

IMPACT OF THE SHARP CHANGES IN THE USE OF CONTRACEPTION IN 2013 ON THE RISK OF PULMONARY EMBOLISM IN FRANCE*

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BACKGROUND

In late 2012, a national pill crisis led French women to promptly change their behavior regarding contraception, with a significant increase in the use of first-/second-generation combined oral contraceptives** (C1G/C2G) to the detriment of third-/fourth-generation products (C3G/C4G). With about four millions women daily exposed to these contraceptives, these sharp modifications should have immediate implications in terms of venous thromboembolism morbidity.

OBJECTIVES

To assess the impact of the shift from C3G/C4G to C1G/C2G on the rate of women aged 15-49 years hospitalized for pulmonary embolism (PE) in France in 2013 compared to 2012 and 2010-2012.

METHODS

Population

All French women aged 15-49 years between 2010 and 2013, excluding those who delivered a live birth during the calendar year.

Outcome

All hospitalized PE in women aged 15-49 years were identified from the French national hospital discharge databases from 2010 to 2013. Only women for whom no hospitalization for PE had been reported in the last 12 months were included. Any PE occurring during a delivery stay was excluded.

Primary analysis

Annual PE hospitalization incidence rates, overall and by age group, were calculated from 2010 to 2013. Rates in 2013 were compared with those in 2012 and with mean rates over the preceding 3-year period (2010-2012). PE hospitalization incidence rates differences, together with 95% confidence interval were computed assuming a normal approximation to a Poisson distribution of the occurrence of PE.

Secondary analysis

- "Control populations": PE hospitalization rates were studied in two populations of non-users of contraceptives: women aged 50-69 years and men aged 15-49 years.
- Expected reduction in pulmonary embolism incidence in women aged 15-49 years, estimated by modeling the number of expected cases based on modifications of combined oral contraceptives exposure.

Assuming that the absolute risk of PE in non-users remained constant over the study period, the expected incidence rates were estimated by:

$$PE\ rate = \frac{\sum_{pop} (Number\ of\ women_{pop} \times absolute\ risk\ of\ PE\ in\ non\ -\ users \times RR_{pop/ref})}{\sum_{pop} (Average\ population\ without\ pregnancy_{pop})}$$

In which:

- pop designs one of the three sub-populations: non-users (ref), users of C1G/C2G and users of C3G/C4G
- $RR_{C1G-C2G/ref} \approx 2$ and $RR_{C3G-C4G/ref} \approx 4$

RESULTS

In France, between 2012 and 2013, PE hospitalization incidence rate decreased from 20.6 to 18.4 per 100 000 person-years, i.e. a 10.6% reduction. The trend was similar for all age groups.

Table 1. Hospitalizations for PE, PE hospitalization rates and differences of cases (Δ PE) in women aged 15-49 years in France in 2013 compared to 2012 and to 2010-2012

	2013		2013 vs. 2012		2013 vs. mean (2010-2012)	
	Nb PE	PE Rate (per 100,000)	Δ PE	95% CI Δ PE	Δ PE	95% CI Δ PE
15-49 Y	2625	18.4	-322	[-458 ; -166]	-227	[-352 ; -63]
15-19 Y	104	5.4	-23	[-53 ; 6]	-40	[-71 ; -9]
20-29 Y	566	15.0	-60	[-124 ; 11]	-61	[-121 ; 14]
30-39 Y	798	20.1	-77	[-148 ; 11]	-59	[-124 ; 34]
40-49 Y	1157	25.3	-162	[-261 ; -65]	-67	[-167 ; 25]

A similar pattern was not observed in the control groups:

- Women aged 50-69 years: 4.4% reduction in hospitalization rate for PE in 2013 compared to 2012 (0.2% reduction compared to 2010-2012).
- Men aged 15-49 years: increase in hospitalization rate for PE in 2013 (by 4.1% and 9.5% compared to 2012 and 2010-2012).

The expected pulmonary embolism reduction is consistent with the observed reduction in hospitalization incidence rate.

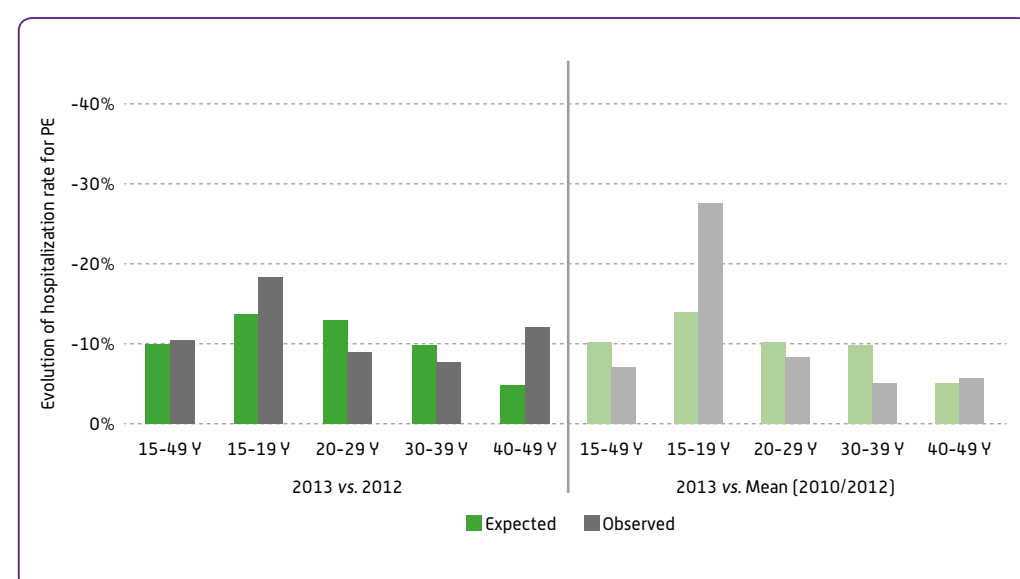


Figure 1. Observed and expected evolution of hospitalization rates for PE in women aged 15-49 years in France in 2013 compared to 2012 and to 2010-2012

CONCLUSION

Sharp change in the use of contraception methods, with a decreased use of C3G/C4G, probably played a major role in the reduction of venous thromboembolism morbidity in France.

* Tricotel A, Collin C, Zureik M. Impact of the sharp changes in the use of contraception in 2013 on the risk of pulmonary embolism in France. *J Thromb Haemost* 2015.

** Combined oral contraceptives were classified according to the progestogen they contain:

- C1G/C2G: norethisterone, levonorgestrel, norgestrel
- C3G/C4G: desogestrel, gestodene, norgestimate, chlormadinone, drospirenone, nomegestrol, dienogest