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Who receives a medical evaluation for infertility in the United States?

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Abstract

Objective—To investigate characteristics of receiving a medical evaluation for infertility among infertile women

Design—Prospective Cohort

Setting—Academic Institution

Patients—Seven thousand four-hundred and twenty two women who reported incident infertility between 1989 and 2009 in the Nurses' Health Study II.

Intervention—None

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Capsule: In addition to financial access influencing who receives a medical evaluation for infertility, demographic and healthy life-style characteristics are associated with a medical evaluation for infertility among infertile women.

Main Outcome Measures—Report of receiving a medical evaluation for infertility

Results—Approximately 65% of women who reported infertility had a medical evaluation for infertility. Infertile women who were parous (RR:0.81, CI:0.78, 0.84), older (P-value, test for linear trend:<0.001), current smokers (RR:0.89, CI:0.83, 0.96), or who had a higher body mass index (BMI)(P-value: 0.01) were less likely to report receiving a medical infertility evaluation. Infertile women who exercised frequently (P-value: 0.04), took multivitamins (RR: 1.03, CI:1.00, 1.07), lived in states with comprehensive insurance coverage (RR:1.09, CI:1.00, 1.19), had a high household income (P-value: 0.05), or who had a recent physical exam (RR:1.15, CI:1.06, 1.24) were more likely to report receiving a medical infertility evaluation.

Conclusions—These findings highlight demographic, lifestyle, and access barriers to receiving medical infertility care. Historically, the discussion of barriers to infertility care has centered on financial access, geographic access, and socioeconomic status. Our findings build off previous literature by supporting previously reported associations and showcasing the importance of demographic and lifestyle factors in accessing care.

Keywords

Infertility; fertility evaluation; fertility treatment; barriers to access; barriers to care

Introduction

In the United States from 2006-2010, approximately 1.5 million couples report being affected by infertility each year (1, 2). Understanding the burden of this disease has become a national priority(3), with the U.S. Department of Health and Human services and Centers for Disease Control and Prevention releasing a National Public Health Action Plan for the Detection, Prevention, and Management of Infertility (4). The National Survey for Family Growth, estimated that among women with fertility problems, in 1982, 1995, and 2006-2010, only 41-46% of women have ever used any type of infertility service (including both medical help to get pregnant and to prevent miscarriage) and this proportion has not varied across time (5).

Data from national surveys and clinic-based studies investigating barriers in access to infertility care have been limited in their scope, focusing on differences by race, age, cause of infertility, and socioeconomic factors (1, 5-15). The most consistently investigated predictors for accessing fertility care are financial access (insurance coverage, income, and high educational attainment) and white race. However, in addition to these factors, healthy behaviors, lifestyle factors, and access to the medical system may all contribute to whether or not an infertile couple has a medical evaluation for their condition; however these factors have not been thoroughly investigated. Additionally, the current research may have methodological limitations due to small samples sizes, poor response rates, and using cross-sectional study designs which could lead to reverse causation or recall bias.

Using data from the Nurses' Health Study II, a large prospective cohort of female medical professionals, we evaluated a broad range of characteristics associated with utilization of fertility evaluation. We hypothesized that previously investigated characteristics including

age, race/ethnicity, income, and insurance coverage would alter fertility care utilization. We also hypothesized that previously uninvestigated lifestyle characteristics such as body mass index (BMI), cigarette smoking, vitamin use, exercise, and routine physical exam history would influence whether women have a medical evaluation for infertility.

Materials and Methods

The Nurses' Health Study II is a prospective cohort study which began in 1989 when 116,430 registered nurses, 25-42 years old, returned a mailed questionnaire regarding their health and lifestyle. At recruitment, women lived in one of fourteen states. However the participants have since moved to all 50 states. Follow-up questionnaires are sent biennially, with a follow-up rate from the original cohort of 92%. Informed consent was obtained from all participants and the study was approved by the Institutional Review Board of Brigham and Women's Hospital. For the current analysis, pre-menopausal women with no history of hysterectomy, oophorectomy, or tubal ligation were followed from 1989, when the cohort began, through 2009.

