ELSEVIER

Journal of Adolescent Health 41 (2007) 14–18

JOURNAL OF ADOLESCENT HEALTH

Original article

STI Research: Recruiting an Unbiased Sample

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Manuscript received September 1, 2006; manuscript accepted February 9, 2007

Abstract

Purpose: Although minors may legally consent for *clinical* care of sexually transmitted infections (STI) in all states, *research* participation often requires parental consent. We examined whether age, race, and parental barriers differed between those adolescents who accepted versus refused enrollment in a minimal risk STI research study.

Methods: A cross-sectional sample (age 13–21 years, sexually active females, presenting to an Emergency Department) was approached to participate in an STI study. Participation required an interview regarding symptoms and sexual history, a vaginal swab and urine sample for STI testing, and parental consent for those under age 18 years. Demographics, enrollment, and reasons for ineligibility or refusal were recorded.

Results: Of 466 females approached, 240 (52%) met eligibility criteria, and 139 (58%) of those eligible refused enrollment. Reasons for refusal included: 32 (23%) lack of parental confidentiality or consent, 65 (47%) no reason, 23 (17%) time constraints, and 19 (13%) other reasons. Parental barriers were only cited by those under age 18. Reasons for refusal did not differ by race. In unadjusted and adjusted analyses, enrollees were more likely to be black and age $\geq$ 18 than nonenrollees. An interaction between age and race is shown in stratified logistic regression analyses: The association of age $\geq$ 18 with enrollment was highly significant for white/other females (odds ratio [OR] 12.5, 95% confidence interval [CI] 3.0–52.7) but not for Black females (OR 1.5, 95% CI .77–3.0).

Conclusions: Requiring parental consent appears to preclude participation in minimal risk STI research, especially for younger non-black females.

Keywords: Adolescent; STI; Research; Recruitment; Bias

State guidelines allow minors to provide consent for clinical care of sexually transmitted infections (STIs) in all states. A minor is defined as those $\geq$ 12 years and $<$ 18 years in all states except six: five limit STI care to those $\geq$ 14 years and one state restricts STI care to those $\geq$ 16 years [1,2]. However, in many institutions, parental informed consent and adolescent assent is required for those $<$ 18 years to participate in any research. This requirement may be a barrier to research examining STIs in adolescents. Consequently, it may result in a study population that differs from the clinical population, as participation is limited to those who agree to disclose their sexual behavior to a parent. The recruited sample may also differ in terms of other factors that are often linked with outcomes, such as age, race, socioeconomic status, sexual history, and other high-risk behaviors. Although the aim is to recruit a research sample that closely reflects the population to be studied, this potential bias must be acknowledged when interpreting study results.

Adolescents are less likely to seek *clinical* care for reproductive health needs if parental notification is required [3]. However, to our knowledge, there is no literature evaluating the effects of parental consent on STI research par-

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1054-139X/07/$ – see front matter
doi:10.1016/j.jadohealth.2007.02.010

ticipation among adolescents. Our Institutional Review Board (IRB) required parental consent for adolescent females < 18 years of age to participate in this STI study. Therefore, the primary objective was to determine the proportion of eligible but unenrolled patients in an STI study who reported a parental barrier as a reason for not enrolling. In addition, because demographic variables including race and age are often reported as risk factors for STIs, we examined the association and interactions of age, race, and parental consent on enrollment.

Methods

This is a study of the enrollment process of a minimal risk STI/UTI study that was IRB approved. The IRB required parental informed consent from each subject < 18 years. The enrollment process was reviewed and exempt from further IRB oversight because it only included de-identified data. For clarification, we will describe the initial study and eligibility criteria, and then the enrollment process.

The STI study was a cross-sectional study evaluating the associations of urinary tract infections (UTI) and STIs in sexually active females. The study was a convenience sample of adolescent females who presented for clinical care to an outpatient teen health clinic or the pediatric emergency department (PED) at our institution between May 2003 and January 2005. In our institution, adolescents presenting for STI-related clinical care may be evaluated and treated confidentially without parental consent. However, to enroll in this research study for those < 18 years, subject assent and parental informed consent was required. Telephone permission was permitted for parents or guardians who did not accompany their child to their clinic or PED visit.

Enrollment process study

For those subjects who presented to the PED, a computerized registration system allowed us to assess initial eligibility requirements, such as age, gender, chief complaint, and triage acuity level. Using this system, we were able to maintain a de-identified enrollment log to document our enrollment process for the subset of subjects (n = 101) who were recruited from the PED. This system was not available in the teen health clinic and thus prevented us from collecting enrollment data in this setting.

