

Hormonal contraception and mental health

Øjvind Lidgaard

Department of Obstetrics & Gynaecology
Rigshospitalet,
Faculty of Health Sciences
University of Copenhagen

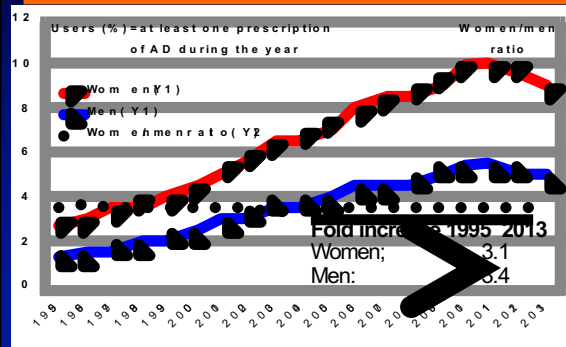
15th ESC congress, Budapest, May 11, 2018

Hormonal contraception and depression

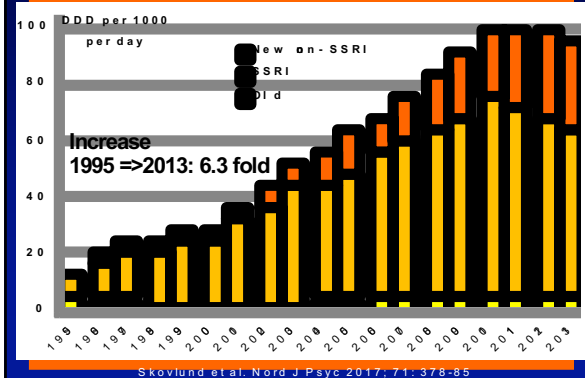
Background

- Female sex hormones have an influence on many women's mood
- Exogenous hormones may likewise have an influence on some women's mood
- But first some descriptive data

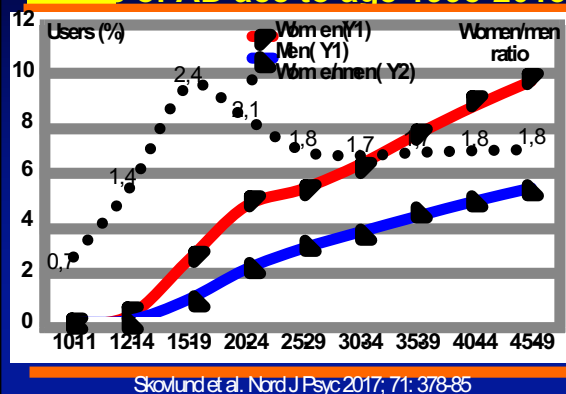
Users of AD in women 15-49 years



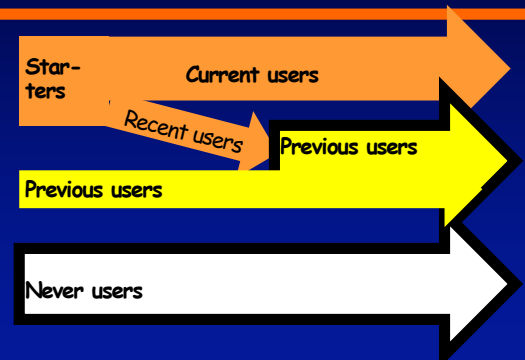
Use of AD in women 1995-2013



Users of AD acc to age 1995-2013



HC & AD: Methodological points



Hormonal contraception, depression and suicides

Charlotte W. Skovlund¹
Lina Steinrud Mørch¹,
Lars Vedel Kessing²,
Øjvind Lidegaard¹

Department of Gynaecology¹ and Psychiatry²,
Rigshospitalet, University of Copenhagen

Hormonal contraception and depression

Aim

- To assess the risk of being user of antidepressants (AD) and of getting a depression discharge diagnosis with use of different types of hormonal contraception