Collection of information on fertility evaluation

To define infertility status, women were asked to self-report if they had "tried to become pregnant for more than one year without success" on every questionnaire cycle from1989-2001, and in 2005 and 2009. We restricted our study population to women who reported incident infertility after the first questionnaire cycle (n=7,422). To define our outcome, women were then asked what the cause for their infertility was and were given the following choices: "not investigated, not found, tubal blockage, ovulatory disorder, endometriosis, cervical mucus factors, spousal infertility, and/or other." Women could report multiple causes for infertility. Women who reported "not investigated" were considered not to have sought infertility evaluation (n=2,598). Women who did not report "Not investigated" but instead reported a cause for infertility or that the cause was "not found" were classified as having reported medical evaluation and diagnosis of infertility (n=4,824).

Reliability and validity of self-reported infertility

While validation data were not available on all types of infertility, a validation study of self-reported ovulatory disorder infertility was conducted among a random subset of 100 women in the Nurses' Health Study II who cited ovulatory infertility as a physician identified infertility cause on the questionnaire. Over 93% of the women who responded to the supplemental questionnaire reported diagnostic test results and/or indicative treatment for ovulatory infertility indicating a conventional infertility workup was performed. Additionally, among a sub-sample of the original 100 women, among 40 random women whose participant medical records were reviewed, 95% of women had indication in their medical records (diagnostic test and/or treatment) confirming medically diagnosed ovulatory disorder infertility and a conventional infertility workup (16). We also see high validity of our measure of self-reported fertility treatment in this cohort across time (≥84% concordance) and with medical records (74% of medical records confirmed women's reported treatment, while the remaining records generally contained no information on

specific treatments) (17). These validation estimates verify the nurses' ability to accurately report their experience with conventional physician-based infertility evaluation.

Covariates

Since we wished to prospectively quantify the association between the self-reported woman's characteristics and her likelihood of seeking fertility evaluation to reduce reverse causation and recall bias, the covariate values were defined approximately two years prior to the first report of infertility, with the exception of marriage which was collected at time of reported infertility. Demographic factors including age (categorized according to the Society of Assisted Reproductive Technology [SART] age guidelines), race, marriage, and male partner's education in 1999 were analyzed. We considered reproductive characteristics including nulliparity, history of uterine fibroids, history of endometriosis, and history of spontaneous abortion. We also considered several self-reported lifestyle factors including, current body mass index (BMI) (kg/m^2) based on weight and height measurements as discussed in detail previously (18), BMI at age 18, cigarette smoking status, alcohol intake, current multivitamin use, and physical activity (measured in Metabolic Equivalent of Task [MET] hours/week based on weekly reported recreational physical activity(19)). Lastly, we considered factors related to access, including at least one routine physical exam, physical exam for general health symptoms, and annual household income. State mandated insurance coverage of fertility treatment was defined as: "comprehensive coverage" (state mandated infertility treatment coverage including ART), "limited coverage" (state mandated infertility coverage that included diagnosis and treatment but may exclude IVF treatment or did not specify treatment coverage), and "offer only" (state mandated offer of an insurance policy that includes fertility treatments available for purchase) based on history of state legislature on fertility treatment, which was updated at each questionnaire cycle (11, 17, 20). All models were mutually adjusted for other demographic, lifestyle, and access covariates.

Data analysis

Log-binomial models were used to estimate relative risks and confidence intervals of seeking an infertility evaluation (21). In a few instances, the models did not converge and log-Poisson models, which provide consistent but not fully efficient estimates of the relative risk and its confidence intervals, were used (22). To test for linear trend, variables were set to mean values within each category and treated as linear. Sensitivity analyses expanded the outcome definition to include women who reported infertility evaluations on a later questionnaire cycle than the reported experience of infertility.

Results

Of the 7,422 women reporting incident infertility, approximately 65% reported a medical infertility evaluation (Table 1). The mean age at first report of infertility was 35.1 years (SD=4.7) among those who reported medical evaluation for infertility and 36.2 years (SD=4.7) among those who did not. Of the women who reported medical evaluation for infertility, 9% reported tubal infertility as a possible infertility cause, 27% reported ovulatory dysfunction, 12% reported endometriosis, 4% reported cervical mucosal factors, 19%

reported male infertility, 19% reported "other" reason, and 33% reported that the reason for infertility was not found.

