

## AHRQ Grant Final Progress Report

### Title of Project: Harnessing Health IT to Prevent Medication---Induced Birth Defects

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## **ABSTRACT**

**Purpose:** To evaluate two types of clinical decision support (CDS) designed to move evidence-based information about risk of medication-induced birth defects to the point of care for primary care providers (PCPs).

**Scope:** 4 clinics operated by two primary care practices in Western Pennsylvania, which together serve over 15,000 women of reproductive age.

**Methods:** Focus groups were conducted with clinicians and patients to inform the design of two CDS systems. We compared the effects of electronically notifying PCPs when they initiated a potentially teratogenic prescription with either a “simple” or “multifaceted” alert. We also evaluated the effect of using patient-facing networked tablet computers to gather information about women’s reproductive plans. We evaluated these interventions using de-identified data abstracted from 35,110 PCP visits. In addition, study PCPs completed surveys pre- and post-intervention, and patients were asked to complete surveys about the counseling they received regarding prescription medications.

**Results:** Both CDS systems increased documentation of family planning services when potential teratogens were prescribed. Simple prescribing alerts were associated with greater clinician satisfaction than multifaceted alerts. However, the multifaceted alerts produced a greater increase in PCP discussions of the risks of medication use during pregnancy. Routine intake assessment of women’s reproductive plans increased documented contraception when potential teratogens were prescribed. However, refinement of these interventions is warranted; despite these interventions, women were not consistently counseled about potentially teratogenic prescriptions. In particular, CDS needs to alert PCPs repeatedly when multiple potentially teratogenic prescriptions are initiated to prevent substitution of one potential teratogen with another.

**Key Words:** decision support; health IT; medication; women; pregnancy; birth defects; preconception counseling; contraception

**IOM priority area for study:** Pregnancy

## PURPOSE

The goal of this project was to develop and evaluate novel ways in which health IT may be able to help clinicians counsel women about the risk of medication---induced birth defects. In particular, we wanted to develop advanced clinical decision support (CDS) that could provide primary care physicians (PCPs) with point---of---care information on medication risks in the context of information on the woman's reproductive plans. The project had two specific aims:

**Aim 1: To develop and implement two decision support systems designed to alert ambulatory clinicians to risk of medication---induced birth defects.**

To inform this effort, we conducted:

- a) focus groups with primary care clinicians
- b) focus groups with women of childbearing age
- c) a modified Delphi process designed to identify which medications require support

**Aim 2: To evaluate the effect of two decision support systems designed to alert ambulatory clinicians to risk of medication---induced birth defects,** we conducted a factorial design cluster randomized controlled trial involving ambulatory clinicians. Outcome measures were obtained by reviewing electronic prescription records, conducting phone interviews with women of childbearing age following their visit to a study clinician, and surveying participating clinicians about their satisfaction with the decision support they receive.

- a) Intervention #1: Compare multifaceted clinical alerts (intervention) to streamlined clinical alerts (control)
- b) Intervention #2: Evaluate whether collecting machine---actionable information about women's risk of pregnancy using a networked tablet computer (intervention) is superior to the way clinicians usually collect this information (control).

For both of these interventions, we planned to evaluate the following hypotheses:

1. Clinicians in the intervention groups will prescribe fewer teratogenic medications than clinicians in the control groups.
2. Clinicians in the intervention groups will be more likely than clinicians in the control groups to prescribe or document use of contraception by women prescribed teratogenic medications.
3. Women seen by clinicians in the intervention groups will report more satisfaction than women seen by clinicians in the control group with the counseling they received about the risk of medication---induced birth defects and contraceptive options.
4. Clinicians in the intervention groups will be more likely than clinicians in the control groups to report that they were satisfied with the decision support they received.

## SCOPE

### Background

Each year U.S. women of reproductive age receive an estimated 12 million prescriptions for potentially teratogenic medications which can cause birth defects.(1) Over the course of one

year, it is estimated that one of every six women of childbearing age fill a prescription for one of the 100+ drugs classified by the US FDA as potentially harmful class D or X medications.(2) Because comparably effective medications that are not teratogenic do not exist for some medical conditions, it is sometimes necessary to treat women of reproductive age with these risky medications.(3) Fortunately, with concurrent use of effective contraception, birth defects associated with teratogenic medications can be prevented. However, the rate of unplanned pregnancy is nearly 50% in the United States(4) and the risk of these medications to the fetus is greatest in early pregnancy, before many women know that they are pregnant. Clinicians who provide preconception and contraceptive counseling at the time a potentially teratogenic medication is prescribed may help women avoid medication---induced birth defects, as women who are using effective contraception at the time they fill potentially teratogenic prescriptions are less likely to become pregnant.(2) However, fewer than 20% of women using these medications receive contraceptive counseling during ambulatory care visits.(1) Consequently, it has been estimated that approximately 6% of US pregnancies are exposed to class D or X medications.(5)

Prior work has shown that primary care physicians (PCPs) prescribe the majority of potentially teratogenic medications to reproductive---age women.(1, 2) PCPs have also assumed a larger role in the provision of women's health care over the last decade.(6) Although some women see both a PCP and a gynecologist, it is estimated that 28% of women see only a PCP and have no regular contact with a gynecologist.(7) Although the US Preventive Services Task Force recommends that primary care providers obtain a history of sexual practices and provide counseling on the prevention of unintended pregnancy and contraceptive options to all sexually active women who do not want to become pregnant(8) only a minority of PCPs routinely ask their female patients about family planning needs. This is due in part to the fact that PCPs have multiple issues to address at a given 15---minute visit, and they must prioritize the information they review.(9) In addition, generalist training in family planning is often limited.(10)

### **Context**

Health IT interventions, such as computerized provider order entry with CDS, hold great promise for improving the safe use of medications by reproductive---age women. Prior efforts to develop drug---pregnancy alert systems have attempted to identify whether patients were pregnant at the time a medication is prescribed, however, have been limited by not considering a women's *chance of becoming pregnant* while using the medication.(11) At the other extreme, are alerts triggered for all pre---menopausal women. However when the threshold for alerting is set this low, clinicians may be inundated with alerts of low clinical significance. This in turn, leads to high override rates and the potential to override even important alerts.(12, 13)

### **Setting**

This project was conducted with the collaboration and support of the University of Pittsburgh Medical Center (UPMC). UPMC is one of the largest integrated delivery systems in the country and has a strong record of investing in Health IT, patient safety and quality improvement. All UPMC ambulatory clinicians routinely use measurement tools to evaluate their patients' experience. All patients and clinicians have access to quality reports on UPMC providers,

including reports of ambulatory care quality and safety of the providers. UPMC began offering patients access to their personal health information in 2008 through a patient portal, *HealthTrak*, which is now used by some 77,000 patients. UPMC has used the EpicCare® electronic medical record (EMR) (Epic Systems Corporation, Verona Wisconsin) with computerized prescribing and order entry since 1999 and has had considerable success developing and implementing CDS systems.

