A Multicenter Study Investigating the Factors that Influence Female Participation in Clinical Research: A Focus on the Mindsets of Pregnant and Fertile Women

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ABSTRACT
The purpose of the Multi-Center Study Investigating the Factors that Influence Participation in Clinical Research is to accumulate enough data and information about female patients to determine factors, barriers, and any resources that could influence their decision to participate in clinical research. The study has three main aims: first is to gain a better sense of women’s general attitudes and involvements concerning clinical research, second the study wishes to ascertain any factors that influence female participation in clinical research, third the study is trying to understand the value and impact of promotional tools directed at creating equality in clinical research. The overall goal is to lessen or eradicate the gender disparity between men and women in clinical research by finally trying to find solutions to the problem. The outcomes indicate that pregnant and fertile women, a part of the initial data collection, are open to educational resources, but do have different motivating factors and barriers that help influence their decisions to participate.

BACKGROUND
In 1977, the FDA issued a ban prohibiting any woman with “child bearing potential” from participating in clinical research. This ban was revoked in 1990, but its effects have left a lasting impact.1 Will the pregnant or fertile women surveyed also still be wary of clinical research because of this stigma? Would there be a difference between the motivating factors, barriers, and resources that influence non-fertile women?

There has been a proven increase in women’s participation in clinical trials since the 1970s, but the ratio of women’s enrollment when compared to both the United States’ entire population and to diseases that impact women more frequently, is much lower than it should be.2 Since the beginning of 1990, different guidelines have tried to correct the mindset that the FDA’s ban created, such as the 1991 Pregnancy Discrimination Act and the Guideline for the Study and Evaluation of Gender Differences in the Clinical Evaluations of Drugs in 1993.3 In 1994, the National Institutes of Health (NIH) guidelines issued by the Office of Research on Women’s Health and Office of Research on Minority Health stated that all human subjects must be included in research. These guidelines were the beginning steps bridging the gap between the sexes in clinical research.2 Guidelines continue to be imposed in the twentieth century. In 2003, the American Heart Association made separate guidelines for women in clinical trials.2 The fact is that women are
more prone to vascular diseases, but men are being enrolled in drug trials much more frequently. The need for new strategies in creating gender specific medicine has become much more apparent. Finally, in 2012, the Canadian Institute of Health Research (CIHR) stated that all their funding applicants must explain whether they’re investigating gender-related factors if their enrollment did not include a significant amount of women. If this is the case, they must explain why more women are not included. This will make researchers think about including women in their trials and could prevent them from excluding women without proper reasoning. (Many times researchers are aware of the increased cost and confounding factors that can come from including women in trials and so choose not to include them.)

As Kingston states in her article “Deadly Gender Gap”, “studying women can teach us a lot about the treatment of and care for chronic diseases, which place far more of a burden on the health care system.” Most importantly, the inclusion of pregnant women with chronic diseases can begin to be tested also, because sadly, most drugs used routinely in pregnancy have not yet been tested on pregnant women.

In a recent research study, the results showed that women can be motivated by different factors to participate in clinical research. Of course, there are still many barriers to overcome, especially when dealing with pregnant women or a woman who may become pregnant. When pregnant women think about taking part in a study, a risk to themselves, their baby, or any kind of required change in their behavior or therapy could deter them. The article, “Women’s Views about Participating in Research While Pregnant”, states that the main problem in surmounting these barriers is that “little is known about issues relevant to women considering research participation during pregnancy.” The Multicenter Study aims to tackle this gap head-on by becoming the first large-scale investigation that tries to recognize the opinions and factors that compel women to not enroll in clinical research.

**METHODS**

The Multicenter Study’s purpose is to be the first research study to investigate and come to conclusions about the experiences, opinions, and obstacles for female participation in clinical research. The goal is to reach out to 500 female patients, at least 18 years old, at each of the project’s sites, which include: Christiana Care, Columbia University, Drexel University, Lehigh Valley Hospital Networks (LVHN), St. Peter’s, and Virtua. In order to target females specifically, the site’s OB/GYN departments were the main point of distribution. The surveys were IRB approved and consisted of 8 pages, one page being designated for consent and was kept by the patients. The research scholars, monitored by each site’s head PI, administered the surveys at each of the six sites; the scholar was able to consent patients and answer any questions regarding the survey in all three languages when necessary. Patients were always informed of the anonymity and voluntary nature of the survey. A screening log was kept of
all women approached at each site. The survey had already been validated by another study at LVHN and was also circulated to 15 non-clinical and 15 non-research staff at LVHN asking for feedback. Data entry was performed by each of the research scholars at her perspective site. The results of 400 surveys given at LVHN's sites were analyzed by the author. Multiple two tailed T-tests with confidence intervals of 95% were calculated in Microsoft Excel for this paper specifically.

