Epidemiology and Adverse Cardiovascular Risk Profile of Diagnosed Polycystic Ovary Syndrome

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Context: Polycystic ovary syndrome (PCOS) is associated with menstrual and reproductive abnormalities, insulin resistance, and obesity.

Objective: The objective of this study was to determine the prevalence of diagnosed PCOS and its association with cardiovascular risk factors.

Setting: The study is set in an integrated health care delivery system in northern California.

Patients: A total of 11,035 women with PCOS were identified by one or more outpatient diagnoses of PCOS using health plan databases. An age-matched sample of women without PCOS was also selected.

Outcome Measures: Prevalence of PCOS and targeted cardiovascular risk factors [hypertension, dyslipidemia, diabetes mellitus, and body mass index (BMI)] were measured.

Results: During 2002–2004, the prevalence of diagnosed PCOS among female members aged 25–34 yr was 2.6% (95% confidence interval 1.6–1.7%). Women with diagnosed PCOS were more likely than those without PCOS to be obese [BMI ≥ 30 mg/m²; odds ratio (OR) 4.21, 3.96–4.47]. Furthermore, PCOS was associated with diabetes (OR 2.45, confidence interval 2.16–2.79), hypertension (OR 1.41, 1.31–1.51) and known dyslipidemia (OR 1.53, 1.39–1.68), even after adjusting for BMI and known confounders. Among women with PCOS, compared with whites, Blacks and Hispanics were more likely and Asians less likely to be obese; Asians and Hispanics were more likely to have diabetes; and Blacks were more likely and Hispanics less likely to have hypertension.

Conclusions: Within a large, community-based population receiving health care, diagnosed PCOS was highly prevalent and associated with a much higher frequency of cardiovascular risk factors that varied by race/ethnicity. Our prevalence estimates likely underestimate the true prevalence of PCOS. Further studies are needed to explore racial/ethnic differences and the extent to which PCOS contributes to future cardiovascular risk. (J Clin Endocrinol Metab 91: 1357–1363, 2006)
nally, we assessed whether clinical findings varied by racial/ethnic group among the women with PCOS.

**Subjects and Methods**

**Source population**

We identified all female health plan members who received ambulatory care within Kaiser Permanente of Northern California, a large, integrated healthcare delivery system that provides comprehensive medical care for more than 35% of ensured adults in the San Francisco and greater Bay area. The Kaiser Permanente of Northern California membership of approximately 3.2 million members covers a 14-county region in northern California; has been shown to have substantial racial, ethnic, and gender diversity; and is highly representative of the surrounding local and statewide population, except for slightly lower representation of the extremes of age and annual household income (19). The Kaiser Foundation Research Institute’s institutional review board approved the study.

**Identification of PCOS**

We used an automated health plan ambulatory visit database to identify all women who received one or more outpatient clinic diagnoses of PCOS [International Classification of Diseases, Ninth Revision (ICD-9) code 256.4] between January 1, 1994 and December 31, 2004. Individuals with diagnosed PCOS who were younger than 15 yr old at the index date (defined as the date of the first identified PCOS diagnosis during the study period) were excluded because of the concern for possible overlap with other conditions associated with androgen excess (e.g. congenital adrenal hyperplasia). Women initially diagnosed at age 45 yr or older were excluded to avoid potential overlap of the index date with menopause transition. Women were also excluded if they had evidence of the following conditions identified using diagnoses from health plan ambulatory visit databases: congenital adrenal hyperplasia, Cushing’s syndrome, adrenal cancer, ovarian tumor or cancer, pituitary tumor (except for nonsecreting pituitary adenoma), prolactinoma, or hyperprolactinemia (if the highest documented prolactin level was more than 20 ng/dl in laboratory databases).