A trained research assistant (RA) was available during 80 8-hour shifts from April 2004 through January 2005. These shifts were varied to cover day, evening, and weekend hours. The RA initially reviewed the computerized registration for basic eligibility: females between the ages of 13 and 21 years who presented with or without urinary symptoms. These patients were recorded in the enrollment log using a code assigned by the RA. Any patient presenting to the emergency department with a chief complaint of significant trauma, sexual assault, psychiatric issues, or who was unstable was excluded from participation.

Those patients who met the basic eligibility criteria were recorded in the enrollment log. The RA attempted to approach every eligible subject; if she could not, she recorded the reason the patient was not approached. The RA assessed the potential subject for complete eligibility: history of sexual activity and no recent antibiotic use or STI testing. In addition, she recorded the patient's self-reported race and genitourinary symptoms. After further questioning of the medical personnel and the patient, those who met complete criteria were offered enrollment, and the study requirements were described. To participate, each adolescent was asked to complete a face-to-face interview regarding her clinical symptoms and sexual history and to provide a vaginal swab and a urine sample for STI and UTI testing. At this time, adolescents < 18 years were informed that parental informed consent would be necessary for enrollment. At any point in the enrollment process, if a patient reported that she was not sexually active, she was deemed ineligible.

For each eligible subject, the RA recorded whether she accepted or declined enrollment. Each subject who declined enrollment was asked to state in her own words the reason for refusal. The first response from the subject was recorded by the RA. If the answer was, "I don't know" or "no reason," the RA did not pursue a reason because the patient already refused enrollment in the study, and we did not want to appear coercive. All three investigators (including the lead RA, J.M.T.) reviewed the individual responses and categorized these reasons into four broad categories: no reason, parental barriers, lack of time, and other. Groupings were not decided a priori, and the authors agreed on 100% of the group assignments.

The proportion of subjects who were approached, eligible, and enrolled was calculated. Bi-variate associations of demographics and refusal variables were assessed using chi-square analysis. A logistic regression model to predict enrollment was developed to assess the odds ratios (OR) and 95% confidence intervals (CI). In addition, we tested for interactions between variables.

Results

During the 10-month period of enrollment from the PED, there were 864 patients who met initial eligibility criteria: female gender between the ages of 13 and 21 years. Of the 864, 398 were not approached due to either time constraints of the potential enrollee (n = 150), ineligibility according to their chief complaint or registration (n = 140), or ineligibility per information communicated by the nurse or physician (n = 108). Of the 466 that were approached for enrollment, 226 (48%) did not meet full study criteria, leaving 240 females eligible for enrollment, and this comprises our study sample.

Of the 240 eligible subjects, 139 (58%) declined to enroll. Reasons to decline enrollment are shown in Figure 1. Many gave no specific reason for refusal. Other reasons

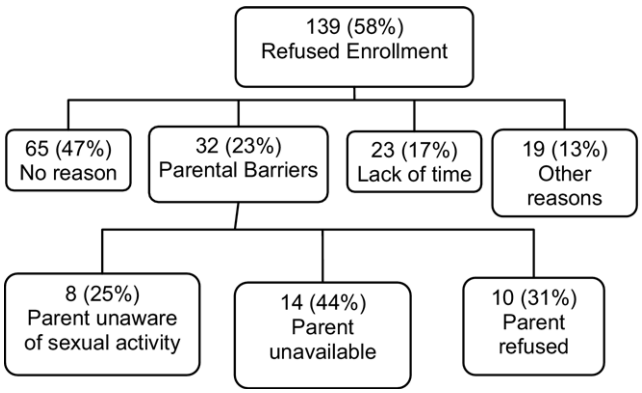

Figure 1. Reasons to decline enrollment after meeting full study criteria for this STI/UTI study.

included discomfort with a vaginal swab, inability to void, or poor mobility. Over 20% of the adolescents refused enrollment due to parental barriers: the parent was unaware of the adolescent's sexual activity, was unavailable, or refused to provide consent.

