Introduction
Ethical constraints surrounding the inclusion of pregnant women in clinical trials are a significant barrier to pre-marketing evaluations of the effects of medication use during pregnancy. As an alternative to pregnancy registries, claims data are increasingly used to identify pregnancies, link pregnancies to offspring, and assess medication use during this period. We describe the use of Military Healthcare System’s (MHS) data to develop a linked mother-child database for adverse event detection and medication utilization analyses during pregnancy.

Methods
To identify pregnancies, pregnancy outcomes, and linkages to offspring, women of reproductive age with at least one pregnancy-related encounter between January 2005 and December 2012 who were eligible to receive care under the MHS were identified as the source population. Building on previously published algorithms, we used pregnancy-related diagnostic and procedure codes, parameterized temporal constraints, and data elements unique to the MHS to identify pregnancies ending in live births, stillbirth, clinical miscarriage, or ectopic pregnancy. Pregnancy ending in live births were matched to presumptive offspring using birth dates and family-based sponsorship identification. Pregnancies with data or outcome conflicts (e.g., start of pregnancy codes but no end of pregnancy codes) were not evaluated. Descriptive information regarding mother-child pairs available for analysis were evaluated. Outpatient opiate agonist or partial agonist and antidepressant medications dispensed to mothers during different periods of the pregnancy were evaluated. Proportion of pregnancies with exposure to an opiate agonist or partial agonist as well as antidepressant use were calculated among all live births that were matched to offspring. Additionally, trend data on both use of opiate and antidepressants are presented by birth year and trimester of pregnancy.

Results
Mother-Child Population
- Overall, our mother-child database contains over one million pregnancies with about 80% ending in live births. Our algorithms are able to match about 90% of all live births occurring in the DoD population. Additionally, our algorithms are able to identify a small percentage of all pregnancies with complete start and end of pregnancy care as stillbirths or clinical or spontaneous miscarriage (Figure 1).

Descriptive Characteristics of Mom-Child Pair
- Of the pregnancies ending in live births with no data conflicts (N=677,147), a slight majority (51%) were male and about a third were three years old or younger. Additionally, about 6.25% of all live-births were preterm (Table 1).

- The majority of mothers (~95%) were less than 35 years old with Active Duty females being the most common group.

Opioids and Antidepressant Use During Pregnancy
- Overall, maternal use of opioids during pregnancy was about 16%. Rates of use remained relatively stable from 2006 until 2010 and started declining thereafter; use during the third trimester was highest, followed by first and second trimester (Figure 2).

- Maternal use of any antidepressant from 2006-2012 was about 7%; the rates for all antidepressant use declined from 2006 to 2007 and remained relatively steady until 2010 with an additional decline thereafter. SSRIs and other antidepressants made up the two most frequently prescribed antidepressant among pregnant females (Figure 3).

Conclusions
- We have developed a large mother-child linked database which is being used for rapid medication utilization and adverse event signal detection and signal strengthening analyses in the MHS. Future plans will focus on validation of intermediate outcomes such as stillbirths and spontaneous miscarriages.
- Examples from our preliminary analysis for outpatient opioid use and antidepressant use are consistent with previous studies published in the literature.

Literature cited

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