**Supporting features of the PCOS diagnosis**

Supportive data for the PCOS diagnosis as well as the number of temporally separate diagnoses of PCOS after the index date were collected from outpatient records and laboratory databases during the study period. We classified women with diagnosed PCOS based on additional supportive outpatient diagnoses they received during the study period using the following diagnostic categories: hyperandrogenism, anovulation, infertility, menstrual irregularity, dysfunctional uterine bleeding, insulin resistance, and acanthosis nigricans. Hyperandrogenism was defined by a diagnosis of hirsutism, hyperandrogenism, acne at more than 21 yr of age, or laboratory evidence of hyperandrogenemia as determined by the reference ranges for the assays used (total testosterone >80 ng/dl, free testosterone >8 pg/ml, or androstenedione >280 ng/dl). Anovulation was defined by a diagnosis of oligomenorrhea, amenorrhea, or ovulatory dysfunction.

**Control subjects**

For analyses pertaining to prevalence of cardiovascular risk factors, we obtained relevant data from identified PCOS women who were also health plan members at any point between January 1, 2002 and December 31, 2004 and compared them with a control group of female members without diagnosed PCOS who were selected in a 1:5 case to control ratio to match on the 5-yr age distribution of the PCOS women. Control group members were also required to have evidence of active health plan membership any time between January 1, 2002 and December 31, 2004, and at least one ambulatory visit during the year corresponding to the matching index PCOS diagnosis date.

**Patient characteristics and cardiovascular risk factors**

We obtained information on self-reported race/ethnicity using multiple Kaiser health plan databases; however, race/ethnicity data were not uniformly collected on all members and were available for 65% of each group. To identify cardiovascular risk factors, we defined the presence of diabetes mellitus based on having two or more outpatient diagnoses or a principal hospital discharge diagnosis using data from a validated longitudinal health plan diabetes registry (20). We defined hypertension as having two or more outpatient diagnoses of hypertension (ICD-9 codes 401–405), hypertension identified from the outpatient significant health problem list, or one outpatient diagnosis plus a filled prescription for an anti-hypertensive drug from the outpatient pharmacy database of the health plan (21). Diagnosed or known dyslipidemia was based on the presence of one or more outpatient diagnoses (ICD-9 codes 272.0, 272.2, 272.4), filled prescriptions for lipid-lowering therapies in an outpatient pharmacy database, and/or serum LDL cholesterol of 160 mg/dl (4.14 mmol/liter) or higher identified from outpatient laboratory databases, consistent with the National Cholesterol Education Program Adult Treatment Panel III guidelines (22). We separately identified individuals who had a measured triglyceride level greater than 200 mg/dl (2.26 mmol/liter) and those with an HDL cholesterol level less than 40 mg/dl (1.04 mmol/liter). Finally, we identified the presence of diagnosed coronary heart disease, ischemic stroke, or transient ischemic attack, and peripheral arterial disease using previously validated methods involving ICD-9 and Current Procedure Terminology (CPT) codes for diagnoses and relevant procedures found in ambulatory visit, hospital discharge, and billing claims databases (21). These characteristics were identified for PCOS and non-PCOS cohort members during the entire period between January 1, 1994 and December 31, 2004. However, it should be noted that because patients present to various clinics for a variety of reasons, not every patient had every test.

We evaluated cigarette smoking status (current or former smoker), BMI (kilograms per square meter), and systolic and diastolic blood pressure obtained at routine outpatient visits between January 1, 2002 and December 31, 2004. Based on the highest BMI recorded in the ambulatory visit database during this period, these women were classified as either normal or below normal (<25 kg/m2), overweight (25–29 kg/m2), obese (≥30 kg/m2) (23). Because measurement of BMI was gradually implemented in clinics starting in August 2002, these data were only available in 61.2% of PCOS and 56.3% of non-PCOS women. Thus, we calculated the proportion of women in each BMI category among the subset of PCOS or non-PCOS women who had a BMI measured. Finally, among those without diagnosed hypertension, we determined the proportion of patients whose highest outpatient blood pressure measurement (ascertained in over 90% of women in both groups) met the 7th Report of the Joint National Committee (JNC 7) criteria of systolic blood pressure greater than or equal to 140 mm Hg and/or diastolic blood pressure greater than or equal to 90 mm Hg (24) on two separate outpatient dates.

