Hormonel kontraception til kvinder I forskellige aldre

Øjvind Lidegaard

Praktisk medicin 2014

Gynækologisk klinik, Rigshospitalet
Københavns Universitet

HC and venous thrombosis according to oestrogen dose & progestogen type

<table>
<tr><th></th><th>NETA
Norethis-terone</th><th>LNG
Levonor-gestrel</th><th>NGM
Norges-timate</th><th>DGS
Deso-gestrel</th><th>GSD
Gesto-dene</th><th>DRSP
Drospire-none</th><th>CPA
Cyproterone-acetate</th></tr>
<tr><td>High Dose</td><td colspan="2">Withdrawn</td><td>Patch</td><td>Nuva Ring</td><td></td><td></td><td></td></tr>
<tr><td>Middle Dose</td><td>1st</td><td colspan="2">2nd gen</td><td colspan="2" rowspan="2">3rd gen</td><td rowspan="2">4th gen</td><td></td></tr>
<tr><td>Low Dose</td><td></td><td></td><td></td><td></td></tr>
<tr><td>POC</td><td></td><td>LNG-IUS</td><td></td><td>Cera-zette</td><td></td><td></td><td></td></tr>
<tr><td>Nat. oe dienog</td><td>Qlaire</td><td></td><td></td><td>Implant</td><td></td><td></td><td></td></tr>
</table>

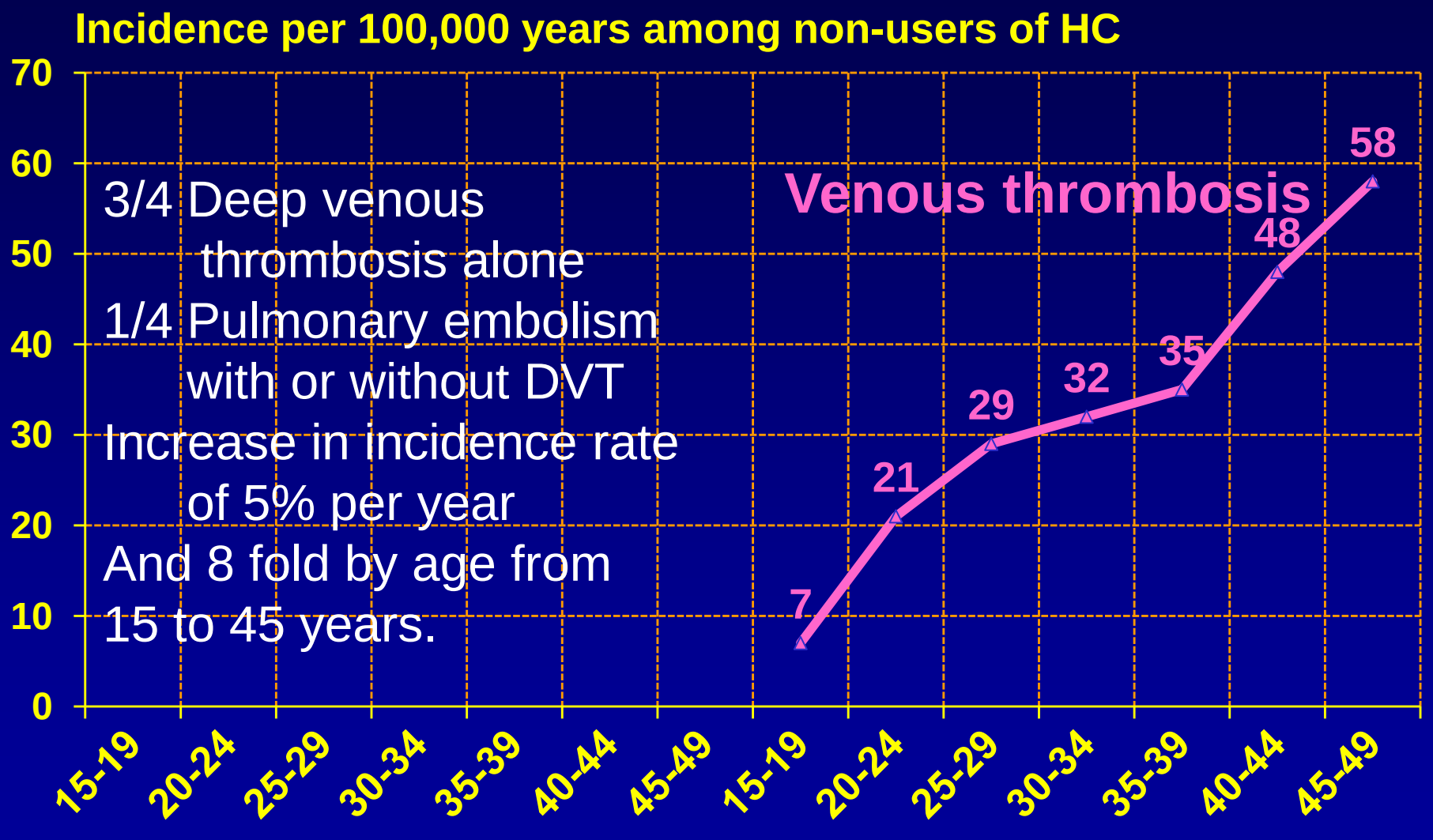
RR of venous thrombosis according to oestrogen dose & progestogen type

	NETA Norethis-terone	LNG Levonor-gestrel	NGM Norges-timate	DGS Deso-gestrel	GSD Gesto-dene	DRSP Drospire-none	CPA Cyproterone-acetate
High Dose	Withdrawn		8 Patch	6.5 NuvaRing			
Middle Dose	3	3	3	6	6	6	6
Low Dose				5	5	6	
POC	1	<1 LNG-IUS		1 Cerazette			
Nat. oe dienog.	4.5 Qlaire			1.4 Implant			

No risk | Low risk | Middle risk | High risk

Venous thrombosis in DK 2001-2009

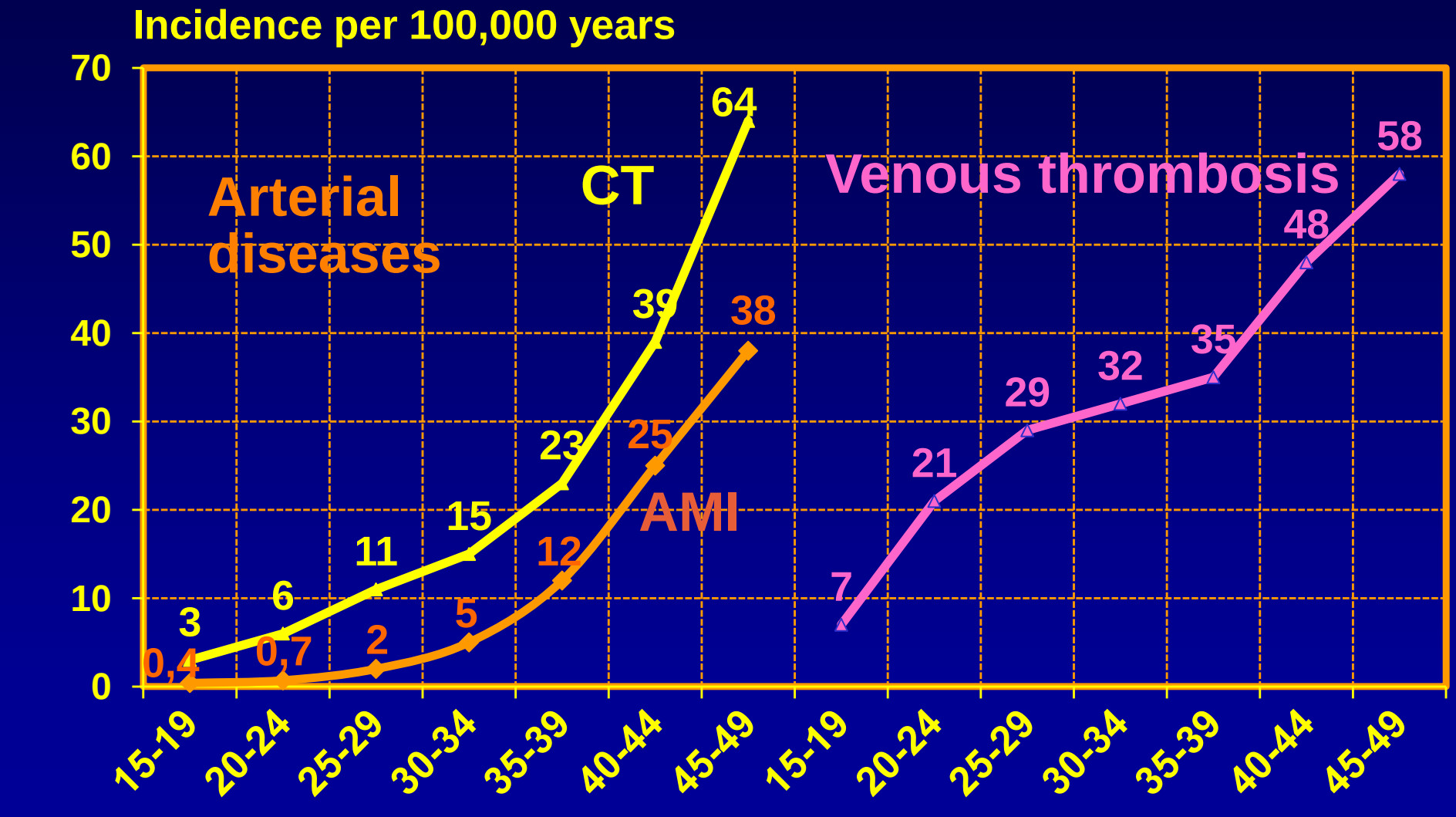
Pregnant and puerperal women excluded



Lidegaard et al BMJ 2011

CT, AMI and VT in DK 2001-2009*

Pregnant and puerperal women excluded



Lidegaard et al NEJM 2012 and BMJ 2011

VT: Acquired risk factors

	Prevalence	RR
Age ≥30 vs <30	50%	2.5
Pregnancy	4%	8
Adiposity (BMI>25)	30%	2
Varicose veins	8%	2
Immobilisation/trauma	?	2-10
Oral contraceptives	30%	3-6
Medical diseases	5%?	2-5

