Enhancing Uterine Fibroid Research Through Utilization of Biorepositories Linked to Electronic Medical Record Data

Lani Feingold-Link, MS[1,*] Todd L. Edwards, PhD,[1,2,3,4,*] Sarah Jones, BA,[3]
Katherine E. Hartmann, MD, PhD[1,3,5,6] and Digna R. Velez Edwards, PhD[3,4,5,6]

Abstract

Background: Uterine leiomyomata (fibroids) affect up to 77% of women by menopause and account for $9.4 billion in yearly healthcare costs. Most studies rely on self-reported diagnosis, which may result in misclassification of controls since as many as 50% of cases are asymptomatic and thus undiagnosed. Our objective was to evaluate the performance and accuracy of a fibroid phenotyping algorithm constructed from electronic medical record (EMR) data, limiting to subjects with pelvic imaging.

Methods: Our study population includes women from a clinical population at Vanderbilt University Medical Center (2008–2012). Analyses were restricted to women 18 years and older with at least one fibroid diagnosis confirmed by imaging for cases or at least two separate pelvic imaging procedures without a diagnosis for controls. We randomly reviewed 218 records to evaluate the accuracy of our algorithm and assess the indications for pelvic imaging. Participant characteristics and indications for imaging were compared between cases and controls in unadjusted and adjusted logistic regression analyses.

Results: Our algorithm had a positive predictive value of 96% and negative predictive value of 98%. Increasing age (odds ratio = 1.05, 95% confidence interval 1.03–1.08) and Black race (odds ratio = 2.15, 95% confidence interval 1.18–3.94) were identified as risk factors for fibroids. The most common indications for imaging in both cases and controls were pain, bleeding, and reproductive factors, and the most common imaging modality was a pelvic ultrasound.

Conclusions: These data suggest that using biorepositories linked to EMR data is a feasible way to identify populations of imaged women that facilitate investigations of fibroid risk factors.

Introduction

UTERINE LEIOMYOMATA, OR FIBROIDS, are benign growths of the uterus and are the most common pelvic tumor in women, accounting for $9.4 billion in healthcare costs each year.[1–3] Fibroid risk increases with age until the hormonal changes of menopause, with prevalence estimates ranging from 20 to 77%.[4–6] Estimates of fibroid prevalence in the population vary greatly due to poor capture of women with asymptomatic fibroids. Studies have shown that as many as 51% of women are misclassified without clinical confirmation through imaging.[7,8] A large proportion of existing fibroid studies are based on study designs that rely on self-reported fibroid diagnosis, with the exception of a few studies that have integrated a standardized fibroid assessment across all enrolled subjects.[7,9] In addition to the significant impact of fibroids on a woman's quality of life and the economic burden in the United States, there is poor understanding of fibroid etiology and risk factors that can only be accomplished by better characterization and phenotyping of those with and without fibroids. Overcoming the bias introduced by underreporting of asymptomatic disease is a key challenge in observational fibroid risk research.

The difficulty in implementing a standardized fibroid assessment that conducts pelvic imaging on a large number of subjects is cost. A potential solution to this would be to utilize large clinical databases with linked electronic medical record (EMR) information to identify fibroid cases and controls that have already been imaged. Furthermore, with the development of large networks of biorepositories that link to EMR

[1]Department of Medicine, [2]Division of Epidemiology; [3]Institute for Medicine and Public Health; [4]Center for Human Genetics Research, [5]Department of Obstetrics and Gynecology; and [6]Vanderbilt Epidemiology Center, Vanderbilt University, Nashville, TN.
*These authors contributed equally to this work.

information, there is an opportunity to conduct studies of fibroids on a large scale to better understand both the epidemiology and etiology of uterine fibroids. Our objective with this study was to evaluate the performance and accuracy of a fibroid phenotyping algorithm constructed from electronic medical record (EMR) data, limiting to subjects with pelvic imaging. We evaluate the algorithm accuracy to identify cases and controls by estimating the positive and negative predictive values (PPV and NPV), as well as sensitivity and specificity. These algorithms are being used to develop a retrospective case-control group for women with and without fibroids. In addition, we characterize our study population with regards to common risk factors, and describe the indications for imaging in the case-control groups.

