

PCOS, hormonal contraception and thrombotic stroke

A national cohort study

*Terese Matthesen,
Lars Hougaard Nielsen,
Anne Mette Rasmussen, and
Øjvind Lidegaard*

**Department of Gynaecology, Rigshospitalet
Faculty of Health Science
University of Copenhagen, Denmark**

Background

- PCOS is the most frequent endocrine disease in women; Prevalence 5-10%
 - Women with PCOS have an increased risk of adiposity, diabetes, hypertension, cardiovascular diseases; metabolic syndr.
 - 1st choice treatment: Oral contraceptives.
 - Hormonal contraception increases the risk of cerebral thrombosis.
 - We found no study assessing the risk of thrombotic stroke among fertile women.
-

Objectives

- To assess the risk of thrombotic stroke in women of reproductive age with PCOS.
 - To compare this risk with the risk in women without PCOS
 - To quantify how much adiposity and use of hormonal contraception contribute to an eventually increased risk of thrombotic stroke in women with PCOS
-

Material

- Inclusion: Women 15-49 years during the period January 2001-December 2012
 - Exclusion: Previous CaVD, cancer, thrombophilia, and women with hysterectomy, sterilisation or bilateral oophorectomy.
 - Censoring: Death, emigration
 - Temporary exclusion: Treatment of infertility and pregnancy.
-