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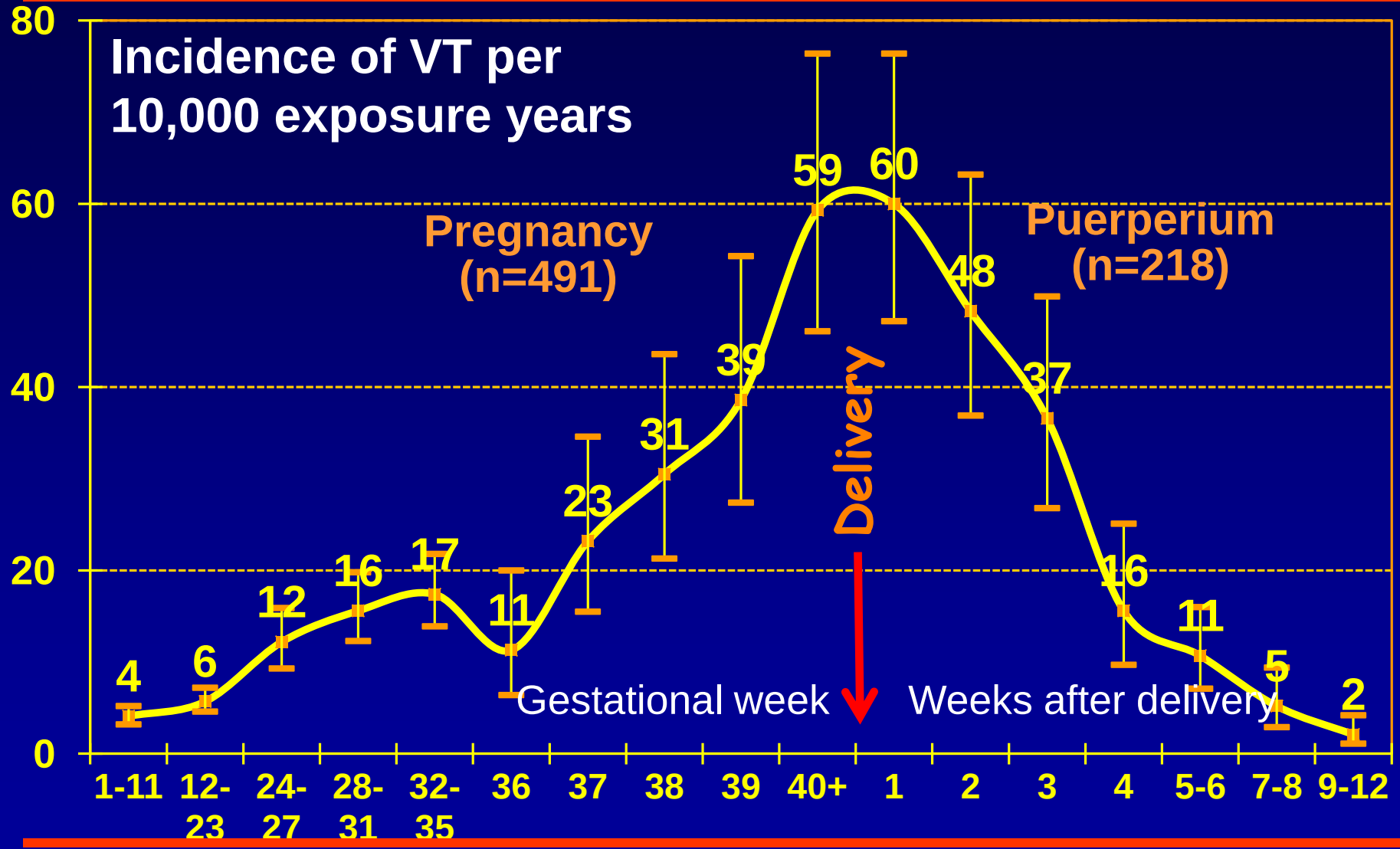
Medical diseases	5%?	2-5

Venous thrombosis in pregnant and puerperal women, DK 1995-2005. N=709



Virkus et al. Thromb Haemost 2011; 106: 304-9

Li/12

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Medical diseases	5%?	2-5

BMJ

Hormonal contraception and risk of venous thromboembolism: national follow-up study

Øjvind Lidegaard, professor,[1] Ellen Løkkegaard, consultant,[2] Anne Louise Svendsen, statistician,[3] Carsten Agger, data manager[4]

[1]Gynaecological Clinic, Rigshospitalet, Copenhagen University, DK-2100 Copenhagen, Denmark

ABSTRACT

Objective To assess the risk of venous thrombosis in current users of different types of hormonal

BMJ

RESEARCH

The venous thrombotic risk of oral contraceptives, effects of oestrogen dose and progestogen type: results of the MEGA case-control study

A van Hylckama Vlieg, research fellow,[1] Helmerhorst, professor of clinical epidemiology of fertility,[1,2] J P Vandenbroucke, professor of clinical epidemiology,[1] C J M Doggen, research fellow,[1] F R Rosendaal, professor of clinical epidemiology, head of department[1,3,4]

risk of venous thrombosis than oral contraceptives with levonorgestrel. Progestogen only pills and hormone releasing intrauterine devices were not associated with

OC and VT: Methods

National Registry of Patients (>1977)

VT diagnoses,

Previous CaVD/canc.

Pregnancies, surgery

National Registry of Medicinal products (>1995): OC use

Medication against

BP↑, DM, Hyperchol.

1995 → 2005

Cause of Deaths Registry (>1977)

Lethal VT

Statistics of Denmark

PIN-codes, education

vital status, emigration

Lidegaard et al. BMJ 2009

OC and VT: Progestagen type adjusted for duration of use

ug EE	Neta	Lng	NGM	Deso	Gest	Drsp	CPA
50	1.4 1.0-2.1	1.2 0.9-1.7	na	na	na	na	na
30-40	1.0 0.7-1.4	1 **Ref**	1.2 1.0-1.5	1.8 1.5-2.2	1.9 1.6-2.2	1.64 1.3-2.1	1.9 1.5-2.4
20	na	na	na	1.5 1.3-1.8	1.5 1.2-1.9	na	na
POP	na	0.3 0.2-0.5		0.5 0.2-1.7			
Mirena	na	0.4 0.3-0.6					

Lidegaard et al. BMJ 2009; 339; b2890

Li/09

VT and drospirenone

	VT no	Risk /10,000	Rate ratio DRSP/2nd gen	
Dinger[07]	118	9.1	1.0 (0.6-1.8)	4th/2nd
Seeger[07]	57	13.0*	0.9 (0.5-1.6)	4th/???
Vlieg[09]	1,524	na	1.7 (0.7-3.9)	4th/2nd
Lidegaard[09]	4.213	7.8	1.6 (1.3-2.1)	4th/2nd

Critique

REVIEW

Risk of venous thromboembolism among users of oral contraceptives: a review of two recently published studies

Samuel Shapiro, Jürgen Dinger

Abstract

Background Two recent studies, a cohort study from Denmark, and a case-control study from The Netherlands, have reported increased risks of venous thromboembolism (VTE) among users of oral contraceptives (OCs) containing desogestrel, gestodene, drospirenone and cyproterone, relative to the use of levonorgestrel.

Critique In the Danish study the comparisons were not valid. (1) VTE risk is highest soon after commencement of OC use, and duration of use was underestimated for levonorgestrel users, but not for drospirenone users; for the remaining compounds duration was only slightly underestimated. The underestimation for levonorgestrel resulted in systematic overestimation of the relative risks for the compared OCs. (2) Duration was also incorrectly estimated: only the duration of current use, *not duration of all episodes of use* was relevant to VTE risk. (3) Confounding was not adequately controlled.

In The Netherlands study the comparisons were not valid. (1) The relative risk for drospirenone versus levonorgestrel was not statistically significant. (2) Extensive publicity had been given to the risk of VTE among users of desogestrel, gestodene, drospirenone and cyproterone: information bias and detection bias were therefore likely. (3) Inadequate allowance was made for duration of use. (4) The combination of two different control groups, both of them likely to have been biased, into a single category was not valid.

Conclusion The best evidence continues to suggest that the increased risk of VTE in OC users is a class effect, dependent on the estrogen dose and duration of use, and independent of the progestogen used.

Keywords combined oral contraceptives, progestogen, risk assessment, venous thromboembolism

J Fam Plann Reprod Health Care 2010; **36**(1): 33–38
(Accepted 25 November 2009)

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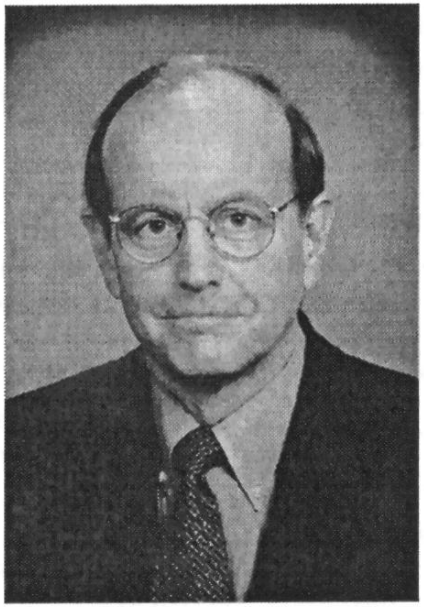
An Editor

Epidemiologic Research Using Administrative Databases

Garbage In, Garbage Out



David A. Grimes, MD

Administrative databases stem from claims made for services by health care providers and institutions.[1] Simply put, they are billing systems. These databases were created for reasons other than epidemiologic research–a key limitation. Data fields commonly include only basic demographic information, drug dispensing, provider visits, and hospitalization. Examples of administrative databases often used by researchers include Medicare, Medicaid, and those of health maintenance organizations such as Kaiser Permanente.

Vital records, such as birth certificates, represent another administrative database commonly used for epidemiologic research.[2,3] Again, these data are collected for civil and legal purposes, not for research.

Research using administrative databases has important strengths and weaknesses. Sample sizes are often large, which provide power to find differences. Those enrolled may be representative of the community of interest. Recording of drug prescriptions occurs contemporaneously, which

Grimes, Obstet Gynecol Nov 2010, 116: 1018-19

Research using vital records should be limited to simple descriptive reports with caveats about data accuracy. Using birth certificate information for epidemiologic analyses is inappropriate because of well documented deficiencies in information quality[3]. Similarly, epidemiologic research using adminstrative databases, such as the Danish National Patient Registry, must at a minimum validate each reported outcome by chart review[9] or by patient interview.