Several demographic characteristics were related to fertility evaluation among women with infertility. Infertile women of older age were less likely to report a fertility evaluation compared to their younger peers (P-value, test for linear trend <0.001) (Table 2). Infertile women whose male partners had graduate level education were more likely to report an evaluation than women whose partners had attained less than a four year college degree (P-value, test for linear trend <0.001). No significant difference was observed by race or marital status. Among reproductive factors, infertile women who were parous were less likely to report a medical evaluation compared to nulliparous infertile women (RR: 0.81, CI: 0.78, 0.84). While infertile women who ever reported ultrasound or hysterectomy-diagnosed uterine fibroids were not more or less likely to report a medical evaluation. Those with a history of surgically-confirmed endometriosis were more likely report having a medical evaluation than infertile women without a prior endometriosis diagnosis (RR: 1.27 CI:1.20, 1.35). History of spontaneous abortion was not associated with evaluation.

Among lifestyle factors, while there was no association between BMI at age 18 years and fertility evaluation (P-value, test for linear trend=0.16), there were significant findings among other lifestyle covariates (Table 3). There was a significant inverse relationship between adult BMI and likelihood of reporting a fertility evaluation among infertile women (P-value, test for linear trend = 0.01). Infertile women who were current smokers were less likely to report having a medical evaluation than never smokers (RR: 0.89, CI: 0.83, 0.96), while alcohol intake was unrelated to infertility diagnosis. In addition, infertile women who exercised frequently were more likely report a fertility evaluation than their sedentary counterparts (P-value, test for linear trend=0.04). Compared to infertile women who did not use multivitamins, those who did were more likely to report an evaluation (RR: 1.03, CI: 1.00, 1.07).

Lastly, infertile women who resided in states with any level of state mandated insurance coverage for infertility treatment were more likely to report having an infertility evaluation compared to those residing in states without mandated insurance coverage (offer only: RR: 1.07, CI:1.03, 1.11; limited coverage: RR:1.09, CI:1.04, 1.14; comprehensive coverage: RR=1.09, CI:1.00, 1.19) (Table 4). Infertile women with higher household incomes were more likely to report having an infertility evaluation (P-value, test for linear trend=0.05). Compared to infertile women who had not reported a physical exam prior to their infertility, women who had a recent (~2 years prior to infertility) general physical exam (RR: 1.14, CI: 1.06, 1.22) or an exam for symptoms of any health condition (RR: 1.15, CI:1.06, 1.24) were more likely to report having a fertility evaluation. In sensitivity analyses, which expanded the outcome definition to include delayed report of fertility investigation, overall trends did not significantly change.

Discussion

Infertile women who reported receiving a medical infertility evaluation were different from their peers with uninvestigated infertility on several important demographic, lifestyle, and

access characteristics. Among this cohort of registered nurses who reported infertility, the majority of women (65%) reported receiving a medical diagnosis of their fertility. To the best of our knowledge, this is the largest prospective study with inclusion of detailed confounding control which investigates a range of predictors of medical evaluation for infertility.

The National Survey for Family Growth has collected nationally representative estimates for infertility service use (both medical help getting pregnant and help preventing miscarriage) for women 15-44 since 1982 (5, 9, 15). While they report no significant difference across time in infertility service utilization for help getting pregnant among women with infertility problems, nulliparous women with infertility problems were less likely to utilize services in 2006-2010 (38%) compared with 1982 (56%)(5). This may reflect societal shifts in delays in age at conception of first child and use of services beyond the age of 44, which are not captured in the NSFG. In our study population, women were eligible to enter the analysis until menopause, and we observed no difference in utilization patterns after adjusting for age (Table 1).