This study was conducted with two UPMC practices in Western Pennsylvania. One was an urban, academic general internal medicine practice comprising one clinic. The other was a suburban, community---based family medicine practice comprising 3 clinics. All PCPs in the 2 practices who were not co---investigators were invited to participate in this project. Since January of 2005, all patients seen in the academic practice have been asked to use a touch screen tablet computer to complete general screening questions as part of routine clinical care. These Functional Assessment Screening Tablets (*FAST*) use branched logic to present appropriate intake questions to patients. *FAST* is also able to use patient responses from previous visits to determine which questions to ask. *FAST* responses from that visit as well as previous visits are summarized in a paper print---out for physicians and are also manually entered into EpicCare®.

### **Participants**

This project focused on improving health outcomes for an AHRQ priority population—women. The academic practice treats over 7,900 unique women of reproductive age (18---50 yrs). People of color (primarily African---Americans and Asians) make up 30% of this clinic’s patient population, while US Census data indicate that minority groups form only 9.4% of the population in the clinic’s general catchments area. The payer mix includes commercial insurance (40%), Medicare (30%), and Medicaid (15%). Fifteen percent of patients are uninsured and either self---pay or receive uncompensated care. The community---based practice serves over 7,100 unique female patients of reproductive age. Most (98%) patients are Caucasian and have commercial insurance (72%). However, the payer mix also includes Medicare (15%), Medicaid (7%), and self---insured (5%) patients.

### **METHODS**

We developed, implemented and evaluated an advanced CDS system consisting of two health IT interventions which sought to integrate information on medication---induced birth defects with current information on a woman’s chance of becoming pregnancy for use by primary care physicians (PCPs). Focus groups with physicians and patients were conducted to inform the design of the health IT systems. The systems were evaluated using a factorial design cluster---randomized controlled trial. Because in most cases there is not an equally effective non---teratogenic medication available, the goal of this project was not to reduce use of potentially teratogenic medications. Rather, we hoped that PCPs who received this CDS would increase the frequency with which they counseled their patients about the risks of medication---induced birth defects and use of contraception. We were interested in the provision of contraceptive prescriptions, contraceptive counseling, pregnancy tests, and referrals to family planning

specialists when teratogenic medications were prescribed, as well as more typical CDS outcomes such as order cancellation, alert override and PCP---acceptance/satisfaction.

### **Aim #1: Design of Interventions**

#### ***Focus Groups with Clinicians and Patients***

Informational letters soliciting input on a clinical alert system were distributed to PCPs at the study practices. We conducted 8 clinician focus groups, with a total of 48 participants. The focus group moderator's guide consisted of open---ended questions designed to solicit recommendations about what decision support would be most valuable to clinicians and to elicit information about the process and content of both ideal and usual clinician---patient risk discussion. Sample questions from the focus group moderator guide included:

- *What makes it hard for clinicians to discuss risk of medication---induced birth defects with patients?*
- *How would you like to obtain information about risk of medication---induced birth defects?*

In addition, we conducted 4 patient focus groups with a total of 36 women of reproductive age. The focus group moderator's guide consisted of open---ended questions designed to elicit information about the process and content of both ideal and usual clinician---patient discussions. Sample questions from the focus group moderator guide included:

- *What makes it hard for women to discuss risk of birth defects with their doctors?*
- *How have you obtained information about risk of medication---induced birth defects in the past?*

All focus group sessions were digitally recorded and transcribed verbatim. Transcripts were entered into ATLAS.ti. We used grounded theory methodology(14) to perform content analysis and develop the codebook, which was then used by two team members to independently code each transcript. Discrepancies in coding were discussed until consensus was reached. Once the transcripts were coded, patterns of responses, both within a particular question or concept and between them, were explored across the various focus groups.

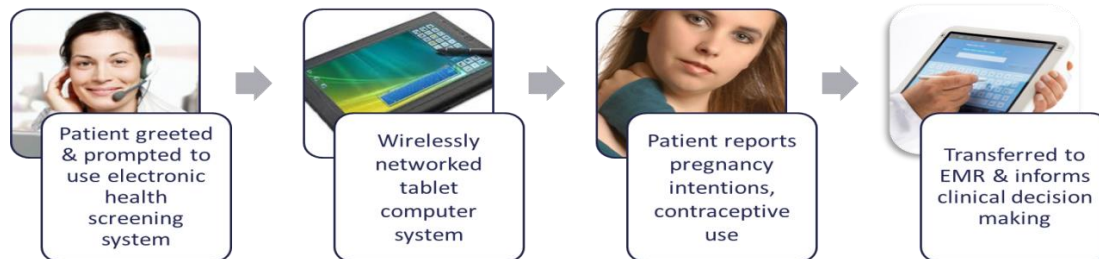
#### ***Modified Delphi Process to Create a List of Teratogenic Medications of Concern***

To achieve consensus regarding which medications should be supported we used a modified Delphi process,(15) via the internet. This process allowed us to combine available evidence from the medical literature with expert judgement. We recruited 6 experts in teratology to serve on a panel. All panelists received a list of medications we felt were potentially worthy of counseling. Panelists were asked to identify any medications they felt should be removed from the list and to add any they felt were missing. Prior to completing a second rating, panelists received an anonymous summary of the ratings of other panelists, with their own prior ratings. After reviewing this information, panelists were asked to identify any changes in their ratings, including any medications they felt should be removed from or added to the list. After 2 rounds, all medications that a majority of panelists felt warranted counseling were included on the list of medications that triggered the CDS we developed.

## Design and Implementation of 2 Health IT interventions

### Intervention #1: Use of tablet computers to collect data on patients' reproductive plans

We evaluated whether collecting information about women's chance of becoming pregnant using wirelessly networked tablet computers is superior to the way that clinicians usually collect this information. As this information was routinely collected at intake like the patients' blood pressure and weight, we refer to this information as their "contraceptive vital sign."



**Figure 1:** Design of electronic intake system including a "contraceptive vital sign"

Participating PCPs were randomized to receive the contraceptive vital sign information collected via the networked tablet computers or to a control group who received only standard intake information. In order to do this, we modified the FAST tablet computer algorithm at the academic practice to ask two additional questions of women aged 18---50 (who had not previously indicated they had undergone menopause, hysterectomy, or tubal ligation) visiting PCPs in the intervention group (Figure 1). Women were asked "Are you currently pregnant or trying to become pregnant?" and provided with 5 response options: "no", "not trying to get pregnant but wouldn't mind being pregnant", "currently pregnant", "been through menopause", and "prefer not answer." Women who responded either "no" or "not trying to get pregnant" were then asked: "There are many ways that people try to avoid becoming pregnant. Which are you using?" and were provided with a list of contraceptive methods.

Included in the list of response options were "no method of birth control", "not sexually active in the past 3 months", and "prefer not to answer." These responses appeared on a paper report that was given to intervention PCPs prior to seeing a patient. If a patient reported that she was pregnant, trying to become pregnant, wouldn't mind becoming pregnant, or trying to avoid pregnancy but not using any contraception, the report provided to PCPs included the warning statement "Consider chance of pregnancy when prescribing" in bold text, unless the woman responded that she had not had sex within the past 3 months.