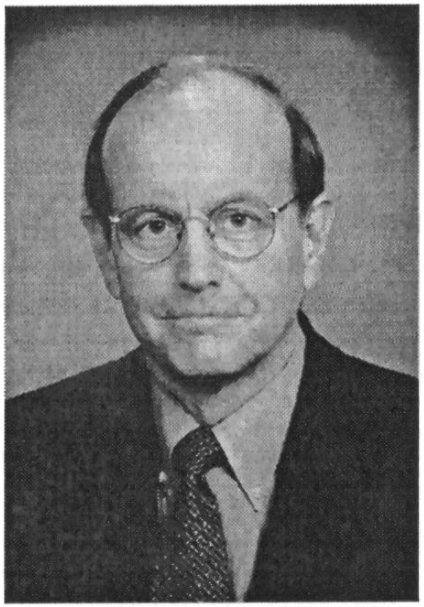
In recent decades, the computer science concept of "GIGO" ("garbage in, garbage out") has somehow come to mean "garbage in, gospel out[10]." When computer software tackles a large database, many accept the "computerized" output as trustworthy, regardless of the quality of the input. Sadly, no fancy statistical machinations can compensate for poor-quality data. Publications relying on unconfirmed database reports of venous thromboembolism should be ignord.

Grimes. Obstet Gynecol 2010; 116: 1018-19

Editorial

Epidemiologic Research Using Administrative Databases

Garbage In, Garbage Out



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Financial Disclosure

Dr. Grimes serves as a consultant (DSMB member) for Bayer.

Grimes, Obstet Gynecol Nov 2010, 116: 1018-19

OC and VT: Methods

National Registry of Patients (>1977)

VT diagnoses,

Previous CaVD/canc.

Pregnancies, surgery

Registry of Medicinal products (>1995):

OC use (>1995)

Anticoagulation therapy

BP↑, DM, Hyperchol.

1995 → 2001 → 2005 → 2009

1.3 million women

Cause of Deaths Registry (>1977)

Lethal VT

Statistics Denmark

PIN-codes, education

vital status, emigration

Lidegaard et al. BMJ 2011

BMJ

BMJ 2011;343:d6423 doi: 10.1136/bmj.d6423

RESEARCH

Risk of venous thromboembolism from use of oral contraceptives containing different progestogens and oestrogen doses: Danish cohort study, 2001-9

OPEN ACCESS

Øjvind Lidegaard *professor of obstetrics and gynaecology*[1], Lars Hougaard Nielsen *statistician*[1], Charlotte Wessel Skovlund *data manager and scientific assistant*[1], Finn Egil Skjeldestad *professor of clinical medicine*[2], Ellen Løkkegaard *senior registrar in obstetrics and gynaecology*[3]

[1]Gynaecological Clinic 4232, Rigshospitalet, University of Copenhagen, Denmark; [2]Department of Obstetrics and Gynaecology, Institute of Clinical Medicine, University of Tromsø, Norway; [3]Department of Obstetrics and Gynaecology, Hillerød Hospital, University of Copenhagen, Denmark

Abstract

Objective To assess the risk of venous thromboembolism from use of

thromboembolism was not increased with use of progestogen only pills or hormone releasing intrauterine devices. If oral contraceptives with

OC and VT: Progestogen type Confirmed versus non-use

ug EE	Neta	Lng	NGM	Deso	Gest	Drsp	CPA
50	6.2 3.0-13.2	4.5 2.9-6.9	Patch	na	na	na	na
30-40	2.2 1.1-4.5	3.0 2.4-4.0	3.5 2.9-4.3	6.6 5.6-7.8	6.2 5.6-7.0	6.4 5.4-7.5	6.4 5.4-7.5
20	na	na	na	4.8 4.1-5.6	5.1 4.4-5.9	6.9 4.2-11.5	na

	Vg. Ring
POP	0.7 0.3-1.5
Mirena	0.7 0.5-1.1

Lidegaard et al. BMJ 2011; 343: d6423

Combined oral contraceptives, venous thromboembolism, and the problem of interpreting large but incomplete datasets

Jürgen Dinger,[1] Samuel Shapiro[2]

[1]Director, ZEG - Berlin Center for Epidemiology and Health Research, Berlin, Germany
[2]Visting Professor of Epidemiology, Department of Epidemiology, University of Cape Town, Cape Town, South Africa

Correspondence to
Dr Jürgen Dinger, ZEG - Berlin Center for Epidemiology and Health Research, Invalidenstrasse 115, 10115 Berlin, Germany; dinger@zeg-berlin.de

Received 11 November 2011
Accepted 14 November 2011

Background

In 2009, Lidegaard *et al.*[1] published findings in the *British Medical Journal*, derived from a Danish retrospective cohort study of the risk of venous thromboembolism (VTE) associated with the use of combined oral contraceptives (COCs). Their analysis was based on data derived from national health registries, and they concluded that "oral contraceptives with desogestrel, gestodene, or drospirenone were associated with a significantly higher risk of VTE than oral contraceptives with levonorgestrel". That report has previously in the publication differ from those mentioned in the re-analysis submitted to EMA (one example is given below).

Since the mid-1990s there has been heated debate regarding the risk of VTE associated with the use of different progestogens, and those who have followed the discussion can only note with concern its confrontational and increasingly sharp tone, which, unfortunately, is also reflected in the published responses to the re-analysis,[5–7] and more particularly in the authors' replies.[8 9]

The heat of the debate may have some-

Dinger & Shapiro, on the road again

We conclude that the best evidence continues to suggest that the increased risk of VTE among COC users is a class effect. In the Danish data an analysis confined to women who used COCs for the first time from 2001 onward did not support any differential effects of progestogens. Surprisingly, this information was neither presented nor discussed in the published re-analysis.[4] Any potential differences, if they exist at all, are probably beyond the resolving power of the 'epidemiological microscope'.

Dinger & Shapiro. J Fam Plan Repr Health Care2011: Nov. 14.

BMJ

BMJ 2012;344:e2990 doi: 10.1136/bmj.e2990

RESEARCH

Venous thrombosis in users of non-oral hormonal contraception: follow-up study, Denmark 2001-10

OPEN ACCESS

Øjvind Lidegaard *professor*[1], Lars Hougaard Nielsen *statistician*[1], Charlotte Wessel Skovlund *data manager*[1], Ellen Løkkegaard *senior registrar*[2]

[1]Gynaecological Clinic 4232, Blegdamsvej 9, DK-2100 Copehagen Ø, Juliane Marie Centre, Rigshospitalet, University of Copenhagen, Denmark; [2]Department of Obstetrics and Gynaecology, Hillerød Hospital, University of Copenhagen, Denmark

Abstract

Objective To assess the risk of venous thrombosis in current users of

Conclusion Women who use transdermal patches or vaginal rings for contraception have a 7.9 and 6.5 times increased risk of confirmed

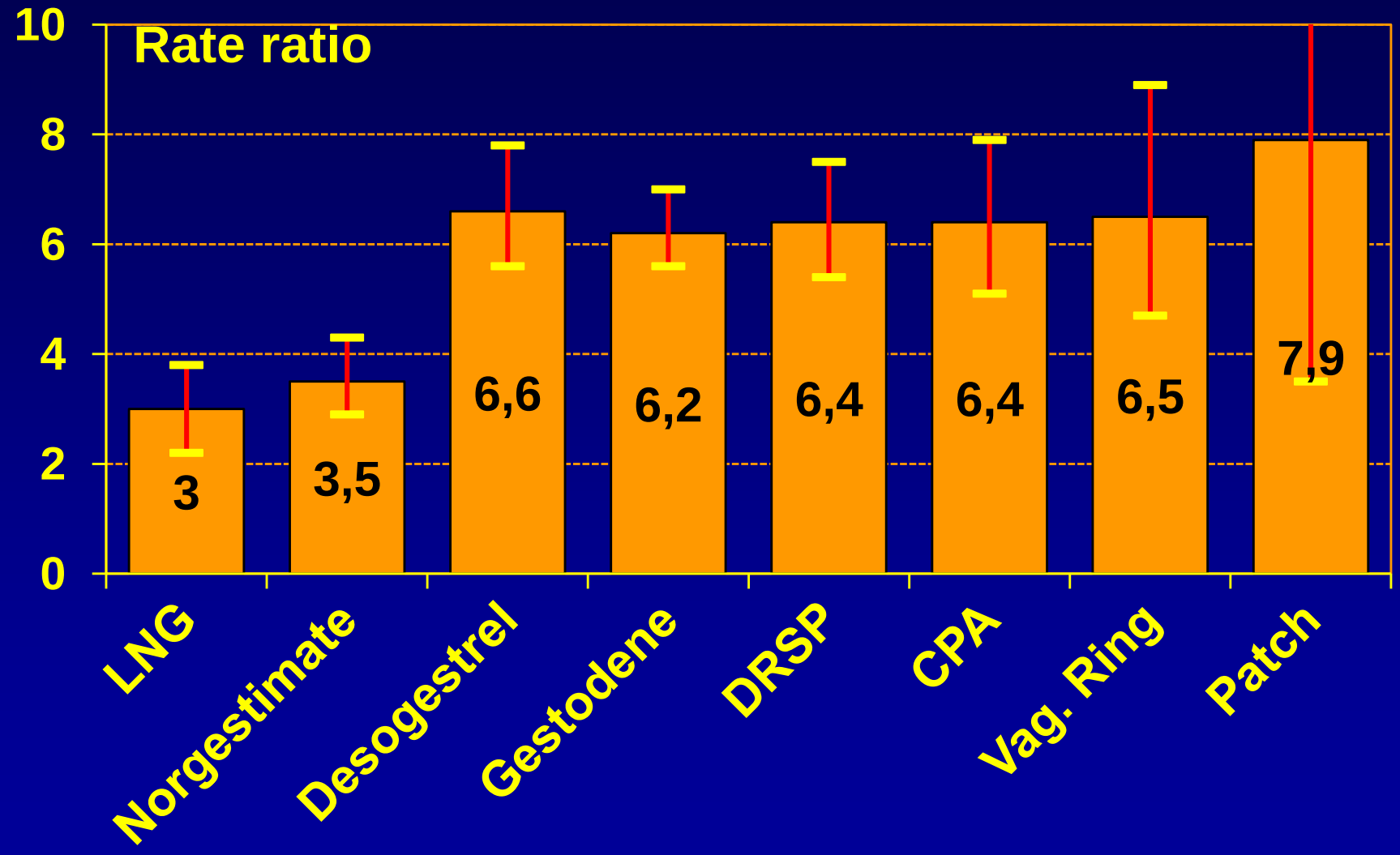
OC and VT: Progestogen type Confirmed versus non-use

ug EE	Neta	Lng	NGM	Deso	Gest	Drsp	CPA
50	6.2 3.0-13.2	4.5 2.9-6.9	7.9 3.5-17.7 ← Patch	na	na	na	
30-40	2.2 1.1-4.5	3.0 2.4-4.0	3.5 2.9-4.3	6.6 5.6-7.8	6.2 5.6-7.0	6.4 5.4-7.5	6.4 5.4-7.5
20	na	na	na	4.8 4.1-5.6	5.1 4.4-5.9	6.9 4.2-11.5	na
				6.5 4.5-8.9 Vaginal Ring			
POP	0.7 0.3-1.5			0.6 0.2-1.9			
Lng-IUS		0.6 0.4-0.8					