Materials and Methods

Study population

We utilized the clinical data available from the Synthetic Derivative (SD) EMR database (2008–2014), located at Vanderbilt University, Nashville, Tennessee.[10] The SD consists of de-identified clinical data obtained from patients at Vanderbilt University Medical Center, including all clinics that are part of the hospital system. Clinical data from multiple sources are available, including diagnostic and procedure codes, basic demographics, discharge summaries, progress notes, health history, multidisciplinary assessments, laboratory values, imaging reports, medication orders, and pathology reports. The IRB of Vanderbilt University approved this study.

Fibroid diagnosis

We created a fibroid case and control algorithm for the purposes of developing a retrospective case-control group of women with and without fibroids using EMR data. Our EMR system allows researchers to electronically evaluate clinical records using all available data in a participants' EMR. Our algorithms used a combination of demographic inclusion and exclusion criteria, *International Classification of Diseases ninth edition* (ICD-9) diagnostic codes, Current Procedural Terminology (CPT) codes, and keyword exclusions from specific notes and reports of a participant in order to identify cases and controls. Keyword searches of EMRs were conducted using natural language processing (NLP) algorithms available for those using our EMR data for research. We found that the NLP approach was able to reliably remove fibroid text mentions in these specific note fields and was able to exclude those subjects that lacked a diagnostic code but had a history of fibroids documented. Our "gold standard" validation of our algorithm was conducted through expert chart review of each participant's notes and reports to confirm that our algorithm accurately diagnosed a subject with or without a fibroid. A detailed summary of our case-control phenotyping algorithm is provided in Fig. 1 and Supplementary Table S1 (Supplementary Data are available online at www.liebertpub.com/jwh).

Subjects included as a fibroid case or control were women 18 years of age and older. All subjects (both cases and controls) were required to have had imaging procedures performed where they would have been identified as having a fibroid if a fibroid was present. Subjects with procedural
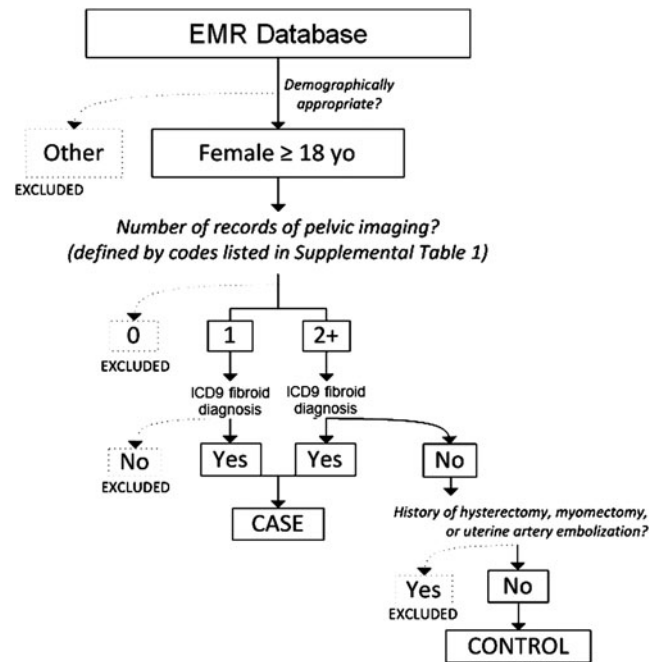

FIG. 1. Summary of study population case inclusion and exclusion criteria. Women aged 18 and older were included in the analysis. A history of pelvic imaging was queried by investigation of Current Procedural Terminology (CPT) codes corresponding to ultrasound, computed tomography (CT), or magnetic resonance imaging (MRI) of the pelvis. Those without evidence of pelvic imaging studies were excluded. In records documenting at least one imaging event, those that also carried a fibroid diagnosis were classified as cases. A fibroid diagnosis was defined by *International Classification of Diseases* (ICD) codes indicating the presence of fibroids or ICD and CPT codes indicating a history of fibroid treatment procedures. Those that did not carry a fibroid diagnosis were included as controls only if a second imaging event on a separate day was also documented. Finally, we determined that since it is unreasonable to assess the fibroid status of women without uteri, we excluded those controls that had a history of hysterectomy. This was accomplished through both the exclusion charts containing certain ICD codes and also with a free text search of records.