**Statistical approach**

The period prevalence of PCOS from January 1, 2002 through December 31, 2004 was estimated using identified PCOS cases who were health plan members and average age-eligible yearly membership files for female members. Point estimates and associated 95% confidence intervals (CI) for the period prevalence of PCOS were calculated overall and stratified by 5-yr age categories based on age at July 1, 2003. We also calculated the period prevalence of all female Kaiser health plan members aged 25–34 yr old who received a diagnosis of hyperandrogenism, hirsutism, oligo/amenorrhea, and/or ovulatory dysfunction during 2002–2004, in the absence of a PCOS diagnosis, to estimate the broader current prevalence of women with PCOS-like symptoms.

The clinical characteristics of women with and without diagnosed PCOS were compared using a χ2 test for categorical variables and Student’s t test for continuous variables. Point estimates with 95% CI were calculated for prevalence data. We examined the independent association between PCOS and each of three cardiovascular risk factors (diabetes, hypertension, and dyslipidemia) in the subgroup of women with measured BMI using separate logistic regression models with PCOS as the primary predictor variable. We also examined whether the relation between PCOS and these vascular risk factors varied by racial/ethnic group using stratified multivariable analyses. Finally, among women with diagnosed PCOS, we examined the association between race/ethnicity and the prevalence of hypertension, diabetes, dyslipidemia, and elevated BMI. All analyses were conducted using SAS statistical
software version 9.0 (Cary, NC). A two-sided $P$ value less than 0.05 was considered statistically significant.

**Results**

**Cases of PCOS and supporting diagnoses**

We initially identified 12,916 women with at least one outpatient diagnosis of PCOS between 1994–2004 who were aged 15–44 yr at the time of the first identified PCOS diagnosis (index date). After excluding 182 women who met exclusion criteria, the final PCOS cohort included 12,734 women who received at least one outpatient diagnosis of PCOS. In the PCOS cohort, 11,679 (92%) received at least one other additional diagnosis supportive of PCOS during the study period. These 11,679 women included 3,643 (31.2%) women with diagnoses indicative of both clinical hyperandrogenism and anovulation, and an additional 6,724 (57.6%) with diagnoses of either hyperandrogenism or anovulation. The remaining 1312 (11.2%) women had diagnoses of infertility, menstrual irregularity, acanthosis nigricans, or insulin resistance. A total of 6999 (55%) received two or more separate outpatient diagnoses of PCOS.

**Period prevalence of PCOS and PCOS-related symptomatology**

The estimated period prevalence of diagnosed PCOS during 2002–2004 among female members aged 20–39 yr was 2.2% (95% CI 2.1–2.2%), and was as high as 2.7% (2.6–2.8%) and 2.6% (2.5–2.7%) among women aged 25–29 and 30–34 yr, respectively (Fig. 1). Of note, we identified an additional 10,498 women aged 25–34 yr who received an outpatient diagnosis of either hyperandrogenism and anovulation, and an additional 6,724 (57.6%) with diagnoses of either hyperandrogenism or anovulation. The remaining 1312 (11.2%) women had diagnoses of infertility, menstrual irregularity, acanthosis nigricans, or insulin resistance. A total of 6999 (55%) received two or more separate outpatient diagnoses of PCOS.

**PCOS and associated cardiovascular risk factors**

The clinical characteristics of age-matched women with and without diagnosed PCOS are shown in Table 1. There was a slightly higher proportion of whites and Hispanics and a smaller proportion of Blacks in women with diagnosed PCOS. Among the subset of women with measured BMI (49.6% of sample), women with PCOS were substantially more likely to be obese than age-matched controls (67.0% vs. 31.4%, $P < 0.001$). Similarly, women with PCOS were more likely than those without PCOS to have received a diagnosis of obesity or morbid obesity during the entire study period (53.1% vs. 15.7%, $P < 0.001$).

