Language as a Barrier in Cancer Clinical Trial Eligibility

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Clinical trials

3-5 % of adult cancer patients enroll in clinical trials
(Bell and Balneaves, 2015; Michaels et al, 2015)

Barriers can be:
1. Patient level
   ◦ Transportation
2. Doctor level
   ◦ Unconscious bias
3. Institutional level
   ◦ Insufficient staffing
   ◦ Lack of institutional support
   ◦ Unsuitable protocols
   ◦ e.g. biased eligibility criteria

Underrepresented groups in clinical trials:
• Racial and ethnic minorities
• Elderly
• Lower socioeconomic class
  (Michaels et al, 2015)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Trial Participants, No. (%)</th>
<th>Proportion of Incident Cancer Patients, %†</th>
<th>Proportion of US Population, %†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Race/ethnicity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White non-Hispanic</td>
<td>64355 (85.6)</td>
<td>83.1</td>
<td>75.7</td>
</tr>
<tr>
<td>Hispanic</td>
<td>2292 (3.1)</td>
<td>3.8</td>
<td>9.1</td>
</tr>
<tr>
<td>Black</td>
<td>6882 (9.2)</td>
<td>10.9</td>
<td>10.8</td>
</tr>
<tr>
<td>Asian/Pacific Islander</td>
<td>1446 (1.9)</td>
<td>2.0</td>
<td>3.8</td>
</tr>
<tr>
<td>American Indian/Alaskan Native</td>
<td>240 (0.3)</td>
<td>0.2</td>
<td>0.7</td>
</tr>
<tr>
<td>Age, y</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30-64</td>
<td>51145 (68.0)</td>
<td>37.5</td>
<td>78.5</td>
</tr>
<tr>
<td>65-74</td>
<td>17851 (23.7)</td>
<td>31.4</td>
<td>11.3</td>
</tr>
<tr>
<td>≥75</td>
<td>6219 (8.3)</td>
<td>31.2</td>
<td>10.2</td>
</tr>
</tbody>
</table>

(Murthy et al. 2004)
Clinical trials

Success of a clinical trial:
• Generalizability
• Safety of patients
• Statistical validity
• Efficiency

“exclusions can bias individual trial results both in favor of the treatment and control.” (Tierney and Stewart, 2004)

Costs of low recruitment:
• Consumption of resources
• Decrease in efficiency
• Loss in external validity and statistical power
• Possible negative health outcomes

“85 % of research investment is wasted” (Dechartres and Ravaud, 2015)
Language Based Eligibility

English Fluency as an eligibility criterion has been increasing in recent years

- 1.7% of trials before 2000; 9.0% of trials in 2010 (Egleston et al, 2015).

- Language-based discrimination
- Exclusion of some racial minorities
- Less Generalizability

Statistics shown as a national average, but how about our ACC?
Prevalence of English fluency as exclusion criteria at ACC

Primary Objective

Assess ACC prevalence of exclusion criteria based on English fluency and consider potential policy change at the institutional level.

Secondary Objectives

Analyze results by Disease site

Analyze results by treatment modality

Assess potential effects on the demographics of clinical trial enrollees
Methods

1. Data collection & IRB
   • Design the protocol and apply for IRB exemption

   • Non-cancer treatment trials
   • Quality of life CTs
   • EmergingMed
   • I-Drive (investigators shared network)

   • Date opened & date closed
Findings – Consort Diagram

Protocols Assessed for Eligibility (n= 246)

Excluded (n= 156)
- Could not be found (n= 136)
- Was not open in CY14 (n= 1)
- Not sponsored by ACC (n= 19)

Protocols assessed (n= 90)

English Fluency as Subj ective Measure

No Exclusion based on English Fluency (n= 70)
- Contains no language that indicates exclusion based on English ability

English Fluency as Explicit Exclusion

No (n= 81)
- Protocol criteria does not explicitly exclude patients who do not speak English fluently

Yes (n= 9)
- Contains language that explicitly excludes patients who do not speak English fluently
  e.g. “Must speak English”

Non-explicit Exclusion Language (n= 11)
- Contains language that indicates a barrier for patients who do not speak English fluently without explicitly stating so
  e.g., “provide independent informed consent”
## Findings – Results Stratified by Disease Site

<table>
<thead>
<tr>
<th>Disease Site</th>
<th>Total trials</th>
<th>Explicit Exclusion</th>
<th>Implicit Exclusion</th>
<th>Both Explicit and Implicit</th>
<th>Implicit + Explicit Exclusion Combined with all cancer types</th>
</tr>
</thead>
<tbody>
<tr>
<td>All cancer types</td>
<td>16</td>
<td>3 (18.8%)</td>
<td>2 (12.5%)</td>
<td>5 (31.3%)</td>
<td>5 (31.3%)</td>
</tr>
<tr>
<td>Metastatic</td>
<td>10</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>5 (19.2%)</td>
</tr>
<tr>
<td>Lung/Mesothelioma</td>
<td>10</td>
<td>2 (20.0%)</td>
<td>1 (10.0%)</td>
<td>3 (30.0%)</td>
<td>8 (30.7%)</td>
</tr>
<tr>
<td>ENT (ear, nose, throat)</td>
<td>9</td>
<td>1 (11.1%)</td>
<td>2 (22.2%)</td>
<td>3 (33.3%)</td>
<td>8 (32.0%)</td>
</tr>
<tr>
<td>Bone marrow/Leukemia/Lymphoma</td>
<td>13</td>
<td>1 (7.7%)</td>
<td>3 (23.1%)</td>
<td>4 (30.8%)</td>
<td>9 (31.0%)</td>
</tr>
<tr>
<td>Pancreas/colorectal/Liver</td>
<td>11</td>
<td>1 (9.1%)</td>
<td>2 (18.2%)</td>
<td>3 (27.3%)</td>
<td>8 (32.0%)</td>
</tr>
<tr>
<td>Prostate/Testes</td>
<td>4</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>5 (25.0%)</td>
</tr>
<tr>
<td>Breast</td>
<td>17</td>
<td>3 (17.6%)</td>
<td>2 (11.8%)</td>
<td>5 (29.4%)</td>
<td>10 (30.3%)</td>
</tr>
<tr>
<td>Head and Neck</td>
<td>8</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>5 (20.8%)</td>
</tr>
<tr>
<td>Gynecologic</td>
<td>5</td>
<td>1 (20.0%)</td>
<td>0 (0%)</td>
<td>1 (20.0%)</td>
<td>6 (28.6%)</td>
</tr>
<tr>
<td>Bone</td>
<td>6</td>
<td>0 (0%)</td>
<td>2 (33.3%)</td>
<td>2 (33.3%)</td>
<td>7 (31.8%)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>90</td>
<td>9 (10%)</td>
<td>10 (11.1%)</td>
<td>19 (21.1%)</td>
<td>-</td>
</tr>
</tbody>
</table>
Findings – Results by Treatment Modality