codes (one or more for cases and two or more on separate dates for controls) for imaging with ultrasound, magnetic resonance imaging (MRI), or computed tomography (CT) were included (Fig. 1 and Supplementary Table S1). Cases required evidence of a fibroid diagnosis defined by either an ICD-9 code indicating the presence of fibroids or ICD and CPT codes indicating a history of fibroid treatment procedures (e.g., myomectomy or uterine artery embolization). An individual was included as a control if they had two imaging events on separate dates and did not have a fibroid diagnosis or history of fibroid treatment procedures. Excluded from controls were women without an intact uterus (e.g., having had a prior hysterectomy) based on CPT procedural codes and text mentions of hysterectomy (see Supplementary Table S1). Our sampling algorithm to define fibroids cases and controls is informed by a published fibroids algorithm by Hartmann and colleagues using EMRs.[3]

We randomly selected 218 participants (104 algorithm-defined fibroid cases and 114 controls) for chart review from our larger pool of 44,900 women who met our fibroid case and control algorithm criteria. The 218 subjects were a random draw from the pool of available women in the EMR, regardless of participant characteristics. We evaluated the notes and reports of these subjects to evaluate the quality of the phenotyping algorithm, as well as for abstraction of characteristics for participants. Algorithms were then assessed by calculating PPV, NPV, sensitivity, and specificity as well as evaluating the associations between patient characteristics and indications for imaging with fibroid risk.[11–13] Indications for pelvic imaging were determined by manual review of participants EMR. All indications were collected and those reported are the most common indications across records.

Statistical analysis

Analyses were conducted with STATA statistical software version 11.2 (StataCorp LP, College Station). We evaluated known correlates with fibroids risk and tested them for association with fibroid risk in our population using logistic regression. Descriptive statistics of covariate data were expressed as means and standard deviations for continuous covariates and as frequencies and proportions for categorical data. Candidate confounders we modeled included age (years), body mass index (BMI, kg/m^2), and indicator variables for race (non-Hispanic white [white, referent], non-Hispanic black [black], other). Although all indications for pelvic imaging were abstracted, here we report only most common indications. Indications for pelvic imaging included pain (pelvic, abdominal, other), bleeding (postmenopausal, dysmenorrhea, menorrhagia, and oligomenorrhea); reproductive (normal pregnancy, pregnancy complications, bleeding during pregnancy, and other); trauma; management of a known issue; malignancy (suspected or known); and other. We evaluated indications for pelvic imaging across cases and controls using logistic regression unadjusted and adjusted for known fibroid candidate confounders. Types of imaging modality included ultrasonography, CT scans, and MRI scans, and were compared between cases and controls using logistic regression adjusted and unadjusted for candidate confounders. We used a two-sided 5% significance level for all statistical inferences for associations between fibroid risk and evaluation of indications and type of modality for pelvic imaging.

Results

Using our phenotyping algorithm, the PPV for cases was 96% and the NPV for controls was 98%, while the sensitivity was 97% and the specificity 98%. The primary reason for case misclassification was due to initial diagnosis or suspicion of fibroid that was later refuted after further evaluation with imaging, and in one circumstance surgery for removal of fibroid proved that it was not a fibroid. Reasons for control misclassification included prior history of fibroid in clinical notes.