There were several challenges to implementing this intervention. Due to a programming error, the contraceptive vital sign questions were not asked on annual preventive visits, which cut our sample size in half. Additionally, although we had hoped to have the FAST tablets directly interface with the EMR, after extensive discussion, UPMC opted to adopt the Welcome tablet program as their preferred electronic intake system, and they thus refused to integrate FAST and EpicCare. This meant that in order to get the FAST contraceptive vital sign information into the EMR, a staff person needed to enter the information from a paper report into the appropriate field in Epic, which in practice rarely happened rapidly enough to support

prescribing alerts (intervention #2). Due to the UPMC decision, the community-based study practices received Welcome tablets instead of FAST. Although the information Welcome tablets collected did directly interface with Epic, the information was filed in a “questionnaire” section which was not part of most clinicians’ work flow or actionable for CDS. In addition, the community-based clinics had difficulty implementing the electronic intake system, as the registration staff did not consistently provide tablets to patients at check-in (i.e., only 16% of visits we hoped would include Welcome tablet data actually did). As the clinic’s medical director chose to use these tablets to ask multiple questions about patients’ alcohol use (in addition to routine intake questions and the contraceptive vital sign), the intake system developed a “you think I’m an alcoholic?” stigma, and regular use of this intake system at these community-based clinics dropped off over time. Thus, we were only able to evaluate the effects of the contraceptive vital sign using a randomized design at the academic clinic.

*Intervention #2: Prescribing alerts when potentially teratogenic medications were ordered:*

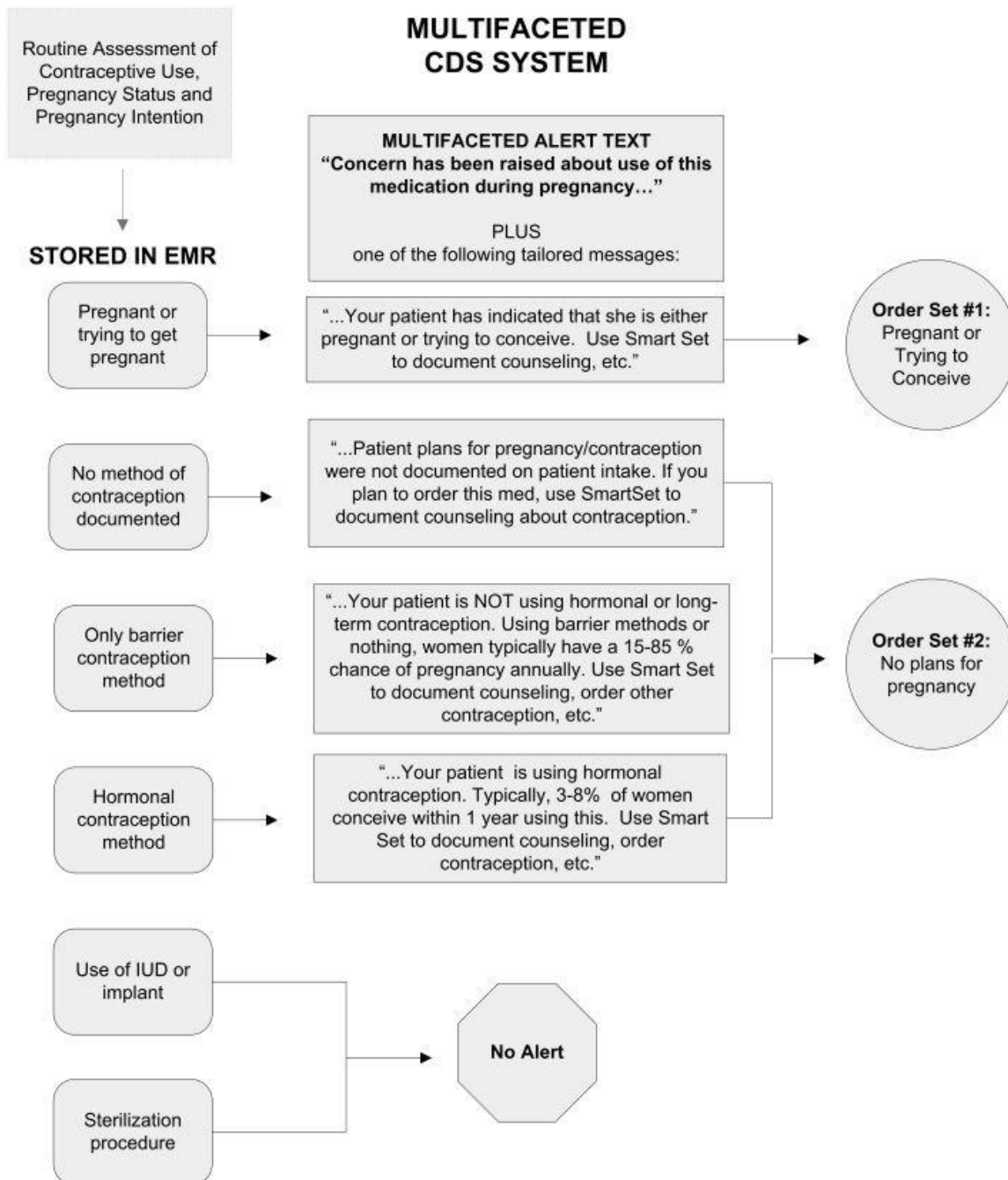
We designed 2 types of clinical alerts when PCPs ordered potentially teratogenic medications (list available on request) for a female patient between 18-50 years of age who did not have an indication of sterilization on her EMR. The ‘simple’ CDS alert stated “Concern has been raised about the use of this medication during pregnancy” when a potentially teratogenic medication was ordered. The ‘multifaceted’ CDS expanded upon this by incorporating data on women’s pregnancy intentions and contraceptive use collected by the tablet computers (Intervention #1) to tailor the alert text and provide a link to a structured order set (Figure 2). Both were disruptive alerts requiring PCP acknowledgement. These alerts fired when the PCP ordered a new prescription or a renewal prescription, but in an effort to avoid “alert fatigue” an alert only appeared for the first potentially teratogenic medication ordered during each encounter. Participating PCPs were randomized to receive either “simple” CDS or “multifaceted” CDS. PCPs were not specifically trained about teratogenesis or contraception or to use this CDS. We hypothesized that multifaceted CDS with tailored alerts incorporating information on women’s likelihood of pregnancy and a structured order set would lead to greater improvements than CDS that simply warned PCPs about the use of medication during pregnancy. We also hypothesized that PCPs would report more satisfaction with the multifaceted CDS alerts.

