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Maximizing the diversity of participants in a phase II clinical trial of optical technologies to detect cervical neoplasia

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Abstract

Introduction—We compare the racial and ethnic demographics of our participants with the populations where our clinics are located (Texas and British Columbia) and investigate the reasons cited for participation.

Methods—We compared the distribution of participants by race/ethnicity to numbers from the 2000 United States Census and the 2001 Census of Canada. Each participant recorded her reasons for enrolling in the trial in her own words. This information was then categorized for analysis. For participants who provided more than one reason for participation, their responses were weighted accordingly to sum 100% for each race. All analyses were performed using SPSS v12.0 (SPSS, Inc, Chicago).

Results—In all, 1,850 women participated in the study. Except for Asians in the Vancouver population and Native Americans in both populations, all minorities were recruited in proportions in excess of their respective proportions in the general population. Distinct differences in the reasons for participating between sites were noted. Houston patients were more likely to cite concern for one's own health as a reason for participating. On the other hand, Vancouver patients were more likely to cite helping others. This trend was found in both the screening and diagnostic populations.

Conclusions—We attribute our success in recruiting minorities to community outreach, our multicultural staff, and efforts to provide uniform care at all sites.

Keywords

participant recruitment; clinical trials; cervical neoplasia; optical technologies

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Introduction

Women who participate in cervical cancer diagnostic trials are usually identified by having a recent or past abnormal Papanicolaou smear; yet only 50% of them are found to have true disease. Likewise, women who participate in cervical cancer screening trials may have never had an abnormal Papanicolaou smear, yet a small portion of them (less than 10%) will have true disease. These data suggest an opportunity for the improvement of current cervical cancer screening methods. To that end, optical technologies, such as fluorescence and reflectance spectroscopy, show great promise for the rapid and accurate detection of cervical neoplasia¹. Still, they must undergo comprehensive efficacy testing against the current standard of care, in this case colposcopically-directed biopsy.

The Littenberg model was established in 1992 as a guideline for the development of emerging biomedical technologies². It includes five components: biologic plausibility, technical efficacy, clinical effectiveness, patient satisfaction, and societal outcomes (cost effectiveness). Our group has tested a spectroscopic point probe for biologic plausibility, technical efficacy, patient satisfaction, and societal outcomes³, and we are now turning our efforts towards determining clinical effectiveness. To accomplish this, we recently completed screening and diagnostic phase II clinical trials of the device, and we have begun a phase III randomized clinical trial (RCT). While RCTs are recognized as the gold standard for assessing the efficacy of any new medical devices⁴, phase II trials still provide valuable information. Clinical trials in cervical diagnostic and screening settings require two populations: a group that undergoes the experimental screening method of detection (e.g. optical technology) and a group that receives the standard of care (biopsy). These groups should be as representative of the general population as possible in order to optimize the generalizability of the results. Unfortunately, women, minorities, and elderly persons have low rates of participation⁵ in clinical trials. Furthermore, particularly important for cancer screening trials, non-symptomatic participants often lack the motivation to seek screening for a condition that they do not perceive as a threat or that they may never develop.

We have already reported our experience with a number of recruitment strategies in phase II trials⁶, and the literature provides additional information concerning the success of several strategies, including: newspaper, television, and/or radio advertisements; word of mouth; billboards; websites; and print mailings⁶⁻⁸. In this manuscript, we first compare the racial/ethnic demographics of our participants with the populations where our clinics are located (Texas and British Columbia). We then investigate the reasons cited for participation, separated first by clinic site and second by race. We conclude by identifying three strategies we used for maximizing the recruitment of minority women into our trials: take the clinic to the patient, establish a reputation for excellence which fosters a high level of trust between the patient and the providers, and recruit research staff of similar socio-demographics as the patients to supplement that trusting environment.