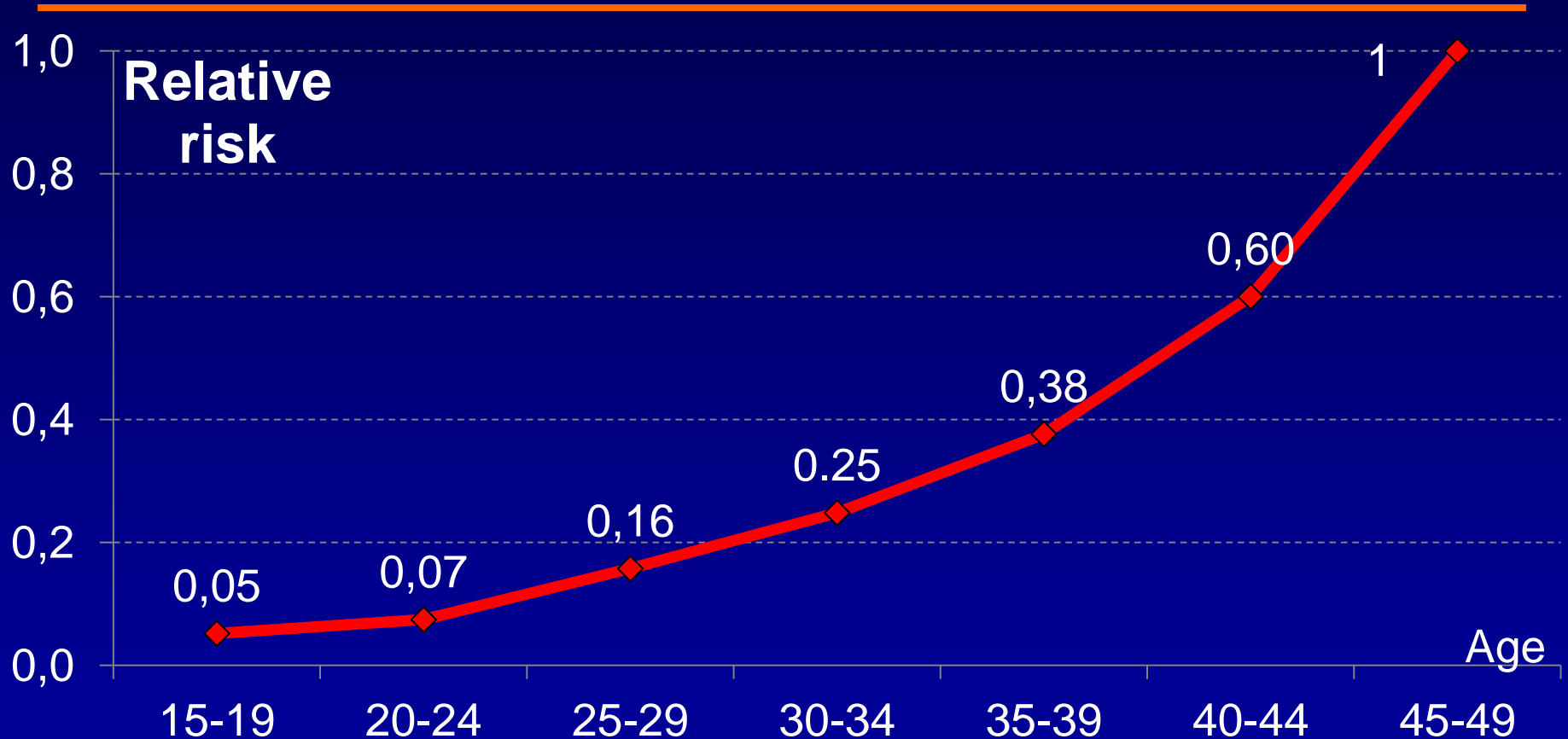
Methods

- Data source: National Health Registry and prescription registry.
 - Poisson regression with adjustment for age, BMI, hormonal contraception, and education.
 - Sensitivity analysis restricted to women with known body mass index.