There were several implementation challenges. Because the FAST tablets (intervention #1) were unable to directly interface with the EMR, the multifaceted alert most frequently provided a general alert, instead of a tailored alert. Although residents at the academic practice were supposed to receive alerts, a programming error excluded them, significantly reducing the number of physicians who actually participated in this study. In addition, 8 months into the intervention, changes to the UPMC EMR that were unrelated to this study inadvertently deactivated the multifaceted CDS. Thus, this group received no alerts for the remainder of the study. Therefore, we were able to compare the effect of simple vs. multifaceted alerts from October 2008 to June 2009, and the effect of the simple alert vs. no alert from July 2009 to April 2010. Finally, although we programmed these alerts to only fire for women that did not have ICD-9 or CPT codes indicating tubal ligation or hysterectomy, the system did not check for ICD-9 codes associated with menopause and infertility, which might have further limited alert fatigue.



Figure 2. Design of the Multifaceted CDS Alert System

COLLECTED AT INTAKE



## Specific Aim #2: Evaluation of Decision Support Systems

We used three sources of data to evaluate these two interventions:

- 1) Physician survey data: PCPs were asked to complete an online survey prior to the intervention and a follow-up survey one year after implementation. The surveys asked the PCPs how many times in the last month they provided preconception counseling or counseled their patients about risks of medication-induced birth defects. PCPs were also asked how many times in the last month they or their staff counseled patients about contraception or provided patients with contraceptive prescriptions or referrals. Finally, PCPs rated their satisfaction with the CDS they received on a 10-point scale. Using the survey data, we compared PCPs' mean level of satisfaction with the CDS they received and self-reported changes in prescribing patterns. Overall changes in PCP practice patterns were assessed using Wilcoxon matched pair signed-rank tests. To compare changes in practice patterns by CDS group, change scores were calculated for each PCP, and differences by study group in the mean change score were assessed using independent samples t-tests or Wilcoxon rank sum tests. Only PCPs with complete pre- and post-intervention surveys were included in this analysis. Surveys from residents who, due to a programming error did not receive the CDS as intended were also removed from this analysis.
- 2) EMR data: We abstracted de-identified EMR data from all visits made to study physicians by females aged 18-50 years regarding the type of clinical encounter (new vs. return, with usual PCP vs. different PCP), all potentially teratogenic medications prescribed, and all pregnancy tests ordered. We also noted whether the patient had an active contraceptive prescription, had documentation of contraceptive counseling within the past 3 months, or had been referred for placement of an intrauterine contraceptive, contraceptive implant, or diaphragm. Finally, we abstracted data regarding patients' age, race and marital status.

To evaluate the effects of the tablet computer intervention, we reviewed de-identified EMR data from all visits with women aged 18-50, with no evidence of sterilization, menopause, or infertility, who started to complete an intake questionnaire using a FAST tablet computer at their visit. We abstracted EHR data from pre-intervention visits (May 2007-Sept 2008) and intervention period visits (Oct 2008-April 2010). Women's responses to the contraceptive vital sign questions were also extracted from the FAST system and linked to their EHR data by an honest broker. We eliminated from this analysis all annual preventive visits which unfortunately did not receive the intervention as originally planned. We had 2 primary outcomes in terms of effectiveness: 1) documentation of use of contraception in the patient's medical record and 2) provision of new family planning services at the visit (i.e. new contraception prescriptions, contraceptive counseling, pregnancy testing, or referral to a family planning specialist). We were interested in these outcomes both overall and specifically for visits where a potential teratogen was prescribed.

To evaluate the effects of the clinical alert intervention, de-identified EMR data were abstracted from 3 time periods: "T0"--- the 10 month period prior to CDS activation, "T1"--- the 9

month period during which physicians received either simple or multifaceted CDS, and “T2”--- the 9 month period during which the multifaceted CDS was deactivated and physicians received either simple or no CDS. Encounters with indication of surgical sterilization, hysterectomy, menopause, or infertility were excluded from this analysis. Our primary outcome, provision of family planning services when a potentially teratogenic medication was prescribed, was defined as evidence of pregnancy testing, a new contraceptive prescription, a non---expired contraceptive prescription, contraceptive counseling, or referral for placement of a contraceptive device.

We used the same analytic approach to evaluate both interventions: we estimated the adjusted absolute difference in improvement in the outcomes of interest over time between the intervention and control groups using mixed effects logistic regression models adjusted for clustering. Models used a difference in differences approach. All models were adjusted for physician type, physician gender, patient age, usual PCP visit (Y/N), and new patient visit (Y/N).

- 3) Patient survey data: Female patients visiting study PCPs during the intervention were invited to complete a survey 5---30 days after their visit. Interested participants provided signed informed consent and received survey access instructions at the time of their clinic visit. Women who preferred to complete the survey by phone were able to do so. The 75 question survey collected detailed information regarding participants’ demographic and reproductive characteristics, as well as details about their visit. Participants who reported receiving a prescription at their last clinic visit were asked “At your last visit, did your doctor spend any time discussing the chance that a medication you are using can cause birth defects?” and “Did your doctor tell you that you may want to avoid becoming pregnant while using any of the medications that were prescribed to you?” Patients were also asked “At your last visit, did your doctor talk to you about birth control?” Those that reported receiving counseling were asked to rank their level of satisfaction with the counseling they received with four response options (‘very satisfied’ to ‘not satisfied’). For those women who granted permission to review their medical records, we abstracted identified EMR data from each clinic visit made during the study period and linked these records to their survey data.

## RESULTS

### Principal Findings

#### *Focus Groups*

The physician focus groups identified barriers to providing contraceptive counseling at the patient, provider, and health system levels. The providers identified patient contraceptive method of preference, outside influences, already on birth control, desire for pregnancy, religion, patient discomfort, and sexual activity confidentiality as patient---level barriers to counseling. Physician---level barriers included: lack of knowledge, training, or comfort; beliefs about certain contraceptive methods; a perceived patient responsibility for initiating discussions; a need for skilled personnel for certain contraceptive methods; and a lack of communication with subspecialists. Finally, health system---level barriers included lack of

reimbursement for counseling, limitations on time, poor access to providers trained to place contraceptive devices, competing medical priorities, and lack of a clinical reminders.

The patient focus groups found that women reported depending a great deal on their PCPs for information about the risks medications might pose to a pregnancy.(16) However, women frequently reported that the information they had received was not comprehensive. Women indicated they wanted their PCPs to initiate discussions about potentially teratogenic medications at the time the medications are prescribed, regardless of whether she was sexually active or planning a pregnancy. Women wanted clear information about all potential fetal outcomes. Factors women reported as being critical to effective teratogenic risk counseling included privacy, sufficient time, and a trusting relationship with their PCP. These concerns were taken into consideration in designing our two health IT interventions.

### **Physician Survey Data**

Seventy---six percent (n=31) of eligible PCPs completed both pre--- and post---intervention surveys. Following implementation of the CDS, PCPs reported significant improvement in several practice patterns (Table 1). When comparing the changes by CDS type, we found that PCPs who received the multifaceted CDS reported a greater increase in the number of times per month they discussed the risk of medication use during pregnancy with their patients than PCPs who received the simple CDS (+4.9±7.0 multifaceted vs. +0.8±3.2 simple, p=0.03). However, PCPs receiving simple CDS reported greater satisfaction with their CDS [median (IQR): 8(3.5) simple vs. 5(3) multifaceted, on a 10---point scale, p=0.006].