Methods

Participants were actively recruited for two separate trials which employed fluorescence and reflectance point spectroscopy to diagnose cervical disease. Participants with a recent or past abnormal Papanicolaou smear were enrolled into the diagnostic trial (high-risk population), while those with a history of normal Papanicolaou smears and no cervical treatments were enrolled into the screening trial (low-risk population). The trials were conducted at The University of Texas M. D. Anderson Cancer Center's Colposcopy and Prevention Clinic and The University of Texas Health Science Center Gynecology Clinics at the Lyndon Baines Johnson Harris County Hospital and Memorial Hermann Hospital in Houston, Texas, United States, and the British Columbia Cancer Agency in Vancouver, British Columbia, Canada. The

trials began in 1999 and concluded in 2005 and enrolled women 18 years of age or older. Due to the nature of the spectroscopic device, women who had a hysterectomy or who were pregnant at the time of enrollment were ineligible. Those who participated in both trials underwent an extensive risk factor interview; a complete medical history; a full physical examination; regular and *ThinPrep* (Cytoc, Corp., Marlborough, MA) Papanicolaou smears; cervical cultures for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* testing; a wet preparation if vaginitis was present; an endo-cervical curettage; specimens for HPV typing; colposcopic examination; two to four fluorescence and reflectance measurements of the cervix; and biopsy of the sites measured by spectroscopy. The institutional review board at each institution approved the protocols, and written consent was obtained from all participants.

Participants were recruited into the screening and diagnostic populations using a variety of methods that have been discussed elsewhere⁶. Briefly, women in the diagnostic trial were recruited either from participating colposcopy clinics or from the community; all women in the screening trial were recruited from the community. Community recruitment methods included radio and television advertisements (including news stories), newspaper and billboard advertisements, newsletters, websites, distribution of study-specific flyers, and health fairs around the city. Participants from the community enrolled in the trials by contacting a research coordinator who was responsible for checking eligibility requirements, registration, and scheduling. In addition, for the diagnostic trial, potential participants were approached by the clinical team in their respective clinics for participation in the study. All demographic information was collected at the time of registration. Information concerning reasons for participation or non-participation (including ineligibility) and brief demographics were recorded for all women who inquired about or were approached for participation.

To compare the recruitment success of minority women into our studies, we compared the distribution of participants by race/ethnicity to numbers from the 2000 United States Census⁹ and the 2001 Census of Canada¹⁰. In addition, each participant was allowed to record her reason for enrolling in the trial in her own words. This information was then placed into one of six categories if the patient was in the screening trial or seven if the patient was in the diagnostic trial. For participants who provided more than one reason for participation, their responses were weighted accordingly to sum 100% for each participant. All analyses were performed using SPSS v12.0 (SPSS, Inc, Chicago).

Results

In all, 1,850 women participated in the study. Differences in the demographics of the screening and diagnostic population (Table 1) as well as between the Houston and Vancouver populations (Table 2) are evident; therefore, we present our findings by study population.

Figures 1 and 2 compare the racial/ethnic demographics of our diagnostic and screening populations with the State of Texas and Province of British Columbia, respectively. For the Houston study population, except for Native Americans, all minorities were recruited in excess of their respective proportions in the general Texas population. For the Vancouver study population, a deficiency was noted in both Native American and Asian participants; however, had the Vancouver site recruited for a longer period, this deficiency may not have been apparent.

Of the women approached about joining the diagnostic trial, only 24 refusals were recorded; this represents only 3% of those approached for the diagnostic trial. Of the refusals, 38% said that the time commitment was too long, 21% only wanted to undergo the necessary treatment for their dysplasia, 17% were not interested in the trial after it was explained to them, 8% were not eligible, and 4% each had child care issues, were uncomfortable with the study

requirements, were concerned about their comfort level during the procedure, or had already received a biopsy for their diagnosis.