Lidegaard, BMJ 2012; 344: e2990

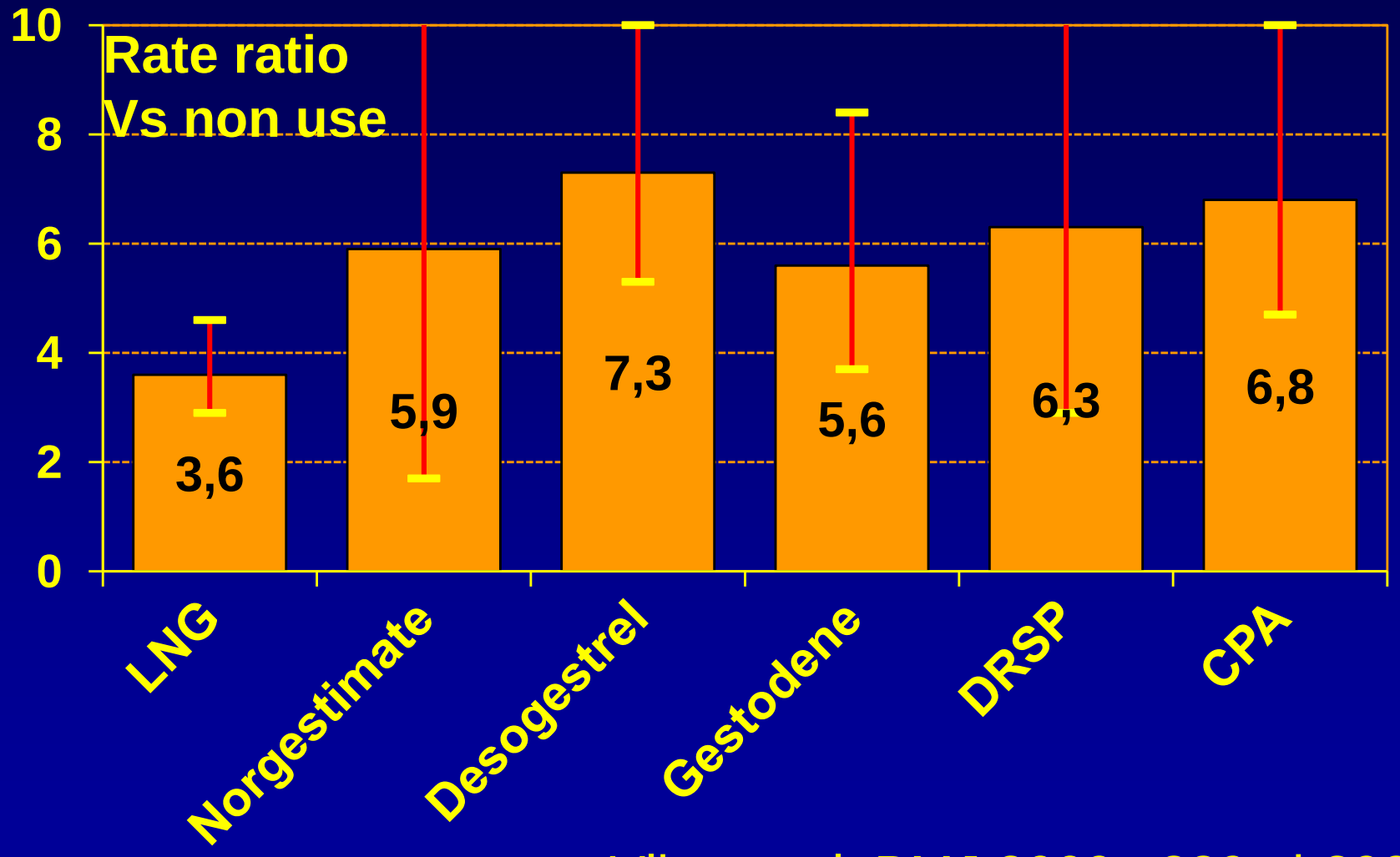
Relative risk versus non-use

Confirmed events only



Lidegaard et al. BMJ 2011; 343: d6423 + 2012; 344: e2990

Relative risk versus non-use



Vlieg et al. BMJ 2009; 339; b2921

…….on the road again

Publication in BMJ on May 10, 2012

- Anne Szarewski (14.5.2012)
  "…biologically nonsensical results"

…….on the road again

Publication in BMJ on May 10, 2012

- Anne Szarewski (14.5.2012)
- Samuel Shapiro (16.5.2012)
  "..the Danish registry is an unsuitable resource for the evaluation of VTE risk"

…….on the road again

Publication in BMJ on May 10, 2012

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- Mary E. Gaffield (16.5.2012)
  "These new data .. may lead to a new (unfounded) scare…."

…….on the road again

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  “Higher abortion rate in areas where ….prescribing restrictions are in place”

…….on the road again

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- Anne L Connolly (18.5.2012)

  "…poor studies such as this one…"

…….on the road again

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- Julie M Chandler (17.5.2012)
- Anne L Connolly (18.5.2012)
- Jørgen Jespersen (19.5.2012)

  "We find no reason to repeat the clear and concise arguments by Anne Szarewski"

VT and drospirenone

	VT no	Risk /10,000	Rate ratio DRSP/2nd gen
Dinger[07]	118	9.1	1.0 (0.6-1.8) 4th/2nd
Vlieg[09]	1,524	na	1.7 (0.7-3.9) 4th/2nd
Lidegaard[09]	4.213	7.8	1.6 (1.3-2.1) 4th/2nd
Dinger[10]	680	na	1.0 (0.5-1.8) 4th/2nd
Parkin[11]	61	2.3	2.7 (1.5-4-7) 4th/2nd
Jick[11]	186	3.1	2.8 (2.1-3.8) 4th/2nd
Lidegaard[11]	4,246	9.3	2.1 (1.6-2.8) 4th/2nd

IR = incidence per 10,000 women years

BMJ Editorial Nov 2011

This new study has tackled many of the concerns expressed about the earlier investigation. Although unpalatable to some, it is difficult not to conclude that combined oral contraceptives with desogestrel, gestodene, or drospirenone confer a higher risk of venous thromboembolism than those with levonorgestrel.

Philip Hannaford. BMJ 2011; 343: d6592

VT and drospirenone

	VT	IR	Rate ratio
Dinger[07]	118	9.1	1.0 (0.6-1.8) 4th/2nd
Vlieg[09]	1,524	na	1.7 (0.7-3.9) 4th/2nd
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Lidegaard[11]	4,246	9.3	2.1 (1.6-2.8) 4th/2nd
FDA Kaiser[11]	625	7.6	1.5 (1.2-1.9) 4th/2nd

IR = incidence per 10,000 women years

Combined hormonal contraceptives and the risk of venous and arterial thromboembolism and cardiovascular death: misuse of automated databases

Samuel Shapiro

Visiting Professor of Epidemiology, Department of Family Medicine and Public Health, University of Cape Town School of Medicine, Cape Town, South Africa

Correspondence to
Professor Samuel Shapiro, Department of Family Medicine and Public Health, University of Cape Town School of Medicine, Anzio Road, Observatory, Cape Town, South Africa;
samshap@mweb.co.za

ABSTRACT

Background In December 2011, the US Food and Drug Administration (FDA) convened a public Advisory Committee meeting to review evidence from a study commissioned by the agency. An analysis of findings derived from four databases was published on the FDA website, and presented at the meeting. Among users of combined hormonal contraceptives containing ethinylestradiol (EE) plus drospirenone (DRSP) the risks of venous (VTE) and arterial thromboembolism (ATE) were higher than

[myocardial infarction (MI) and stroke combined], in users of recently introduced combined estrogen/progestogen hormonal contraceptives (CHCs).[1] At the time of the meeting the findings had only been published on the FDA website, but not in a peer-reviewed journal.

The investigators concluded that their data "[provided] another positive finding to the increasing body of evidence linking [drospirenone (DRSP)] to increased risk of VTE relative to standard low-dose

Shapiro, critique of FDA

Conclusions The best evidence continues to suggest that the increased risk of VTE in combined hormonal contraceptive users is dependent on the dose of estrogen, and independent of the progestogen used. The best evidence also suggests that DRSP does not increase the risk of ATE, and may reduce it.