**Table 1: Changes in physician self-report of counseling, referral, and prescribing behaviors (N=31)**

<i>"In the last month, in your outpatient clinical experience, how many times did you or your staff..."</i>	<b>Pre--- Intervention Median (IQR)</b>	<b>Post--- Intervention Median (IQR)</b>	<b>Change Score Mean (SD)</b>	<b>P---value<sup>†</sup></b>
Discuss the risk of medication use during pregnancy	(3)	3 (9)	+3.3 (6.1)	0.001
Provide preconception counseling	(3)	2 (6)	+1.8 (3.6)	0.007
Order a pregnancy test	(2)	2 (3)	+1.0 (3.5)	0.17
Discuss contraception with a patient	(8)	7 (9)	+1.6 (9.4)	0.08
Discuss emergency contraception with a patient	(2)	0 (2)	+0.5 (2.7)	0.39
Prescribe hormonal birth control	(5)	5 (9)	+2.0 (3.9)	0.05
Refer to a family planning specialist	(0)	0 (1)	+0.4 (1.0)	0.03
Refer for IUD placement	(1)	0 (2)	+0.5 (1.1)	0.008

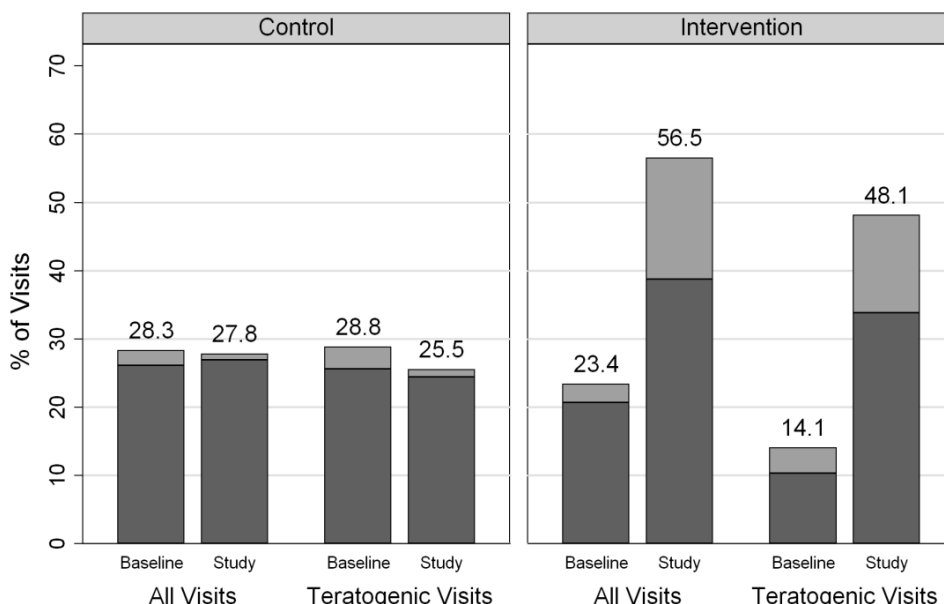
<sup>†</sup>P-values from Wilcoxon matched pair signed-rank tests.

**Electronic Medical Record Data**

**Intervention #1:** Fifty---three PCPs (intervention=26; control=27) contributed data from 5,371 visits with 2,304 women aged 18---50 years. During the 816 visits on which women were asked the contraceptive vital sign questions, 93% provided answers for their PCP. The remaining 7% either skipped the question or did not make it to that part of the questionnaire before being called to see the clinician. Of those who answered the contraceptive vital sign questions, 92.3% indicated that they were not trying to get pregnant; 6.3% said they wouldn't mind being pregnant; 0.3% were trying to get pregnant; 0.4% were currently pregnant and 0.7% preferred not to answer. Among those who were not currently pregnant or trying to get pregnant, 53% reported contraceptive use (34% were using hormonal or more effective contraceptive; 19% were using barrier or behavioral methods), 29% said that they had not had sex within the past 3 months, and 12% reported sexual activity without contraception; 6% said that they preferred not to answer the question about contraceptive use. In total, intervention PCPs were notified to "consider chance of pregnancy when prescribing" on 13.5% (n=110/816) of visits in which contraceptive vital sign data was collected. Overall, 17% of visits involved the prescription of a potentially teratogenic medication.

Figure 3 shows the proportion of all visits and proportion of teratogenic visits with medical record documentation of contraceptive use during the baseline and intervention periods for both the intervention and control groups. Following implementation of this intervention, 57% of visits made to PCPs in the intervention group had documentation of contraception vs. 28% of visits to PCPs in the

control group. In mixed effects models, this represented a significantly greater improvement in documentation in the intervention group compared to the control group [intervention: +77.4(70.7 to 84.1) vs. control: +3.1(1.2 to 5.0) adjusted percentage points, p<0.001]. A similar pattern was seen



**Figure 3. Change in proportion of visits with medical record documentation of contraception before and after introduction of a contraceptive vital sign** (dark gray=hormonal or more effective, light gray=barrier or behavioral)

for documented use of hormonal or more effective contraception; in adjusted mixed effects models this represented a significantly greater improvement in documentation of hormonal or more effective contraception in the intervention group [intervention: +37.8(26.6 to 48.9) vs. control: +2.9(1.3 to 4.5) adjusted percentage points, p<0.001]. The same patterns were seen

amongst the high-risk visits involving a teratogenic prescription; in mixed effects models predicting documentation of contraception and adjusting for visit-level covariates, significantly greater improvement in documentation was seen in the intervention group than the control group [intervention: +61.5(35.8 to 87.1) vs. control: -0.3(-4.3 to 3.6) adjusted percentage points,  $p < 0.001$ ]. A similar pattern was seen for documented use of hormonal or more effective contraception: in mixed effects models this represented a significantly greater improvement in documentation of hormonal contraception in the intervention group [intervention: +22.2(1.3 to 43.2) vs. control: +0.5(-2.1 to 3.1) adjusted percentage points,  $p = 0.004$ ].

At baseline, new contraceptive prescriptions or other family planning services were provided at 11% of control group visits and 9% of intervention group visits ( $p = 1.0$ ). After introduction of the contraceptive vital sign, intervention PCPs who saw patients with contraceptive vital sign data were not significantly more likely to provide new contraceptive prescriptions or other family planning services [intervention: +0.3(-2.8 to 3.3) vs. control: -1.4(-3.3 to 0.4) adjusted percentage points,  $p = 0.3$ ]. In the subgroup of visits involving a teratogenic prescription, family planning services were provided at 12% of control group visits and 7% of intervention group visits ( $p = 0.7$ ). However, again there was only minimal increase in provision of new family planning services by intervention PCPs [+3.3(-5.4 to 12.0) vs. control: -1.7(-6.6 to 3.3),  $p = 0.3$ ].