Figures 3 through 6 show the reasons for participation for Houston screening patients, Vancouver screening patients, Houston diagnostic patients, and Vancouver diagnostic patients, respectively. Upon examining the reasons for participation, distinct differences were seen between clinic sites. Houston screening patients (Figure 3) in all racial/ethnic groups were more likely to enroll for reasons pertaining to their own health (e.g., they were due for a Papanicolaou smear, they needed a physical, etc.). On the other hand, Vancouver screening patients (Figure 4), regardless of race/ethnicity, were much more likely to cite helping others as a reason for participating. This effect was also noted for both sites in the diagnostic population. A majority of the Houston participants of all races in the diagnostic trial (Figure 5) reported their own health as the main reason for their participation. On the other hand, Vancouver diagnostic participants (Figure 6) of all races overwhelmingly reported wanting to help others as the main reason for their participation. Interestingly, more of the Vancouver participants in the diagnostic trial reported that they preferred the care offered under the study to that which would be standard care for their dysplasia. A larger number of the Houston participants in the diagnostic trial were referred to the study by a friend or family member compared to the Vancouver participants. There was also a larger number of patients in the screening trial in Houston who reported having an interest in the study as their primary reason for participating when compared to the Vancouver group.

Reasons that were categorized as “Help” included both wanting to help others and wanting to help the research itself. Participants who stated their reason as “Why not?” were also included in this category. Reasons that were categorized as “Health” included need for an annual check-up, wanting to follow-up on an abnormal Papanicolaou smear, wanting a second opinion, and wanting a more thorough examination. Women whose reasons were classified as “Referred” included those who had heard about the studies through a friend or family member, or were recruited by a member of our research staff. Women who were classified as “Interest” had stated that they found the study and the underlying technology interesting. It is important to note that many of the women who listed reasons which were categorized under “Incentive” did so because they did not possess medical insurance which would cover well-woman exams. Only three patients indicated that they completed the study for the compensation offered to participants. The “Preferred Over SOC [standard of care]” classification includes women who wanted a more thorough exam and women who felt that the research protocol offered a better alternative to the standard of care. That is, they felt that spectroscopy was less painful and more desirable than both biopsy and Papanicolaou smear.

Discussion

We were successful in recruiting two racially and ethnically diverse and representative populations for our screening and diagnostic trials of cervical dysplasia using optical spectroscopy techniques. We attribute this success to three major factors: bringing our staff to the sites in which patients were seen, community outreach, and our multicultural staff. These factors have been cited as key factors in the recruitment of women, minority, and underserved populations into cancer clinical trials^{11, 12}.

Level of patient care

Not only do we provide consistent levels (as compared to the University of Texas M. D. Anderson Cancer Center and the British Columbia Cancer Agency) of patient care to our participants, but we try to do so in environments that are conducive to high-quality research in facilities that are convenient for all sectors of the target population. The inclusion of colposcopy clinics at the University of Texas Health Science Center-LBJ Hospital and the British Columbia

Cancer Agency allow the inclusion of higher proportions of black, Hispanic, and Asian women than would be feasible at M. D. Anderson alone. We also strive to provide the same level of patient care at each of our performance sites. By offering high-quality care to all of our participants, we increase their trust in our providers and research staff, thereby increasing the participation of the community in future studies.

Community outreach

The community outreach efforts of M. D. Anderson and the British Columbia Cancer Agency increase the visibility of the institutions to our target populations. We build upon this strength by bringing the clinic to the patients rather than having them travel to our clinics. Often large medical centers that can support large clinical research are located in urban areas where parking and travel can be problems for participants. In addition, by bringing medical equipment and trained personnel into the community, we are also building that trust in the staff and institution that makes potential participants more likely to become involved in research projects that appeal to them. We are also able to leverage resources of large research institutions to establish clinics with high standards in the community. For instance, we can review biopsies back at the host institutions, but can ensure that treatment is offered where the patients are located.

Multicultural staff

Our research group is a diverse mix of male and female researchers from many different racial and ethnic backgrounds. In addition, the medical care providers, including five gynecologic oncologists, two gynecologists, one family practitioner, four nurse practitioners, six study nurses, and ## interviewers are mostly female. It has been reported that many women are uncomfortable to attend a clinic with predominantly male providers¹³. We found this is especially true when confronted with the opportunity to participate in research protocols that require more patient care time involved with experimental procedures. In addition, the multicultural make up of our research team allows minority women the opportunity to interact with researchers with whom they may more closely identify. Mistrust in the medical system has been repeatedly cited as a major reason for nonparticipation among minority populations¹⁴. Finally, many members of our staff are multilingual (in addition to English many of them speak Spanish, Vietnamese, Mandarin, and Cantonese), allowing us to recruit patients who may be otherwise overlooked due to a language barrier. The level of trust built between our research team and our target population has allowed us to build a research program that reaches more of the women for whom our results could have major implications in health care and disease prevention.

