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# Physician characteristics and prescription drug use during pregnancy: a population-based study

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#### ABSTRACT

*Purpose:* We aimed to explore the relationship between physician characteristics and their prescribing behavior regarding category D and X drugs for pregnant women by using a population-based data set in Taiwan.

Methods: The sampled population for the study included 14,430 women. These women received a total of 198,420 prescriptions during pregnancy. We performed multivariate logistic regression analysis by using generalized estimated equations to assess the odds ratio (OR) of the prescription for categories D and X drugs among doctors after adjusting for maternal age and chronic disease.

Results: Of the total 198,420 prescriptions, 4.2% were prescribed category D and X drugs. The covariate-adjusted odds for physicians aged between 40 and 49 years and 50 and 59 years for prescribing category D and X drugs to pregnant women were 1.22 (95% confidence interval [95% CI], 1.15—1.31) and 1.51 (95% CI, 1.40—1.64) times that of physicians aged between 30 and 39 years, respectively. Male physicians were less likely to prescribe category D and X drugs to pregnant women than female physicians (OR, 0.69; 95% CI, 0.63—0.75). In addition, physicians specializing in "other" specialties were more likely (OR, 1.46; 95% CI, 1.41—1.54) to prescribe category D and X drugs compared with those specializing in obstetrics/gynecology, whereas physicians practicing in central Taiwan were less likely (OR, 0.85; 95% CI, 0.80—0.89) than their counterparts in other regions of Taiwan to prescribe category D and X drugs.

Conclusions: We conclude that physician characteristics, including sex, age, specialty, and practice location, were associated with the prescription of category D and X drugs for pregnant women.

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#### Introduction

Safety regarding the use of prescription drugs during pregnancy became a major concern starting with the discovery of birth defects resulting from thalidomide in 1960s [1,2] To guide safe drug use during pregnancy, the U.S. Food and Drug Administration (FDA) has developed a scheme rating the potential fetal risk of pharmaceuticals by classifying them into five major categories: A, B, C, D, and X [3]. Most drugs are classified into category C and should only be prescribed to pregnant women if the

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potential benefits outweigh the potential risks to the fetus. Category D and X drugs clearly indicate that there is evidence for fetal risk [4–6].

Yet despite recommendations, in a large number of studies researchers still find that many pregnant women are exposed to drugs with evidence for potential fetal risk. In one investigation conducted in the United States, the authors found that 4.8% of pregnant women filled one or more prescriptions for a drug classified by the FDA as demonstrating increased risks during pregnancy (category D) and that 4.6% filled a prescription for one or more drugs rated by the FDA as contraindicated during pregnancy (category X) [7]. In another study of pregnancies in Italy, researchers found that 2% of pregnant women filled one or more prescriptions for a category D drug and 1% filled one or more prescriptions for a category X drug [8]. Moreover, in a study from

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France, investigators found that more than one-half of pregnant women filled a prescription for a category D drug [9].

The high rates of exposure to category D and X drugs during pregnancy emphasize the need to develop and implement systems to prevent exposures to drugs that are known to pose a potential risk to the fetus. Therefore, it is necessary to evaluate the behavior of physicians in prescribing high-risk drugs to develop approaches aimed at mitigating the prescription of contraindicated drugs. Some studies indicate that prescription behavior may be influenced by nonclinical, nonpharmacological factors, such as a physician's specialty, his or her geographic setting, sex, and age [10–13]. However, whether physician characteristics truly have any impact on the prescription of category D and X drugs for pregnant women remains unclear.

To fill this gap in the literature, we aimed to explore the relationship between physician characteristics and the prescription behavior of category D and X drugs for pregnant women by using a nationwide population-based data set in Taiwan. Our study can help policymakers understand the patterns of variation in prescription behavior among doctors, which should in turn help them to devise strategies aimed at decreasing the use of prescription drugs with real or potential fetal risk.

#### Methods

#### Database

We sourced the data used in this study from the Taiwan Longitudinal Health Insurance Database 2005 (LHID2005). This database includes all the original claims and registration data for 1,000,000 beneficiaries randomly sampled from the year 2005 registry of beneficiaries of the National Health Insurance (NHI) program. The health care use records for these 1,000,000 beneficiaries were then retrieved from 1996 through 2010. The representativeness of the LHID2005 corresponding to the whole population of NHI beneficiaries in terms of sex, age distribution, and average insured payroll-related amount has been confirmed by The Taiwan National Health Research Institute. Numerous researchers have used the LHID2005 to conduct and publish their studies in internationally peer-reviewed journals [14-16]. This study was exempted from full review by the Taipei Medical University Institutional Review Board because the LHID2005 consists of anonymized secondary data released to the public for research purposes.

