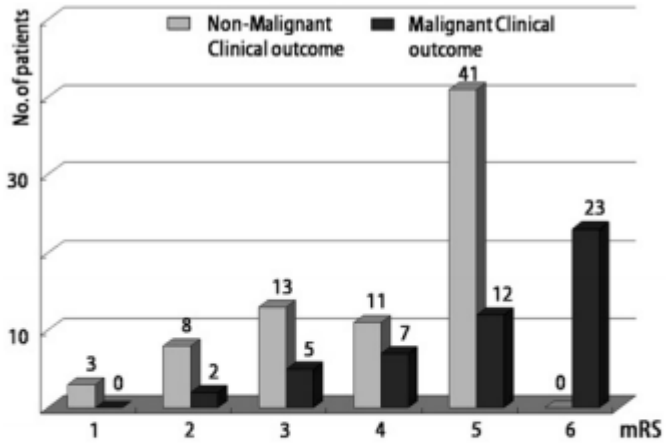


Figure 2 The distribution of patients according to modified Rankin scale[10] at 6 months after stroke onset. The grey bar indicates the group of patients who did not experienced the malignant clinical outcome during admission to hospital and the black bar indicates the group of patients who did.

Brain atrophy may have an association with clinical outcome after a large stroke by a trend of saving patients from an MCO but also by interfering with their functional recovery.

Lee et al, JNNP, 2010

Safety Challenges Can Increase in Some Older Adults

- Underlying disease or comorbidity progress
  - Frailty
  - Polypharmacy
- Physiology changes with aging affects absorption, distribution, metabolism and excretion*
- Risk of interactions as well as adverse drug reactions is increased

*Ruiter et al, British J Clinical Pharmacology, 2019

Opportunities to Address Barriers

- **Forge partnerships** with trusted community leaders, patient advocacy groups
- **Educate Investigator and site staff/HCPs** who care for the population to reduce recruitment gatekeeper
- **Elicit and incorporate patient and caregiver feedback** into protocol and patient facing materials, so that older populations can appropriately participate
- **Address common problems** as appropriate (e.g. travel vouchers, reminders via multiple channels, study update)
- Carefully **balance inclusion/exclusion criteria and ability to recruit** representative population

Summary

- Clinical development is a step-wise assessment that protects subject safety and provides information required for regulatory review
- Older aged group or people have recruitment and retention barriers in common with other age groups and others that are largely unique
- Careful consideration of study design and the anticipated effect of older age groups on efficacy and safety outcomes should inform inclusion and exclusion criteria
- Additional data in frail older adults or a broader age range may still be needed to guide safe and effective use

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