

Thromboembolic complications in users of estradiolvalerate/dienogest oral contraceptives

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Hormonal contraception: History

1960: First combined pill on the market, 1st gen.

1970's: 2nd gen. OC with levonorgestrel with middle dose of ethinylestradiol (EE)

1980's: 3rd gen. OC (desogestrel or gestodene)

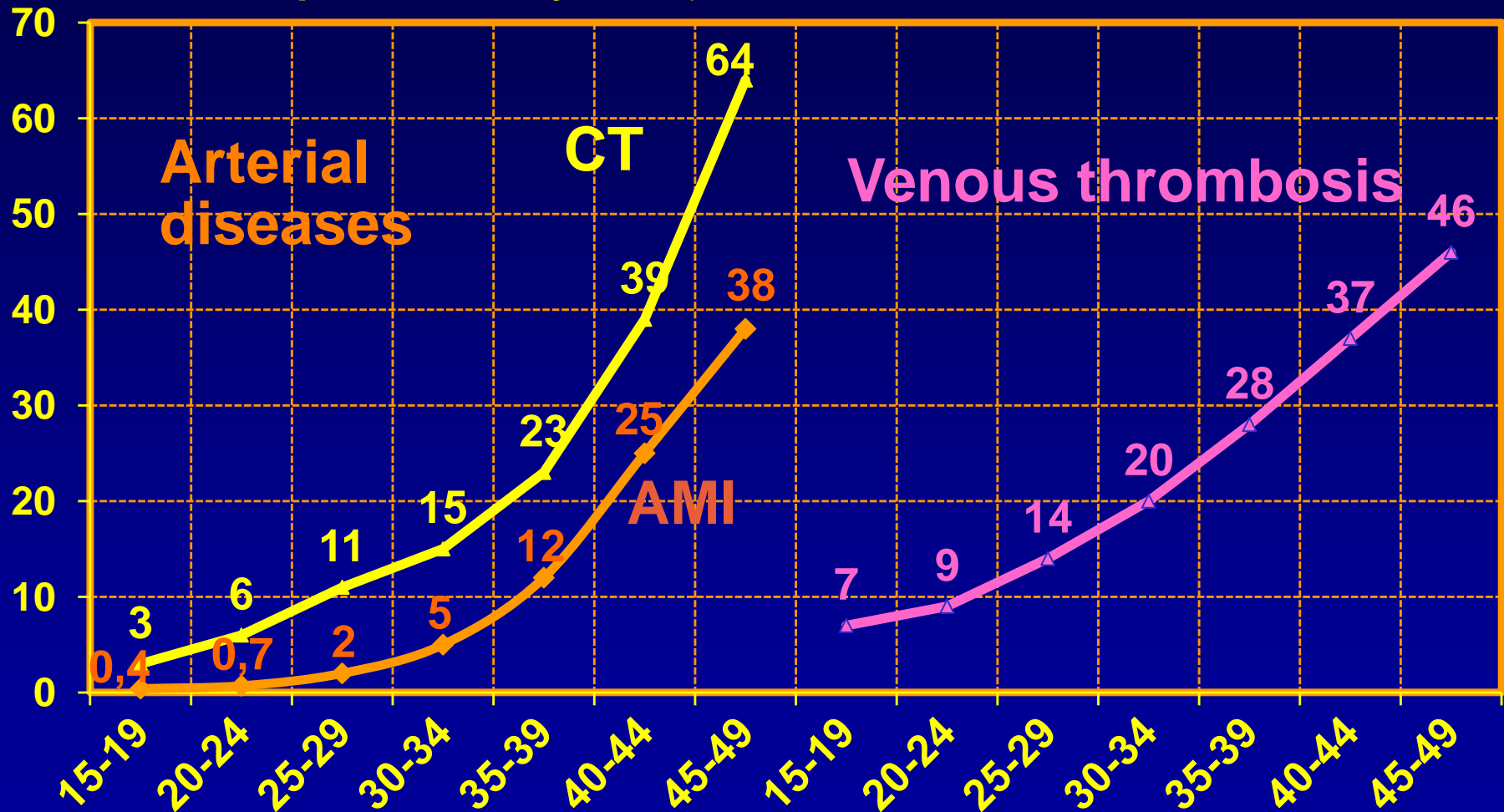
1990's: 20 ug EE OC, levonorgestrel-IUS

2000's: 4th gen. OC (drospirenone), implant, vaginal ring, natural oestrogen OC

CT, AMI and VT in DK 2001-2009

Pregnant and puerperal women excluded

Incidence per 100,000 years (including users of hormonal contraception)



Qlairra & venous thrombosis: Methods

National Health Registry (>1977)

VT diagnoses,
Previous CaVD/canc.
Pregnancies, surgery

Registry of Medicinal products (>1995):

OC use (>1995)

Anticoagulation therapy

BP↑, DM, Hyperchol.

