

# Hormonal contraception, PCOS, BMI, and venous thrombosis

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# Background

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- Two recent studies found a doubled risk of venous thrombosis in women with PCOS\*.
- Which influence has hormonal contraception on that risk?
- Which influence has BMI on that risk?
- Which influence has PCOS on the risk of VT in users of different types of hormonal contraception?

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\*) Bird et al. CMAJ 2013 and Okoroh et al. ACOG 2012

# Two new studies

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- Data from US IMS claims database 1.6 mio users of HC 2001-2009. Women with PCOS matched with propensity scores. VT
  - +PCOS: n= 46,867 (2.9%)      34/10,000 wy
  - - PCOS: n= 43,506              11/10,000 wy
  - RR +PCOS/-PCOS:              2.1 (1.4-3.2)
  - RR in non-users of HC:        2.1 (1.6-3.1)
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\*) Bird et al. CMAJ 2013

# PCOS and venous thrombosis

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- Data from US Thomson Reuters MarketScan database 2003-2008.

- Relative risk of VT

|                 | 18-24          | 25-34          | 35-45          |
|-----------------|----------------|----------------|----------------|
| +HC +PCOS/-PCOS | 2.9<br>2.2-3.9 | 2.0<br>1.7-2.4 | 1.8<br>1.5-2.1 |
| -HC +PCOS/-PCOS | 3.8<br>2.6-5.4 | 2.7<br>2.3-3.2 | 2.2<br>1.9-2.5 |

# Venous thrombosis and drospirenone

|                          | <b>VT</b> | <b>IR</b> | <b>Rate ratio</b> |         |
|--------------------------|-----------|-----------|-------------------|---------|
| Dinger <sup>07</sup>     | 118       | 9.1       | 1.0 (0.6-1.8)     | 4th/2nd |
| Vlieg <sup>09</sup>      | 1,524     | na        | 1.7 (0.7-3.9)     | 4th/2nd |
| Lidegaard <sup>09</sup>  | 4,213     | 7.8       | 1.6 (1.3-2.1)     | 4th/2nd |
| Dinger <sup>10</sup>     | 680       | na        | 1.0 (0.5-1.8)     | 4th/2nd |
| Parkin <sup>11</sup>     | 61        | 2.3       | 2.7 (1.5-4.7)     | 4th/2nd |
| Jick <sup>11</sup>       | 186       | 3.1       | 2.8 (2.1-3.8)     | 4th/2nd |
| Lidegaard <sup>11</sup>  | 4,246     | 9.3       | 2.1 (1.6-2.8)     | 4th/2nd |
| FDA Kaiser <sup>11</sup> | 625       | 7.6       | 1.5 (1.2-1.9)     | 4th/2nd |
| Gronich <sup>11</sup>    | 518       | 8.6       | 1.7 (1.0-2.7)     | 4th/2nd |
| Bird <sup>13</sup>       | 354       | 18.0      | 1.9 (1.5-2.4)     | 4th/2nd |

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# Methods

## National Health Registry (>1977)

BMI, VT diagnoses,  
Previous CaVD/canc.  
Pregnancies, PCOS

## Registry of Medicinal products (>1995):

OC use (>1995)

Anticoagulation therapy

BP↑, DM, Hyperchol.

1995



2001

1,417,473 women

2012

## Cause of Deaths Registry (>1977)

Lethal VT

## Statistics Denmark

PIN-codes, education  
vital status, emigration

# Hormonal contraception and VT: Confirmed 2001-12, non-use ref.

**ug EE NETA LNG NGM DSG GSD Drsp CPA**

|       |                 |                |                 |                               |                |                |                |
|-------|-----------------|----------------|-----------------|-------------------------------|----------------|----------------|----------------|
| 50    | 6.2<br>2.9-13.1 | 4.0<br>2.9-6.9 | 6.8<br>3.2-14.4 | 6.1 ← Vaginal ring<br>4.6-8.0 |                |                | na             |
| 30-40 | 2.3<br>1.2-4.5  | 3.3<br>2.9-3.9 | 3.7<br>3.1-4.3  | 6.7<br>5.8-7.7                | 6.6<br>6.0-7.2 | 6.3<br>5.5-7.2 | 6.3<br>5.2-7.6 |
| 20    | na              | na             | na              | 5.3<br>4.7-6.0                | 5.2<br>4.6-5.9 | 6.6<br>4.9-8.9 | na             |