With regard to other traditional cardiovascular risk factors (Table 1), women with PCOS were substantially more likely than non-PCOS women to have diagnosed diabetes mellitus or known hypertension. Among the subgroup of women without diagnosed hypertension, those subjects with PCOS were more likely to have elevated blood pressure (systolic 140 or greater and/or diastolic 90 mm Hg or greater on two separate occasions) compared with control subjects. Diagnosed dyslipidemia, low HDL cholesterol, and elevated triglyceride level were also more prevalent in PCOS vs. non-PCOS women. Documented current or former cigarette smoking was similar in both groups. Known cardiovascular disease was rare overall and did not significantly differ between groups.

We additionally investigated the independent association of PCOS and targeted cardiovascular risk factors in the subgroup of PCOS (n = 6,220) and no PCOS (n = 26,622) women who had measured BMI. Women with PCOS had 4-fold increased odds of being obese or morbidly obese as defined by BMI 30 kg/m² or greater [odds ratio (OR) 4.21, 95% CI 3.96–4.47, adjusted for age and diabetes status]. We also noted a much higher prevalence of diabetes (15.1% vs. 3.1%, $P < 0.001$) and diagnosed hypertension and/or elevated

![Fig. 1. Period prevalence of diagnosed PCOS among female health plan members between January 1, 2002 and December 31, 2004. Numbers in parentheses represent the average annual number of female health plan members in each specified age group during this time period. Error bars represent 95% confidence limits.](https://academic.oup.com/jcem/article-lookup/doi/10.1210/jc.2005-0452)
Among the subgroup of women with diagnosed PCOS, we observed several racial/ethnic differences (Table 2). For instance, among those with measured BMI, Asian women had the lowest prevalence of obesity (BMI ≥ 30 kg/m²), whereas Blacks and Hispanics had the highest. There was also a slightly higher proportion of individuals with diabetes among Asian and Hispanic women. In multivariable logistic regression analysis that adjusted for BMI category and age, women who were Asian (OR 2.16, 1.63–2.85) or Hispanic (OR 1.33, 1.03–1.71) had an increased odds of having diabetes mellitus, compared with women who were white. The crude prevalence of diagnosed hypertension or elevated blood pressure was lowest among Asians and Hispanics and highest among Blacks, and after adjusting for age, BMI category, and diabetes status, the odds of hypertension and/or high blood pressure remained highest in Blacks (OR 1.32, 1.19–1.48) and lower in Hispanics (OR 0.68, 0.62–0.75) but were not significantly

**TABLE 1.** Clinical characteristics of women with diagnosed PCOS and age-matched female controls who were health plan members from January 1, 2002 to December 31, 2004