Our study was consistent with previous work during this time period and found that after adjusting for confounding, “demographic characteristics” (age at infertility, parity, husband’s education) and “access characteristics” (income, connection with the medical system, and insurance status) were significant predictors of reporting having received an infertility evaluation (1, 5-13, 15, 23-25). Being older was predictive of not reporting having had an evaluation to a similar extent as having been previously parous. In previous studies from this cohort, women who were older were also less likely to utilize advanced levels of fertility treatment (17). Additionally, partners’ education level was predictive of being more likely to report having received an infertility evaluation, which is consistent with the previous literature that found couples with high education are more likely to seek care as it may stand in as a marker for socio-economic status (5, 7-9, 11, 12, 15). Access also played an important role in whether individuals reported receiving a medical diagnosis. Not surprisingly, having financial means, insurance coverage, and connection with the medical system (recent physical exam) were all predictive of reporting a medical evaluation for infertility in our cohort. We did not find significant differences between race and marital status and fertility evaluation, which have been reported previously (5, 7, 11, 14, 26). This may be a reflection of our highly educated, relatively homogenous population among which there may be limited power to detect such differences (n black women=68) or this may support previous work in which, after adjustment, the effect of race was attenuated by other socio-economic factors (9, 15). Historically, the discussion of barriers to infertility care has centered on financial access, geographic access, and socioeconomic status (5-7, 9, 12, 15, 27). However, our findings build off of previous literature by showcasing how lifestyle, demographic, and access factors independent of one another are associated with reporting having received an evaluation for infertility.

Our analyses found that independent of markers of access, there are several predictors of reporting receipt of an infertility evaluation related to lifestyle characteristics. When evaluating the association between lifestyle factors and fertility evaluation, a consistent pattern emerged. Infertile women who reported behaviors which are generally regarded as

"healthy lifestyle" were more likely to report having had an evaluation than their peers who exhibited less "healthy lifestyle" behaviors. For example, women who had a lower BMI preceding infertility, who never smoked, who used multivitamins, and who exercised regularly were more likely to have reported having received an infertility diagnosis compared to their less healthy counterparts independent of all other characteristics.

When looking at reproductive health factors that could represent an individual's past engagement with the reproductive medical system (uterine fibroids diagnosis, endometriosis diagnosis, and spontaneous abortion) no clear pattern emerged. Those who had ever been diagnosed with endometriosis were more likely to reported having received a medical evaluation for their infertility two years later; however those with a uterine fibroid diagnosis and those with a spontaneous abortion were not statistically more likely to reported having received an evaluation. The former may be confounded by indication, given the strong correlation between infertility and endometriosis.

The findings of this work, specifically the associations with demographic and healthy lifestyle factors, may help guide clinicians who serve as first line providers for many women who are suffering from uninvestigated infertility. There are important barriers to utilizing infertility care that are not fully addressed by differences in financial access and insurance coverage. In our data we are unable to determine whether these differences were a product of referral patterns or differences in seeking access by the individual. Therefore, these barriers need to be thoughtfully considered by doctors administering care to reproductive aged women and may be targeted for public health interventions encouraging women to seek medical evaluation for their infertility.

This study also highlights potential methodological limitations of research restricted to women enrolled from a fertility-clinic setting. Our findings suggest that associations seen within studies using only infertility clinic populations should be interpreted carefully. If couples who present in the fertility clinic setting exhibit healthier lifestyle characteristics (lower BMI, multivitamin use, regular exercise) in addition to markers of higher socioeconomic status (higher household income, higher education) than their infertile peers who do not receive a medical evaluation, then results from studies restricted to fertility clinic practices may not be generalizable to the broader population of women experiencing infertility. Additionally, depending on the causal question of interest, using a population restricted to fertility clinic patients may result in selection bias.

As with all studies, there are limitations of this current research. Covariates and outcomes of interest were based on self-report, which may cause concern about the potential for misclassification. In addition, given the health knowledge of our cohort, there is potential for misclassification of report of fertility evaluation. Given validation evidence and the specificity of our questions, we are making the assumption that all participants who reported a specific infertility cause and who also did not report that their infertility was "not investigated", in fact had their fertility investigated in a medical setting. While we were not able to validate reports on all types of infertility, our validation studies on report of ovulatory infertility and fertility treatment provided evidence that misclassification of the participant's infertility experience is unlikely. Indeed, among women reporting ovulatory infertility there

is high concordance (95%) with medical records indicating that nearly all women who reported ovulatory infertility had a diagnosis and medical evaluation for infertility. Additionally, if misclassification of our outcome did exist, we would expect any possible misclassification to be non-differential (i.e., random with respect to our exposures) and thus would attenuate our results toward the null which would thus lead to underestimation of true effects.