**E2V/dienogest 4.7** 2.0-11.3

**POP 0.9** 0.5-1.7      **1.1** 0.6-1.9

**Lng-IUS 0.6** 0.5-0.8

Lidegaard et al. BMJ 2011 and 2012



# Results, BMI

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| <b>BMI</b> | <b>Women</b> | <b>VT</b>  |             | <b>RR<sub>adj</sub>*</b> |
|------------|--------------|------------|-------------|--------------------------|
|            | <b>years</b> | <b>All</b> | <b>Conf</b> |                          |
| <18.5      | 108,098      | 32         | 20          | 0.94 0.6-1.5             |
| 18-24.9    | 1,763,896    | 566        | 372         | Reference                |
| 25-30      | 614,167      | 277        | 175         | 1.31 1.1-1.6             |
| >30        | 360,131      | 273        | 167         | 2.20 1.8-2.6             |

\*) Adjusted for age, year, education, PCOS and hormonal  
contraceptin

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# Results, PCOS

| Group   | Women     | Relative risk of VT |        |         |
|---------|-----------|---------------------|--------|---------|
|         | years     | VT                  | RRadj* | RRadj** |
| No PCOS | 7.002.784 | 4.088               | 1      |         |
| + PCOS  | 55.739    | 54                  | 1.9    | 1.5-2.5 |

## Restricted to women with known BMI

|         |           |     |     |            |
|---------|-----------|-----|-----|------------|
| No PCOS | 2.809.138 | 719 | 1   | 1          |
| + PCOS  | 37.154    | 15  | 1.7 | 1.4 08-2.3 |

\* Adjusted for age, year, education and hormonal contraception

\*\*Adjusted for the same + body mass index

# Results 30-40 µg EE

|      | Wom yrs VT |     | RR*         | RR**         |
|------|------------|-----|-------------|--------------|
| NETA | 29,275     | 9   | 2.3 1.2-4.5 | 3.6 1.1-11.3 |
| LNG  | 303,789    | 186 | 3.3 2.9-3.9 | 3.7 2.3-6.0  |
| NGM  | 384,231    | 165 | 3.7 3.1-4.4 | 4.2 3.0-6.0  |
| DSG  | 214,875    | 219 | 6.7 5.8-7.7 | 5.5 3.7-8.2  |
| GSD  | 839,361    | 773 | 6.6 6.0-7.2 | 7.5 6.0-9.4  |
| DRSP | 353,894    | 253 | 6.3 5.5-7.2 | 7.4 5.4-10.0 |
| CPA  | 156,991    | 119 | 6.2 5.1-7.4 | 8.2 5.5-12.3 |

\*) Adjusted for age, year, education, and PCOS

\*\*\*) Adjusted for age, year, education, PCOS and BMI

# Results 20 µg EE and non-oral

|          | Wom yrs VT |     | RR* |         | RR** |          |
|----------|------------|-----|-----|---------|------|----------|
| LNG      | 303,789    | 186 | 3.3 | 2.9-3.9 | 3.7  | 2.3-6.0  |
| DSG      | 648,034    | 387 | 6.7 | 5.8-7.7 | 5.5  | 3.7-8.2  |
| GSD      | 660,635    | 355 | 6.6 | 6.0-7.2 | 7.5  | 6.0-9.4  |
| DRSP     | 62,743     | 44  | 6.3 | 5.5-7.2 | 7.4  | 5.4-10.0 |
| Vag ring | 69,178     | 52  | 6.2 | 5.1-7.4 | 8.2  | 5.5-12.3 |
| DSG only | 57,969     | 11  | 1.1 | 0.6-1.9 | 0.8  | 0.2-3.4  |
| LNG-IUS  | 341,505    | 52  | 0.6 | 0.5-0.8 | 0.8  | 0.4-1.5  |

\*) Adjusted for age, year, education, and PCOS

\*\*\*) Adjusted for age, year, education, PCOS, and BMI

# Conclusion

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- Women with PCOS has a doubled risk of VT
  - Half of this increase is due to adiposity
  - The increased risk is not explained by HC use
  - The difference in risk of venous thrombosis between users of 3<sup>rd</sup>/4<sup>th</sup> and 2<sup>nd</sup> generation oral contraceptives is not explained by PCOS or by differences in body mass index.
  - First choice for PCOS is 2<sup>nd</sup> gen. pills
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# PCOS-HT-BMI and venous thrombosis

