



Medical condition Obesity, family history and VTE

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- Definition of obesity
- Obesity and VTE risk
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- Contraception after bariatric surgery

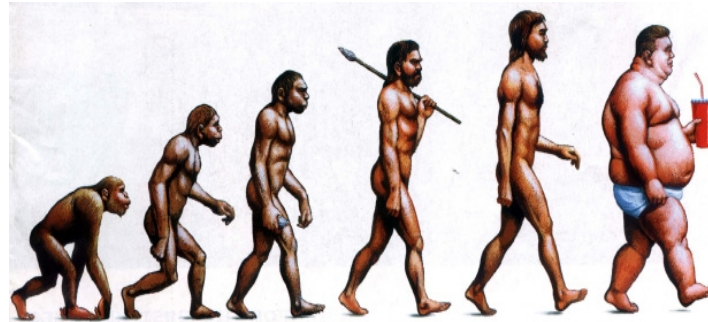
Part 2 Family history and VTE

- Contraception after VTE
- Definition of positive family history for VTE
- Efficient and safe contraception if FH is positive
- VTE risk in women with positive FH



Part 1 Obesity

Obesity today is an epidemic



In Europe prevalence of obesity is 20-30%.
Consequently, knowledge on safe and effective
contraceptive methods is of paramount importance

Medical condition obesity definition

Obesity is defined according to body mass index (BMI kg/m²)

- BMI categories:

- Underweight < 18.5 kg/m²
- Normal 18.5– 24.9 kg/m²
- Overweight 25– 29.9 kg/m²
- Obese 30– 39.9 kg/m² or

- Class I obesity 30– 34.9 kg/m² /

- Class II obesity 35 – 39.9 kg/m²

- Class III very obese > 40 kg/m²

- or otherwise referred to as severe, extreme, obesity or morbid.



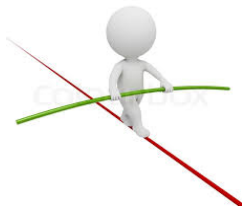
Medical condition Obesity
VTE risk

Medical condition Obesity VTE risk

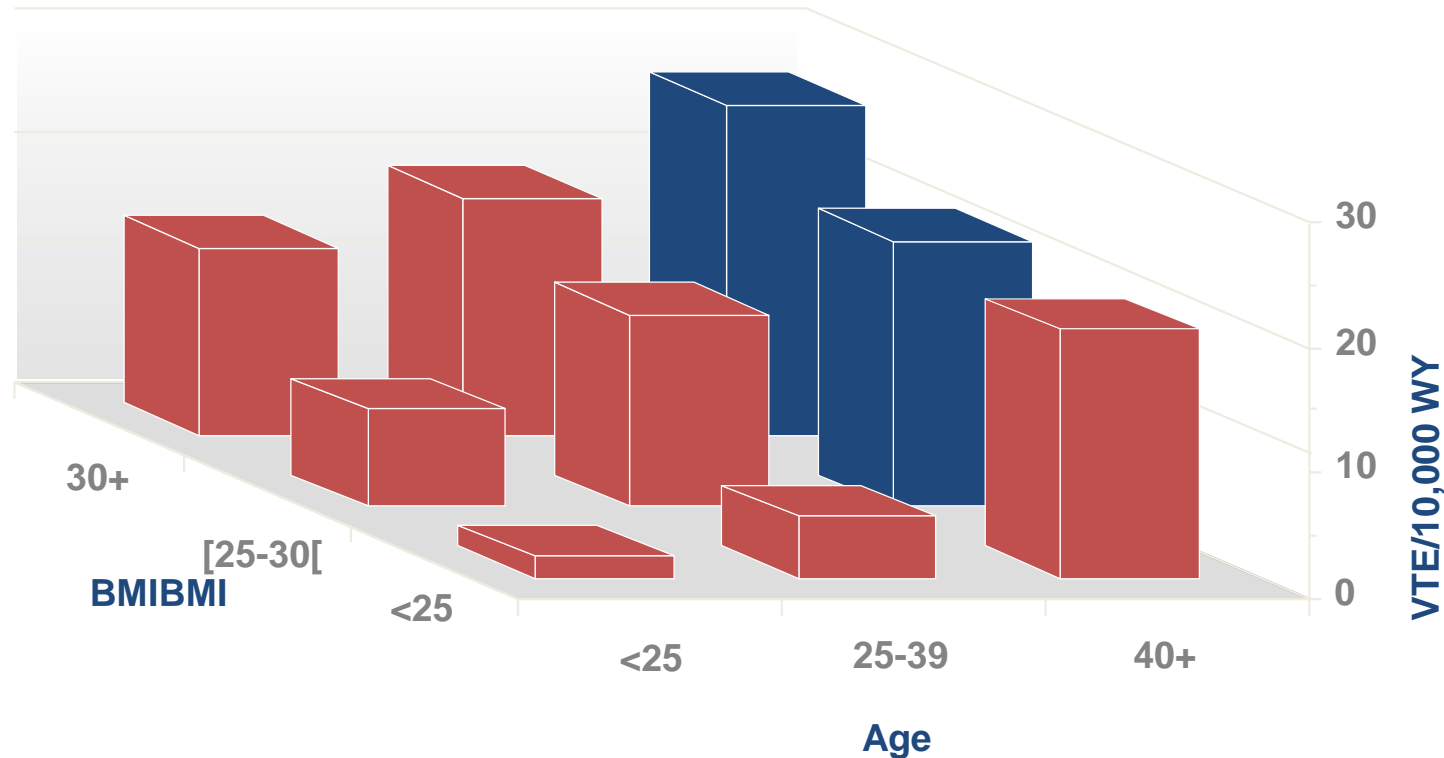
- Obesity increases the VTE risk two-to three fold
 - The risk increases further with age
 - The risk multiplies with use of CHC
- *graph next slide*

