Increasing enrolment in Clinical Trials and the PREDICT Study (www.predicteu.org) (Increasing the Participation of the Elderly in Clinical Trials)

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Increasing the **Pa**R**t**icipation of the **E**l**D**erly **I**n **C**linical **T**rials

- The PREDICT consortium aimed at identifying, addressing and resolving the issues related to the exclusion of older people from CTs using full range of relevant scientific and clinical disciplines.

- EC project no: HEALTH-F4-2008-201917

  * WP1.1 - Systematic literature review.
  * WP1.2 - Review of ongoing CTs.
  * WP2 - Questionnaires for professionals
  * WP3 - Opinion of patients and carers (focus groups)
  * WP4 - Production of a Patient Charter
  * WP5 - Dissemination

WP1.1 Systematic reviews

University of BRISTOL

What evidence is there that the elderly have been excluded from clinical trials?

PREDICT

MRC Medical Research Council

Andrew Beswick

WP1.1 Results

- ✓ Heart failure
- ✓ Hypertension
- ✓ Statin treatment in coronary heart disease
- ✓ Alzheimer disease
- ✓ Depression
- ✓ Colorectal cancer

Barriers and promoters to participation of older people in clinical trials

Promoter	Barrier
Health professional (19)	
Specialist contribution to decision making	No obligation to promote RCTs in older people
	Physician perception of implications of trial participation to patient and to practice
	Physician views on research topic

Promoter	Barrier
Patient (24)	
Perceived health benefits	Unwillingness to compromise care
Altruism	Risk and fear of trial treatment
	Problems with transportation
Financial incentives	Dislike of randomisation
Social interaction	Time/ scheduling conflicts
	Financial implications
	Lack of interest/ Poor self rated health
	Concerns about information and consent

Strategies to improve participation of older people in clinical trials

Commissioners and ethics committees

- Eligibility criteria in clinical trials to be justified by trial designers
- Trial design / Larger sample size /Simplified protocols / few exclusion criteria
- Inclusion of patient preference arm
- Involvement of clinical staff in research design and implementation
- Minimal demands on clinical and support staff
- On-site coordination by clinical staff
- Employment of data manager, age/ sex registers and a good tracking system Training for research staff
- Conducting trials in well established clinical settings
- Comprehensive geriatric assessment

Recruitment process

- Recruitment by specialised research staff/ PI / GP / specialist
- Mass advertising / Postal and telephone two-step strategy Community outreach/ lectures / face-to-face recruitment
- Initial communication with trusted professional
- Emphasise benefits of participation to others
- Make expectations clear at initial contact
- Easy physical access to research institutions
- Provide or reimburse transport costs and parking /home visit
- Allow sufficient study time
- Extended patient recruitment period
- Financial incentives

Trial conduct (adherence)

- Be alert and responsive to potential signs of drop out
- Remind of commitment, reiterate motivations, emphasise need for complete data
- Minimise respondent burden
- Give instrumental or tangible support
- Enlist support from relatives, friends, physician and healthcare professionals
- Establish best time to call including evenings and weekends. Schedule study visits to coincide with other appointments (e.g. outpatient)
- Frequent follow up and contact

Trial conduct (adherence)

- Individualise number of contacts
- Reminder letters prior to visit
- Home assessment visits
- Offer phone/ postal/ e-mail/ surrogate follow up. Pay postage costs
- Provide incentives or small tokens of appreciation, study specific items
- Birthday/ Christmas/ thank you/ illness cards
- Newsletters/ feedback on study

Interventions to improve participation of older people in clinical trials

- Methods of recruitment
- Informed consent
- Follow-up visits

WP1.2 Ongoing trials

EXCLUSION OF OLDER SUBJECTS FROM ONGOING CLINICAL TRIALS ON HEART FAILURE

ORIGINAL INVESTIGATION

The Persistent Exclusion of Older Patients From Ongoing Clinical Trials Regarding Heart Failure

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Background: Much clinical research of relevance to elderly patients examines individuals who are younger than those who have the disease in question. A good example is heart failure. Therefore, we investigated the extent of exclusion of older individuals in ongoing clinical trials regarding heart failure.

Methods: In the context of the Increasing the PaRticipation of the ElDerly in Clinical Trials (PREDICT) study, data from ongoing clinical trials regarding heart failure were extracted from the World Health Organization Clinical Trials Registry Platform on December 1, 2008. Main outcome measures were the proportion of trials excluding patients by an arbitrary upper age limit or by other exclusion criteria that might indirectly cause limited recruitment of older individuals. We classified exclusion criteria into 2 categories: justified or poorly justified.