The population under study was a group of medical professionals and was relatively homogenous in terms of race and education level. In fact, the distribution of infertility differs slightly from previous reports among the population that utilizes ART in the U.S. (28) and the proportion of women who reported having received a fertility evaluation was higher (65%) than estimates previously reported from the National Survey for Family Growth, which estimated that among women with fertility problems, in 2006-2010, 36% of women reported having ever used medical help to get pregnant, this prevalence has not statistically significantly changed over time among NSFG cross-sectional sample populations (5). These results represent a group with high medical knowledge and access, among whom we still observed meaningful disparities in reporting receiving an infertility evaluation. We hypothesize that these differences in access would be even greater among the less homogeneous general population of women experiencing infertility.

Despite these limitations, this study has several strengths including its large sample size, detailed temporal evaluation of predictors and confounders, high response rate, and validated exposure and outcome measures. Our analysis utilized log binomial regression to quantify relative risks, as opposed to logistic regression to quantify odds ratios which are known to overestimate associations when the outcome is common (29).

Conclusions

The Centers of Disease Control and Prevention has recently stated that the detection of infertility and management of infertility care is a national public health priority (3, 4). This research furthers our understanding of the wide range of barriers to infertility care and may be used to guide proposed scientific and programmatic projects to encourage increased medical evaluation for infertility. The Public Health Action Plan calls for more research in the detection of infertility, prevention of infertility, and management of infertility including better understanding the safety and efficacy of infertility treatments (4). The findings from our current work highlight important issues of external and internal validity that may arise if future research is conducted solely within infertility-clinic settings. Understanding the many facets of infertility is a newly stated national priority in the United States and the findings of this study help to elucidate our understanding of the utilization of infertility care.

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Table 1

Age-standardized characteristics of women by whether they sought a medical evaluation for infertility: Nurses' Health Study II (1989-2009)

	Medical evaluation for infertility	
	No (n=2,598)	**Yes (n=4,824)**
Age at infertility *	36.19(4.72)	35.14(4.70)
Race		
- White, %	91	91
Nulliparous		
- Yes, %	47	61
State of residence with mandated insurance coverage for infertility treatment		
- No coverage, %	56	50
- Comprehensive coverage, %	2	3
- Limited coverage, %	18	20
- Offer only, %	24	27
Body Mass Index (BMI) (kg/m^2)		
- <18.5, %	4	4
- 18.5-24.9, %	62	65
- 25-29.9, %	20	18
- 30+, %	15	12
Annual household income		
- <$50,000, %	16	13
- $50,000 - 99,999 %	49	49
- $100,000 - 149,999 %	23	22
- >$150,000, %	12	16
Partner's highest level of education		
- < 4-yr college, %	35	30
- 4-yr college, %	30	32
- graduate school, %	30	33
Recent physical exam		
- No, %	11	8
- Yes, for symptoms, %	23	25
- Yes, for screening, %	66	68
Smoking status		
- Never smoker, %	68	69
- Past smoker, %	20	22
- Current smoker, %	12	9
Exercise (Met-hours/week)		
- MET < 3, %	15	13
- MET 3-8.9, %	22	21

	Medical evaluation for infertility	
	No (n=2,598)	**Yes (n=4,824)**
- MET 9-17.9, %	22	22
- MET >18, %	41	45
Multivitamin use		
- Yes, %	53	57
- No, %	47	43
Year of first infertility report		
- 1989-1992, %	51	51
- 1993-1996, %	32	30
- 1997-2009, %	18	19
Fertility diagnosis among those who had a medical evaluation **		
Tubal, %		9
Ovulatory dysfunction, %		27
Endometriosis, %		12
Cervical mucosal factors,%		4
Male factor infertility, %		19
Other reason, %		19
Reason not found, %		33

Values are means (SD) or percentages and are standardized to the age distribution of the study population.