Of visits to intervention PCPs that involved prescription of a potential teratogen during the study period ( $n = 133$ ), 20% ( $n = 27$ ) still had no documentation of the patient's contraceptive status (either because they did not complete the contraceptive vital sign questions ( $n = 14$ ) or responded "prefer not to answer" ( $n = 13$ )), and 11% ( $n = 14$ ) had documentation of non-use of contraception. Of the 14 visits with documentation of contraceptive non-use when a potential teratogen was prescribed, only one (7%) received a referral for family planning services; none received pregnancy testing or a new contraceptive prescription.

When the Welcome tablets were used at the community-based clinics ( $n = 1,445$  visits with female patients of reproductive age over a 25-month period), we found that most (70%) women completed the questionnaires and few (1%) declined to answer the contraceptive vital sign questions. Further, the women reported information with the potential to affect PCP prescribing decisions 30% of the time: pregnancy or a desire for pregnancy (4%), ambivalence towards pregnancy (3%), breastfeeding (1%), and lack of effective contraception despite a desire to avoid pregnancy (22%).

Intervention #2: Forty-one PCPs (multifaceted=24; simple=17) contributed 35,110 visits made by 9,972 female patients who had no EMR indication of sterilization, infertility or menopause. There was minimal change in the prescription of teratogenic medications during the study period and no significant difference between clinical alert groups (Table 2). All study PCPs received clinical alerts when ordering potentially teratogenic medications. However, PCPs receiving the multifaceted alerts opted to access the linked order set only 16% of the time.

Prior to alert implementation (T0), 24.2% of the visits in which a potentially teratogenic medication was prescribed had documented provision of family planning services. Following

alert implementation (T1), the proportion of visits with concurrent documentation of provision of family planning services when a potentially teratogenic medication was prescribed increased to 26.5%, an increase of +1.0 adjusted percentage points (95% CI:---0.2 to 2.1, p=0.08). This slight increase was observed in both groups, but the difference in change between the groups was not significant (Table 2). After the multifaceted CDS was deactivated (T2), observed improvement in the group formerly receiving the multifaceted CDS slowed, while further improvement was seen among PCPs continuing to receive the simple CDS, however there was not a significant difference between the groups in adjusted models (Table 2).

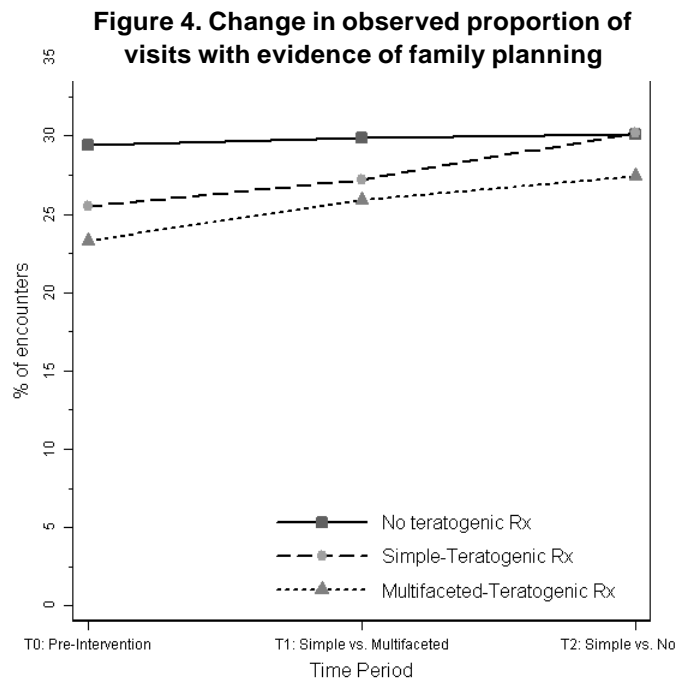
**Table 2: Change in outcomes by intervention group following implementation of clinical alerts**

Time period	PCPs randomized to Simple CDS (n=17)			PCPs randomized to Multifaceted CDS (n=24)			T to T1 Difference between groups <sup>†</sup> (95% CI), P-value	T to T2 Difference between groups <sup>†</sup> (95% CI), P-value
	T0	T1	T2	T0	T1	T2		
CDS received	None	Simple	Simple	None	Multi	None		
No. of encounters	5,433	4,397	4,745	7,243	6,962	6,330		
With a potentially teratogenic prescription	14.2% (772)	13.9% (610)	14.4% (683)	14.3% (1,035)	13.0% (906)	13.5% (857)	-0.5 (-1.5,0.5) 0.30	0.0 (-1.2,1.2) 0.94
With family planning services	25.5% (197)	27.2% (166)	30.2% (206)	23.3% (241)	25.9% (235)	27.4% (235)	-0.2 (-2.6, 2.1) 0.87	-0.4 (-3.1, 2.3) 0.78

<sup>†</sup>Represents the absolute difference in improvement between groups, calculated as the adjusted percentage point change among physicians randomized to receive multifaceted CDS *minus* the adjusted percentage point change among physicians randomized to receive simple CDS.

PCPs receiving the simple CDS displayed a significant upward linear trend over the 3 time points in the provision of family planning services when a potentially teratogenic medication was prescribed (Figure 4, adjusted p=0.03). In contrast, provision of family planning services during visits that did not include the prescription of a potentially teratogenic medication stayed relatively flat; representing a significantly greater improvement in provision of family planning services over time for the visits receiving simple CDS for potentially teratogenic prescriptions compared to the visits without teratogenic prescriptions (adjusted p=0.008).

The CDS alerts had similar effects in the academic and community-based practices: [(academic: +2.6 adjusted percentage points (95% CI: -1.5 to 6.6) vs. community-based: +0.4 adjusted percentage points (95% CI: -0.3 to 1.2)]. The clinical indication for which a potentially teratogenic medication was prescribed did not affect the frequency with which family planning services were documented, with two exceptions: women receiving isotretinoin were most likely to have documented receipt of family planning services (92.3% of such encounters), while women receiving warfarin were least likely (11.5% of such encounters). Of concern, 13% of the time that physicians received an alert they cancelled the prescription that triggered the alert and prescribed another potentially teratogenic medication which would have also triggered an alert, if the system had been designed to repeatedly alert clinicians when a teratogen was prescribed.



### Patient Survey Data

Complete analysis of the patient survey data collected during the intervention period is in progress. As a preliminary analysis, we divided surveys into 3 groups of visits: visits with no teratogenic prescription, visit with a teratogenic prescription received while CDS was up and running and visit with a teratogenic prescription received while CDS was turned off (during the T2 period). Women who did not receive teratogenic prescriptions reported receiving counseling about risk of medication-induced birth defects 19% of the time. Women who received teratogenic prescriptions without CDS support reported receiving such counseling 31% of the time compared to 35% of the time with CDS support. Over 90% of women who received counseling reported that they were 'satisfied' or 'very satisfied' with the counseling provided by their physician, whether or not the physician received CDS.