Results: Among 251 trials investigating treatments for heart failure, 64 (25.5%) excluded patients by an arbitrary upper age limit. Such exclusion was significantly more common in trials conducted in the European Union than in the United States (31/96 [32.3%] vs 17/105 [16.2%]; $P=.007$) and in drug trials sponsored by public institutions vs those by private entities (21/59 [35.6%] vs 5/36 [13.9%]; $P=.02$). Overall, 109 trials (43.4%) on heart failure had 1 or more poorly justified exclusion criteria that could limit the inclusion of older individuals. A similar proportion of clinical trials with poorly justified exclusion criteria was found in pharmacologic and nonpharmacologic trials.

Conclusion: Despite the recommendations of national and international regulatory agencies, exclusion of older individuals from ongoing trials regarding heart failure continues to be widespread.

Arch Intern Med. 2011;171(6):550-556

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WP2. PROFESSIONAL PERCEPTIONS

P.Crome,
Frank Lally
Keele University,
UK

WP2. Methods (II)

- **Final questionnaire:** 43 questions to be answered in a 6 point Lickert scale & 4 open questions.

- **Four major topics:**
  - 3 general questions on under-representation of older people in CTs.
  - 22 questions on barriers to participation of older people in CTs.
  - 18 questions on promoters to participation of older people in CTs.
  - 4 questions on regulation of CTs and possible improvements.

- **60 health professionals in each country (n=540).**

  6 professional groups: geriatricians, GPs, nurses, ethicists, pharma industry, trialists.

WP2. Promoters to inclusion in clinical trials.

Physicians may be more likely to recruit older persons into trials if..

1. It is a specific requirement to recruit older people	90%
2. There are specific age related recruitment figures	90%
3. Financial payment recognises extra-work load	70%

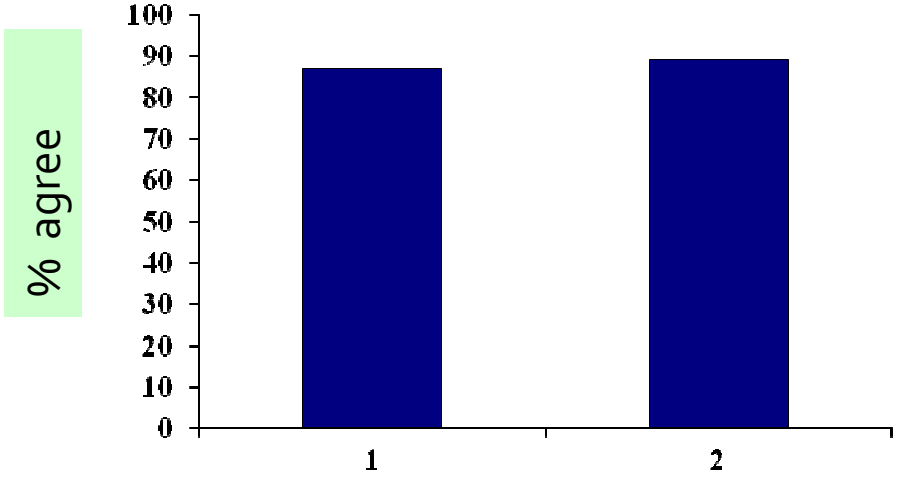
Older patients may be more likely to enter a clinical trial if...

1. If follow-up evaluations are performed at home	97%
2. There are perceived health benefits in taking part	95%
3. If participation is encouraged by their doctors	95%
4. Trials are made as simple as possible	95%
5. Appointments are scheduled flexibly in keeping with patients' life style	92%
6. They are reinbursed for transportation costs	92%

PREDICT

WP2. Promoters to inclusion in clinical trials. Sponsors.

Sponsors may be more likely to recruit older people into trials if...