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>PCOS</th>
<th>No PCOS</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age in 2003 (yr)</td>
<td>30.7 ± 7.2</td>
<td>30.8 ± 7.5</td>
<td>1.0</td>
</tr>
<tr>
<td>Age group in 2003, yr (N %)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15–19</td>
<td>850 (7.7)</td>
<td>4,250 (7.7)</td>
<td></td>
</tr>
<tr>
<td>20–24</td>
<td>1,663 (15.1)</td>
<td>8,315 (15.1)</td>
<td></td>
</tr>
<tr>
<td>25–29</td>
<td>2,616 (23.7)</td>
<td>13,080 (23.7)</td>
<td></td>
</tr>
<tr>
<td>30–34</td>
<td>2,821 (25.6)</td>
<td>14,105 (25.6)</td>
<td></td>
</tr>
<tr>
<td>35–39</td>
<td>1,856 (16.8)</td>
<td>9,280 (16.8)</td>
<td></td>
</tr>
<tr>
<td>40–44</td>
<td>977 (8.9)</td>
<td>4,885 (8.9)</td>
<td></td>
</tr>
<tr>
<td>≥ 45</td>
<td>252 (2.3)</td>
<td>1,260 (2.3)</td>
<td></td>
</tr>
<tr>
<td>Race/ethnicity</td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>White</td>
<td>3,778 (34.2)</td>
<td>17,752 (32.2)</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>552 (5.0)</td>
<td>3,707 (6.7)</td>
<td></td>
</tr>
<tr>
<td>Asian/Pacific Islander</td>
<td>1,117 (10.1)</td>
<td>5,634 (10.2)</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>1,324 (12.0)</td>
<td>6,375 (11.6)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>432 (3.9)</td>
<td>2,276 (4.1)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>3,892 (34.7)</td>
<td>19,431 (35.2)</td>
<td></td>
</tr>
<tr>
<td>Peak BMI (kg/m²)</td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI measured</td>
<td>6,220 (56.4)</td>
<td>26,622 (48.3)</td>
<td></td>
</tr>
<tr>
<td>Among subjects with measured BMI:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal or underweight (BMI &lt; 24)</td>
<td>847 (13.6)</td>
<td>10,549 (39.6)</td>
<td></td>
</tr>
<tr>
<td>Overweight (BMI 25–29)</td>
<td>1,209 (19.4)</td>
<td>7,713 (29.0)</td>
<td></td>
</tr>
<tr>
<td>Obese (BMI ≥ 30)</td>
<td>1,464 (67.0)</td>
<td>8,860 (31.4)</td>
<td></td>
</tr>
<tr>
<td>Cardiovascular risk factor</td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>988 (9.0)</td>
<td>1,136 (1.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diagnosed hypertension</td>
<td>1,341 (12.2)</td>
<td>2,693 (4.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diagnosed hypertension and/or elevated blood pressure</td>
<td>2,939 (26.6)</td>
<td>6,466 (11.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diagnosed dyslipidemia or LDL ≥ 160 mg/dl (4.14 mmol/liter)</td>
<td>1,610 (14.6)</td>
<td>3,253 (5.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HDL cholesterol &lt; 40 mg/dl (1.04 mmol/liter)</td>
<td>2,500 (22.7)</td>
<td>4,125 (7.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Triglyceride &gt;200 mg/dl (2.26 mmol/liter)</td>
<td>1,769 (16.0)</td>
<td>2,570 (4.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Current or former smoker</td>
<td>2,325 (21.1)</td>
<td>11,761 (21.3)</td>
<td>0.56</td>
</tr>
<tr>
<td>Diagnosed cardiovascular disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coronary heart disease</td>
<td>24 (0.22)</td>
<td>134 (0.24)</td>
<td>0.62</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>27 (0.24)</td>
<td>104 (0.19)</td>
<td>0.23</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>19 (0.17)</td>
<td>82 (0.15)</td>
<td>0.56</td>
</tr>
</tbody>
</table>

*Among those with a diagnosis of dyslipidemia, lipid lowering treatment or at least one total cholesterol or LDL cholesterol measurement during the overall study period (n = 7,997 PCOS and n = 29,053 no PCOS), the proportion of those with diagnosed dyslipidemia or LDL cholesterol level greater than or equal to 160 mg/dl (4.14 mmol/liter) remained significantly higher among women with PCOS vs. no PCOS (20.1 vs. 11.2%, P < 0.001). A total of 8,012 PCOS and 29,154 no PCOS women had any lipid or lipoprotein measurement.

*Among those with evidence of at least one HDL cholesterol level measurement during the overall study period (n = 7,209 PCOS and n = 24,220 no PCOS), the proportion who had HDL cholesterol level less than 40 mg/dl (1.04 mmol/liter) remained significantly higher among women with PCOS vs. no PCOS (34.7 vs. 17.0%, P < 0.001).

*Among those with evidence of at least one triglyceride level measurement during the overall study period (n = 6,189 PCOS and n = 18,009 no PCOS), the proportion who had a triglyceride level greater than 200 mg/dl (2.26 mmol/liter) remained significantly higher among women with PCOS vs. no PCOS (28.6 vs. 14.3%, P < 0.001).
TABLE 2. Clinical characteristics of the 7203 (65%) women PCOS who were health plan members from January 1, 2002 to December 31, 2004 with known race/ethnicity information