Good balancing of risk and benefits is necessary:

- Check for other risk factors including age!
- Are POC and IUD acceptable ?



Medical condition Obesity VTE risk



Effect of age and BMI on VTE risk in COC users*

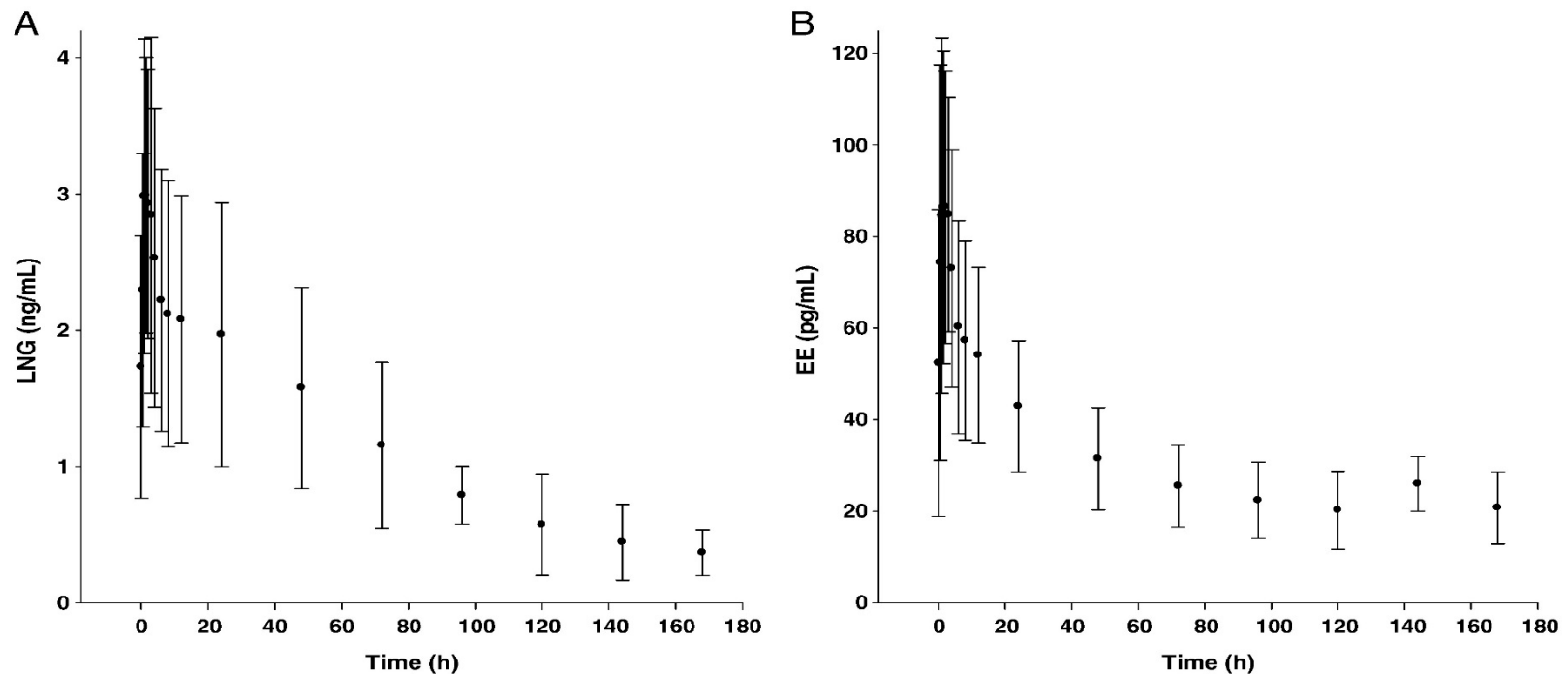
Risk estimates based on 115 VTEs in 116,708 WY of exposure

