Perspectives of Faculty and Patients Regarding Issues in Research Ethics

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Introduction

• Medical research has increased in the Middle East during the past decade.
• Research regulations do not exist in many countries.
• Commentators have expressed concerns regarding the extent of individual/institutional capacity in Research Ethics.
Ethical Practices for Health Research in the Eastern Mediterranean Region of the World Health Organization: A Retrospective Data Analysis

Mohammad Abdur Rab¹, Mohammad Afzal², Alaa Abou-Zeid², Henry Silverman³*

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<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>REC Review</th>
<th>Informed Consent</th>
<th>Confidentiality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biological Samples</td>
<td>49</td>
<td>28 (58%)</td>
<td>37 (76%)</td>
<td>43 (88%)</td>
</tr>
<tr>
<td>Qualitative Studies</td>
<td>30</td>
<td>10 (33%)</td>
<td>19 (65%)</td>
<td>30 (100%)</td>
</tr>
</tbody>
</table>
The underlying reasons for these less than optimal practices of faculty are not known.

Determine Faculty’s

- Extent of ethics training
- Attitudes towards RECs and research ethics
- Alleged practices in research ethics
Prior Ethics Training
Cairo University

Percentage of Faculty with Prior Ethics Training

- Course and Read Materials: 52%
- Only read materials: 20%
- No prior exposure: 28%

Asem A et. al. PRIM&R 2009
Faculty had significant relation with prior research ethics training; *p<0.01
Prior Ethics Training
Ain Shams and King Abdul-Aziz

Percentage of Dental Faculty with Prior Ethics Training

- Workshop/Course: 38%
- No prior exposure: 62%

Prior Ethics Training
Alexandria, Mansoura, Suez Canal, Ain Shams

Percentage of Faculty with Prior Ethics Training

- Both Course and Workshop: 18%
- Either Course or Workshop: 30%
- No Prior Exposure: 52%

Kandeel A. In Press 2011
Prior Ethics Training

No Prior Exposure to Research Ethics

28 – 62%
## Attitudes Towards Research Ethics

<table>
<thead>
<tr>
<th>Item</th>
<th>% of Faculty Who Agreed</th>
</tr>
</thead>
<tbody>
<tr>
<td>There should be measures to protect data from disclosure</td>
<td>93.6</td>
</tr>
<tr>
<td>Informed consent should be obtained from each patient</td>
<td>91.2</td>
</tr>
<tr>
<td>All Investigators should have training in research ethics</td>
<td>97.6</td>
</tr>
<tr>
<td>Patients should not be told about research risks as they may not enroll</td>
<td>7.2</td>
</tr>
<tr>
<td>It is not necessary to obtain research consent to do research on blood samples obtained for clinical tests</td>
<td>29.5</td>
</tr>
<tr>
<td>If no surrogate is available to give informed consent for vulnerable person, they could still be enrolled</td>
<td>7.2</td>
</tr>
<tr>
<td>It is okay to fabricate data to improve outcome of research if there is no harms to patients</td>
<td>11.2</td>
</tr>
</tbody>
</table>

## Attitudes Towards Research Ethics Committees

<table>
<thead>
<tr>
<th>Item</th>
<th>% of Faculty Who Agreed</th>
</tr>
</thead>
<tbody>
<tr>
<td>There is a need for an REC in each University</td>
<td>85.3</td>
</tr>
<tr>
<td>Research must be reviewed by an REC</td>
<td>91.4</td>
</tr>
<tr>
<td>REC members should have training in research ethics</td>
<td>93.1</td>
</tr>
<tr>
<td>Ethics review of research should be restricted to international collaborative research</td>
<td>25.1</td>
</tr>
<tr>
<td>Review by an REC would delay research and make it harder for the researcher</td>
<td>32.9</td>
</tr>
<tr>
<td>Reviewing research by an REC is not necessary since there is a scientific committee</td>
<td>18.9</td>
</tr>
</tbody>
</table>

# Practices in Informed Consent

<table>
<thead>
<tr>
<th>Informed Consent Practices</th>
<th>% Agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gave participants adequate information</td>
<td>90.2</td>
</tr>
<tr>
<td>Allowed adequate time for discussion</td>
<td>90.2</td>
</tr>
<tr>
<td>Gave a copy of the consent form to participants</td>
<td>37.7</td>
</tr>
<tr>
<td>Used a method to assess understanding</td>
<td>53.8</td>
</tr>
<tr>
<td>Used other methods to explain information to patients who were illiterate</td>
<td>69.8</td>
</tr>
</tbody>
</table>

Asem N, et.al. PRIM&R 2009
Patients’ Perspectives

• Several studies have examined the views of patients from Western countries.
• There is limited empirical research involving the perspectives of patients from developing countries.
• Perspectives of participants from the Middle East would help clarify the concerns regarding research participation.