Values of polytomous variables may not sum to 100% due to rounding

* Value is not age adjusted

** Categories not mutually exclusive

Table 2

Demographic Factors and the Risk of Seeking an Infertility Evaluation in the Nurses' Health Study II, 1989-2009

Demographic factor		N (% work-up)	Crude Risk Ratio (95% Confidence Interval)	Adjusted* Risk Ratio (95% Confidence Interval)
Age	<35	2306 (69.3%)	1.00 (Referent)	1.00 (Referent)
	35-37	991 (62.8%)	0.91 (0.87, 0.95)	0.92 (0.88, 0.97)
	38-40	621 (64.8%)	0.93 (0.89, 0.98)	0.93 (0.88, 0.98)
	40+	906 (58.1%)	0.84 (0.80, 0.88)	0.85 (0.81, 0.89)
		*P-value, test for trend***	<0.001	<0.001
Race	White	4412 (65.2%)	1.00 (Referent)	1.00 (Referent)
	Black	68 (58.1%)	0.89 (0.76, 1.04)	0.91 (0.79, 1.06)
	Asian	141 (68.4%)	1.05 (0.95, 1.15)	1.02 (0.93, 1.12)
	Other	203 (60.2%)	0.92 (0.85, 1.01)	0.93 (0.85, 1.02)
Marital status	Never married	539 (67.5%)	1.00 (Referent)	1.00 (Referent)
	Married/Domestic Partnership	3458 (64.7%)	0.96 (0.91, 1.01)	1.04 (0.97, 1.11)
	Divorced/separated/widowed	246 (59.1%)	0.88 (0.80, 0.96)	0.99 (0.91, 1.08)
Partner's education	<4 year college	1286 (61.2%)	1.00 (Referent)	1.00 (Referent)
	4 year college	1394 (66.3%)	1.08 (1.04, 1.14)	1.05 (1.01, 1.10)
	Graduate school	1436 (66.6%)	1.09 (1.04, 1.14)	1.07 (1.02, 1.12)
		P-value, test for trend	<0.001	<0.001
		Reproductive Factors		
Nulliparous	Yes	2731 (71.1%)	1.00 (Referent)	1.00 (Referent)
	No	1711 (56.7%)	0.80 (0.77, 0.83)	0.81 (0.78, 0.84)
Ever Uterine Fibroids	No	4527 (64.9%)	1.00 (Referent)	1.00 (Referent)
	Yes	297 (66.4%)	1.02 (0.96, 1.10)	1.06 (0.99, 1.14)
Ever Endometriosis	No	4595 (64.3%)	1.00 (Referent)	1.00 (Referent)
	Yes	229 (84.2%)	1.31 (1.24, 1.38)	1.27 (1.20, 1.35)
Ever Spontaneous Abortion	No	4101 (65.5%)	1.00 (Referent)	1.00 (Referent)
	Yes	522 (61.7%)	1.01 (0.93, 1.10)	0.93 (0.85, 1.01)

*Log binomial regression adjusted for age, race, nulliparity, insurance coverage in state of residence, sexual identification, marital status, living arrangement, income, husband's education level, recent physical exam, BMI, smoking status, exercise, multivitamin use, spontaneous abortion, and recent illness or surgery

**Wald test used to assess linear trend among categories

Table 3

Lifestyle Factors and the Risk of Seeking an Infertility Evaluation in the Nurses' Health Study II, 1989-2009