-

Results

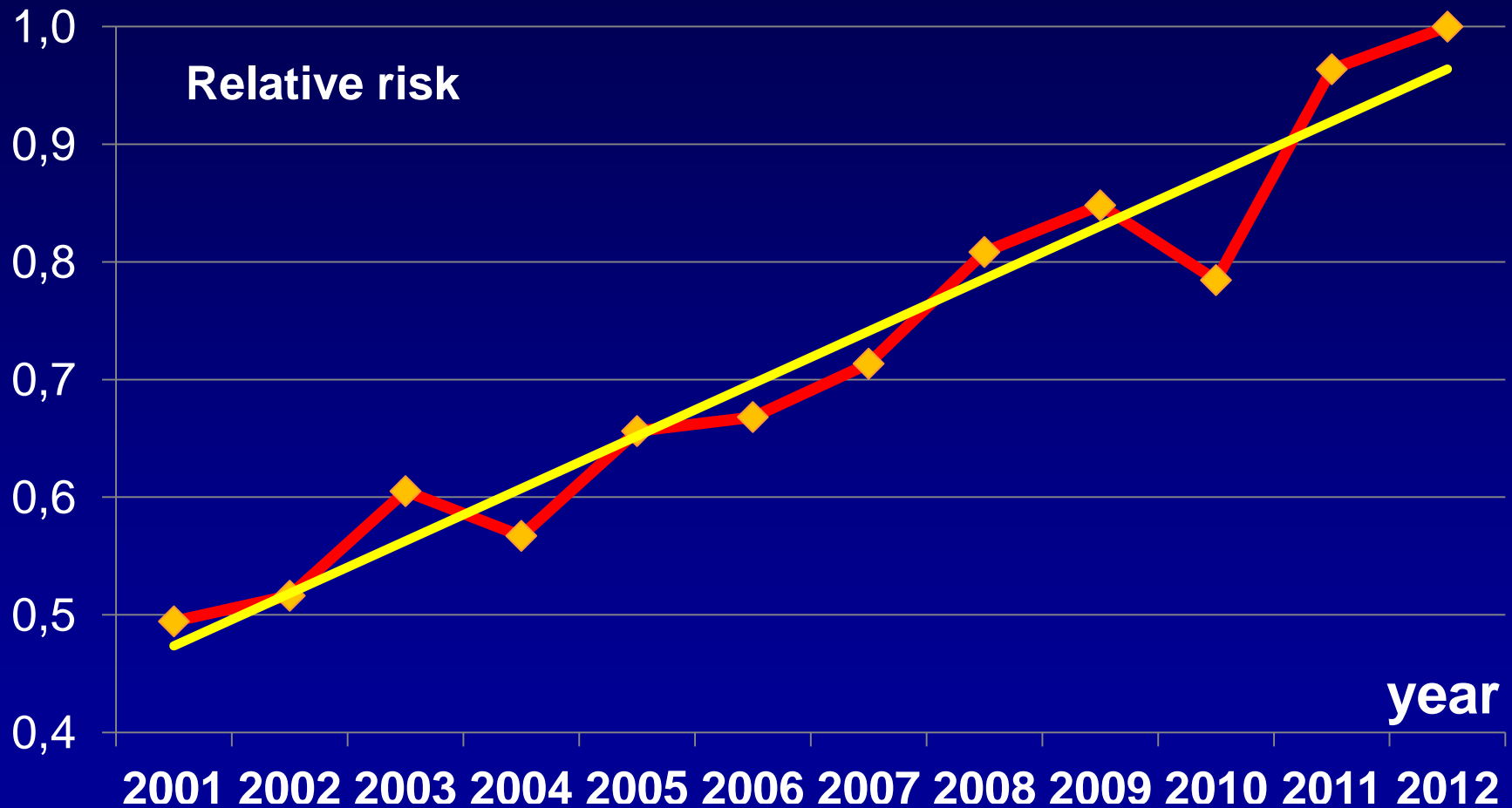
- 11.3 million women-years included.
 - 3,251 women with thrombotic stroke
 - 90,038 women-years with PCOS
 - 42 thrombotic strokes in women with PCOS
 - The Incidence rate of TS increased
 - 2000% with increasing age
-