  • Enhance recruitment efforts
  • Improve the informed consent process
  • Enhance trust between patients and investigators.
Perspectives of Patients

• Objectives:
  – Attitudes towards Research
  – Perception of the Informed Consent process
  – Understanding of research methods
  – Ability to distinguish between research and clinical care (therapeutic misconception).
Research article

**Attitudes, understanding, and concerns regarding medical research amongst Egyptians: A qualitative pilot study**
Susan S Khalil¹, Henry J Silverman*², May Raafat¹, Samer El-Kamary² and Maged El-Setouhy¹

Research article

**Expression of therapeutic misconception amongst Egyptians: a qualitative pilot study**
Mayyada Wazaify*¹, Susan S Khalil² and Henry J Silverman*³

Parental attitudes towards and perceptions of their children’s participation in clinical research: a developing-country perspective
Mona Nabulsi¹, Yvette Khalil¹, Jihad Makhoul²

Collection, storage and use of blood samples for future research: views of Egyptian patients expressed in a cross-sectional survey
Alaa Abou-Zeid¹, Henry Silverman², Magdi Shehata³, Mohamed Shams⁴, Mervat Elshabrawy⁵, Tamer Hfnawy⁶, Safa Abdel Rahman⁷, Bahiga Galal⁸, Hany Sleem⁹, Nabil Mikhail¹⁰, Nadia Moharram¹¹
Attitudes Towards Research Participation
Reasons to Enroll in a Study

% of Participants who answered

- Doctor asked and I could not refuse
- Doctor thought it is a good idea
- Help other patients
- Only way to get hospital care
- Only way to get specific treatment
- Chance to get better treatment

Abou Zeid A, et.al. 2009
Reasons to Refuse to Enroll in a Study

% of Participants

I am afraid of being a social outcast
I am too busy at home
My husband won't let me
I don't feel like being a guinea pig
I don't trust my doctors
I am afraid of procedures

Abou-Zeid A, 2009
Reasons for participation in clinical trials

- Receive expensive / unavailable drugs: 47%
- Receive free hospital care: 16%
- Receive money/gifts: 4.9%

Motives of Participants to Enroll In Dental Research

Al-Amad S, et.al. 2010
Most participants expressed trust in doctors and in the research process.
Perspectives Regarding Informed Consent
Informed Consent as an Important Value

All (15) participants valued the importance of informed consent and some framed their answer in the language of rights.

Responses of Participants:

• "Definitely, it's important to respect the rights of a patient."

• "Yes, definitely, since you have to ask the patient first and everyone has this right."

• "Yes, of course... Aren't I the one that's going to join with my body and my health? I mean, who else would they ask."

Kahlil S, et.al. BMC Medical Ethics 2007
Problems with Informed Consent

Informed consent (33 in-depth interviews)

• Only four parents from the vaccine study remembered the consent process and that it was voluntary.

• Many of the participants found the form difficult because of the complex medical terminology and its length, which required time to read and comprehend and was therefore a source of anxiety for them.

• Parents required the opinion of other trusted people, such as their husband, their pediatrician or a lawyer, before signing it.
Risks and Benefits
Relationship between the type of study and willingness to participate in the study. Studies are listed in order of increasing risk levels.

<table>
<thead>
<tr>
<th>Type of study</th>
<th>Willingness to participate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood sampling study</td>
<td>13/15</td>
</tr>
<tr>
<td>Survey study with sensitive information</td>
<td>12/15</td>
</tr>
<tr>
<td>Skin biopsy study</td>
<td>3/14</td>
</tr>
<tr>
<td>Endoscopy study</td>
<td>1/14</td>
</tr>
<tr>
<td>Drug trial</td>
<td>5/15</td>
</tr>
</tbody>
</table>

Kahlil S, et.al. BMC Medical Ethics 2007
Which types of dental research would patients agree or disagree to participate in?

- Survey: 74.2%
- Swabs: 46.2%
- Saliva collection: 47.3%
- Topical medication: 44.1%
- Fillings: 35.5%
- Biopsy: 17.2%
- Drilling/extraction: 14.0%

Al-Amad, S, 2010
Understanding Research Methods
Physician Uncertainty Regarding Which Drug is Better in a Clinical Trial

Most (12/15) reported discomfort with such uncertainty. Many expressed disbelief that the physician-investigator would not know which drug is better for them.

"I don't know, I'd be very surprised how my doctor doesn't know, I might be worried how he's a doctor and doesn't know. He's specialized in this and doesn't know, so how should I feel but worried."