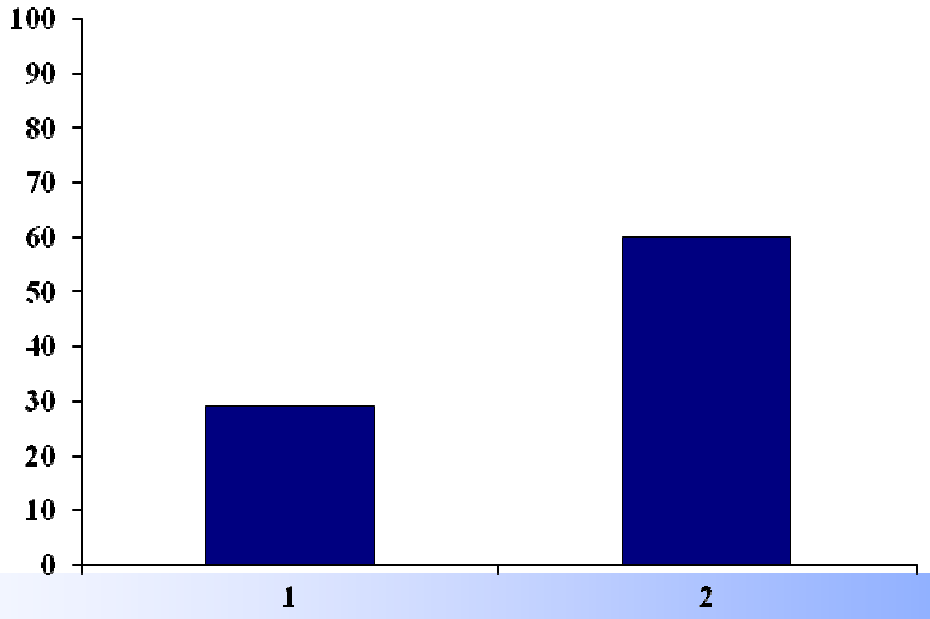


1. They received appropriate financial compensation
2. There is a legal requirement to include older people.

WP2. Promoters to inclusion in clinical trials. Regulation.

1. Overall, do you believe that present arrangements for clinical trials relating to older people are satisfactory?

2. Do you believe that either European or national regulations of clinical trials need alteration?



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WP3. PATIENT AND CARER PERCEPTIONS

Bernadette Bartlam
P.Crome, Keele University, UK

WP3. Aim

To understand the views of older people and carers on:

- Whether older people ought to be included in clinical trials, and under which conditions.

- The degree to which legislation ought to be developed to require the inclusion of older people, and the usefulness of a Charter.

WP3. Results

Focus Groups	nEU
Cardiovascular disease	6
Heart Failure	7
Cancer	7
Dementia	4
Diabetes	1
Depression	5
Cerebrovascular disease carers	3
Dementia carers	4
Carers (other)	5
TOTAL	42

WP3. Findings

Several themes emerged:

Ageism

Diversity in ageing: different outcomes

Awareness of advantages and disadvantages of participation (pros & cons): personal health benefits, altruism, transportation, home follow-up

Trust as key to participation: information, informed consent, protection

Charter for the Rights of Older People in Clinical Trials (www.predicteu.org)

1.OLDER PEOPLE HAVE THE RIGHT TO ACCESS EVIDENCE-BASED TREATMENTS

2.PROMOTING THE INCLUSION OF OLDER PEOPLE IN CLINICAL TRIALS AND PREVENTING DISCRIMINATION

3.CLINICAL TRIALS SHOULD BE MADE AS PRACTICABLE AS POSSIBLE FOR OLDER PEOPLE

4.THE SAFETY OF CLINICAL TRIALS IN OLDER PEOPLE

5.OUTCOME MEASURES SHOULD BE RELEVANT FOR OLDER PEOPLE

6.THE VALUES OF OLDER PEOPLE PARTICIPATING IN CLINICAL TRIALS SHOULD BE RESPECTED.

Conclusions

- The PREDICT study confirmed the persistent exclusion of older people from clinical trials
- The PREDICT project identified some interventions that might increase participation of older people in clinical trials
- It is time to move from research to implementation

Centres

MERCS. Sheffield. UK.: Mills, Edbroke, Sinclair Cohen

MRC. Oxfordshire Medical Research Council. UK: Beswick, Dieppe

Gerontología e Geriatría. Univ. Perugia. Italia: Cherubini, Ruggiero

Keele University. UK: Crome, Lally, Bartram

Corporació Parc Tauli. Sabadell, Spain: Oristrell-Salva

University Medical Centre Amsterdam. Netherlands: Hertogh

Institute of Public Health. Jagiellonian University. Poland: Szczerbinska

Kaunas University of Medicine. Lituania: Lesauskaite

Ana Aslan National Institute of Geriatrics. Romania: Prada

Soroka Hospital. Ben-Gurion University Beer-sheva. Israel: Clarfield

Dept. de Geriatria. Charles University, Praga. Czech Repúblic: Topinkova