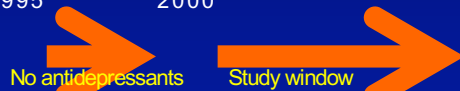
HC & AD: Methods

Included

- All women (& men) in Denmark 1995-2013
- 15-49 years old with a Danish PIN

Exclusion/censoring

- Delivering women + 6 months after delivery
- Women with cancer or previous VTE
- Pregnant and infertile women
- Women with previous psychiatric diagnoses 1995-2000 and 2013



Skovlund et al. JAMA Psychiatry 2016; 73:1154-1162

HC & AD: Methods

Included confounders

- Age, Calendar year
- Education
- Endometriosis and PCOS
- Parity: Nulliparous versus parous

Statistical analysis

- Poisson regression analysis
- First use of antidepressants in starters/users of hormonal contraception
- First depression diagnosis in users of HC

Skovlund et al. JAMA Psychiatry 2016; 73:1154-1162

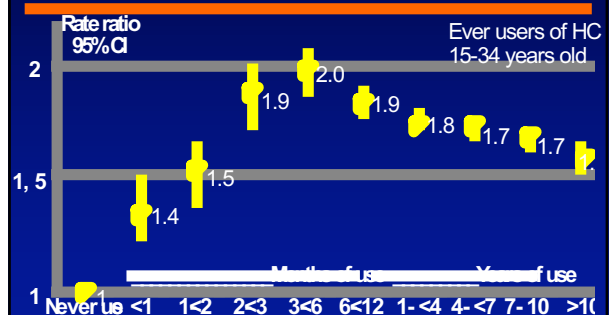
HC & AD: Results

Included

- 1.1 mio women 15-49 years included
- 6.8 mio women years of observation
- 441,523 starters of hormonal contraception
- 135,750 first users of antidepressants
- 14,691 first depression diagnoses
- Categorisation of hormonal contraceptives:

Skovlund et al. JAMA Psychiatry 2016; 73:1154-1162

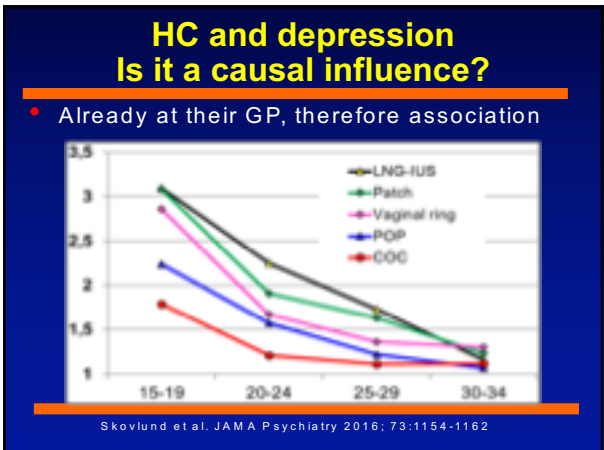
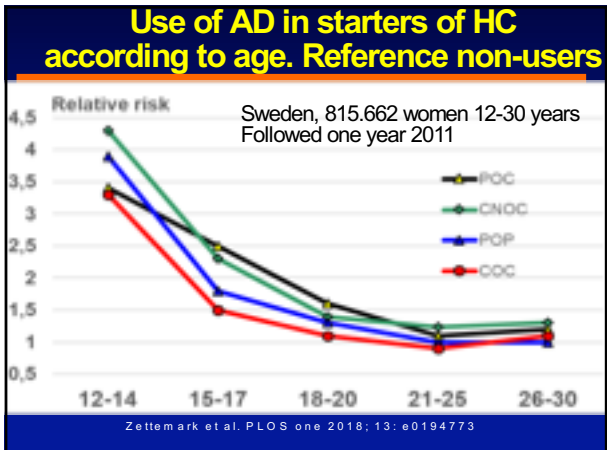
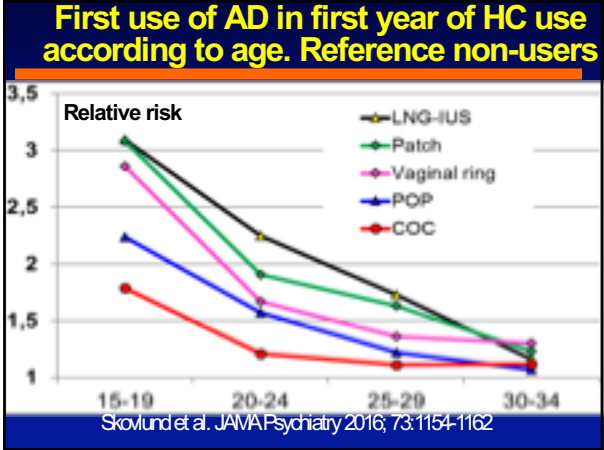
First use of AD according to length of first use of hormonal contraception



