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

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Increasing the Participation of the Elderly In Clinical Trials

- 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

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

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
<table>
<thead>
<tr>
<th>Promoter</th>
<th>Barrier</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Health professional (19)</strong></td>
<td>No obligation to promote RCTs in older people</td>
</tr>
<tr>
<td>Specialist contribution to decision making</td>
<td>Physician perception of implications of trial participation to patient and to practice</td>
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<tr>
<td></td>
<td>Physician views on research topic</td>
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<tr>
<td>Promoter</td>
<td>Barrier</td>
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<tr>
<td><strong>Patient (24)</strong></td>
<td></td>
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<tr>
<td>Perceived health benefits</td>
<td>Unwillingness to compromise care</td>
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<tr>
<td>Altruism</td>
<td>Risk and fear of trial treatment</td>
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<td></td>
<td>Problems with transportation</td>
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<tr>
<td>Financial incentives</td>
<td>Dislike of randomisation</td>
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<tr>
<td>Social interaction</td>
<td>Time/ scheduling conflicts</td>
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<td></td>
<td>Financial implications</td>
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<td></td>
<td>Lack of interest/ Poor self rated health</td>
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<td></td>
<td>Concerns about information and consent</td>
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</table>
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
EXCLUSION OF OLDER SUBJECTS FROM ONGOING CLINICAL TRIALS ON HEART FAILURE
The Persistent Exclusion of Older Patients From Ongoing Clinical Trials Regarding Heart Failure

Antonio Cherubini, MD, PhD; Joaquim Oristrell, MD, PhD; Xavier Pla, MD; Carmelinda Ruggiero, MD, PhD; Roberta Ferretti, MD; Germán Diestre, MD; A. Mark Clarfield, MD, FRGCP; Peter Crome, MD, DSc; Cees Hertogh, MD, PhD; Vita Lesauskaite, MD, PhD; Gabriel-Ioan Prada, MD, PhD; Katarzyna Szczerbinska, MD, PhD; Eva Topinkova, MD, PhD; Judith Sinclair-Cohen, BSD; David Edbrooke, MD, FRCA; Gary H. Mills, MD, PhD

**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*
Increasing the Participation of the Elderly in Clinical Trials

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..

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

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

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<tbody>
<tr>
<td>1. If follow-up evaluations are performed at home</td>
<td>97%</td>
</tr>
<tr>
<td>2. There are perceived health benefits in taking part</td>
<td>95%</td>
</tr>
<tr>
<td>3. If participation is encouraged by their doctors</td>
<td>95%</td>
</tr>
<tr>
<td>4. Trials are made as simple as possible</td>
<td>95%</td>
</tr>
<tr>
<td>5. Appointments are scheduled flexibly in keeping with patients’ life style</td>
<td>92%</td>
</tr>
<tr>
<td>6. They are reimbursed for transportation costs</td>
<td>92%</td>
</tr>
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</table>
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.
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?
Increasing the Participation of the Elderly in Clinical Trials

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

<table>
<thead>
<tr>
<th>Focus Groups</th>
<th>nEU</th>
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<tbody>
<tr>
<td>Cardiovascular disease</td>
<td>6</td>
</tr>
<tr>
<td>Heart Failure</td>
<td>7</td>
</tr>
<tr>
<td>Cancer</td>
<td>7</td>
</tr>
<tr>
<td>Dementia</td>
<td>4</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1</td>
</tr>
<tr>
<td>Depression</td>
<td>5</td>
</tr>
<tr>
<td>Cerebrovascular disease carers</td>
<td>3</td>
</tr>
<tr>
<td>Dementia carers</td>
<td>4</td>
</tr>
<tr>
<td>Carers (other)</td>
<td>5</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>42</strong></td>
</tr>
</tbody>
</table>
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
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.

Charter for the Rights of Older People in Clinical Trials (www.predict.eu.org)
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 Taulí. 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 República: Topinkova