



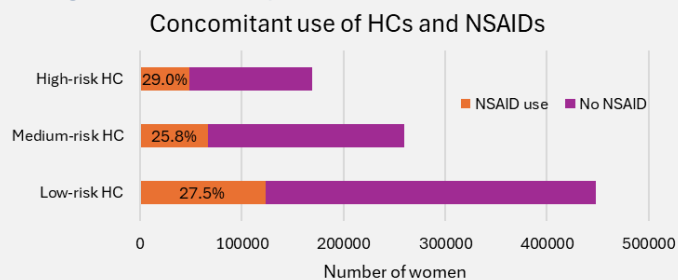
Is NSAID use associated with an increased risk of venous thromboembolism among hormonal contraceptive users?

Recently, a Danish nationwide study reported that the use of non-steroidal anti-inflammatory drugs (NSAIDs) was associated with an increased risk of venous thromboembolism (VTE) in women aged 15-49 years, particularly among those with concomitant use of high- and medium-risk hormonal contraception (HC). The aim of this DARWIN EU® study was to evaluate this association across European data sources.

Study overview

- Design: Population-level drug utilization study and self-controlled case series in Denmark, Norway, Spain, and the UK.
- Population: 876,932 women using HCs from Norway, 2018-2023.
- Exposure: Initiation of an oral NSAID (ibuprofen, diclofenac, and naproxen), with a grace period of 30 days to identify treatment episodes.
- Outcome: Incident (first-ever) VTE, including deep vein thrombosis and pulmonary embolism. Main risk period: 1-7 days after NSAID initiation.

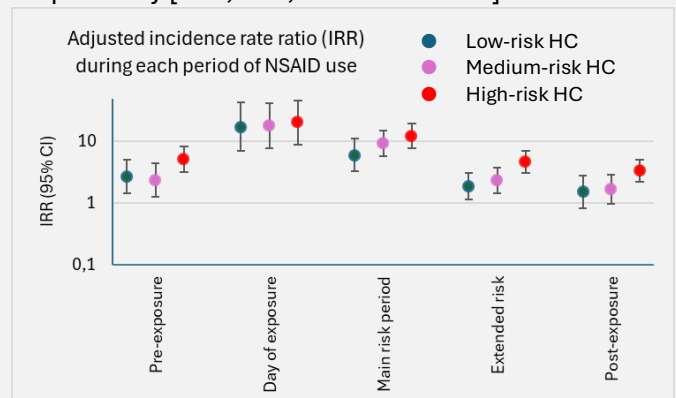
Characteristics of NSAID users among women using HCs in Norway



- At start of HC use, the median age was 27 years (IQR 20–35) for low-risk HC, 23 years (IQR 18–29) for medium-risk HC, and 25 years (IQR 21–31) for high-risk HC.
- The most common comorbidities at HC initiation were anxiety (26-31%), asthma (15-16%), and depression (10-11%).

Norway-specific results

The IRRs during concomitant use of NSAIDs with low-, medium-, and high-risk HC were 6.0 (95% CI 3.3-11.1), 9.4 (5.8-15.1), and 12.3 (7.8-19.3), respectively [188, 212, and 243 events].



In the analysis of negative control exposure, paracetamol use showed similar associations as with any NSAID use.

Data & Methods notes

- The self-controlled case series design accounts for time-fixed confounding by the using same person with an event (case) as their own control.
- Most women (79%) initiating NSAIDs while on HCs did not have a record of a potential indication for NSAIDs. This limited the ability to adjust for confounding by indication.
- NSAIDs are commonly purchased over-the-counter. The resulting misclassification is expected to bias the results towards the null.

How was this useful?

During all oral NSAID exposure risk periods, a positive association with VTE was observed. Counterintuitively, positive associations were also observed in the 2 weeks prior to NSAID initiation and in most scenarios also in the post-exposure period. Similar associations in VTE risk before and during use of paracetamol were found. These findings were not specific to Norway and consistent across all databases.

These results indicate that protopathic bias (reverse causation) and residual confounding may explain the observed association between NSAID use and VTE in women taking HC. However, it is impossible to rule out the possibility that part of the increased risk may directly be linked to NSAID use.

Access to the full report

[DARWIN EU® - Association of venous thromboembolism with NSAID use in women 15-49 years using hormonal contraceptives](#)

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