Shapiro S. J Fam Plan Reproduc Health Care 2013: 39: 89-96

VT and drospirenone

	VT	IR[4]	Rate ratio
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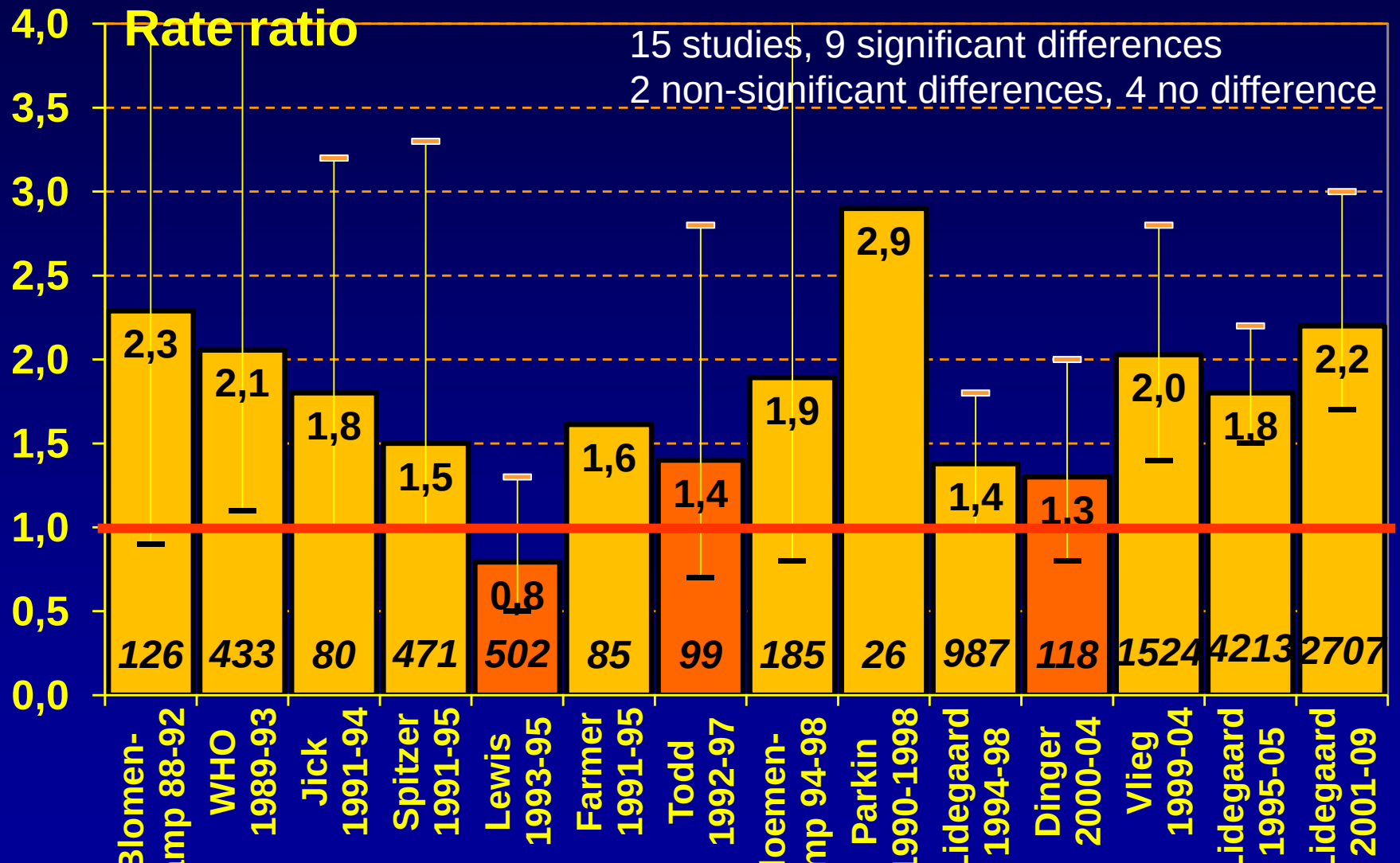
FDA Kaiser[11]	625	7.6	1.5 (1.2-1.9) 4th/2nd
Gronich[11]	518	8.6	1.7 (1.0-2.7) 4th/2nd
Bird[13]	354	18.0	1.9 (1.5-2.4) 4th/2nd

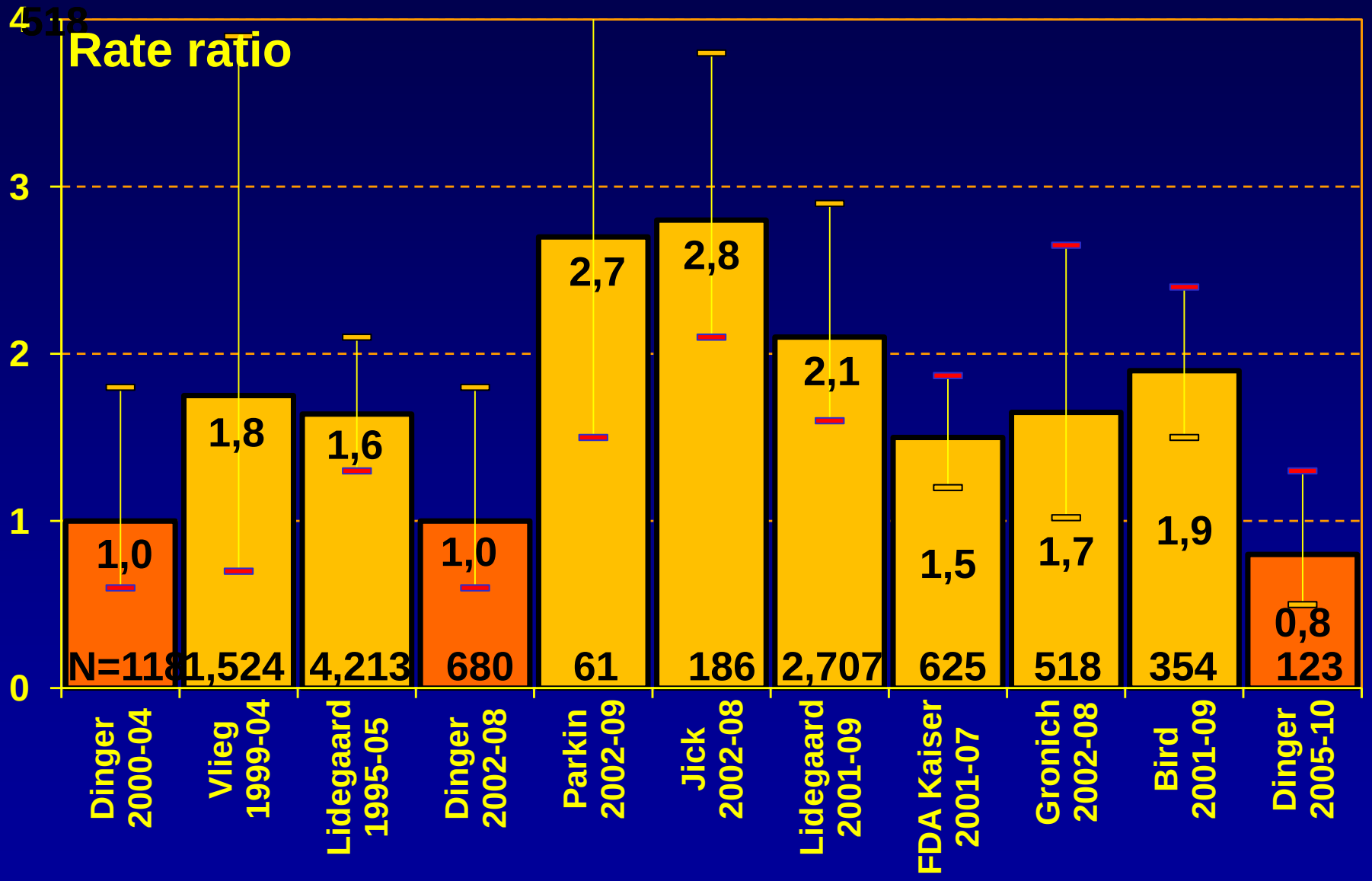
VT and drospirenone

	VT	IR	Rate ratio
Dinger[07]	118	9.1	1.0 (0.6-1.8) 4th/2nd
Vlieg[09]	1,524	na	1.7 (0.7-3.9) 4th/2nd
Lidegaard[09]	4.213	7.8	1.6 (1.3-2.1) 4th/2nd
Dinger[10]	680	na	1.0 (0.5-1.8) 4th/2nd
Parkin[11]	61	2.3	2.7 (1.5-4-7) 4th/2nd
Jick[11]	186	3.1	2.8 (2.1-3.8) 4th/2nd
Lidegaard[11]	4,246	9.3	2.1 (1.6-2.8) 4th/2nd
FDA Kaiser[11]	625	7.6	1.5 (1.2-1.9) 4th/2nd
Gronich[11]	518	8.6	1.7 (1.0-2.7) 4th/2nd
Bird[13]	354	18.0	1.9 (1.5-2.4) 4th/2nd
Dinger[14]	123	7.2	0.8 (0.5-1.3) 4th/2nd

3rd versus 2nd generation COC



COC with DRSP vs LNG

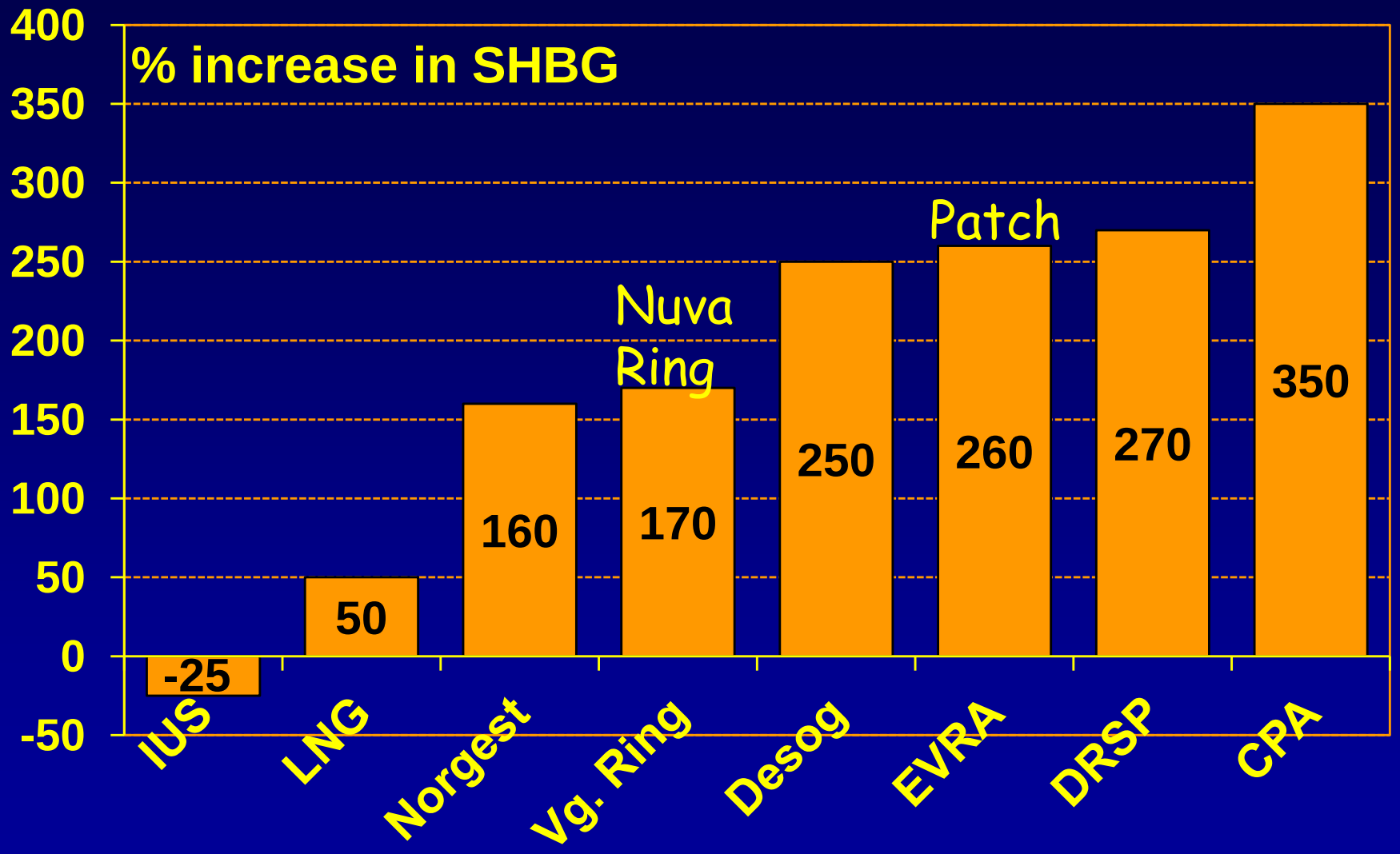


George Monbiot

One of the most widespread human weaknesses is our readiness to accept claims that fit our beliefs and reject those that clash with them. We demand impossible standards of proof when confronted with something we don't want to hear, but will believe any old cobblers if it confirms our prejudices:

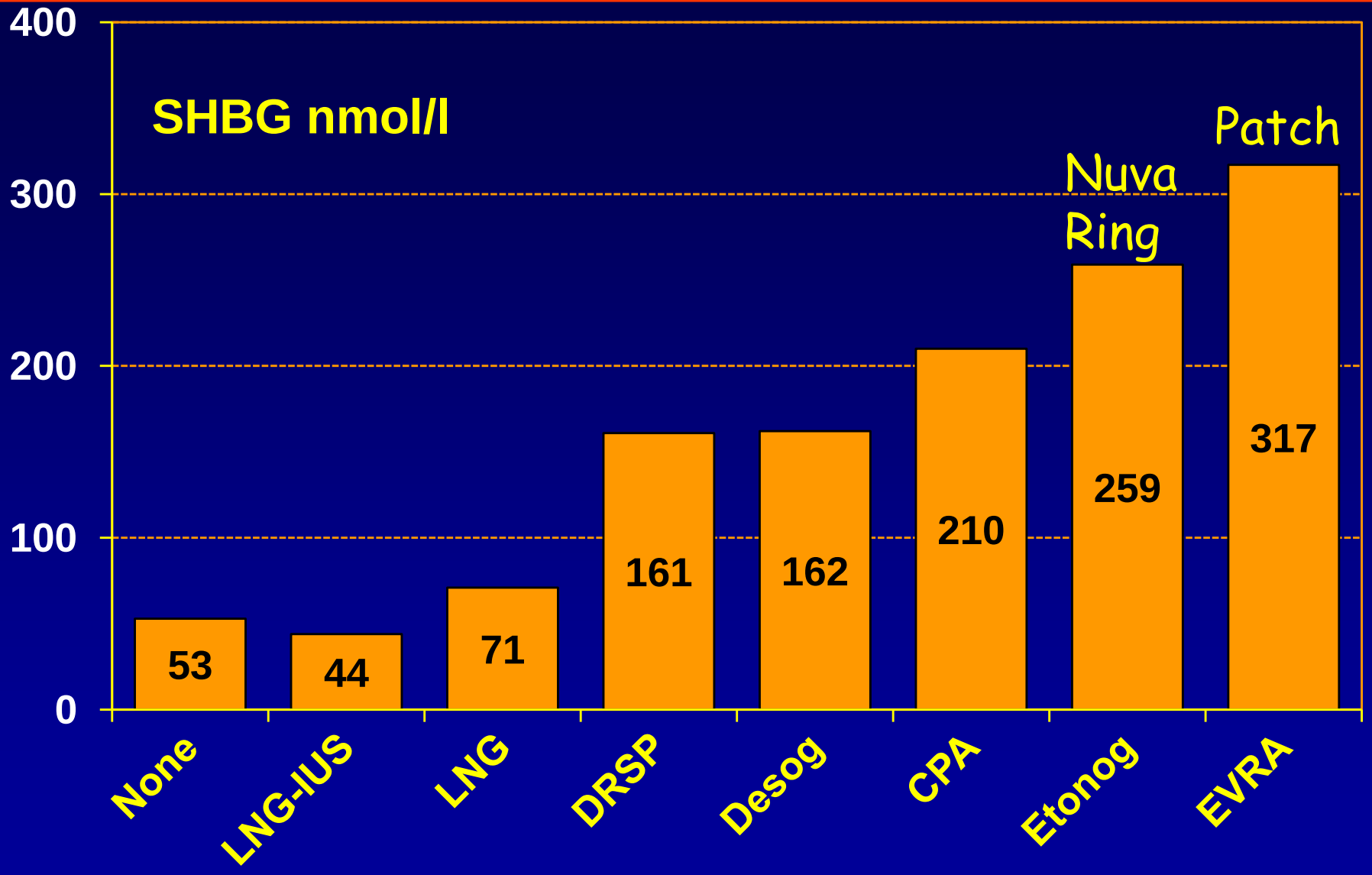
Guardian, November 22, 2011

Hormonal contraception and SHBG



Odlin et al. Acta Obstet Gynecol Scand 2002; 81: 482-90

Hormonal contraception & SHBG



Raps et al. Thrombosis Haemostasis 2012; doi: 10.1111

OCs and venous thrombosis

Current status March 2014

POP:	**1**	
LNG-IUS:	**<1**	
2nd gen:	**3**	
3rd gen:	**6**	(Vg. Ring)
4th gen:	**6**	(also low dose)
Patch	**7**	

COC and VT: Conclusion

- COC increase the risk of VT 3-6 fold

The risk with COC use is influenced by

- The progestogen type ~100 %
- The oestrogen dose ~50 % => 20%
- The length of use ~50 %

We need low-dose oral contraceptives with 1st and 2nd generation progestogens and low-dose pills with natural oestrogen

HC and thrombotic stroke Reference: Non-users

- All women in Denmark 15-49 years old during the period January 1995 through December 2009 (15 years)
- Data from four National registries
- Included: 1,626,158 women

  14,251,063 women years

  4,914,401 current use

  3,311 thrombotic strokes

Lidegaard et al. N Engl J Med 2012; 366: 2257-66

HC and thrombotic stroke
Reference: Non-users

ug EE	Neta	Lng	NGM	DSG	Gest	Drsp	CPA
50	1.3 0.7-2.5	2.3 1.6-3.2	3.2 0.8-12.6	2.5 1.4-4.4	Vg.Ring	na	na
30-40	2.2 1.5-3.2	1.7 1.4-1.9	1.5 1.2-1.9	2.2 1.8-2.7	1.8 1.6-2.0	1.6 **1.2-2.2**	1.4 1.0-2.0
20	na	na	na	1.5 1.3-1.9	1.7 1.4-2.1	0.9 0.2-3.5	na
POP	1.4 0.9-2.0			1.4 0.7-2.6	Cerazette		
Mirena		0.7 0.5-1.0		0.9 0.3-2.6	Implant		

Lidegaard et al. N Engl J Med 2012; 366: 2257-66

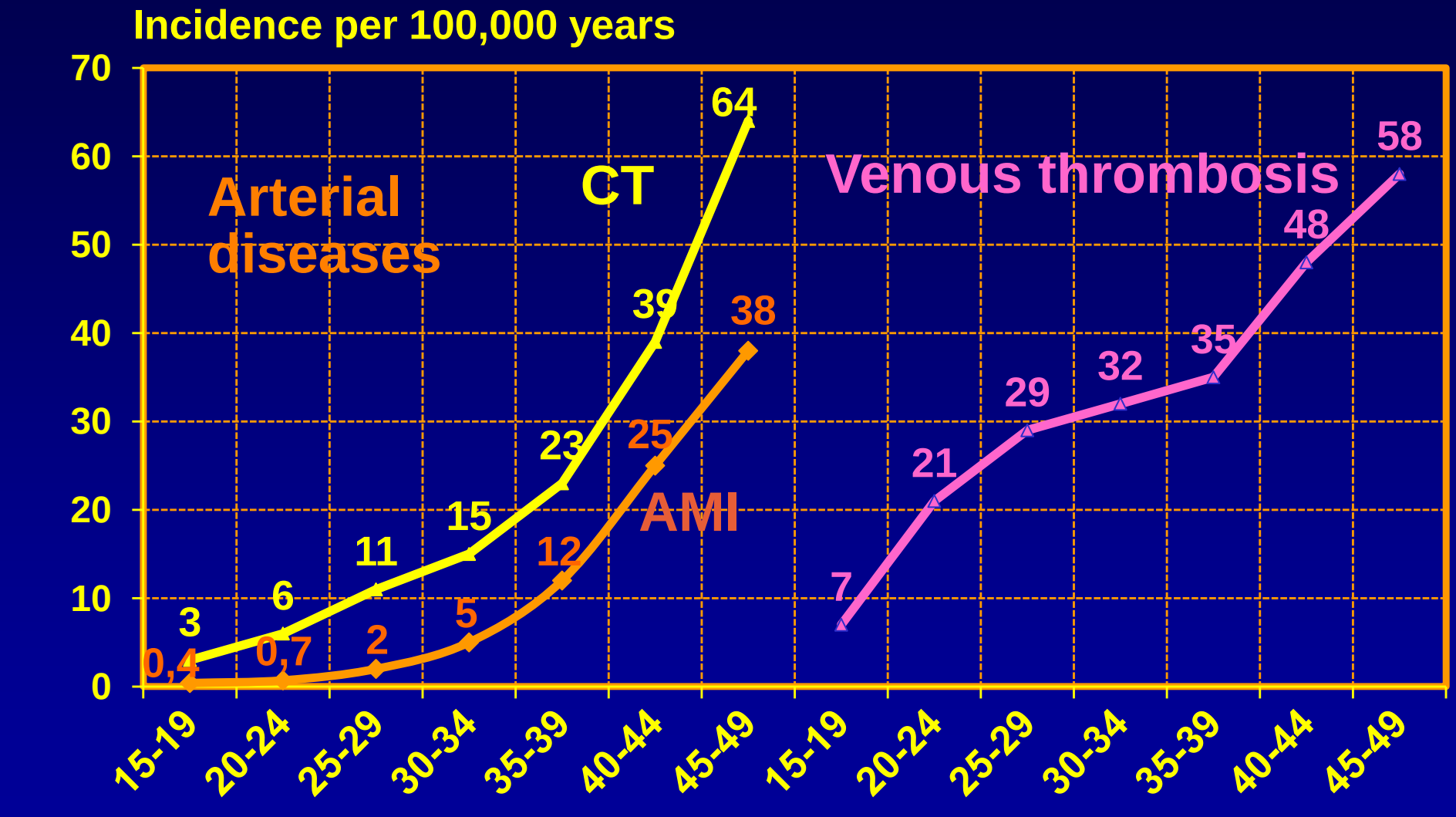
OCs and thrombosis

Current status March 2014

	VT	CT
POP:	1	1.4
LNG-IUS:	<1	1
2nd gen:	3	1.7
3rd gen:	6	1.8
4th gen:	6	1.6
Patch	7	3.2

CT, AMI and VT in DK 2001-2009*

Pregnant and puerperal women excluded



Lidegaard et al NEJM 2012 and BMJ 2011

IRF
Rationel
Farmakoterapi
September 2012
7

Hormonel kontraception og tromboemboliske aspekter

*Af Øjvind Lidegaard**

Hormonel kontraception omfatter p-piller, p-plaster, vaginalring, hormonspiral, subkutant implantat samt intramuskulært gestagendepot, altså seks forskellige administrationsveje. Ud over at yde en effektiv kontraceptiv effekt indebærer brugen af hormonel kontraception også en række non-kontraceptive gevinster, for eksempel blødningskontrol og bedring af akne, som har stor betydning for den udbredte brug af hormonel kontraception.