Efficacy of contraceptive methods in obese women CHCs

Obesity and contraceptive use

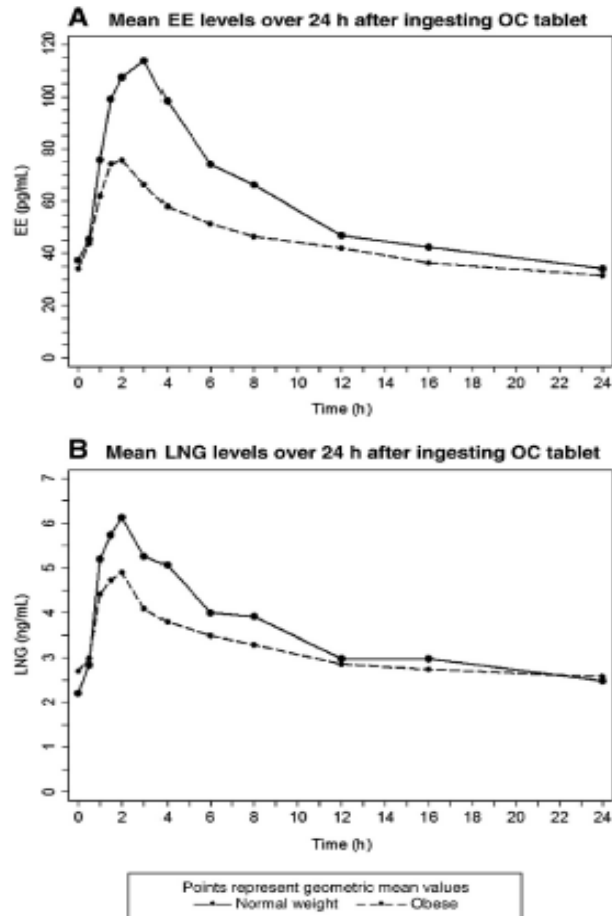
- Obese women have higher odds of female sterilization compared to women with normal BMI
 - BMI 30-34,9: aOR: 1.96 (95%CI: 1,45-2,66)
 - BMI > 35: aOR: 1,56 (95%CI: 1,13-2,14)
- Odds of hormonal contraceptive use are reduced
 - aOR: 0,78 (95%CI:0,62-0,98)
- Weight concerns and obesity affect contraceptive decision making

Variability of EE and LNG plasma levels in obese women (EE 30/LNG 150)



Plasma levels of the hormone components in CHCs show a high variability. In obese women

Plasma levels of EE and LNG in normal weight and obese women (EE 30/LNG 150)



- OC hormone peak levels are lower compared to normal-weight women, but their trough levels are similar.
- Based on pharmacokinetic studies with EE/LNG pills it is unlikely that effectiveness is reduced in obese women

Fig. 2. Serum concentrations of EE and LNG in 13 normal-weight and 15 obese study participants.

