Introduction
The risk of venous thromboembolism (VTE) with oral contraceptives (OCs) is well documented. Recently, questions have been raised about an increased risk of VTE of 4th generation OCs (containing drospirenone) compared to 2nd generation containing levonorgestrel.

Objective
This IMEDS Evaluation pilot used a distributed network of FDA Sentinel data partners to examine the rate of VTE in new users of 2nd and 4th generation OCs using the standardised data analytics capabilities of the IMEDS Evaluation pilot

Methods
The analytic cohort consisted of women aged 15-44 who were new OC users in 2nd or 4th generation. Patients with VTE risk factors were excluded. Dispensings were defined by National Drug Code in databases containing ICD9 codes 415.1 or 419.x, occurring in the prior history or emergency department setting. Nine Sentinel data partners participated. Publicly available Sentinel modular programs were used. Feasibility data were reviewed to inform use of the more complex modular analyses. Consistent with typical FDA use of these programs, the analysis did not include direct comparison or statistical testing; rather, the results include rates of VTE stratified by age, sex, and year.

Results
Between January 1, 2008 and April 30, 2010 there were 350,572 new users of 4th generation OCs and 317,363 new users of 2nd generation OCs. There were 158 new VTE events for 4th generation OCs, and 121 for 2nd generation OCs. The rate of VTE events per 10,000 person-years was 8.56 for 4th generation and 6.58 for 2nd generation OCs (interquartile range from 5.81 to 11.26 for 4th generation OCs and from 0 to 7.07 for 2nd generation OCs across the data partners).

Conclusions
In line with the literature, rates of VTE were greater for 4th generation than 2nd generation OCs. Limited variation was seen across data partners, although some partners had few events. Limitations include lack of confounding control, no direct comparisons or matching, and VTE defined only by the plot. The plot shows the value of the large distributed data network as such differences are explored in observational databases such as those available in the FDA’s Sentinel network(3).

Background
The risk of venous thromboembolism (VTE) with oral contraceptives (OCs) is well documented. Recently, questions have been raised about an increased risk of VTE of 4th generation OCs (containing drospirenone) compared to 2nd generation containing levonorgestrel.

Objectives
The aim of this pilot assessment was to examine rates of 2nd and fourth generation oral contraceptives (OCs) with respect to the occurrence of venous thromboembolism (VTE) in the Sentinel data network using the standardised data analytics capabilities of the IMEDS Evaluation pilot (figure 2).

Methods
The cohort for this analysis consisted of women aged 15-44 who are new users of 2nd generation OCs (containing levonorgestrel) and 4th generation (drospirenone-containing) OCs. Patients with evidence of VTE risk factors were excluded: cancer, renal failure, chronic-cardiovascular diseases, inflammatory or autoimmune conditions, epilepsy, anticoagulant use, NuvaRing use major surgery, trauma, or pregnancy. Dispensings were defined by National Drug Code in outpatient pharmacy claims records. VTE was defined as ICD9 codes 415.1 or 419.x, occurring in the prior history or emergency department setting. Age stratification was conducted into three age groups (15-29, 30-39, 40-44).

Results
Analyses were conducted across nine Sentinel data partners participating in the plot. Publicly available Sentinel modular programs and summary table query tools (Modular Program QRP version 2.09). Summary Table version 5.0) were used. Summary table data were reviewed to inform use of the more complex modular analyses. Consistent with typical FDA use of these programs, the analysis did not include a direct comparison or statistical testing, rather, the results include rates of VTE stratified by age, sex, and year.

Conclusions
This rapid analysis approach shows rates of VTE were greater for 4th generation than 2nd generation OCs in line with the literature. Limited variation was seen across data partners, although some partners had few events. Limitations include lack of confounding control, no direct comparisons or matching, and VTE defined solely by diagnosis code. The plot shows the potential of the large distributed data network in exploring safety issues and the value in leveraging Sentinel data and analytic tools.

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References