Increasing age was associated with increased risk of developing a fibroid (Table 1). The mean age and standard deviation for cases was 44 ± 10 years and 36 ± 14 years for controls. Black race was also associated fibroid risk with an odds ratio (OR) = 2.15, and 95% confidence interval (95%

CI) of 1.18–3.94. Although we observed increased risk for fibroids among overweight and obese subjects, these associations were not statistically significant (overweight OR = 1.68, 95% CI 0.78–3.59; obese OR = 1.56, 95% CI 0.77–3.18). Among fibroid cases, the most common type of fibroid was intramural, consistent with published literature, followed by submucous, subserous, and pedunculated fibroids. The majority of cases had only one fibroid, and the average largest diameter dimension was $46 \, mm \pm 39 \, mm$. The primary surgical treatment for fibroids was hysterectomy (40%) and did not differ by race (data not shown).

Evaluation of the indications for pelvic imaging in both cases and controls (Table 2) showed that on average more cases than controls had experienced bleeding as the primary reason they were evaluated with imaging (39% of cases, 8% for controls). However, there were more controls that were evaluated for reproductive indications occurring during pregnancy (2% of cases and 48% of controls). Pain, trauma, management of a known issue, and malignancy were other common indications, and these did not differ significantly between cases and controls. Since controls required two or more distinct imaging events to be eligible, we evaluated indications across the first and second imaging and did not find significant differences across indications in these two groups among controls (Table 2). Evaluation of indications for imaging were evaluated both unadjusted (Table 2) and adjusted for age, BMI, and race (results not shown) and effect sizes were consistent across both analyses.

A detailed summary of indications for imaging are provided in Table 3. More controls than cases had indications that included abdominal pain, irregular periods/metrorrhagia, pregnancy complications, and suspected malignancy. More cases than controls had indications that included pelvic pain, menorrhagia, normal pregnancy, and known malignancies.

The mean age between the first and last pelvic imaging within cases (if they had more than one imaging event) and controls was 4 ± 5 years for cases and 6 ± 4 years for controls, with a mean of 4 ± 3 and 7 ± 6 imaging events for cases and controls, respectively. The most common type of imaging used to evaluate the pelvis was ultrasound in both cases and controls [88% cases, 59% controls (first image), 65% controls (second image), Table 4]. However, more controls than cases also had imaging performed through CT scans (6% cases, 38% controls).

Discussion

We evaluated the utility of EMR data to construct a fibroid case-control cohort of imaged women and demonstrated the accuracy of our phenotyping algorithm for identifying fibroid status. Furthermore, we evaluated the indications for pelvic imaging in both our cases and controls to assess whether indications differed by status. Overall, the most common indications for imaging were pain, bleeding, and pregnancy-related. However, more cases than controls had imaging performed for bleeding, specifically menorrhagia, and more controls than cases had imaging performed related to pregnancy such as routine obstetric ultrasounds or for pregnancy complications. Finally, across cases and controls, ultrasounds were the most common type of imaging modality used, and were more common in cases.

TABLE 1. CHARACTERISTICS OF STUDY POPULATION

Characteristic	n	Fibroid cases (n=100) %/mean (SD)	Controls (n=112) %/mean (SD)	OR	95% CI Lower	95% CI Upper
Age mean (SD)[1]	212	44 (10)	36 (14)	1.05	1.03	1.08
Age categories						
<25	28	2	23	1.00	Reference	
25 to 29	24	3	19	1.86	0.28	12.16
30 to 34	29	11	16	7.94	1.57	40.23
35–49	73	49	21	26.54	5.81	121.22
50–64	36	19	15	14.53	3.00	70.54
≥65	22	16	5	34.67	6.22	193.06
BMI mean (SD)	204	30 (7)	28 (7)	1.04	0.99	1.08
BMI categories						
Underweight (<20)	12	3	8	0.51	0.12	2.12
Normal weight (20–24.9)	48	19	26	1.00	Reference	
Overweight (25–29.9)	63	33	27	1.68	0.78	3.59
Obese (≥30)	89	45	39	1.56	0.77	3.18
Race						
White	138	55	75	1.00		Reference
Black	63	37	23	2.15	1.18	3.94
Other	10	8	2	6.04	1.24	29.50
Fibroid type[2]						
Any submucous	9	16	-	-	-	-
Any intramural	26	47	-	-	-	-
Any subserous	19	35	-	-	-	-
Any pedunculated subserosal	1	2	-	-	-	-
Fibroid number						
1	43	52	-	-	-	-
>1	39	48	-	-	-	-
Fibroid largest dimension (mm)	71	46 (39)	-	-	-	-
Surgical treatment of fibroid[3]						
Hysterectomy	40	40	-	-	-	-
Myomectomy	10	10	-	-	-	-
Uterine artery embolization	4	4	-	-	-	-