<table>
<thead>
<tr>
<th>Modality of treatment</th>
<th>Total trials</th>
<th>Explicit English Requirements</th>
<th>Implicit English Requirements</th>
<th>Total Explicit and Implicit Requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemotherapy</td>
<td>35</td>
<td>0 (0%)</td>
<td>9 (25.7%)</td>
<td>9 (25.7%)</td>
</tr>
<tr>
<td>Radiotherapy</td>
<td>22</td>
<td>2 (9.1%)</td>
<td>1 (4.6%)</td>
<td>3 (13.6%)</td>
</tr>
<tr>
<td>Other</td>
<td>39</td>
<td>7 (17.9%)</td>
<td>2 (5.1%)</td>
<td>9 (23.1%)</td>
</tr>
<tr>
<td>Total</td>
<td>90</td>
<td>9 (10%)</td>
<td>10 (11.1%)</td>
<td>19 (21.1%)</td>
</tr>
</tbody>
</table>
Conclusions

• 21.1% of ACC clinical trials have a language barrier
  • 10% Explicit
  • 11.1% Implicit

• By Disease Site
  • Ear, nose and throat as well as bone cancer clinical trials had the highest incidence of explicit and implicit criteria (33.3% each)

• Stratification by Modality
  • Chemotherapy has relative highest incidence of possible implicit exclusion
Limitations

Causation

- The reasons for why some trials include English fluency as an eligibility criterion and others do not were not explored in this study.
Future Directions

• Analyze clinical trial data from 2015 & 2016 to increase power of results
• Determine effects of English fluency as a eligibility criteria on enrollment demographics
• Develop method to spread awareness of ACC inclusion policy/resources
  • Penn IRB has existing protocols to allow for Non-English speakers
• Incorporate policy changes such as:
  ◦ Using standardized project management procedures and protocols
  ◦ Realistic budgeting to support challenges in recruitment (translators)
  ◦ Research staff cultural competency
  ◦ Communication training

(Bernadette et al, 2015)

Consent Form - Short Forms

- ICD-8.1 - English Template
- ICD-8.2 Chinese
- ICD-8.3 Haitian Creole
- ICD-8.4 Italian
- ICD-8.5 Korean
- ICD-8.6 Russian
- ICD-8.7 Spanish
- ICD-8.8 Vietnamese
- ICD-8.9 Arabic
- ICD-9.10 - Portuguese
- ICD-8.11 Polish
UNIVERSITY OF PENNSYLVANIA
RESEARCH SUBJECT
INFORMATION FORM

Protocol Title:

Principal Investigator:

Emergency Contact:

You are being invited to participate in a research study. Before you agree, the investigator must explain a number of things to you. These things include:

- The purpose of the study
- How many people will be enrolled in the study and how long the study will last
- The risks, procedures or treatments that will be done
- Which tests, procedures or treatments are experimental
- Any risks from the study. There may be risks from a study drug or device, or from a study test or procedure
- If the study will benefit you in any way
- How you will be told if there is new information about the study that could affect your decision to continue with the study
- Other options you have rather than participating in the study
- What to do if you are injured or hurt during the study
- Whether there are any costs to you for participating
- Whether you will be paid anything for participating
- Reasons the investigator may halt your participation in the study
- Who can use our research information about you from the study
- How your information and privacy will be protected

Your participation in this research study is voluntary. If you decide not to participate, you are free to leave the study at anytime. Withdrawal will not interfere with your future care. If you have questions about your participation in this research study or about your rights as a research subject, make sure to discuss them with the study investigator or members of the study team. You may also call the Office of Regulatory Affairs at the University of Pennsylvania at (215) 898-2614 to talk about your rights as a research subject.

You will be asked to sign this form to show that

- You agree to participate in the study
- You agree to provide the information above and discussed with you

You will receive a copy of this signed form and the summary of the study that will be discussed with you.

Subject’s Name [print]  Subject’s Signature  Date

Witness [print]  Witness’ Signature  Date

Version Date

Template Version 1/30/2007
Acknowledgments

Our beloved advisor, Carmen Guerra, MD, MSCE, FACP
The student who did the preliminary research for the project, Edgar Guzman
Our main resource at ACC, Vicki Sallee
Our resource at Penn’s IRB, Megan Kasimatis
References


(Bell and Balneaves, 2015)