Lifestyle factors		N (% work-up)	Crude	Adjusted*
			Risk Ratio (95% Confidence Interval)	
BMI at age 18**	<18.5	827 (66.3%)	1.02 (0.98, 1.07)	1.02 (0.98, 1.07)
	18.5-24.9	3411 (64.8%)	1.00 (Referent)	1.00 (Referent)
	25.5-29.9	378 (64.8%)	1.00 (0.94, 1.07)	1.00 (0.94, 1.07)
	30+	151 (61.4%)	0.95 (0.86, 1.05)	0.95 (0.86, 1.05)
		*P-value, test for trend****	0.13	0.16
BMI	<18.5	196 (69.5%)	1.05 (0.97, 1.14)	1.05 (0.97, 1.13)
	18.5-24.9	2880 (65.9%)	1.00 (Referent)	1.00 (Referent)
	25.5-29.9	808 (62.9%)	0.95 (0.91, 1.00)	0.99 (0.95, 1.04)
	30+	529 (59.2%)	0.90 (0.85, 0.95)	0.96 (0.90, 1.01)
		P-value, test for trend	0.02	0.01
Smoking Status	Never Smoker	3338 (65.6%)	1.00 (Referent)	1.00 (Referent)
	Past Smoker	1026 (65.9%)	1.00 (0.96, 1.05)	1.04 (1.00, 1.09)
	Current Smoker	437 (58.8%)	0.90 (0.84, 0.95)	0.89 (0.83, 0.96)
Alcohol intake	No Alcohol	1385 (63.6%)	1.00 (Referent)	1.00 (Referent)
	<5 g/d	1772 (65.7%)	1.06 (1.00, 1.13)	0.98 (0.94, 1.02)
	5.01-10 g/d	522 (67.5%)	1.03 (0.99, 1.08)	1.00 (0.94, 1.06)
	>10g/d	421 (62.0%)	0.97 (0.91, 1.04)	0.94 (0.88, 1.00)
		P-value, test for trend	0.69	0.12
Exercise (Met hours/week)	MET <3	542 (60.4%)	1.00 (Referent)	1.00 (Referent)
	MET 3-8.9	895 (63.2%)	1.05 (0.98, 1.12)	1.02 (0.96, 1.09)
	MET 9-17.9	951 (65.0%)	1.08 (1.01, 1.15)	1.04 (0.97, 1.10)
	MET 18-26.9	581 (65.6%)	1.09 (1.01, 1.17)	1.05 (0.98, 1.13)
	MET 27-41.9	628 (66.5%)	1.10 (1.03, 1.18)	1.05 (0.98, 1.12)
	MET 42+	751 (68.3%)	1.13 (1.06, 1.21)	1.07 (1.00, 1.14)
		P-value, test for trend	<0.001	0.04
Multivitamin Use	No	1858 (63.2%)	1.00 (Referent)	1.00 (Referent)
	Yes	2383 (65.9%)	1.04 (1.01, 1.08)	1.03 (1.00, 1.07)

*Log binomial regression adjusted for age, race, nulliparity, insurance coverage in state of residence, sexual identification, marital status, living arrangement, income, husband's education level, recent physical exam, BMI, smoking status, exercise, multivitamin use, spontaneous abortion, and recent illness or surgery

**adjusted for race/ethnicity

***Wald test used to assess linear trend among categories

Table 4

Access Factors and the Risk of Seeking an Infertility Evaluation in the Nurses' Health Study II, 1989-2009

Access factor		N (% work-up)	Crude	Adjusted*
			Risk Ratio (95% Confidence Interval)	
Mandated Insurance Coverage	No Coverage	2452 (63.6%)	1.00 (Referent)	1.00 (Referent)
	Offer only	1274 (66.7%)	1.05 (1.01, 1.09)	1.07 (1.03, 1.11)
	Limited Coverage	953 (66.0%)	1.04 (0.99, 1.08)	1.09 (1.04, 1.14)
	Comprehensive Coverage	145 (69.0%)	1.09 (0.99, 1.19)	1.09 (1.00, 1.19)
Household Annual Income	<$50,000	377 (59.1%)	0.94 (0.87, 1.01)	0.94 (0.87, 1.00)
	$50,000-99	1414 (63.0%)	1.00 (Referent)	1.00 (Referent)
	$100,000- 149	647 (62.5%)	0.99 (0.94, 1.05)	0.97 (0.92, 1.03)
	>$150,000	469 (68.7%)	1.09 (1.03, 1.16)	1.03 (0.97, 1.09)
		*P-value, test for trend***	<0.001	0.05
Recent Physical Exam**	No	349 (56.5%)	1.00 (Referent)	1.00 (Referent)
	Yes for symptoms	1110 (65.8%)	1.17 (1.09, 1.25)	1.15 (1.06, 1.24)
	Yes for screening	3081 (65.9%)	1.17 (1.08, 1.26)	1.14 (1.06, 1.22))
Recent Major Illness or Surgery	No	4085 (64.7%)	1.00 (Referent)	1.00 (Referent)
	Yes	739 (66.8%)	1.03 (0.99, 1.08)	1.01 (0.97, 1.06)

*Log binomial regression adjusted for age, race, nulliparity, insurance coverage in state of residence, sexual identification, marital status, living arrangement, income, husband's education level, recent physical exam, BMI, smoking status, exercise, multivitamin use, spontaneous abortion, and recent illness or surgery

**This includes physical exams outside of an infertility work-up, measured 2 years before reported infertility

***Wald test used to assess linear trend among categories