[1]Age is at fibroid diagnosis for cases and second imaging for controls.
[2]Fibroid type values do not sum to total number of fibroids because subjects may have had more than one fibroid type observed.
[3]Surgical treatment percentages do not add to 100 because women have undergone more than one procedure.
95% CI, 95% confidence interval; BMI, body mass index; OR, odds ratio; mean (SD), mean (standard deviation).

In addition to evaluating the indications for imaging and assessing the accuracy of our phenotyping algorithm, we evaluated a few common fibroid risk factors (age, race, and BMI) to assess whether we had comparable effect sizes within our population. Consistent with prior research, we

TABLE 2. SUMMARY OF INDICATIONS FOR PELVIC IMAGING

Indication	n	Fibroid cases % (N=90)	Controls %[a] (N=111)
Pain	80	22	28
Bleeding	51	39	8
Reproductive	86	2	48
Trauma	5	0	3
Management of known issue	20	8	4
Malignancy	10	2	3
Other	57	27	17

[a]Summarized data are for the first pelvic imaging procedure for controls.

observed increasing age and Black race to be risk factors for fibroids (age OR = 1.05, and Black race OR = 2.15).[2,4,5,14–17] Our effect sizes for both age and Black race were consistent with prior studies that have observed 2-fold or higher odds of fibroids in Black women compared with White.[2,4,5,14–17] Although high BMI has previously associated with fibroid risk, we did not observe a strong association with BMI, although there was evidence that increasing BMI is associated with increasing risk (overweight OR = 1.68; obese OR = 1.56).[18–20] However, the associations between BMI and fibroids have been inconsistent in prior published literature.

The SD is linked to a biorepository of DNA samples (BioVU) that provides a unique resource for conducting genetic epidemiology studies of uterine fibroids. The motivation behind this study was to develop a phenotyping algorithm that could be portable into biorepositories like BioVU that would allow us to pursue large-scale genetic studies of fibroid risk. It would be very difficult and expensive to collect imaging data in a prospective manner in order to properly classify fibroid cases and controls. The major strengths of using populations like BioVU to conduct fibroid

TABLE 3. DETAILED SUMMARY OF INDICATIONS
FOR PELVIC IMAGING

Indication	n	Fibroid cases % (N=90)	Controls %[a] (N=111)
Pain			
Pelvic	15	70	4
Abdominal	27	20	82
Other	6	10	14
Bleeding			
Postmenopausal	8	21	25
Dysmenorrhea	4	11	13
Menorrhagia	19	57	38
Oligomenorrhea	3	11	25
Reproductive			
Normal pregnancy	28	100	63
Pregnancy complication	13	0	32
Bleeding during pregnancy	1	0	2
Other	1	0	2
Malignancy	5		
Suspected malignancy	1	0	33
Known malignancy	4	100	67

A portion of women were missing indications for pelvic imaging
due to incomplete information in their records.

[a]Summarized data are for the first pelvic imaging procedure for
controls.

genetic analyses are that this information is already available
in the EMR, and with the tools described here we show that
we can extract that information reliably. Furthermore, the
imaging reports available in BioVU essentially provide a
''gold standard'' diagnosis of fibroid status and ''off-the-
shelf'' DNA samples also allow an investigator to immedi-
ately conduct studies of fibroids without waiting for sample
accrual. BioVU is part of network of biorepositories linked to
EMR data called the electronic medical records and geno-
mics (eMERGE) network (http://emerge.mc.vanderbilt.edu),
thus phenotyping algorithms can be shared across network
sites to develop large-scale genetic studies evaluating EMR-
derived traits.