Combined vaginal ring

N=20 normal weight women

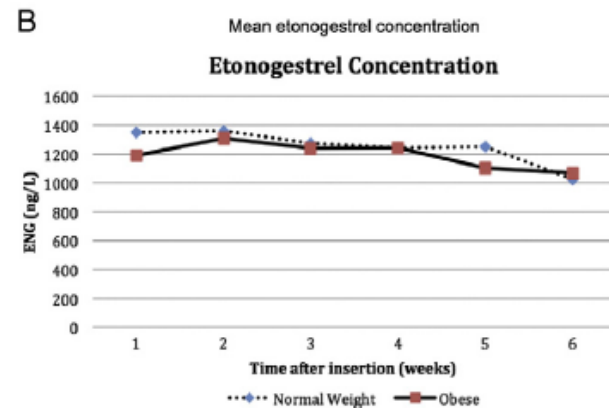
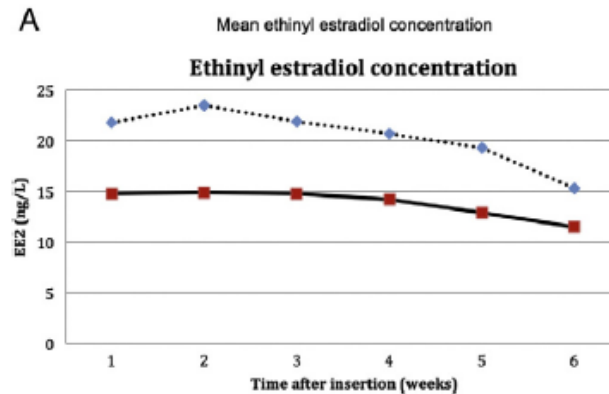
N= 20 obese women

6 weeks follow-up

No ovulations

Obese women did not have lower etonogestrel plasma levels. than normal weight women.

EE levels were lower but were in the therapeutic range up to week 6.



All levels are in the therapeutic range

Conclusion

Optimise efficacy of CHC in obese women

- A small increase in CHC failure in women with **BMI > 35 kg/m²** cannot be excluded .
- Use COC containing 30 µg EE
- Continuous use of 20 µg EE/100 µg LNG is better than a 21/7 regimen, but breakthrough bleeding may occur.
- Recommend condoms in newstarters for 10 days as steady state takes longer to achieve
- The **combined transdermal patch** is less efficient in women with body weight > 90 kg and, potentially BMI > 30 kg/m² .
- The **combined vaginal ring** is probably as efficient as a COC.
- Discuss alternatives as VTE and ATE risk is increased with CHC





Medical condition: Obesity
Progestin only methods and IUDs

Medical condition: Obesity Progestin only methods and IUDs

- **POP:** At present no data indicate a decreased efficacy of Desogestrel 75 μg in obese women.
- **Implant:** Etonogestrel levels are lower in obese women. Caution is recommended. Replacement after 24 months instead of 36 months might contribute to safety.
- **DMPA:** Highly efficient in obese women

Medical condition: Obesity Progestin only methods and IUDs

- **Copper-IUDs** are highly recommended in obese women, after contraindications have been excluded
- The **LNG-IUS** is a safe and effective contraceptive method for obese women without contraindications for this method.
- The LNG-IUS is advantageous in women with heavy menstrual bleeding.

Medical condition: Obesity Emergency contraception

- In obese women at high risk of pregnancy after unprotected intercourse, the insertion of a copper IUD is the method of choice
- If this is not possible ulipristal acetate 30 mg may be a better option than Levonorgestrel 1.5 mg.

Medical condition: Obesity Bariatric surgery



- A COC or POP might be less efficient in post-bariatric patients with malabsorptive procedures (CDC medical eligibility criteria).
- IUDs and DMPA are efficient.
- Desogestrel pharmacokinetics does not change after Roux-en-Y gastric bypass surgery (probably efficient).
- In women with surgical procedures not including malabsorption there is no reason to restrict COCs, but take the VTE and ATE risk into account.
- In women who returned to a BMI < 30 kg/m² non-oral CHC are another option.

Case

Medical condition: Obesity

17 year old adolescent with a BMI of 31 kg/m², non-smoker, no further risk factors, wants hormonal contraception with regular cycles. She does not use tampon and does not like to touch her vagina. For her only CHC are acceptable.

Which CHC might be the preferred option in this teenager ?

- Does use of a 20µg EE pill decrease VTE risk ?
- What type of progestin should be chosen ?
- Will a long-cycle be more efficient in obese women ?
- Is a pill containing 30EE µg/150 µg LNG more efficient ?
- Is the CTP an option ?
- What should be discussed in addition ?