RESULTS

<table>
<thead>
<tr>
<th>Participant Information</th>
<th>Responses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age Range</td>
<td>18-76</td>
</tr>
<tr>
<td>Pregnant</td>
<td>56.48%</td>
</tr>
<tr>
<td>Not Pregnant</td>
<td>43.52%</td>
</tr>
<tr>
<td>Fertile*</td>
<td>85.71%</td>
</tr>
<tr>
<td>Not Fertile*</td>
<td>14.29%</td>
</tr>
<tr>
<td>Participated in a Clinical Trial Previously</td>
<td>5.8%</td>
</tr>
</tbody>
</table>

*Fertility is defined as less than 40 years in age for the purpose of this data analysis by the author

Table 1: General description of 400 women that participated in the survey

Explanation of statistics will be referenced in Discussion and Conclusion selection below
Figure 1 displays the percentage of women who have participated in clinical research but are still able to have children.

Figure 2 displays the percentage of women who have participated in clinical research but are not able to have children.

Summary of the Ethnicities of Women Surveyed

Figure 3 displays the range of ethnicities answered by the women surveyed.
Figure 4 displays the total votes for the factors that could influence participation.

Figure 5 displays the total votes for the factors that could influence participation.
Opinions of Women Still Able to Have Children about Factors Motivating Participation

Figure 6 displays the total votes for the factors that could influence participation.

Opinions of Women No Longer able to have Children about the Factors Motivating Research

Figure 7 displays the total votes for the factors that could influence participation.
Figure 8 displays the total votes for the barriers that could influence participation.

Figure 9 displays the total votes for the barriers that could influence participation.
Figure 10 displays the total votes for the barriers that could influence participation.

Figure 11 displays the total votes for the barriers that could influence participation.
Figure 13 displays the total votes for the resources that could influence participation.

Figure 12 displays the total votes for the resources that could influence participation.
Figure 14 displays the total votes for the resources that could influence participation.

Figure 15 displays the total votes for the resources that could influence participation.
DISCUSSION/ CONCLUSION
For the purpose of the author’s specific data analysis of this initial data, the difference between pregnant and non-pregnant women will be compared, along with the differences between fertile and non-fertile women. These groups will be focused on in order to assess whether previous bans placed on pregnant and fertile women has created a lasting stigma for women, leading to more of a rift in the gender disparity related to clinical research.
The age range of women surveyed was 18-76, 56% of the women surveyed were pregnant when surveyed, and 86% of the women were fertile when surveyed. Fertility is defined by the author as less than 40 years old for the purpose of this analysis. Of the 400 women whose responses were analyzed, only about 6% of them had participated in a clinical trial previously. By looking at this summary, it is possible that, because of some factor, women are deterred from participating in clinical trials.
When the women who had previously participated in clinical trials are compared, depending upon their fertility, there is no significant difference. (See figures 1 and 2). Both fertile women and non-fertile women seem just as likely to participate from their responses. As figure 3 shows, the women surveyed were of diverse racial backgrounds; this means that when analyzing the data, conclusions can be drawn about the feelings of minorities and women concerning influences, barriers, and helpful resources concerning participation in clinical research.

When comparing the mindsets of the pregnant and non-pregnant women concerning factors that could influence their participation in clinical research, there was no significant difference. Both groups agreed that the factor, “How well the research is explained to me”, is the most important. Being offered money seemed to have no importance in women’s decision making overall, even though the average self-reported income was less than $30,000 a year.

Surprisingly, even though it is hypothesized women may feel more comfortable being approached by a female doctor; the results seemed to show the opposite. Both pregnant and non-pregnant women voted “0” most often for this factor on the ascending scale used, meaning this factor was “No Motivation” to their participation. In this ascending scale, 0= “No motivation”, 1= “Very little motivation”, 2= “Some motivation”, 3= “Significant Motivation”, and 4= “Most Motivation”.