Adjusted* relative risk of first ever thrombotic stroke according to age

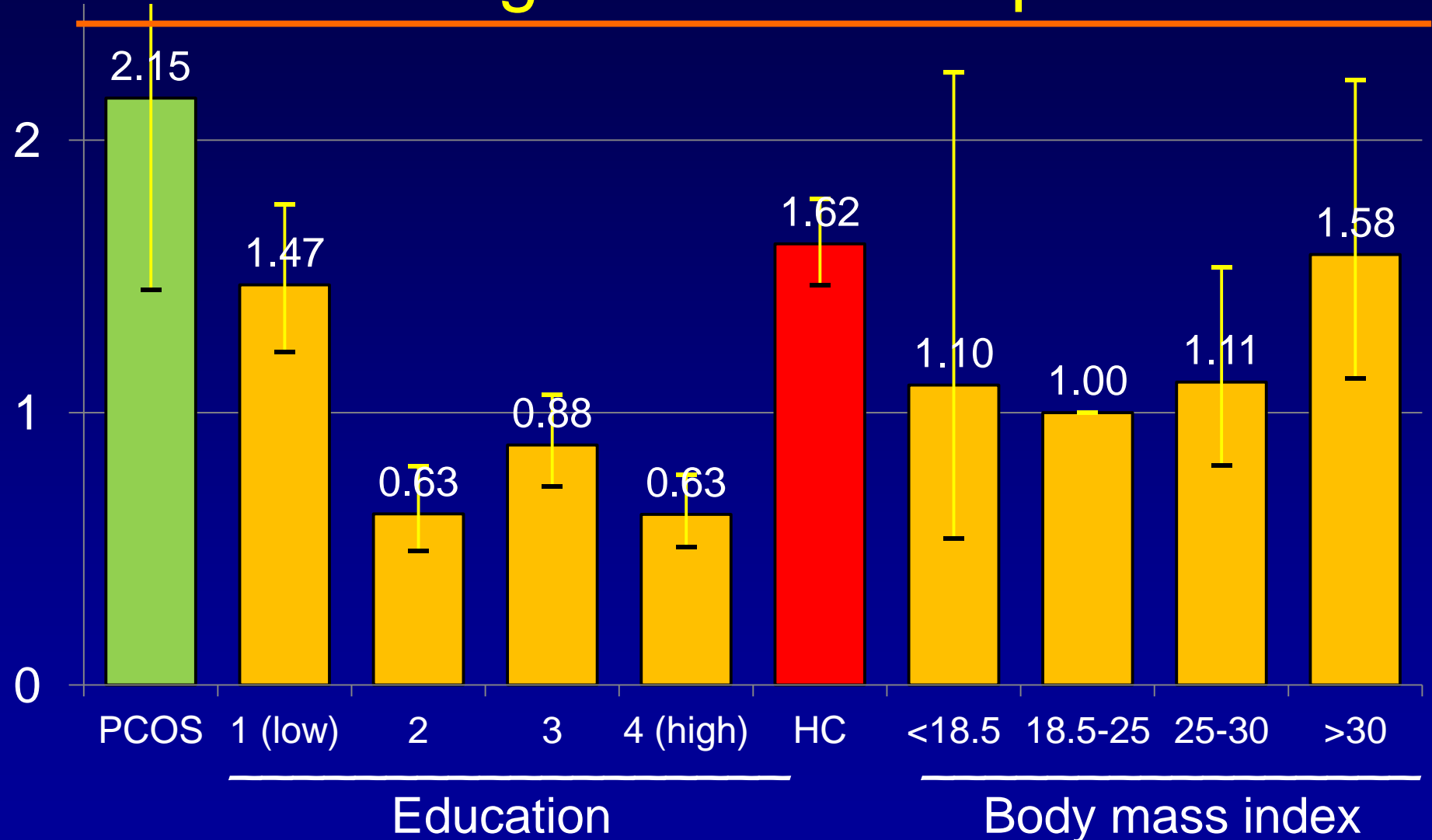


*) Adjusted for calendar year, education, use of hormonal contraception, and body mass index.

Relative risk of first ever thrombotic stroke by time



Adjusted relative risk of cerebral infarction according to different exposures



*) Adjusted for year, education, hormonal contraception, and BMI

Results

- Women with PCOS had twice the risk of thrombotic stroke than women without PCOS after adjustment for HC
 - Sensitivity analysis demonstrated an 11% reduction in risk of thrombotic stroke with adjustment for BMI (NS)
-

Conclusion

- Fertile women with PCOS have a doubled risk of thrombotic stroke which is not explained by a higher BMI or use of hormonal contraception.
 - Three studies have demonstrated also a doubled risk of venous thrombosis in women with PCOS.
-

HC according to risk of VTE

No risk <1.5	Low risk 1.5-4	High risk 5-7	Few data	No data
----------------------------------	---------------------------------	--------------------------------	-----------------	----------------

EE dose	NETA Norethisterone	LNG Levonorgestrel	NGM Norgestimate	DGS Desogestrel	GSD Gestodene	DRSP Drospirenone	CPA Cyproteroneacetate
----------------	-------------------------------	------------------------------	----------------------------	---------------------------	-------------------------	-----------------------------	----------------------------------

Combined products

Middle	3	3		6		6	6
Low		2.5?		5			
Nat o/e	E2V-DNG 4.5			E2 NOMAC			
N-oral			Patch 7	Vaginal ring 6			

Progestogen only products

Oral	POP 1			Cerazette 1			<i>WHO</i>
N-oral	Depot 1	IUS 1		Implant 1.4			<i>2014</i>

HC and thrombotic stroke

No risk <1.5	Low risk 1.5-4	High risk 5-7	Few data	No data
-----------------	-------------------	------------------	----------	---------

EE dose	NETA Norethisterone	LNG Levonorgestrel	NGM Norgestimate	DGS Desogestrel	GSD Gestodene	DRSP Drospirenone	CPA Cyproteroneacetate
---------	------------------------	-----------------------	---------------------	--------------------	------------------	----------------------	---------------------------

Combined products

Middle	2.2*	1.7*	1.5*	2.2*	1.8*	1.6*	1.4
Low				1.5*	1.7*	0.9	
Nat oie	E2V-DNG			E2 NOMAC			
N-oral			Patch 3.2	Vaginal ring 2.5*			

Progestogen only products

Oral	POP 1.4			Cerazette 1.4			<i>WHO</i>
N-oral	Depot	IUS 0.7		Implant 0.9			<i>2014</i>

Conclusion

- Fertile women with PCOS have a doubled risk of thrombotic stroke which is not explained by a higher BMI or use of hormonal contraception.
 - Three studies have demonstrated also a doubled risk of venous thrombosis in women with PCOS.
 - Also women with PCOS should therefore have 2nd generation hormonal contraception as first choice
-

Thanks for your attention

www.lidegaard.dk/slides

Strengths

- >11 million observation years
- 12 years complete follow-up.
- Information on hormonal contraception from prescription registry => no recall bias
- Adjustment for the two most important confounders: BMI and use of hormonal contraception.

Limitations

- The definition of PCOS has changed through the study period.
 - Only women referred to hospital were recorded with a PCOS diagnosis code.
 - No information about family disposition, physical exercise, smoking, hypertension, diet, and hyperlipidaemia.
-