Medical condition: Obesity, VTE, efficiency
Case 1

Is the VTE risk with CHC use acceptable in this young woman, who wants to use a method with regular bleeding ?



Yes, if she refuses all other methods and has no further risk factors.

Medical condition: Obesity ,VTE, efficiency Case: Counselling aspects

Discuss the long-term risks associated with her weight and advice her to exercise and visit a nutrition course to learn, how to lose weight



- COC containing $\leq 20 \mu\text{g}$ EE are not associated with a lower VTE risk than those with 30-35 μg EE. Therefore use 30 μg EE COCs to increase efficacy.
- Advise use of a COC with EE/LNG (lower VTE risk CHC containing third or fourth generation progestins)
- As steady state is achieved delayed, use of condoms can be recommended for the initial 10 days in newstarters.

Medical condition: Obesity ,VTE, efficiency Case: Efficacy of non-oral CHC

CTP and CVR

- Efficacy of the CTP may be reduced. Her BMI is just a bit above 30 kg/m². The CTP could be used, if she would not accept oral contraception
- The CVR could be used if she would prefer vaginal application
- Both methods are associated with a twofold VTE risk in relation to a COC with levonorgestrel (6-12/10000 woman-years vs 5-7/10000 woman-years)

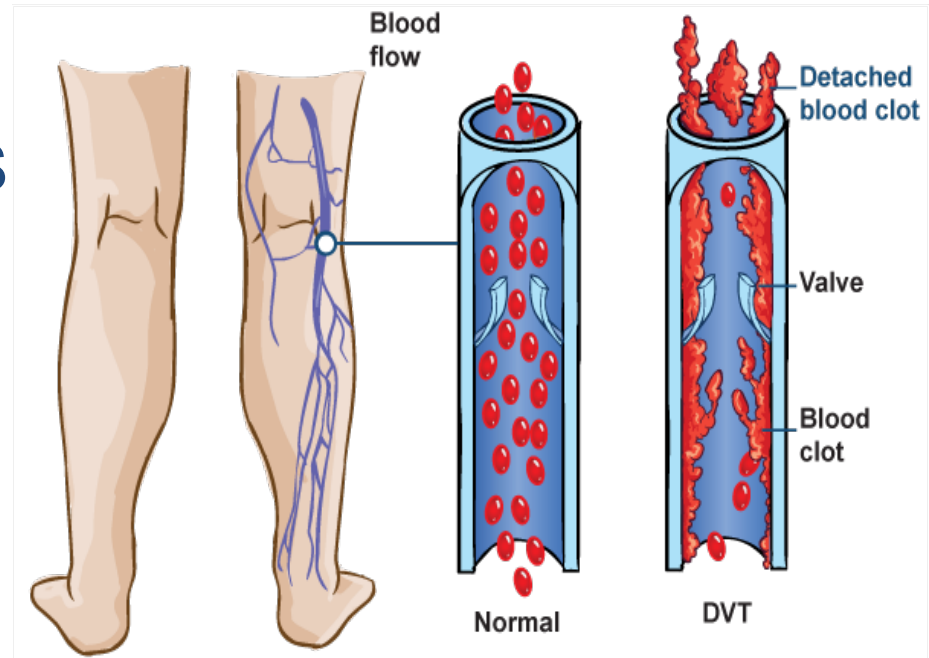


Part 2 Family history and VTE

Medical condition Contraception after VTE

Efficient and safe options

- Copper IUD and LNG-IUS
- POP Desogestrel
- Implant
- DMPA
- Permanent methods



Definition of Family history for VTE



Positive family history

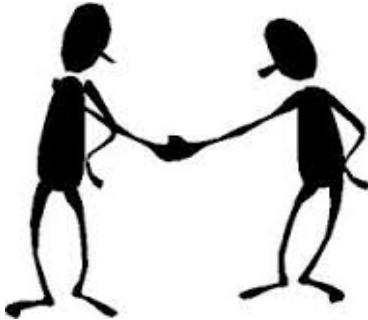
Having a member of your family who has had a blood clot, a deep vein thrombosis, ischaemic stroke or pulmonary embolism

Strong-risk family history

If the first-degree relative had the event at age <50 years the VTE risk is especially high and CHCs should be avoided

Only 30% of women with a positive family history suffer from any type of thrombophilia

Medical condition Positive family history



Efficient and safe options for contraception

- Copper IUD and LNG-IUS
- POP Desogestrel
- Implant
- DMPA
- Permanent methods

Positive family history

How high is the VTE risk in non-CHC users?