#### Study sample

The sampled population for this retrospective study included 14,430 women who had live singleton births between January 1, 2004, and December 31, 2008. If a woman had more than one singleton birth during this study period, we only included the first birth in the study group. In addition, the gestational age and delivery date of each infant was available in the dataset, thus allowing us to calculate the period of pregnancy for each selected woman.

#### Variable of interest

In Taiwan, the NHI recommends and provides 10 prenatal visits for all pregnant women free of charge to remove financial barriers to care and to reduce the risk of poor pregnancy outcomes. In addition, the very low copayments for ambulatory care visits (only about U.S.\$5 per visit) under the NHI provides beneficiaries with a strong incentive to receive medical care at contracted medical facilities. Therefore, we believe that the data used in this study allowed us to capture nearly every prescription written for the sampled women during their pregnancies. In this study, the primary

outcome was "whether a category D or X drug was prescribed during pregnancy," with "prescription" as the unit of analysis. The key independent variables were physician characteristics including age group (<30, 30–39, 40–49, 50–59, and >59 years), sex, practice type (hospital-based vs. office-based), specialty (obstetrics and gynecology [OB/GYN] vs. others), and location (northern, central, southern, and eastern Taiwan). The "others" specialty included family practice, internal medicine, surgery, orthopedics, urology, ENT (ie, ear, nose, and throat), ophthalmology, dermatology, and rehabilitation.

We also took potential confounding factors into consideration in the regression models to examine the relationship between physician characteristics and the prescription of a category D or X drug for pregnant women. These factors included maternal age and whether the woman had a chronic disease [17,18]. Under the NHI program, approximately 40 diseases were classified as chronic, including diseases such diabetes, hypertension, gout, hyperthyroidism, chronic hepatitis, glaucoma, cancer, rheumatoid arthritis, ankylosing spondylitis, and migraine.

#### Statistical analysis

We performed all the analyses conducted in this study using the SAS package (SAS System for Windows, Version 8.2, SAS Institute Inc, Cary, NC). We used  $\chi^2$  tests to compare differences between physician characteristics and the prescription of category D or X drugs. We also performed multivariate logistic regression analysis using generalized estimated equations to assess the odds ratio (OR) of the prescription for categories D and X drugs among doctors after adjusting for maternal age, chronic disease, and the clustering of sampled patients among particular doctors and the clustering of the sampled physicians within practices. A two-sided P<.05 was considered statistically significant in this study.

#### Results

Of the 14,430 sampled women, the mean age  $(\pm SD)$  was 27.4  $(\pm 4.7)$  years; approximately 73% were between 25 and 34 years of age (Table 1). In total, 2.4% of the sampled women had at least one type of chronic disease. Furthermore, 9929 physicians had prescribed pharmaceuticals for the sampled women during their pregnancies. Among these physicians, almost 40% were between 40 and 49 years of age, and 87% were male.

The percentages of prescriptions for category D and X drugs with regard to the total number of all prescriptions by physician characteristics are provided in Table 2. Of the total 198,420 prescriptions, 4.2% were prescribed category D and X drugs. The results of Pearson  $\chi^2$  tests show that there were significant differences in the percentage of category D and X drugs prescribed in terms of maternal age (P < .001), chronic disease status (P < .001), physician age (P < .001), sex (P < .001), specialty (P < .001), and practice location (P < .001). There was no significant difference in the percentage of category D and X drugs prescribed between hospital-based and office-based physicians (P = .069).

Table 3 shows the results of the regression analysis when we used generalized estimated equations. After we adjusted for maternal age group and chronic disease status, the covariate-adjusted odds for physicians between 40 and 49 and 50 and 59 years of age for prescribing category D and X drugs to pregnant women were 1.22 (95% confidence interval [95% CI], 1.15–1.31) and 1.51 (95% CI, 1.40–1.64) times that of physicians aged between 30 and 39 years, respectively. The adjusted OR for prescribing category D and X drugs for physicians specializing in "other" specialties was 1.46 (95% CI, 1.41–1.54) compared with physicians specializing in OB/GYN. Male physicians were less likely to

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