Den væsentligste bivirkning ved

Tromboemboliske komplikationer blandt yngre kvinder

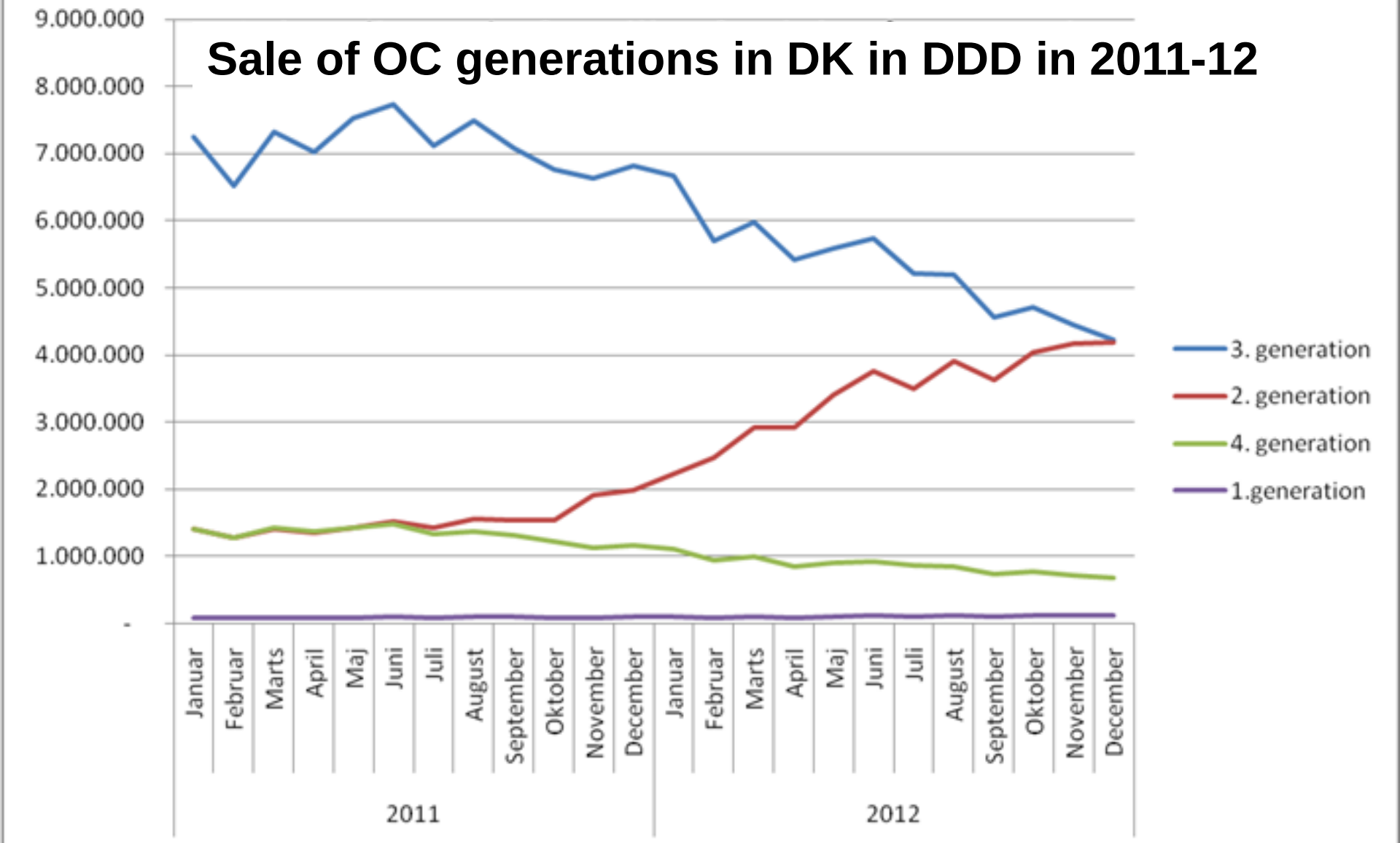
Venøs trombose

Blandt ikke-gravide kvinder under 30 år er den hyppigste tromboemboliske komplikation til hormonel kontraception den venøse trombose, som blandt kvinder, der ikke anvender hormonel kontraception, optræder med to tilfælde pr. 10.000 kvinder pr. år. Blandt kvinder i alderen 30-49 år er baggrundsincidensen i gennemsnit dobbelt så høj eller fire pr. 10.000 kvinder pr. år.

kardieinfarkt (*AMI*) samt cerebral trombose og tromboemboli. Blandt ikke-gravide kvinder under 30 år forekommer der 0,6 arterielle tromboser pr. 10.000 pr. år, mens der blandt kvinder mellem 30 og 49 år i gennemsnit forekommer fem tilfælde pr. 10.000 kvinder pr. år. De vigtigste risikofaktorer for arteriel trombose er høj alder, rygning, hyperkolesterolæmi, diabetes, hypertension og migræne, især migræne med aura.

Hormonel kontraception

Sale of OC generations in DK in DDD in 2011-12



http://laegemiddelstyrelsen.dk/da/topics/bivirkninger-og-forsoeg/bivirkninger/nyheder/laeger-foelger-anbefalinger-for-brugen-af-p-piller

IPPF

From choice, a world of possibilities

February 2013

IMAP= International Medical Advisory Panel

IPPF Medical Bulletin

IMAP Short Statement on the Safety of Third and Fourth Generation Oral Contraceptives

Based on the analysis conducted by the United States Food and Drugs Administration (FDA) (2013) and the recommendations contained on the publications "Family Planning: a Global Handbook for Providers" by WHO (2011) and Medical Eligibility Criteria (WHO, 2010),[i] IMAP Members provide guidance to IPPF's Member Associations on the safety of third and fourth generation oral contraceptives. This statement is developed in response to recent public alarm in European countries, where women sued manufacturers for potential fatal blood clots (Venous Thromboembolism) as a result of using Meliane (Gestodene-containing oral contraceptive pill). The conclusions presented below do not apply to implants, IUS or other products containing the active components in third and fourth generation oral contraceptives.

What are third and fourth generation

What is Venous Thromboembolism

The term venous thromboembolism (VTE) refers to both deep vein thrombosis (DVT) – a blood clot in one of the deep veins of the body; and pulmonary embolism – a blood clot that travels through the bloodstream and lodges in one of the lungs.

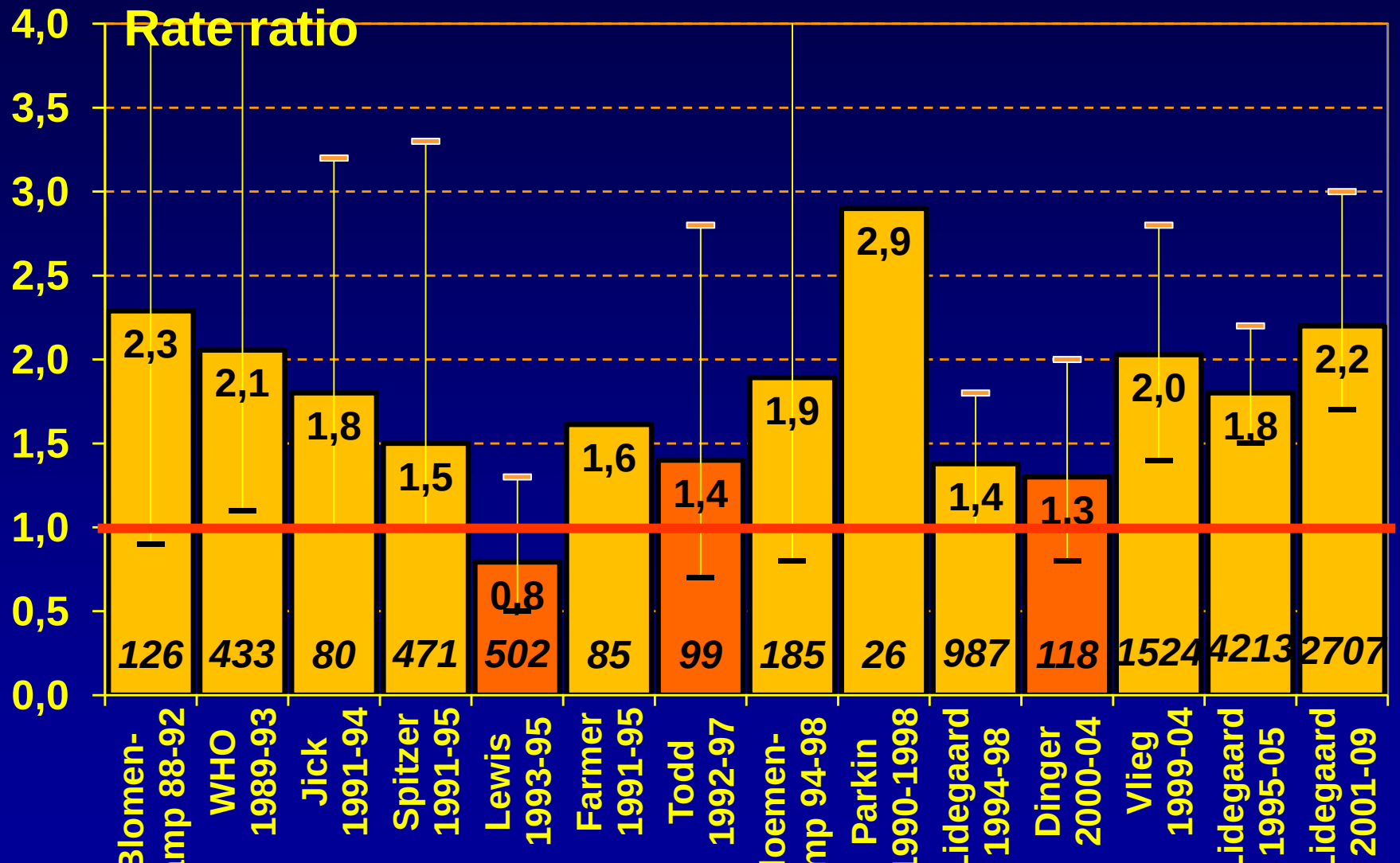
Evidence on third and fourth generation pills