Although using EMR data overcomes a major barrier in
fibroid research by helping to eliminate the bias introduced
by asymptomatic disease, there are still limitations to con-
sider. Our algorithm may classify some women as controls
who will develop fibroids in the future but do not have disease

TABLE 4. IMAGING MODALITIES USED
IN UTERINE FIBROID DIAGNOSIS

Modality	n	Fibroid cases % (N=100)[a]	Controls % (N=112)
Ultrasound	214	88	59
CT Scan	85	6	38
MRI	3	0	2
Diagnosis as part of surgical proceduredel number	6	7	0

[a]These women either had a fibroid visualized as part of surgical
procedure or had imaging where a mass was seen but not diagnosed
until after a follow-up surgical procedure.

CT, computed tomography; MRI, magnetic resonance imaging.

at the time of imaging and being sorted by our algorithm. One
strategy to minimize this potential confounder would be to
limit the control group to women who are less likely to go on
to develop fibroids, such as postmenopausal women. When
limiting to the subset of women whom were 55 and older
($n=15$) among the women evaluated in our study, the algo-
rithm was very reliable with none of the women being mis-
classified. The majority of these women had pelvic imaging
through CT scans. We did not deem it prudent to restrict our
control group in our preliminary analyses although the size of
the SD and availability of demographic data provide us with
ample opportunity to do this in the future. There is also the
limitation that when using EMR data it is difficult to assess
history of fibroids and/or treatment that occurred outside of
the Vanderbilt EMR system. Among cases we can only
evaluate women diagnosed and/or treated for fibroids at
Vanderbilt; however, for controls we can have the ability to
evaluate records through NLP and are able to determine the
patient self-reported a fibroid diagnosis and/or treatment of if
the diagnosis was reported in their EMR notes and exclude
the subjects accordingly. Among controls we also require the
women to have had their pelvic imaging at Vanderbilt,
therefore, at least at the time of imaging no fibroid was ob-
served and no fibroid was mentioned in their EMR. We also
note that our algorithm is only applicable to other clinical
populations with similar EMR systems and is meant to be
used for retrospective assessment of fibroid status for con-
struction of case-control groups. As a result of the retro-
spective assessment of fibroid status we cannot apply our
algorithm to a prospective design or evaluate accurate fibroid
prevalence estimates. Furthermore, our findings show that we
capture more symptomatic and severe fibroids due to our data
coming from a clinical population. This is due to the fact that
pelvic imaging is usually performed for women who present
with clinical symptoms, and thus are more likely to have
more severe fibroids. Our algorithm is intended to accurately
identify case and control individuals particularly for EMR
DNA biorepositories that focus on genetic research, where
having a more severe condition is a strength in the design.
Additionally, in contrast to a prospective cohort where all
subjects are imaged, having different indications for imaging
across controls results in a pool of subjects that do not rep-
resent the general population, as a result evaluation of spe-
cific exposures of interest may be confounded by indication
for pelvic imagery. A final limitation that cannot be ac-
counted for in this study is the potential physician bias to
underreport fibroids in a patient's record, for example, during
pregnancy when a fibroid may change in both appearance
and/or concentration.

Here we showed that our phenotyping algorithm classifies
fibroid case and controls with high accuracy. Despite some
differences in indications for pelvic imaging between cases
and controls, overall the indications and modalities used to
classify subjects were comparable. While the majority of
both cases and controls were assessed with ultrasound, more
controls were assessed with CT scans. This difference is
unlikely to produce an important bias, as MRI is more sen-
sitive for detecting fibroids than ultrasound and so there
should not be differential misclassification of controls. Little
is known about fibroid pathophysiology or genetic risk fac-
tors beyond what has been learned from cell culture studies
and tumor biology. The barriers faced by fibroid researchers

today include lack of imaging, limited racial diversity in cohorts, and availability of DNA samples. Populations like BioVU that leverage available information regarding the study population, pelvic imaging, and banked DNA samples provide an opportunity to study the molecular causes of uterine fibroids.

Acknowledgments

Disclosure Statement

No competing financial interests exist.