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>White (n = 3778, 52.4%)</th>
<th>Black (n = 552, 7.7%)</th>
<th>Asian (n = 1117, 15.5%)</th>
<th>Hispanic (n = 1324, 18.4%)</th>
<th>Other (n = 432, 6.0%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age ± SD in 2003</td>
<td>32.6 ± 7.4</td>
<td>31.7 ± 7.9*</td>
<td>32.2 ± 6.4</td>
<td>30.8 ± 6.7*</td>
<td>31.7 ± 6.5*</td>
</tr>
<tr>
<td>Peak BMI measured (kg/m²)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI &lt; 24</td>
<td>15.0%</td>
<td>15.6%</td>
<td>16.4%</td>
<td>15.5%</td>
<td>16.2%</td>
</tr>
<tr>
<td>BMI 25–29</td>
<td>17.6%</td>
<td>22.9%</td>
<td>24.2%</td>
<td>20.8%</td>
<td>23.2%</td>
</tr>
<tr>
<td>BMI ≥ 30</td>
<td>67.5%</td>
<td>80.3%</td>
<td>80.2%</td>
<td>73.8%</td>
<td>78.7%</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>9.5%</td>
<td>8.9%</td>
<td>9.7%</td>
<td>8.0%</td>
<td>8.0%</td>
</tr>
<tr>
<td>Diagnosed hypertension</td>
<td>13.9%</td>
<td>21.7%</td>
<td>13.9%</td>
<td>12.2%</td>
<td>12.9%</td>
</tr>
<tr>
<td>Diagnosed hypertension or high blood pressure</td>
<td>32.0%</td>
<td>40.9%</td>
<td>25.8%</td>
<td>26.6%</td>
<td>32.4%</td>
</tr>
</tbody>
</table>

* P < 0.05 compared with whites.

Discussion

Among a large, community-based population of women receiving health care, we found PCOS was diagnosed in approximately one in 38 women aged 25–34 yr. Because we included in the denominator all age-eligible female health plan members rather than those who received outpatient care in medicine and gynecology clinics (where the opportunity to receive a diagnosis of PCOS is greater), this is a conservative estimate of the true prevalence of PCOS. The actual prevalence of PCOS is likely higher, as suggested by the large number of women (5.1% of all women aged 25–34 yr) with diagnoses related to PCOS symptomatology but without an identified PCOS diagnosis.

One of the strengths of our study is the inclusion of a community-based, ethnically diverse population of over one half million reproductive aged women who receive medical care within a large integrated health care delivery system in northern California. As such, these data are likely to be representative of a typical clinical population and reflect the current burden of this disease within health care systems. Many more reproductive age women likely have undiagnosed PCOS, highlighting the clinical and public health importance of this condition.

The Kaiser Permanente Northern California PCOS study is also currently the largest contemporary sample of women with diagnosed PCOS and one of the most ethnically diverse PCOS cohorts, with 18.4% Hispanic, 15.5% Asian/Pacific Islander, and 7.7% Black among those in whom this information was available. We note that in our study, Asian women with PCOS were much less likely to be obese as defined by current WHO criteria; however, there are increasing data that cardiovascular risk may be evident at lower BMI among Asians compared with other white/European populations (25). We also found that women with PCOS who were Asian or Hispanic were more likely to have diabetes mellitus, independent of age and BMI. Furthermore, Black women with PCOS had higher odds of hypertension, and Hispanic women lower odds, compared with white women, even after adjustment for age, BMI, and diabetes status.

Our data also demonstrate that PCOS is independently associated with higher odds of major cardiovascular risk factors such as diabetes, hypertension, dyslipidemia, and obesity. These results support and extend previous studies that observed an association between PCOS and these risk factors that is independent of age and BMI in selected populations (8, 11, 12, 14, 15). Furthermore, we found that the relations between PCOS and cardiovascular risk factors were consistent across racial/ethnic groups. However, although predicted cardiovascular risk is clearly higher among PCOS women, the extent to which PCOS—a disorder which primarily affects women during their reproductive years—impacts on future cardiovascular events during older age remains to be determined. As expected, given the young age of the cohort, clinically diagnosed cardiovascular disease was extremely rare in both PCOS women and controls.