The recruitment of minority and women participants in clinical research studies has been further supported by the NIH Revitalization Act (PL 103-43). Subsequently, tremendous effort has gone into understanding the barriers to involvement of women and minority populations in clinical research. This is particularly important for trials examining technologies for cervical cancer screening and diagnosis. Historically, women at increased risk for cervical cancer are minority women and women at lower socio-economic status. Studies show that the identified barriers to involvement in clinical trials include: historical, educational, cultural, linguistic, economic, geographic, and social barriers¹⁵. These barriers have lead women, especially minority women, to be cautious or unwilling to join clinical studies; however, their participation is crucial in understanding the effectiveness of cancer prevention measures that could ultimately impact their rates of incidence and mortality. We have shown that providing quality health care in a familiar setting by a multi-cultural research team greatly increases the participation of minority women in our research trials. Furthermore, we feel that these factors could greatly increase participation at other institutions and allow a more accurate assessment of investigational devices for the diagnosis and treatment of cervical cancer.

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Figure 1.

Comparison of the racial demographics of the State of Texas and the Houston study populations. Black women constitute 12% of the Texas population. Enrollment of black women into our trials were 18% for the screening trial and 17% for the diagnostic trial. Hispanic women were enrolled to the screening trial in equal proportion to their statewide numbers (32%) and slightly lower (20%) for the diagnostic trial. Asian women were over-enrolled in the screening trial (6%) and equally enrolled in the diagnostic study (3%) compared to the Texas demographics (3%). Native American women were enrolled equally in both studies (0.2%) compared to the state demographics (0.3%).

Figure 2.

Comparison of the racial demographics of the Province of British Columbia and the Vancouver study populations. Women of Asian decent constitute 19% of the British Columbia population. Enrollment of Asian women into our trials were 12% for the screening trial and 7% for the diagnostic trial. Enrollment for both black and Hispanic women in the screening trial (1.3%) over-estimated their contribution to the British Columbia population (0.7% for black women and 0.6% for Hispanic women); however, the contributions to the diagnostic trial were similar (0.7%). Asian women represent constitute 11.5% of the Texas population. Native American women were under-represent in the screening (0.6%) and diagnostic (0.4%) trials when compared to the province demographics (4%).

Figure 3.

Reasons for participation by race/ethnicity, Houston screening patients. The majority of participants in the Houston screening trial cited wanting to improve their health (46 - 66% among the minority groups) as the primary reason for participating in the trial. 10 – 19% presented wanting to help others as their reason for participating; and 14 – 25% cited interest in the study as their reason.

Figure 4.

Reasons for participation by race/ethnicity, Vancouver screening patients. The majority of participants in the Vancouver screening trial cited wanting to help others (61 - 100% among the minority groups) as the primary reason for participating in the trial. 75% of the Hispanic women and all of the Native American women who participated listed a family history of cancer as a reason for participating. Personal health reasons were cited less frequently by the Vancouver participants than the Houston participants.

Figure 5.

Reasons for participation by race/ethnicity, Houston diagnostic patients. The majority of participants in the Houston diagnostic trial cited wanting to “know more” (38 - 63% among the minority groups) as the primary reason for participating in the trial. 10 – 39% presented wanting to help others as their reason for participating. The highest proportion of participants that were recruited by family or friends into the study was among the Asian women (17%), which was much higher than the other groups.

Figure 6.

Reasons for participation by race/ethnicity, Vancouver diagnostic patients. The majority of participants in the Vancouver diagnostic trial cited wanting to help others (61 - 100% among the minority groups) as the primary reason for participating in the trial.