References

1. Cardozo ER, Clark AD, Banks NK, et al. The estimated annual cost of uterine leiomyomata in the United States. Am J Obstet Gynecol 2012;206:211–219.
2. Day BD, Dunson DB, Hill MC, Cousins D, Schectman JM. High cumulative incidence of uterine leiomyoma in black and white women: ultrasound evidence. Am J Obstet Gynecol 2003;188:100–107.
3. Hartmann KE, Birnbaum H, Ben-Hamadi R, et al. Annual costs associated with diagnosis of uterine leiomyomata. Obstet Gynecol 2006;108:930–937.
4. Cramer SF, Patel A. The frequency of uterine leiomyomas. Am J Clin Pathol 1990; 94:435–438.
5. Marshall LM, Spiegelman D, Barbieri RL et al. Variation in the incidence of uterine leiomyoma among premenopausal women by age and race. Obstet Gynecol 1997;90:967–973.
6. Vollenhoven B. Introduction: the epidemiology of uterine leiomyomas. Baillieres Clin Obstet Gynaecol 1998;12:169–176.
7. Baird DD, Dunson DB, Hill MC, Cousins D, Schectman JM. High cumulative incidence of uterine leiomyoma in black and white women: ultrasound evidence. Am J Obstet Gynecol 2003;188:100–107.
8. Myers SL, Baird DD, Olshan AF et al. Self-report versus ultrasound measurement of uterine fibroid status. J Womens Health (Larchmt) 2012;21:285–293.
9. Laughlin SK, Baird DD, Savitz DA, Herring AH, Hartmann KE. Prevalence of uterine leiomyomas in the first trimester of pregnancy: an ultrasound-screening study. Obstet Gynecol 2009;113:630–635.
10. Pulley J, Clayton E, Bernard GR, Roden DM, Masys DR. Principles of human subjects protections applied in an opt-out, de-identified biobank. Clin Transl Sci 2010;3:42–48.
11. Meystre SM, Savova GK, Kipper-Schuler KC, Hurdle JF. Extracting information from textual documents in the electronic health record: a review of recent research. Yearb Med Inform 2008;128–144.
12. Ritchie MD, Denny JC, Crawford DC et al. Robust replication of genotype-phenotype associations across multiple diseases in an electronic medical record. Am J Hum Genet 2010;86:560–572.
13. Wilke RA, Berg RL, Peissig P et al. Use of an electronic medical record for the identification of research subjects with diabetes mellitus. Clin Med Res 2007;5:1–7.
14. Laughlin SK, Baird DD, Savitz DA, Herring AH, Hartmann KE. Prevalence of uterine leiomyomas in the first trimester of pregnancy: an ultrasound-screening study. Obstet Gynecol 2009;113:630–635.
15. Faerstein E, Szklo M, Rosenshein NB. Risk factors for uterine leiomyoma: a practice-based case-control study. II. Atherogenic risk factors and potential sources of uterine irritation. Am J Epidemiol 2001;153:11–19.
16. Faerstein E, Szklo M, Rosenshein N. Risk factors for uterine leiomyoma: a practice-based case-control study. I. African-American heritage, reproductive history, body size, and smoking. Am J Epidemiol 2001;153:1–10.
17. Ojeda VJ. The pathology of hysterectomy specimens. N Z Med J 1979;89:169–171.
18. Moore AB, Flake GP, Swartz CD et al. Association of race, age and body mass index with gross pathology of uterine fibroids. J Reprod Med 2008;53:90–96.
19. Takeda T, Sakata M, Isobe A et al. Relationship between metabolic syndrome and uterine leiomyomas: a case-control study. Gynecol Obstet Invest 2008;66:14–17.
20. Wise LA, Palmer JR, Spiegelman D et al. Influence of body size and body fat distribution on risk of uterine leiomyomata in U.S. black women. Epidemiology 2005;16:346–354.

Address correspondence to:
Digna R. Velez Edwards, PhD
Vanderbilt Epidemiology Center
2525 West End Avenue
Suite 600, 6th Floor
Nashville, TN 37203

E-mail: digna.r.velez.edwards@vanderbilt.edu