From general PED registration data, 49% of 13–21-year-old females seeking care are black, 46% are white, and 5% are other races; however, we do not know the racial distribution of the sexually active females in this age group. In our sample, of those who acknowledged sexual activity and met full enrollment criteria, the majority of subjects were black (65%) or white (28%), with only three subjects reporting other race. For 15 subjects, self-reported race was not documented. As shown in Table 1, of those who met full eligibility criteria, bi-variate analysis showed those who enrolled were more likely to be black and older than those not enrolled. When examined as a categorical variable, enrollment increased by age: 21% of those aged 13–14 years, 38% of those aged 15–16 years, 48% of those aged 17–18 years, and 56% of those ≥ 19 years enrolled (Fisher's exact, $p = .02$). Although this overall trend was significant, the difference in participation between each age category did not reach statistical significance. As shown in Table 1, statistical significance was reached ($p = .002$) in participation between subjects aged ≥ 18 years and age < 18 years.

Table 2
Enrollment stratified by race and age (n = 225)[a]

Race	Age (years)	Enrolled n (%)	*p*-value (chi-square)	OR	95% CI
Black n = 155	≥18 n = 50	29 (58)	.23	1.5	.77–3
	<18 n = 105	50 (47)			
White/other n = 70	≥18 n = 13	10 (77)	<.001	12.5	3–52.7
	<18 n = 57	12 (21)			

[a] Row percentages are displayed.

To examine the effects of both race and age, further analysis was done using a logistic regression model including the only demographic variables available for 225 subjects: race and age. Race was examined as black vs. white/other. Because parental consent was needed in those < 18 years, age was examined as a dichotomous variable (≥ 18 years vs. < 18 years). Parental barriers did not enter the model because all of those with parental barriers declined enrollment. Both black race (OR 4.1, 95% CI 2.1–8.1) and age ≥ 18 (OR 6.6, 95% CI 2.6–17) predicted enrollment; however, there was a significant interaction between race and age (OR .29, 95% CI .09–.86). We stratified the sample by race to make this effect easier to interpret (Table 2). After stratifying by race, the differential effect of age on enrollment is clear: white females, age ≥ 18 years increases the odds of enrolling by 12-fold, compared with a nonsignificant increase for black females.

Because we found a difference in enrollment by race and age, we examined the reasons for refusing enrollment. There was no statistical difference between the proportion of black and white/other adolescents who refused for the following reasons: no reason (54% vs. 42%, respectively, $p = .2$), unavailable parent (13% vs. 6%, respectively, $p =$

Table 1
Demographic variables for a sample of patients who met eligibility requirements[a]

	Complete eligibility n = 240 n (%)	Enrolled n = 101 n (%)	Not enrolled n = 139 n (%)	*p* value
Race				
Black	155 (65)	79 (78)	76 (55)	<.001
White/other[b]	70 (29)	22 (22)	48 (34)	
Missing	15 (6)	0	15 (11)	
Parental barriers[c]	32 (13)	0	32 (23)	<.001
Age (mean ± SD)	16.6 (± 1.7)	17 (± 1.6)	16.2 (± 1.7)	.001
Age ≥ 18 years	67 (28)	39 (39)	28 (20)	.002

[a] Column percentages are displayed.
[b] Includes 3 Other/mixed race subjects.
[c] Parental barriers = unavailable parent, parent unaware of adolescent's sexual activity, and parental refusal.

.2), parent refusal (8% vs. 5%, respectively, $p = .7$), and parent unaware (5% vs. 4%, respectively, $p = .8$). Parental barriers were cited only by those aged < 18 years, but no other reasons differed by age. Among subjects < 18 years, the proportion citing parental barriers did not differ by age groups: 10.7% of younger (aged 13–14 years) and 20.4% of middle (aged 15–16 years) adolescents reported a parental barrier ($p = .2$). Age and reasons for refusal did not differ for the 15 subjects for whom the race variable was missing.

Discussion

Our study in which the IRB required parental consent demonstrated that parental barriers such as the parent being unaware of sexual activity, unavailable, or unwilling to consent, appear to prevent a substantial proportion of eligible adolescents from participating in STI research. Additionally, some adolescents were ineligible because they denied sexual activity. However, many of these adolescents did so with parents present in the room, demonstrating the difficulty in obtaining a confidential interview in a busy PED setting. Therefore, we may have underestimated the proportion who truly met full enrollment criteria because of their reluctance to divulge their sexual activity.

We know that adolescents value confidential care for highly sensitive clinical issues [3], and our study supports that the same holds true of research settings. For example, a longitudinal HIV (human immunodeficiency virus) study involving adolescents demonstrates that honoring privacy and altruism were two of the most important factors that affected study recruitment and retention [4]. There are at least two studies that have shown that the requirement of parental consent can affect adolescent participation in survey research. One study in which parental/guardian consent was required for a survey on adolescent condom use failed to collect 81% of the questionnaires [5]. A second study was fairly successful (89%) in obtaining parental consent for an adolescent school-based health survey, but estimated spending $20,000 to do so [6].