### Discussion

The cluster randomized trial of the tablet computers demonstrated that the introduction of a contraceptive vital sign was acceptable to the large majority of women served by a primary care practice and significantly improved primary care documentation of contraception. However, the intervention had minimal impact on PCP provision of new family planning services, and a substantial number of patients prescribed potentially teratogenic medications were found to remain at risk for unintended pregnancy. Although the intervention was designed to limit PCP liability when a potential teratogen is prescribed, it may have inadvertently increased liability when contraceptive non-use was explicitly documented alongside a potentially teratogenic



prescription. As PCPs frequently discuss contraception during annual preventive visits, it is unfortunate that these visits were inadvertently excluded from this study by a programming error, and the final sample size was smaller than intended. With only 110 intervention visits in which PCPs received a warning message, we had limited power to detect significant improvement in physician behaviors. In addition, we have no way of verifying that PCPs reviewed the contraceptive vital sign data provided to them as a paper report. Finally, as PCPs have little incentive to code provision of counseling services, PCPs likely provided preconception and contraceptive counseling more often than is reflected in the EMR data.

The cluster randomized trial of the clinical alerts found that CDS can be useful in promoting safe prescribing to women of reproductive age. Specifically, we found that PCPs receiving either type of CDS reported an increase in the number of times they provided counseling about the risks of medication---induced birth defects to women prescribed potentially teratogenic medications; EMR data corroborated a slight increase in provision of contraceptive prescriptions when potentially teratogenic medications were prescribed. The development of this CDS within the context of EpicCare®, a widely---used ambulatory care EMR increases the external validity of the findings. The lack of significant differences between the CDS types is not surprising as PCPs infrequently accessed the supplemental links provided by the multifaceted CDS and the multifaceted CDS did not operate as originally intended. We could not corroborate provision of counseling regarding medication risk because ICD---9 codes for counseling are not used regularly. In addition, the EMR does not document use of non---prescription contraceptives such as condoms, whether a woman's partner has had a vasectomy, or contraceptive services obtained from other clinics. Nor does it reliably document women's sexual orientation or fertility, and there is no way to tell which women were currently pregnant or trying to get pregnant; prior studies in this patient population have shown that the large majority (74%) of fertile patients seen in primary care settings are trying to avoid pregnancy.(17) Our effort to reduce alert fatigue by programming this CDS to fire only once during an encounter may have led to an underestimate of the true potential of this CDS intervention, as doctors ultimately substituted another potential teratogen 13% of the time they received a CDS alert. Finally, because this study did not have a true control group, we cannot conclude that the changes observed are due solely to the introduction of CDS.

### **Conclusions and Implications**

The advanced CDS developed through this grant has potential to increase physician awareness of potentially teratogenic medications and is acceptable to patients and physicians. An adaptation of the prescribing alert which combines aspects of both the simple and multifaceted CDS has therefore been rolled out to all UPMC ambulatory practices and now has the potential to impact patients in a number of rural areas served by UPMC practices, in communities where health IT diffusion has historically been low. However, several refinements could improve upon the value of these systems. In particular, in order to avoid having physicians inadvertently replace one potentially teratogenic medication with another, CDS should alert PCPs to medication risk as many times as needed during a given encounter. If the tablet computers had successfully integrated with the EMR, the multifaceted support would have provided additional information that may have instigated further discussion with patients. It may also be helpful to

incorporate information about the safety of different contraceptive options into future CDS, particularly for women receiving warfarin, who were least likely to receive family planning services, likely due to limited PCP awareness of contraceptives that do not increase risk of thrombosis. Alternatively, systems that facilitate referral of women who need contraception to clinicians with expertise in family planning may be of value.

## DISSEMINATION ACTIVITIES AND PRODUCTS

### Products

“Preventing Medication---Induced Birth Defects PLUS CARE Guide“: Provides instructions for other Epic users on how to implement this CDS within their health system. Available at <https://userweb.epic.com/> This health IT intervention conformed to established standards and is a certified product. Public use version available on AHRQ’s Health IT website under “AHRQ Funded Project Resources Archives.”

### Presentations

1. Schwarz EB, Santucci A, Nikolajski C, Gold M. It’s harder than you’d think: the challenges of providing teratogenic information in primary care settings. Oral abstract presented at the *Annual Meeting of the Organization of Teratology Information Specialists* Monterey, California, June 2008.
2. Santucci A, Nikolajski C, Gold M, Schwarz EB. Doing it right: women’s perspectives on receiving information on medication---induced birth defects. Oral abstract presented at the *Annual Meeting of the Organization of Teratology Information Specialists* Monterey, California, June 2008.
3. Schwarz EB, Handler S, Shevchik G, Kapoor WN, Koren G, Fischer G. Clinical Decision Support to Promote Counseling about Risk of Medication---induced Birth Defects. *AHRQ 2009 Annual Meeting*, Washington, DC, September 14, 2009.
4. Schwarz EB, Borrero S, Douglas E, Akers A. Contraceptive counseling and ambivalence towards pregnancy in primary care settings. *Annual Meeting of the Association of Reproductive Health Professionals and Society of Family Planning* Los Angeles, California, October 2, 2009.
5. Martensis M, Schwarz EB, Sobota M, Nothnagle M, Chuang C. Insurance Coverage of Contraception and Abortion: What Do Physicians Think? *33rd Annual Meeting of the Society of General Internal Medicine* Minneapolis, Minnesota April 30 2010.
6. Schwarz EB, Parisi SM, Handler SM, Kapoor WN, Fischer, GS. Physician Perceptions of Clinical Decision Support to Promote Counseling about Risk of Medication---induced Birth Defects. Poster presented at the *AHRQ Health IT Grantee and Contractor Meeting* Washington, DC, June 2---3, 2010.
7. Schwarz EB, Parisi SM, Fischer, GS, Handler SM, Hess, R. Effect of ‘Contraceptive Vital Sign’ in Primary Care: Randomized Controlled Trial. Poster presented at the *Reproductive Health Conference* Atlanta, GA September 22---25, 2010.
8. Schwarz EB, Parisi SM, Handler SM, Koren G, Kapoor WN, Fischer, GS. Use of Computerized Clinical Decision Support Systems to Promote Counseling about Risk of Medication---induced Birth Defects. Oral abstract presented at the *1st European Congress on Preconception Care and Health* Brussels, Belgium, October 6---9, 2010.
9. Schwarz EB, Parisi SM, Sobota M, Nothnagle M, Chuang C. Primary Care Provider Perceptions of Rates of Unintended Pregnancy and Contraceptive Effectiveness. Oral abstract presented at the *Society for General Internal Medicine Annual Meeting*

Phoenix, Arizona, May 5, 2011.