Family history	VTE-Risk odds ratio (1)
negative	1
positive any relative	2.2
positive relative < 50 years	2.9
> 1 relative	2.9
2 relatives, one <50 years	4

Relation to proband	VTE-Risk odds ratio (2)
Sibling	2.5
Son/daughter	2.6
Parent	2.1
Second degree relative	1.5-2.3
2 relatives, one <50 years	4

Consider that age of the first degree relative < 50 or not does not make such a difference!

Positive family history Probable VTE risk for CHC users

- The VTE risk with a first-degree relative is two-threefold
- The risk with additional use of CHC is 15 fold
- CHCs should rather not be prescribed in such a situation

Siblings and family history

Siblings with VTE vs. Siblings without VTE

All			Siblings +VTE		
Age	n	IR	n	IR	Faktor
10-19	711	6.8	14	44.6	<u>7.5</u>
20-29	3063	29.2	75	110.3	3.8
30-39	3604	33.9	113	89.9	2.3
50-59	6328	76.1	396	181.6	2.3
all	23358	36.2	1141	147.7	4.1

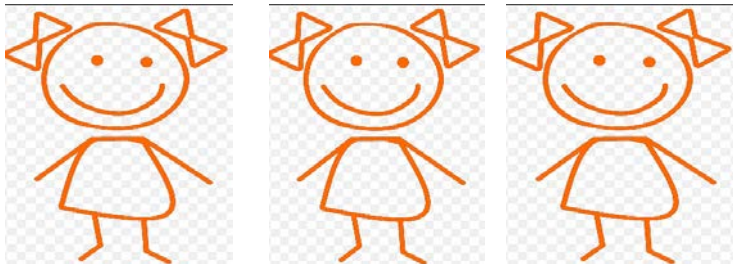
Age-specific number of VTE and Incidence rate (100000 Person-years in siblings)

FH of a sibling with VTE is associated with an especially high risk in young age

Medical condition

Positive Family history - VTE risk

Case: How to handle siblings



Siblings of 14, 17 and 21 years

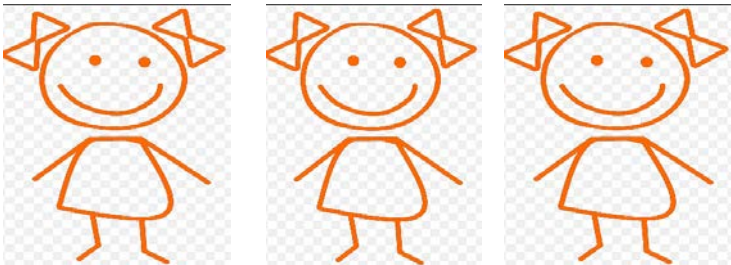
The 17 year old girl experienced a DVT around 8 weeks after CHC start

Medical condition

Positive Family history - VTE risk

Case: How to handle siblings

Risk balancing in women with positive FH



Siblings of 14,17 and 21 years

No genetic mutations were found.

Can she continue with COC?

Can her sister continue with the pill, she is 21 years old and started pill with 18 years?

Can her younger sister, today 14 years old use CHCs in the future?

Medical condition

Positive Family history - VTE risk

Case: How to handle siblings



Risk balancing in women with positive FH

What has to be considered ?

- **17 year old girl after DVT**
- DVT event in 17 year old newstarter occurred typically in the early phase of use
- No thrombophilia
- No other cases of VTE in first or second degree relatives
- 17 year old cannot use CHC after having had DVT (WHO 4)

Medical condition

Positive Family history - VTE risk

Case: How to handle siblings



- **VTE risk in 21 year old sister**
 - With a 1 first degree relative < 50 years the DVT risk is 15-fold.
 - She already used the pill without problems, which decreases the probability that she suffers from a genetic predisposition in the family
 - She might continue with the CHC, but changing to a POC or IUD would reduce her nevertheless elevated DVT risk
- **For the sister aged 14**
 - She will be a newstarter
 - Her VTE risk with CHC use and a 1. first degree relative < 50 y is 15 fold !
 - Do not start with CHC recommend POC or IUD.