Skovlund et al. JAMA Psychiatry 2016; 73:1154-1162

First use of antidepressants in prevalent users of hormonal contraception 15-34 years. Never use ref.

	Low risk <1.5	Med. Risk 1.5-1.9	High risk ≥2	No data
EE dose				
NETA Norethisterone				
LNG Levonorgestrel				
NGM Norgestimate				
DGS Desogestrel				
GSD Gestodene				
DRSP Drospirenone				
CPA Cyproterone-acetate				
Combined products All COC: 1.7 (1.66-1.71)				
Middle 30-40 ug	1.4 1.3-1.6	1.7 1.67-1.77	1.7 1.6-1.7	1.8 1.74-1.87
Low 20 ug EE			1.6 1.55-1.62	1.6 1.55-1.62
Nat E2				1.9 1.76-1.95
Non oral				2.0 1.96-2.10
Progestogen only products All POP: 1.8 (1.7-1.9)				
Oral				1.9 1.8-2.0
Non oral				2.8 2.7-3.0
				3.6 3.3-3.9



HC and depression Is it a causal influence?

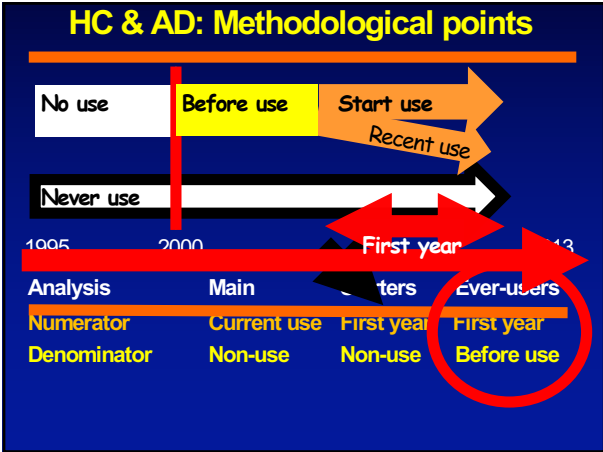
- Already at their GP, therefore association
- Nasty men are met first time at first HC

Skovlund et al. JAMA Psychiatry 2016; 73:1154-1162

HC and depression Is it a causal influence?

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- Nasty men are met first time at first HC
- Users of HC are more neurotic, and therefore disposed for depression

Skovlund et al. JAMA Psychiatry 2016; 73:1154-1162



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- Danish registry data are garbage