In our study, enrollees were more likely to be aged ≥ 18 years than nonenrollees. This effect was highly significant for white females. Although there may have been other, unmeasured developmental reasons for this age gradient, one explanation is that subjects aged ≥ 18 years can legally participate in research without parental consent. Although in all states adolescents may consent independently for clinical care of STIs [1,2], the ability to consent for STI research is more variable. One study from 1995 demonstrates that 70% of IRBs required parental consent for *all* research on minors. Interestingly, over half of these IRBs support changes in federal regulations to allow waiver of parental informed consent in a majority of adolescent research scenarios [7]. Although the Society for Adolescent Medicine (SAM) and the American College of Obstetricians and Gynecologists endorse a waiver of parental consent for adolescent research involving STIs [8,9], in our institution for this study, parental consent was required. We have shown that this requirement may bias enrollment toward those ≥ 18, especially for white females. Thus, we are missing a critical portion of the adolescent population that we aimed to include in this study.

The reluctance of local IRBs to allow minors to consent for STI research may stem from the wording of the Code of Federal Regulations (CFR). Informed consent has been mandated to protect the welfare of human subjects participating in research, particularly those who are considered vulnerable [10]. Consequently, research involving minors has historically required parental informed consent. As early as 1977, The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research recommended that IRBs may waive the requirement of parental consent for "a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects." Examples of circumstances included "research designed to identify factors related to the incidence or treatment of certain conditions in adolescents for which, in certain jurisdictions, they legally may receive treatment without parental consent" [11]. Despite this recommendation, the CFR only includes the general language and not the specific examples [12,13]. The CFR allows wide interpretation among IRBs, and consequently, IRBs differ in how they address assent and consent in adolescent research [7,14,15].

A surprising majority of enrollees in our study were black. In our PED, we know that 49% of the 13–21-year-old females seeking care are black, compared with 65% of those who met full eligibility criteria, and 78% of those enrolled. The key limitation is that we do not know what proportion of 13–21-year-old females who are seeking care acknowledge sexual activity to compare with the population in our study. Historically, blacks have been less likely to enroll in research studies in general due to the history of research abuse [16]. In addition, an adult study showed that patients who consented to participate were less likely to be female or black than those who declined [17]. There may be several reasons for the higher proportion of black females enrolling in our study. Black adolescents may differ from white adolescents in their willingness to acknowledge their sexual activity to either parents or health care providers [18]. Attitudes regarding STIs or the stigma attached to reporting STIs may differ between races. A previous study demonstrated that women and blacks are three times more likely to report having an STI than men and whites [19]. Additionally, a 10-dollar movie coupon incentive was offered to those who enrolled in the study. It is possible that the socioeconomic status may have differed by race in our population, but that data was unavailable for this analysis. However, one would expect that younger females without income would perceive this as a greater incentive than older females, which was not demonstrated in our findings. Age ≥ 18 years did not appear to influence enrollment for black

females, however, the effect of age may have been obscured by the high participation rate of black females. Further research is needed to explore the interesting interaction between race and age.

Although our findings are important, there are several limitations to this study. First, this was a convenience sample of patients. Second, we have limited demographic data. Determining the sexual activity of the adolescents was based on the information provided by the adolescent, although every attempt was made to provide a confidential environment. Finally, the study was not designed to uncover all possible reasons for refusal, and many subjects could not articulate a specific reason. Nor was this study powered to detect age or race differences in reasons for refusing enrollment.

It is important that those involved in adolescent research assess their study samples for possible recruitment bias. In our study, parental barriers account for a large percentage of reasons that patients refuse enrollment. Requiring parental consent appears to bias recruitment toward older females, which is more pronounced in whites than in blacks. The low participation by white females aged < 18 years results in a study sample that does not reflect the demographics of our population. Unfortunately, if these adolescents are not included in STI research studies, research that may enhance their health and development cannot be conducted accurately. For these reasons, we believe that the requirement for parental consent should be waived for minimal-risk STI research. However, further study is needed to assess whether the differential enrollment by age and race that we detected persists when parental consent is not required, or whether it can be attributed to other factors that we were unable to measure.

Acknowledgment

The original STI/UTI study was supported by NIH/NIAID grant R03 A1054616-02 (Huppert, PI), but no additional funding was sought for the enrollment log analysis.

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