10. Williams SL, Hess R, Parisi SM, Handler S, Shevchik G, Kapoor W, Schwarz EB. Integrating Patient--- Reported Information into an Electronic Medical Record to Ensure Safe Prescribing to Women of Childbearing Potential. Oral abstract presented at the *Society for General Internal Medicine Annual Meeting* Phoenix, Arizona, May 6, 2011.
11. Schwarz EB and Fischer GS. Beauty and the Beast: Preventing Medication---Induced Birth---Defects. Oral presentation at the *Epic Users Group Meeting* Verona, Wisconsin, September 20, 2011.
12. X H, Parisi SM, Schwarz EB. Perceptions of intrauterine contraceptives among women seeking primary care. Poster presented at the *North American Forum on Family Planning* Washington, DC, October 22---24, 2011.
13. Russo J, Parisi SM, Creinin M, Schwarz EB. Sources of contraceptive information among primary care patients. Poster presented at the *North American Forum on Family Planning* Washington, DC, October 22---24, 2011.
14. Lee JK, Parisi SM, Schwarz EB. Perceived health status, receipt of contraceptive counseling, and contraceptive use. Poster presented at the *North American Forum on Family Planning* Washington, DC, October 22---24, 2011.
15. Parisi SM, Handler SM, Koren G, Fischer GS, Schwarz EB. Clinical decision support to promote safe prescribing to women of reproductive age: differential effects by subgroup. Poster presented at the *33rd Annual Meeting of the Society for Medical Decision Making* Chicago, IL, October 23, 2011.

## Publications

1. Schwarz EB, Santucci A, Borrero S, Akers A, Nikolajski C, Gold M. Perspectives of primary care clinicians on teratogenic risk counseling. *Birth Defects Res Clin Mol Teratol* 200 Oct;85(10):858--- 63. Epub 200 Jul 8. [PMID: 19591115; PMCID: PMC2805273].
2. Santucci A, Gold M, Akers A, Borrero S, Schwarz EB. Women's Perspectives on Counseling about Risks for Medication---Induced Birth Defects. *Birth Defects Res Clin Mol Teratol* 201 Jan;88(1):64---9. Epub 200 Jul 27. [PMID: 19637252; PMCID: PMC2806515].
3. Akers AY, Gold MA, Borrero S, Santucci A, Schwarz EB. Providers' perspectives on challenges to contraceptive counseling in primary care settings. *The Journal of Womens Health* 2010 Jun;19(6):1163---70. Epub 201 April 26. [PMID: 20420508; PMCID: PMC2940510].
4. Lee JK, Parisi SM, Akers AY, Borrero S, Schwarz EB. The Impact of Contraceptive Counseling in Primary Care on Contraceptive Use. *Gen Intern Med* 201 Jul;26(7):822. Epub 201 Feb 8. [PMID: 21301983; PMCID: PMC3138576].
5. Parisi SM, Zikovich S, Chuang CH, Sobota M, Nothnagle M, Schwarz EB. Primary care physicians' perceptions of rates of unintended pregnancy. *Contraception* Scheduled for publication in the August 2012 issue.
6. Chuang CH, Martenis ME, Parisi SM, Delano R, Sobota M, Nothnagle M, Schwarz EB. Contraception and abortion coverage: What do primary care physicians think? Under 2<sup>nd</sup> round review at *Contraception*.
7. Schwarz EB, Parisi SM, Williams SL, Shevchik GJ, Hess, R. Promoting Safe Prescribing in Primary Care with a Contraceptive Vital Sign: a Cluster---Randomized Controlled Trial. Under review at *Annals of Family Medicine* submitted on August 24, 2011.
8. Schwarz EB, Parisi SM, Handler S, Koren G, Cohen ED, Shevchik GJ, Fischer GS.

Clinical Decision Support to Promote Safe Prescribing to Women of Reproductive--age: A Cluster---Randomized Trial. Under review at the *Journal of General Internal Medicine*, submitted on September 14, 2011.

9. Lee JK, Parisi SM, Schwarz EB. Contraceptive Counseling and Use among Women with Poor Health. Under review at the *American Journal of Obstetrics & Gynecology* submitted November 7, 2011.

## REFERENCES

1. Schwarz EB, Maselli J, Norton M, Gonzales R. Prescription of teratogenic medications in United States ambulatory practices. *Am J Med* 2005;118(11):1240---9.
2. Schwarz EB, Postlethwaite DA, Hung YY, Armstrong MA. Documentation of contraception and pregnancy when prescribing potentially teratogenic medications for reproductive---age women. *Ann Intern Med* 2007;147(6):370---6. Epub 2007/09/19.
3. Briggs GG, Freeman RG, Yaffe SJ. *Drugs in Pregnancy and Lactation*. Philadelphia: Lippincott Williams & Wilkins; 2002.
4. Finer LB, Zolna MR. Unintended pregnancy in the United States: incidence and disparities, 2006. *Contraception* 2011;84(5):478---85. Epub 2011/10/25.
5. Andrade SE, Gurwitz JH, Davis RL, Chan KA, Finkelstein JA, Fortman K, et al. Prescription drug use in pregnancy. *Am J Obstet Gynecol* 2004;191(2):398---407.
6. Scholle SH, Chang JC, Harman J, McNeil M. Trends in women's health services by type of physician seen: data from the 1985 and 1997---98 NAMCS. *Womens Health Issues* 2002;12(4):165---77.
7. Gallagher TC, Geling O, Comite F. Use of multiple providers for regular care and women's receipt of hormone replacement therapy counseling. *Med Care* 2001;39(10):1086---96.
8. Chapter 63, Counseling to Prevent Unintended Pregnancy. *Guide to Clinical Preventive Services*. 2nd edition. 1996. p. 739---53.
9. Yarnall KS, Pollak KI, Ostbye T, Krause KM, Michener JL. Primary care: is there enough time for prevention? *Am J Public Health* 2003;93(4):635---41.
10. Schreiber CA, Harwood BJ, Switzer GE, Creinin MD, Reeves MF, Ness RB. Training and attitudes about contraceptive management across primary care specialties: survey of graduating residents. *Contraception* 2006;73(6):618---22.
11. Shah NR, Seger AC, Seger DL, Fiskio JM, Kuperman GJ, Blumenfeld B, et al. Improving acceptance of computerized prescribing alerts in ambulatory care. *J Am Med Inform Assoc* 2006;13(1):5---11.
12. Weingart SN, Toth M, Sands DZ, Aronson MD, Davis RB, Phillips RS. Physicians' decisions to override computerized drug alerts in primary care. *Arch Intern Med* 2003;163(21):2625---31.
13. van der Sijs H, Aarts J, Vulto A, Berg M. Overriding of drug safety alerts in computerized physician order entry. *Am Med Inform Assoc* 2006;13(2):138---47.
14. Glaser BG, Strauss A. *Discovery of Grounded Theory Strategies for Qualitative Research*: Sociology Press; 1967.
15. Jones J, Hunter D. Consensus methods for medical and health services research. *BMJ*. 1995;311(7001):376---80.
16. Santucci AK, Gold MA, Akers AY, Borrero S, Schwarz EB. Women's perspectives o counseling about risks for medication---induced birth defects. *Birth Defects Res Clin Mol Teratol* 2010;88(1):64---9. Epub 2009/07/29.
17. Lee JK, Parisi SM, Akers AY, Borrero S, Schwarz EB. The impact of contraceptive counseling in primary care o contraceptive use. *Gen Intern Med* 2011;26(7):731---6. Epub 2011/02/09.