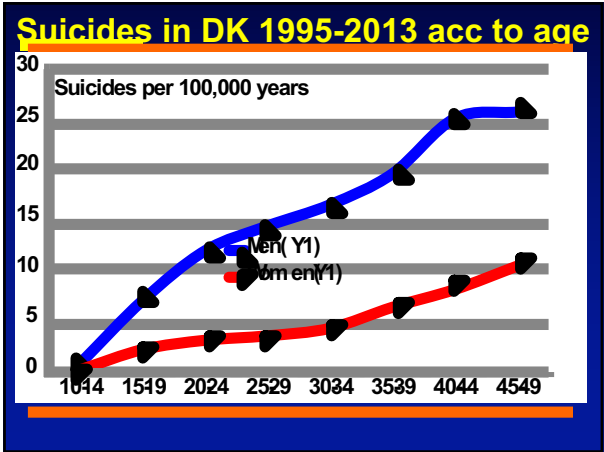
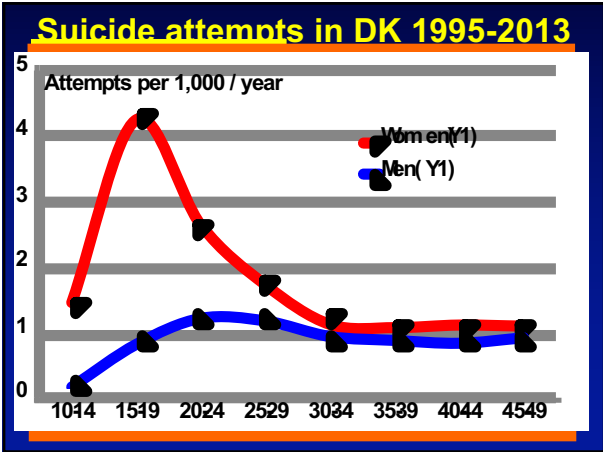
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HC and depression Is it a causal influence?

- Already at their GP, therefore association
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- Users of HC are more neurotic, and therefore disposed for depression
- Previous studies did not find any association
- Danish registry data are garbage.

Conclusion
Nobody has so far explained the association

Skovlund et al. JAMA Psychiatry 2016; 73:1154-1162



Hormonal contraception, suicide attempts and suicides

Charlotte W. Skovlund¹
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 Lars Vedel Kessing²,
 Theis Lange³
 Øjvind Lidegaard¹

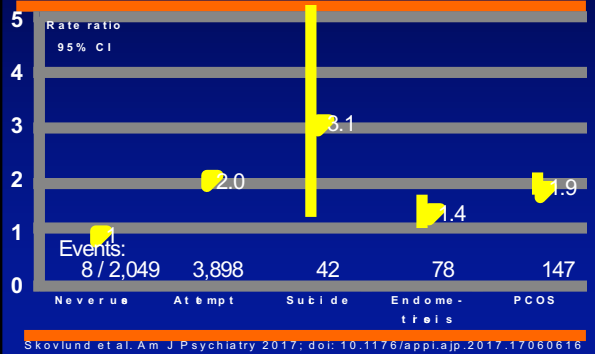
Department of Gynaecology¹ and Psychiatry²,
 Rigshospitalet, Dept. Biostatistics³, all
 University of Copenhagen

HC and suicide attempt and suicide

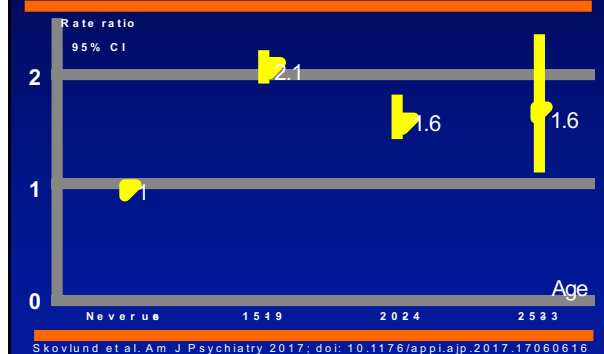
- Included: 475,802 women
- Followed from 15 years
- During the period 1996-2013 (18 years)
- 54% of user time were with use of HC
- 6,999 suicide attempts and 71 suicides
- Confounder control for age, year, education, endometriosis and PCOS
- Reference group: Never users.

