Women using combined oral contraceptives (COCs) are exposed to an increased risk of venous thromboembolic events (VTEs), particularly those using third- and fourth-generation COCs. In France, about four million women are daily exposed to COCs. Consequences of this large exposure needed to be assessed.

**OBJECTIVES**
To estimate the number of VTEs and related-premature deaths (i.e. mortality within 5 years due to recurrent VTEs, including immediate in-hospital lethality) attributable to the use of COCs in women aged 15-49 years between 2000 and 2011 in France.

**METHODS**
**Exposure**
Three sources of national data were combined to estimate the annual number of women exposed to COCs by age and by generation:
- population census
- data from 2 cross-sectional surveys investigating contraception behaviours
- sales of COCs claimed to the ANSM.

**Outcomes**
- Absolute risk of first time VTE in non-users of hormonal contraception and increased risk of VTE in users (vs. non-users of hormonal contraception) were estimated from the literature.
- Immediate in-hospital lethality due to pulmonary embolism and premature mortality due to recurrent VTE were estimated from both national database of hospitalisation and literature data.

**RESULTS**
In France, from 2000 to 2011, the estimated mean annual number of VTEs attributable to COCs was 2529 (778 cases attributable to first-/second-generation COCs and 1751 to third-/fourth-generation COCs), corresponding to:
- 843 estimated cases of pulmonary embolism
- 20 premature deaths, including 8 to 9 immediate in-hospital deaths.

In 2011, higher VTE cases were observed in women aged 25-29 years and 40-44 years (474 and 473 respectively). Overall, 31% of users over 35 years contributed to 46% of VTE cases attributable to COCs.

When compared to the use of first-/second-generation COCs, exposure to third-/fourth-generation COCs led to a mean annual excess of 1167 VTE cases, among which:
- 394 estimated cases of pulmonary embolism
- 9 premature deaths, including 3 immediate in-hospital deaths.

**CONCLUSION**
Risk minimisation actions have been conducted: information for healthcare professionals and patients, modifications of SmPCs. In France, they have led to limit exposure to third- and fourth-generation COCs, and thus optimise the benefit-risk ratio of COCs. Impact of such actions needs to be further assessed.

The results of this study have been published: Tricotel A et al. PLoS ONE, 2014.