Our study had several limitations. As mentioned earlier, our reliance on physician-assigned ambulatory diagnoses of PCOS among women seeking medical attention likely led to incomplete ascertainment of cases. Certainly fewer women would be classified as having PCOS within the context of clinical care (where routine screening is not performed) in contrast to systematic screening of selected populations to identify both diagnosed and undiagnosed cases. These include, for example, women screened at a preemployment physical in the Southeastern United States (4–6.6%) (3, 4), a community population in Greece (6.8%) (5), and female white blood donors in Spain (6.5%) (6). Nevertheless, our study demonstrates that the prevalence of clinically recognized PCOS remains high in a typical clinical practice setting.

There is also likely variability in PCOS diagnosis and evaluation across time and the type of outpatient medical clinic, especially given the changing consensus on the criteria for PCOS, both nationally and internationally, during the study period (26–28). Limitations of our electronic databases precluded full validation of cases identified by a single PCOS diagnosis. However, we used a diagnostic strategy that incorporated various data sources to provide support for the PCOS diagnosis, including ascertainment of additional features, when coded as diagnoses, related to PCOS symptomatology. We also note that, whereas supporting diagnoses provide additional evidence for PCOS, absence of specific supporting diagnoses does not necessarily diminish the likelihood of an intended PCOS diagnosis, because only diagnoses, and not necessarily symptoms, were intended for capture in the ambulatory databases. Nevertheless, it is possible that some PCOS women did not have components of both hyperandrogenism and anovulation (e.g., nonandrogenic disorder). Systemic imaging or surgical data relating to ovarian morphology were also not available in our study. It is un-
likely that PCOS diagnoses were made solely based on ovar-
ian morphology because ultrasound screening for PCOS is
not generally advocated nor routinely performed within our
health plan. Overestimation of PCOS prevalence is possible
because ascertainment was based on a diagnosis and not
specific diagnostic criteria. However, improved physician
identification of PCOS would likely have increased the over-
all reported prevalence of PCOS, because there are probably
many more unrecognized cases of PCOS than cases of over-
diagnosed PCOS, and also magnify the results we observed.

We also lacked complete data on selected demographic
and clinical characteristics, including race/ethnicity, BMI,
and serum lipid and lipoprotein levels. For the latter, al-
though misclassification may have occurred for some tri-
glyceride levels obtained in the nonfasting state, fasting is not
required for accurate HDL cholesterol measurement, and the
prevalence of HDL less than 40 mg/dl (1.04 mmol/liter) was
much higher in PCOS compared with non-PCOS women
overall and among women who were tested.

In conclusion, we found that PCOS affects at least one in
38 women between ages 25–34 yr old within a large, diverse
community-based insured population, with an additional
one in 20 women in this age group manifesting PCOS-related
symptomatology (e.g. oligomenorrhea and hirsutism). The
rise in prevalence of PCOS in young adulthood achieving
peak levels in the 25- to 34-yr age groups followed by ta-
pering off in the older age groups is likely a consequence of
several factors. There has been increased awareness of PCOS
and its recognition in the last 5–10 yr, and by default, in-
creased recognition of PCOS among younger women during
initial presentation. Women in the 25- to 34-yr age group are
more educated, in their peak reproductive years, and more
likely to seek clinical attention for symptoms of androgen
excess, menstrual dysfunction, or infertility. Likewise, new
PCOS symptomatology is less likely or may be less concern-
ing to individuals after age 35 yr, resulting in fewer identified
PCOS cases among older women. The high prevalence of
multiple cardiovascular risk factors among women with
PCOS at a relatively young age highlights the public health
relevance of this condition. Indeed, PCOS has been described
as the female-specific manifestation (“Syndrome XX”) of
the metabolic syndrome (2), a clustering of metabolic risk factors
that has gained increasing attention as an independent pre-
dicator of cardiovascular events. Future studies are needed to
further delineate the racial/ethnic differences in PCOS-as-
associated clinical features and cardiovascular risk factors
and the impact of lifestyle changes or pharmacologic interven-
tion on these factors. Finally, careful longitudinal studies are
needed to examine the long-term cardiovascular outcomes
and underlying mechanisms in these women and to develop
strategies to prevent future cardiovascular events.

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