Skovlund et al. Am J Psychiatry 2017; doi: 10.1176/appi.ajp.2017.17060616

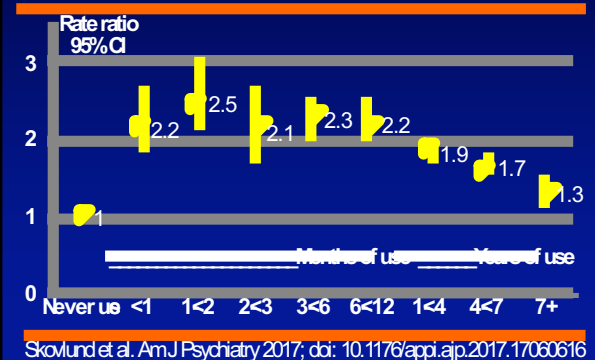
Relative risk of first suicidal attempt and suicide in users of hormonal contraception



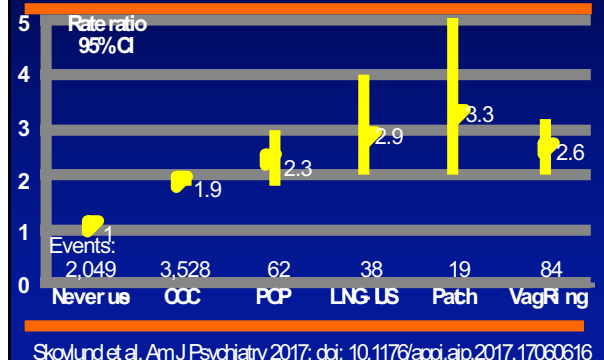
Relative risk of first suicidal attempt in users of hormonal contraception according to age



Relative risk of first suicidal attempt according to length of first use of HC



Relative risk of first suicidal attempt in users of different types of hormonal contraception



First suicide attempt in prevalent users of hormonal contraception. Ref: never-users

EE dose	NETA Norethisterone	LNG Levonorgestrel	NGM Norgestimate	DGS Desogestrel	GSD Gestodene	DRSP Drospirenone	CPA Cypoterone-acetate
Combined products All COC: 1.9 (1.8-2.0)							
Oral 20-40 ug	2.0 1.4-2.9	1.8 1.6-2.1	1.9 1.7-2.2	1.9 1.7-2.1	1.9 1.7-2.0	2.1 1.9-2.3	1.8 1.5-2.2
Non oral	Patch		3.3 2.1-5.2	2.6 2.1-3.2	Vaginal Ring		
Progestogene only products All POP: 2.3 (1.8-3.0)							
Oral	LNG-IUS		2.8 1.3-4.1	2.9 2.1-4.0	Cerazette	2.0 1.4-2.8	Depot
Non oral	LNG-IUS		2.9 2.1-4.0	4.4 3.6-5.4	Implant	6.4 5.0-8.5	

Skovlund et al. Am J Psychiatry 2017; doi: 10.1176/appi.ajp.2017.17060616

Relative risk of suicide in previous studies

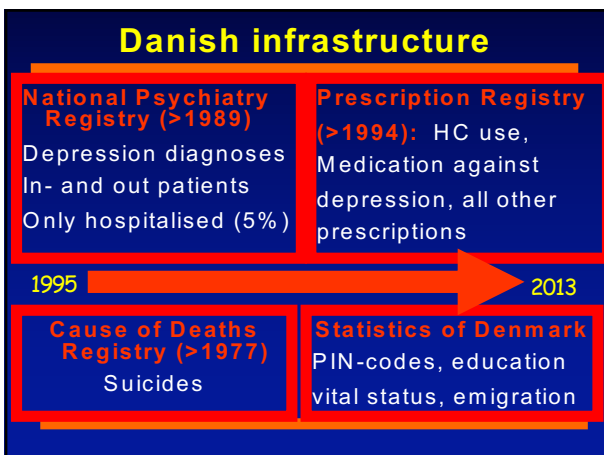
Author Year	Study design	Exp	Reference	Population	Age	Events	Persons years	Relative Risk (95%CI)
Vessey 1989 England	Cohort	OC	Diaphragm or IUD	Married women visiting family planning clinics	25-39*	16	272,512 1968-1986	1.1 (0.3-3.6)
Beral 1999 Britain	Cohort	OC	Never use	Women from general practices	29*	55	0.85 million 1968-1993	1.5 (0.8-2.3)
Colditz 1994 USA	Cohort	OC	Never use	Nurses Health study	30-55*	114	1.3 million 1976-1988	1.3 (0.9-2.0)
Hannaford 2010 UK	Cohort	OC	Never use	Married women or living as married	29*	67	1.2 million 1968-2007	1.3 (0.7-2.2)
Charlton 2014 USA	Cohort	OC	Never use	Nurses Health study	30-55*	241	3.6 million 1976-2012	1.4* (1.1-1.9)
Skovlund 2017 Denmark	Cohort	OC HC	Never use	All women in Denmark	15-33	71	3.9 million 1996-2013	3.1* (1.3-7.1)