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Thanks for your attention

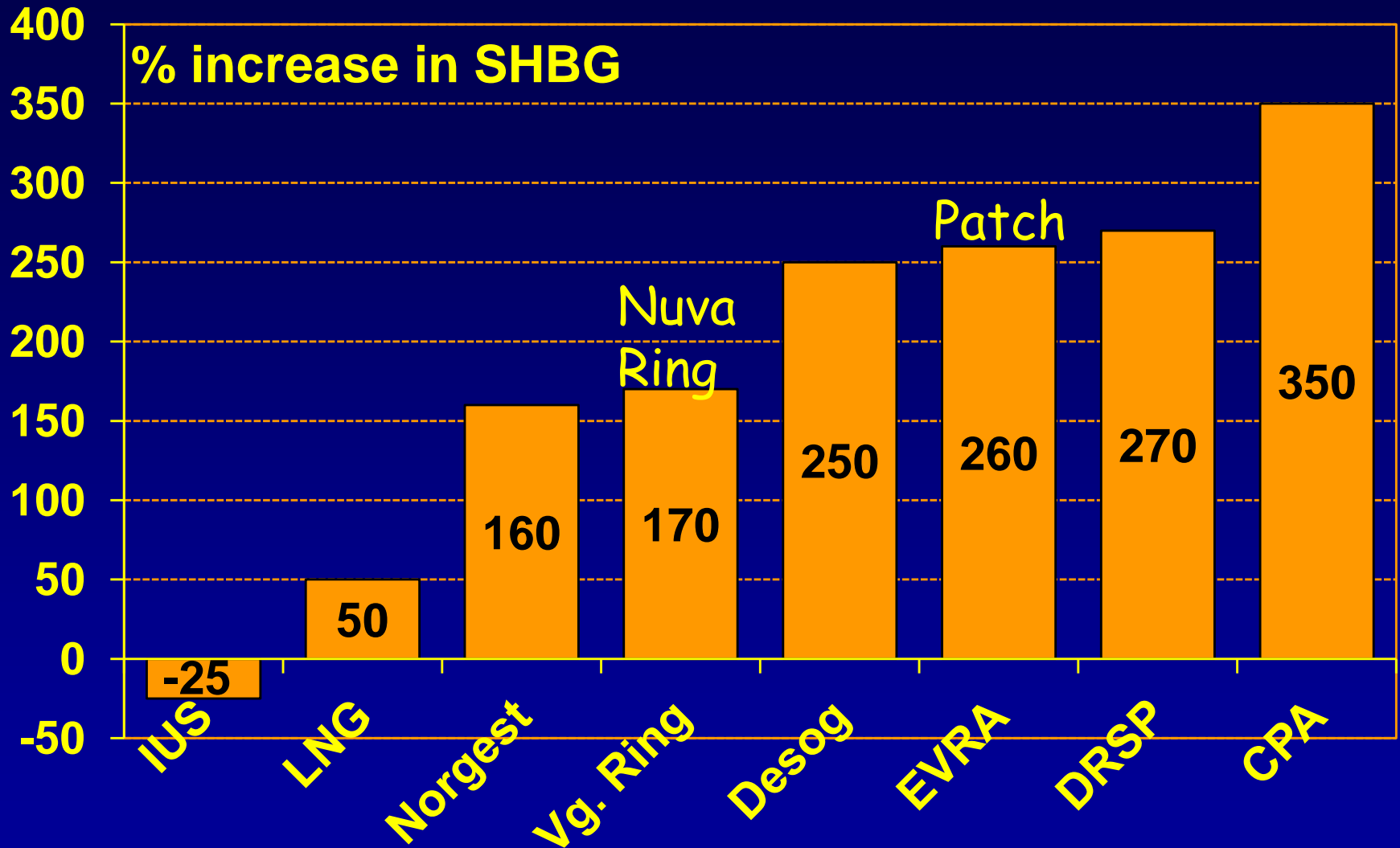
[www.lidegaard.dk/slides](http://www.lidegaard.dk/slides)

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**Conflicts of interest:** Lidegaard has been an expert witness in a legal process in USA in 2011 and 2012.

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# Hormonal contraception and SHBG



# Hormonal contraception & SHBG