1995



2001

1,528,171 women

2012

Cause of Deaths Registry (>1977)

Lethal VT

Statistics Denmark

PIN-codes, education
vital status, emigration

Results VTE

	Women-years	VTE*	RR _{adj}
Non users	7,058,523	1,489	ref
LNG 30-40	305,171	186	3.3 2.9-3.9
E2V/dienogest	5,202	5	4.7 2.0-11.3
Vaginal Ring	69,818	52	6.1** 5.0-8.0
Patch	8,254	7	6.8 3.2-14.4
Implant	38,700	5	1.1 0.4-2.6

*) Only confirmed venous thrombosis included. **p<0.01

Adjusted for age, year, education, hypertension, hyperlipidaemia, and diabetes

Results VTE

	Women-years	VTE*	RR_{adj}
LNG 30-40	305,171	186	1 (ref)
E2V/dienogest	5,202	5	1.3 0.6-3.2
Vaginal Ring	69,818	52	1.7** _{1.3-2.3}
Patch	8,254	7	1.9 0.9-4.1
Implant	38,700	5	0.3 0.1-0.8

*) Only confirmed venous thrombosis included. **p<0.01

Adjusted for age, year, education, hypertension, hyperlipidaemia, diabetes and duration of use

Results AMI

	Women-years	AMI	RR_{adj}
Non users	7,058,523	1,171	ref
LNG 30-40	305,171	87	2.2 1.8-2.7
E2V/dienogest	5,202	1	1.3 0.2-9.3
Vaginal Ring	69,818	5	1.6 0.7-3.9
Patch	8,254	0	na
Implant	38,700	4	1.9 0.7-5.0

Adjusted for age, education, hypertension, diabetes, hyperlipidaemia, year

Thrombotic stroke (TS)

	<u>Women-years</u>	<u>TS*</u>	<u>RR_{adj}</u>
Non users	7,058,523	2,328	ref
LNG 30-40	305,171	128	1.5 1.3-1.8
E2V/dienogest	5,202	2	1.3 0.3-5-1
Vaginal Ring	69,818	22	2.2 1.4-3.4
Patch	8,254	3	2.4 0.7-7.5
Implant	38,700	12	2.1 1.2-3.7

*) cerebral infarction + cerebral apoplexy

Adjusted for age, education, hypertension, diabetes,
hyperlipidaemia, year

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

ug EE NETA LNG NGM DSG GSD Drsp CPA

50	6.2 2.9-13.1	4.0 2.9-6.9	6.8 3.2-14.4	6.1 ← Vaginal ring 4.6-8.0			na
30-40	2.3 1.2-4.5	3.3 2.9-3.9	3.7 3.1-4.3	6.7 5.8-7.7	6.6 6.0-7.2	6.3 5.5-7.2	6.3 5.2-7.6
20	na	na	na	5.3 4.7-6.0	5.2 4.6-5.9	6.6 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 2013 update

HC and thrombotic stroke 2001-12

Reference: Non-users

ug EE NETA LNG NGM DSG GSD Drsp CPA

50		Patch	3.2 0.8-12.6	2.5 1.4-4.4	Vg.Ring	na	na
30-40	2.0 1.1-3.8	1.5 1.3-1.8	1.5 1.2-1.8	2.2 1.8-2.7	1.8 1.6-2.0	1.6 1.3-2.1	1.6 1.1-2.2
20	na	na	na	1.6 1.3-1.9	1.4 1.1-1.7	0.6 0.2-1.5	na

E2V/Dienogest: 1.3 0.3-5.1

POP 1.5 1.0-2.1 1.2 0.7-1.9 Cerazette

Mirena 0.9 0.7-1.0 2.1 1.2-3.8 Implant

E2V/dienogest: Conclusion

- The risk of venous thrombosis was significantly increased with RR of 4.7, just in between 2nd and 3rd/4th generation COC.
 - The risk of AMI and thrombotic stroke was not increased, and with RR estimates below the RR of 2nd generation COC.
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E2V/dienogest and venous thrombosis

Thanks for your attention

www.lidegaard.dk/slides

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Conflicts of interest: The primary investigator has been an expert witness in a legal process in USA in 2011 and 2012.