Skovlund et al. Am J Psychiatry 2017; doi: 10.1176/appi.ajp.2017.17060616

- HC and mental health: Conclusion**
- Ten per cent of women of reproductive age are on antidepressant therapy
 - Depression is a serious disease
 - HC use increases risk of depression by 70%
 - Suicide attempts are doubled and suicides are tripled in users of hormonal contraception
 - Women should be informed about this risk
 - We should be a little more nuanced when prescribing hormonal contraception

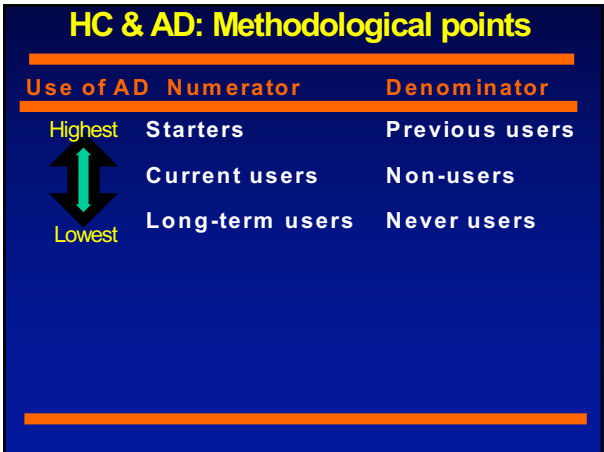
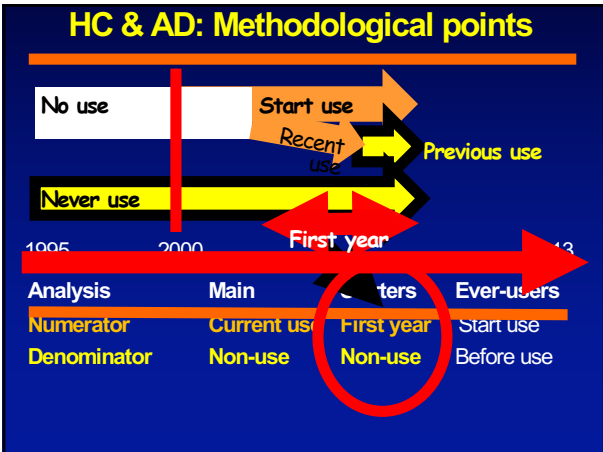
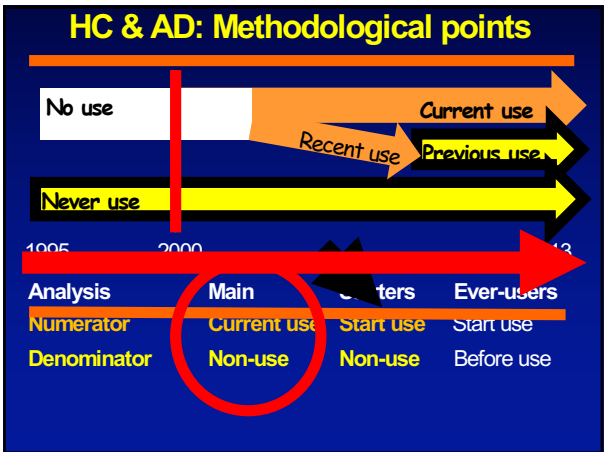
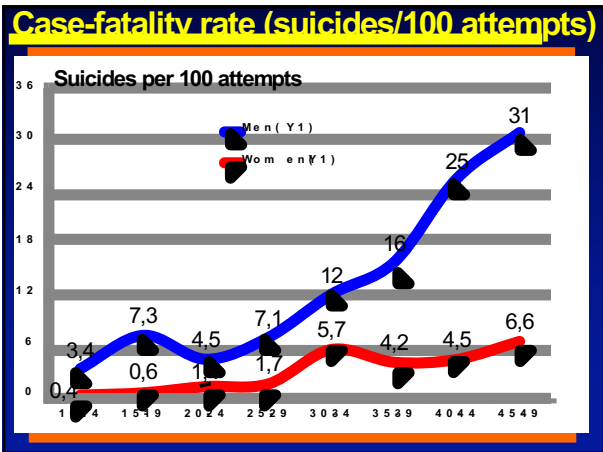
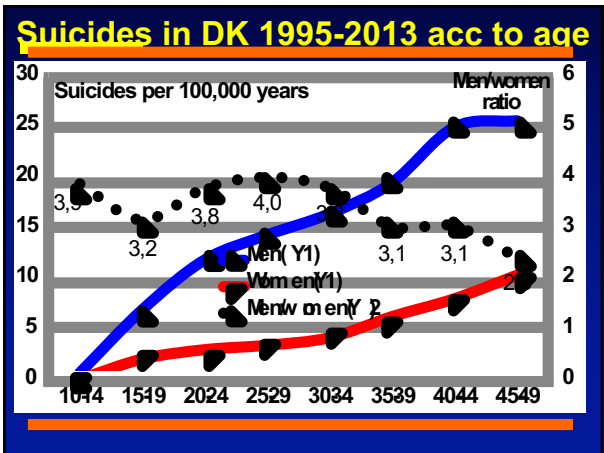
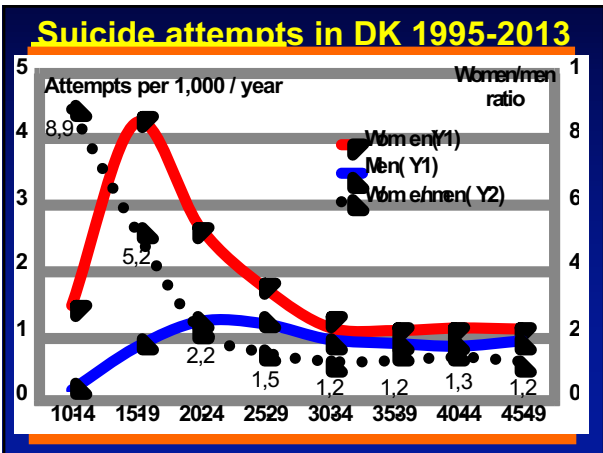
HC, depression & suicides

Thanks for your attention



Hormonal contraception Combined – route – e-dose – e/p type

EE dose	NETA Norethisterone	LNG Levonorgestrel	NGM Norgestimate	DGS Desogestrel	GSD Gestodene	DRSP Drospirenone	CPA Cypoterone-acetate
Combined products							
Middle	1st	2nd gen		3rd gen		4th gen	
Low		2nd					
Nat oe	E2V-DNG		Qas	E2 NOMAC		Zdy	
N-oral			Patch	Vaginal ring			
Progestogen only products							
Oral	POP			Desogestrel		DRSP	
N-oral	IUS		Implant		Depot		



HC & AD: Methodological points


Use of AD	Nominator	Denominator
Highest	Starters	Previous users
	Current users	Non-users
Lowest	Long-term users	Never users

What is the most correct:

What is the least correct:

What is the most used:

HC & AD: Methodological points

Use of AD	Nominator	Denominator
Highest	Starters	Previous users
	Current users	Non-users
Lowest	Long-term users	Never users

What is the most correct: Starters/never us.

What is the least correct: Long-term/non-us.

What is the most used: Current users / non-us