When comparing the fertile and non-fertile women’s opinions of motivating factors, the only factor with statistically significant results is “Knowledge gained will benefit someone in the future” (p=0.0225) (see figure 6 and 7). The average response of a fertile woman was 2.72, while the average response of non-fertile women was 3.18. This may suggest that women who are not concerned about harm to their fertility can be motivated by altruistic circumstances. Other circumstances, such as these, can be looked at by examining potential barriers influencing participation.
When comparing pregnant and non-pregnant women, the barrier “Time commitment” was an important factor to both groups, with an average response of 2.96, but this was still less important in both groups than “Risk of unknown side effects” and “Risk to fetus/fertility” which were both more frequently voted as a “4” on the ascending scale. When comparing the responses of both groups, the barrier “risk to fertility/fetus” had statistically significant results (p=0.0004). The difference can be observed in figures 8 and 9 above. It seems obvious that pregnant women would be more worried about their fetus or fertility, but this fear may have been heightened by past history of bad outcomes in clinical trials for pregnant women. This mindset makes it hard to enroll pregnant women in trials, and is a major factor that has to be overcome in order to continue to improve medicine for pregnant women and their unborn children.

The results of the T-tests when comparing the same factors for fertile and non-fertile women were similar to the results above. The barrier “Risk to fetus/fertility” had very statistically significant findings (p=0.0133). The reasons and consequences of these results have already been discussed, but by looking at figures 10 and 11 other interesting observations can be noted. In general, the non-fertile women are more concerned with “Risk of unknown side effects” than the fertile women and a little less concerned with “Time commitment”. An important point to note is that even the women classified as non-fertile are still concerned with “Risk to fetus/fertility”. A large portion of the non-fertile women did vote this barrier as a “0” on the ascending scale, but 30 non-fertile women still voted “4” for this factor. Again, these observations point to some influencing factor that has impacted women’s mindsets, because this factor should be of little importance to them after they reach 40 years old.

Important factors to look at are the resources that could help the recruitment of women. In the survey, six resources were provided to rate on the ascending scale. These resources were based upon original assumptions about women’s motivation and previous studies analyzed. When looking at the data collected from pregnant and non-pregnant women, there was no significant difference between the opinions for any of the resources. The most helpful resource was “Having all material provided in my own language” (average=2.88 for pregnant women and 2.91 for non-pregnant women). The least important resource for these two groups of women was “Having access to a medical interpreter throughout the study”. The collective average for all the resources was 2.62. Figure 12 and 13 show the similarities of the two groups of women’s mindsets about the resources. This reaffirms the hypothesis that all women and minorities are open to educational and supportive resources.

When comparing the same data collected from fertile and non-fertile women, there are some similarities between the data discussed above and some statistically significant points to note. The data continues to indicate that “Having all material provided in my own language”, is the most important resource and “Having access to a medical interpreter throughout the study” is the least important.
The resource, “Written material explaining the research study”, is significantly different when comparing these two groups of women. Fertile women (average response= 2.668) are less concerned with this resource than non-fertile women (average response= 3.063). Evaluating this difference (p= 0.0401) could lead to assuming that younger women are less concerned with written information, as compared to verbal explanations. This could imply that younger women are more trusting of medical staff, or that they are more likely to make quick decisions about participating. It is possible that older women like to think about the choice longer, or are less trusting.

Surprisingly, “Having all material provided in the same language” has a p value of 0.0459. By comparing the averages, 2.83, for fertile women, and 3.24 for non-fertile women, it is apparent that the older women are more concerned with the language spoken to them, while the younger women are not as concerned. This could indicate that the younger women surveyed are more likely to speak more than one language well or they are more open to having research presented in another language, no matter the circumstances. This point is worth being researched further, because it could impact the way that researchers approach recruiting women of different ages.

There are some limitations that could have confounded the data analysis. Some confounding factors include: unanswered questions depending on the participant’s comfort with certain questions, or the subjects’ understanding that another person will see their answers, even if it is anonymous. More confounding factors are the smaller sample size of “non-fertile” women, as compared to the fertile women, and that “non-pregnant” and “fertile” are not mutually exclusive. The findings from those two groups of data cannot be compared to each other.

The final findings for this small amount of data, looking specifically at pregnant and fertile women, cannot negate the hypothesis that a stigma has continued to impact women’s mindsets concerning clinical research participation. It seems as though pregnant, non-pregnant, fertile, and non-fertile women are all as equally likely to participate in clinical research. These different categories of women, though, may respond to different tactics in order to recruit them. Altruism, written information, side effects, and the way the research is presented can be used to persuade each group of women differently and this information must be used accordingly. The 400 surveys pertaining to this author’s research cannot provide enough data to draw conclusive findings. After all six sites’ data has been collected and analyzed, final conclusions can be made and a course of action can be planned to help shrink the gender disparity.

RECOMMENDATIONS
After analyzing the results of the study, it is clear that one kind of recruitment tactic does not work for all women. Further consideration must be made to try and change the mindset of pregnant women considering clinical research. Hopefully, this change can be made and it will have a positive impact on the future of research and women’s health.
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WORKS CITED