"Uncomfortable is not a term that's enough to describe how I feel...I go to the doctor with my health in their hands, which is the most precious thing to me. The fact that there's some knowledge that they lack, which will affect my health, I see that as a big problem."

Kahlil S, et.al. BMC Medical Ethics 2007
Discomfort with Doctor being blind to treatment assignment

Five respondents would not accept to be in such a study:

• three said they needed to know which drug they were receiving, while the other two stated that their doctor had to know which drug they were receiving.

• Responses from five respondents indicated they lacked an understanding of the physician-investigator being blinded to the treatment option.

• Three participants said they would participate in such a study, but would be either "worried" or uncomfortable with such a situation.

Kahlil S, et.al. BMC Medical Ethics 2007
"No, I'm not comfortable with it. He [the physician] should tell me what the risks and benefits of each drug are and I should have the freedom to decide which of the drugs I want [I'll take]."

"I don't like the idea of it being random. I know that one that's on the market is available in the pharmacy, and there's the newer one. I'll just take the older one."

"This random selection method is not guaranteed [safe] at all...It's like I said, it's just not safe. I just can't see how it can be safe to randomly assign something in medicine [medical care]."

Kahlil S, et.al. BMC Medical Ethics 2007
These parents struggled with the term ‘randomisation’ and its purpose, despite interviewers’ lengthy attempts to explain it.

The Arabic translation for the word ‘randomisation’ is ‘ashwa’l’ meaning happening in a haphazard way.

Parental anxiety about this process, understood as ‘going into the unknown’ is therefore understandable.

“In contrast, parents visiting private clinics, who belong to middle and high socioeconomic classes, seemed to have a better understanding of randomisation and understood the English term. For them, it was an appropriate or ‘fair’ method of conducting research, of which they approved.”
Attitudes Towards Placebo: Dental Patients

I wouldn't choose

I wouldn't know

My doctor wouldn't know

very comfortable

somewhat comfortable

not comfortable

not comfortable at all

I don't care
Conclusions

• Most potential participants have difficulty with concepts in research
  – Uncertainty
  – Double Blindness
  – Randomization
Children Research
A main barrier to parental consent to children’s enrolment in clinical trials was parental fear of possible harm to their children from the study and fear of associated painful procedures.
Mixed reactions toward giving permission for children participation in research (n=15)

Three stated the study would need to be associated with benefits for their children.

Another said that she would "be hesitant if it has risks“

Another respondent mentioned that there needs to be assurances that the study would not involve experimenting on her child.

Kahlil S, et.al. BMC Medical Ethics 2007
Perspectives on Stored Tissue Samples Research
Collection, storage and use of blood samples for future research: views of Egyptian patients expressed in a cross-sectional survey

Alaa Abou-Zeid,¹ Henry Silverman,² Magdi Shehata,³ Mohamed Shams,⁴ Mervat Elshabrawy,⁵ Tamer Hfnawy,⁶ Safa Abdel Rahman,⁷ Bahiga Galal,⁸ Hany Sleem,⁹ Nabiël Mikhail,¹⁰ Nadia Moharram¹¹

ABSTRACT
Objective To determine the attitudes of Egyptian patients regarding their participation in research and with the collection, storage and future use of blood samples for research purposes.
Design Cross-sectional survey.
Study population Adult Egyptian patients (n=600) at rural and urban hospitals and clinics.
Results Less than half of the study population (44.3%) felt that informed consent forms should provide research participants the option to have their blood samples stored and used for future, unspecified research. Differing opinions have included: offering research participants up to six separate choices regarding their prospective consent for future research; re-contacting participants each time new research on their biological samples is proposed; and re-contacting participants only for research that poses a greater than minimal risk.

Finally, as research has become increasingly globalised, ethical issues also arise from collaborative international research in which samples are
Methods:

– Survey distributed to patients in rural, urban, public, and private hospitals
– Public and private clinics
– N = 600
### Response Regarding Storage and Use of Blood Samples in Future Research (n=600)

<table>
<thead>
<tr>
<th>Item</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Give to other researchers without contact</td>
<td>53.3</td>
</tr>
<tr>
<td>Time limit for storage of samples</td>
<td>21.7</td>
</tr>
<tr>
<td>Right to withdraw samples</td>
<td>28.8</td>
</tr>
<tr>
<td>Right to share in profits</td>
<td>32.8</td>
</tr>
<tr>
<td>Be given results of samples if there is an implication for health</td>
<td>88.8</td>
</tr>
<tr>
<td>Samples may be used for future genetic research</td>
<td>66.2</td>
</tr>
</tbody>
</table>
### Responses Regarding Sharing and Exportation of Blood Samples