- Recent epidemiological studies reviewed by the FDA have not shown the magnitude of increased risk of Venous Thromboembolism (VTE) reported in earlier studies as a result of using third and fourth generation oral contraceptives[ii].
- Earlier studies reporting increased risk of VTE produced conflicting results and had methodological limitations that call into question the validity of their findings and conclusions about the magnitude of the additional risk associated with using these products.
- Changes in the results of coagulations tests as a result of using third and fourth generation oral contraceptives suggested in earlier studies have not been shown to be directly responsible

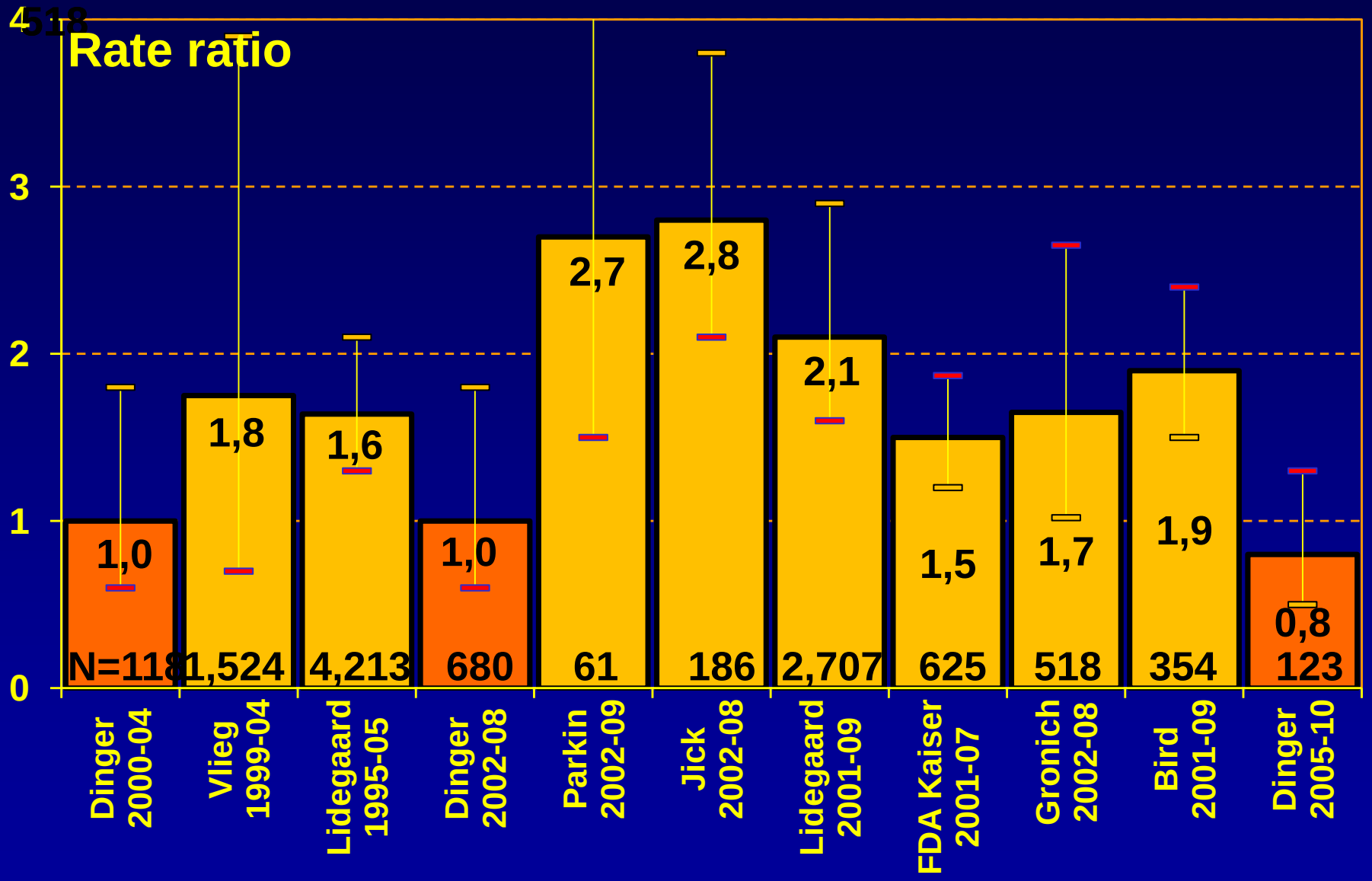
Evidence on third and fourth generation pills

- Recent epidemiological studies reviewed by the FDA have not shown the magnitude of increased risk of Venous Thromboembolism (VTE) reported in earlier studies as a result of using third and fourth generation oral contraceptives[ii].
- Earlier studies reporting increased risk of VTE produced conflicting results and had methodological limitations that call into question the validity of their findings and conclusions about the magnitude of the additional risk associated with using these products.

3rd versus 2nd generation COC



COC with DRSP vs LNG



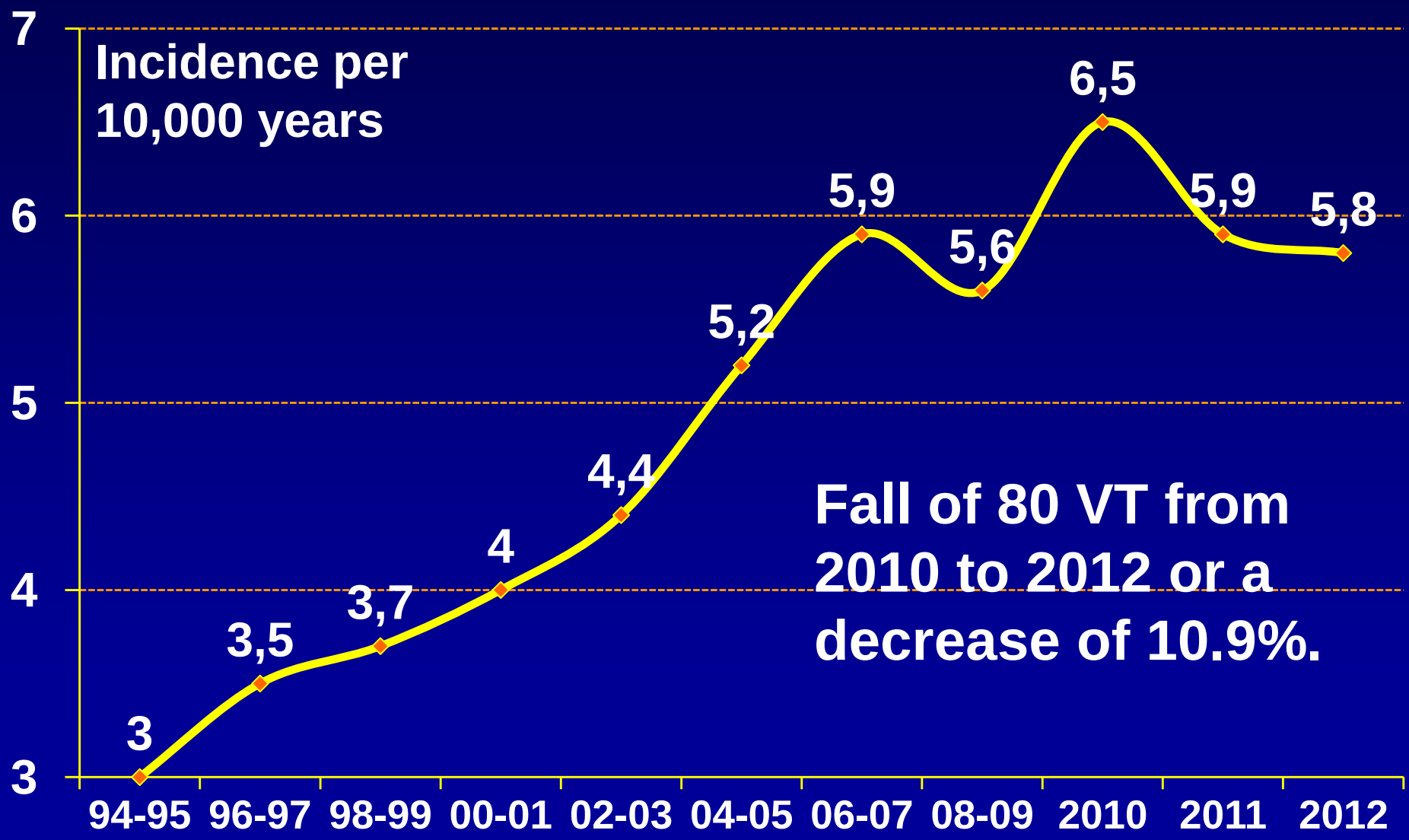
Basic question

Is there a differential risk of VT with use of hormonal contraceptives with different progestogens?

If no: You should expect no change in the occurrence of VT when women shift from 3rd/4th generation pills to 2nd generation.

If yes: You should expect a 50% fall in VT in non-pregnant women shifting from the newer products to 2nd gen. pills

Venous thrombosis in DK 1994-2012 in non-pregnant women 15-44 years old



Hormonal contraception - age

Young women (<35 years)

1st choice	Lowest dose 2nd generation OC
2nd choice	LNG-IUS (fx Jaydess)
3rd choice	3rd or 4th generation OC

Women from 35 years or women at risk

1st choice	LNG-IUS
2nd choice	Lowest dose 2nd generation OC
3rd choice	Non hormonal contraception

Dinger - again

1st world congress in Contraception
Copenhagen, Friday, May 24, 2013
16.30-18.00 (one of four parallel sessions)

(Auditorium 12)

16:30 - 18:00	**Congress Session 17: Venous thromboembolism and contraception – myths and facts** *Chairs: Thomas Rabe, (Germany) & Jørgen Jespersen, (Denmark)*
16:30 - 16:55	Mechanisms of haemostasis in healthy women and women at risk of VT *Beate Luxembourg, (Germany)*
16:55 - 17:20	Summary of relevant epidemiological studies on VTE and contraception *Jeffrey T Jensen, (USA)*
17:20 - 17:45	Methodological limitations of studies on VTE and contraception *Jürgen Dinger, (Germany)*

Hormonal contraception and venous thrombosis

- George Monbiot, Guardian, March 2010

”In fighting for science, we subscribe to a comforting illusion: That people can be swayed by the facts”

http://www.monbiot.com/2010/03/08/the-unpersuadables/

Hormonal contraception and venous thrombosis

Thanks for your attention

www.lidegaard.dk/slides