Table 1
Demographic characteristics of women enrolled by trial, Houston, TX, USA and Vancouver, British Columbia, Canada, [1999-2005]

Characteristic	Total N=1,850	Screening N=1,000	Diagnostic N=850	p-Value
Race				<0.001
White	1,034 (56%)	491 (49%)	543 (64%)	
Black	248 (13%)	154 (15%)	94 (11%)	
Hispanic	388 (21%)	276 (28%)	112 (13%)	
Asian	130 (7%)	67 (7%)	63 (7%)	
Native American	11 (<1%)	3 (<1%)	8 (<1%)	
Other	39 (2%)	9 (<1%)	30 (4%)	
Age [Mean (SE)]	40.6 (0.29)	44.1 (0.38)	36.6 (0.41)	<0.001
Education				0.010
<HS	159 (9%)	71 (7%)	88 (10%)	
HS/Some college	1,032 (56%)	567 (57%)	465 (55%)	
College degree	466 (25%)	249 (25%)	217 (26%)	
Advanced degree	186 (10%)	112 (11%)	74 (9%)	
Refused/don't know	7 (<1%)	1 (<1%)	6 (<1%)	
Marital Status				<0.001
Married	886 (48%)	554 (55%)	332 (39%)	
Not married	961 (52%)	446 (45%)	515 (61%)	
Annual Income *				<0.001
<\$20,000	338 (18%)	177 (18%)	161 (19%)	
\$20,000-49,999	670 (36%)	388 (39%)	282 (33%)	
\$50,000 +	628 (34%)	361 (36%)	267 (32%)	
Refused/don't know	211 (11%)	74 (7%)	137 (16%)	
Study Site				<0.001
Houston	1,368 (74%)	845 (85%)	523 (62%)	
Vancouver	482 (26%)	155 (15%)	327 (38%)	

* Income was assessed using the currency of the patient's home country, USD or CAD

Table 2
Demographic characteristics of women enrolled by city, Houston, TX, USA and Vancouver, British Columbia, Canada, [1999-2005]

Characteristic	Total N=1,850	Houston N=1,368	Vancouver N=482	p-Value
Race				<0.001
White	1,034 (56%)	670 (49%)	364 (76%)	
Black	248 (13%)	243 (18%)	5 (1%)	
Hispanic	388 (21%)	379 (28%)	9 (2%)	
Asian	130 (7%)	63 (5%)	67 (14%)	
Native American	11 (<1%)	3 (<1%)	8 (2%)	
Other	39 (2%)	10 (<1%)	29 (6%)	
Education				<0.001
<HS	159 (9%)	131 (10%)	28 (6%)	
HS/Some college	1,032 (56%)	771 (56%)	261 (54%)	
College degree	466 (25%)	309 (23%)	157 (33%)	
Advanced degree	186 (10%)	151 (11%)	35 (7%)	
Refused/don't know	7 (<1%)	6 (<1%)	1 (<1%)	
Marital Status				<0.001
Married	886 (48%)	708 (52%)	178 (37%)	
Not married	961 (52%)	658 (48%)	303 (63%)	
Unknown	2 (<1%)	1 (<1%)	1 (<1%)	
Annual Income*				<0.001
<\$20,000	338 (18%)	242 (18%)	96 (20%)	
\$20,000-49,999	670 (36%)	481 (35%)	189 (40%)	
\$50,000 +	628 (34%)	485 (36%)	143 (30%)	
Refused/don't know	211 (11%)	160 (12%)	51 (11%)	
Smoking				
Current	307 (16.6%)	208 (15%)	99 (21%)	
Former	404 (21.8%)	276 (20%)	128 (27%)	
Never	1136 (61.4%)	881 (64%)	255 (53%)	
Unknown	3 (0.2%)	3 (<1%)	0 (0%)	
Age [Mean (SE)]	40.64 (0.29)	41.22 (0.33)	38.99 (0.60)	<0.001
BMI [Mean (SE)]	27.20 (0.18)	28.25 (0.22)	24.23 (0.23)	<0.001