<table>
<thead>
<tr>
<th>Item</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Samples may be sent to another Arab Country</td>
<td>62.0</td>
</tr>
<tr>
<td>Samples may be sent to an European Country</td>
<td>41.8</td>
</tr>
<tr>
<td>Samples may be sent to the USA</td>
<td>37.2</td>
</tr>
<tr>
<td>Source country should have access to drugs derived from analysis</td>
<td>89.0</td>
</tr>
<tr>
<td>Gov’t approval for sample exportation</td>
<td>88.2</td>
</tr>
</tbody>
</table>
Clinical Orientation to Clinical Trials
Therapeutic Misconception
Perceptions Of Research Procedures, Informed Consent, And Therapeutic Misconception Among Egyptian Research Participants

Hala Mansour, Nadia Zaki, Rehab Abdelhai, Nehad Sabry, Henry Silverman, Samer El-Kamary
# Introduction

- **Therapeutic misconception in clinical trials**
  - Participants attributes therapeutic impact from the research
  - Participant’s failure to understand how their individual care may be compromised by participating in the research
  - Obscures distinction between research and medical care

<table>
<thead>
<tr>
<th></th>
<th>Medical Care</th>
<th>Research</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Purpose</strong></td>
<td>Enhance Patient’s Welfare</td>
<td>Produce Generalizable Knowledge</td>
</tr>
<tr>
<td><strong>Methods</strong></td>
<td>Clinically necessary procedures to enhance health</td>
<td>Randomization, Placebos, Fixed dose regimens, Protocol-defined restrictions on drug doses, Procedures performed to obtain research data</td>
</tr>
</tbody>
</table>
Definition of Therapeutic Misconception

- **TM(1)**: express an incorrect belief that their individualized needs (or what will benefit them the most) will determine assignment to treatment conditions.
  - Believes that intervention will be chosen based on what the physician believes will be best, rather than on a random process.

- **TM(2)**: offer an unreasonable assessment of the nature or likelihood of medical benefit from participation in the research.
  - Physician would not suggest enrollment unless it was very likely to be of help
  - Risks of research must be low
• Total number of subjects that expressed therapeutic misconception about clinical trials in this study sample.

Total: 9/15

• Belief that medical care would be individualized for themselves

TM1: 8/15

• Unreasonable belief in the likelihood of benefits

TM2: 6/15

Waizaify, et.al. 2009
Examples of Therapeutic Misconception TM (1)

• I: “How would you feel if your doctor would not know which drug you would be taking?”
• P: “There’s no way that my doctor doesn’t know what I’m taking”

• I: “Would this study [clinical trial] be acceptable for you...?”
• P: “If the doctor says it’s better then I’ll try it. If he tells me it’s not good, then I won’t try it.

• I: “Would you agree to participate in this study?”
• P: “I think my physician would know better...I’ll take what they suggest.”
• P: “He’ll probably try the new drug to see how it helps me.”

• I: “If a research study involves comparing a new drug with a current one....?”
• P: “I’d prefer to pick the one with the fewer side effects.”
Examples of Therapeutic Misconception TM (2)

• I: Would you agree to be in a research study?
• P: “I definitely would agree to participate, but the new drug must have a better impact than the old drug.”
• P: “Certainly, these studies won’t have side effects, the goal is to improve health and not cause harm.”
• P: “It must have some guidelines that guarantee that it will protect me.”
• P: “I must be at least 90% reassured that it’s something safe.”
• P: “I’ll take it if my doctor tells me that it’s better.”
Conclusions Regarding TM

• The majority of the participants demonstrated misconception regarding
  – how research participation may involve the sacrifice of some degree of personal/individualized care
  – the likelihood of benefits from the research

• Ethical Problems from the presence of TM
  – Present challenges in obtaining valid informed consent, because participants fail to appreciate adequately the risk/benefit ratio
  – Vulnerable to exploitation
Summary

Overall, individuals in our sample recognize the value of medical research and have a great deal of trust regarding medical research and their participation in research.

Informed consent is considered an important value.

Concerns with the level of research risks associated with several types of medical research. Most would not participate in research that involved more than minimal risk.
Summary

• Many participants had discomfort with or difficulty in the understanding several research concepts: randomization, double-blind, and clinical equipoise.

• There are concerns with the presence of the therapeutic misconception in clinical trials
Recommendations

We recommend:

1) enhanced educational efforts regarding general research concepts to enhance the validity of informed consent
2) further survey studies in other areas of the Arab Region to determine the generalizability of our results.
Thank you!!