The ‘pill’: balancing risks

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The ‘Pill’ Oral Combined Hormonal Contraceptive pill

- What is the pill ?
- Safe prescribing
- VTE risk
- Health benefits
- Choice contraception

What is the pill?

Estrogen & progestogen

- **Estrogen:**

  Ethinyl estradiol (20-30mcg)

  Estradiol valerate

  17 B estradiol

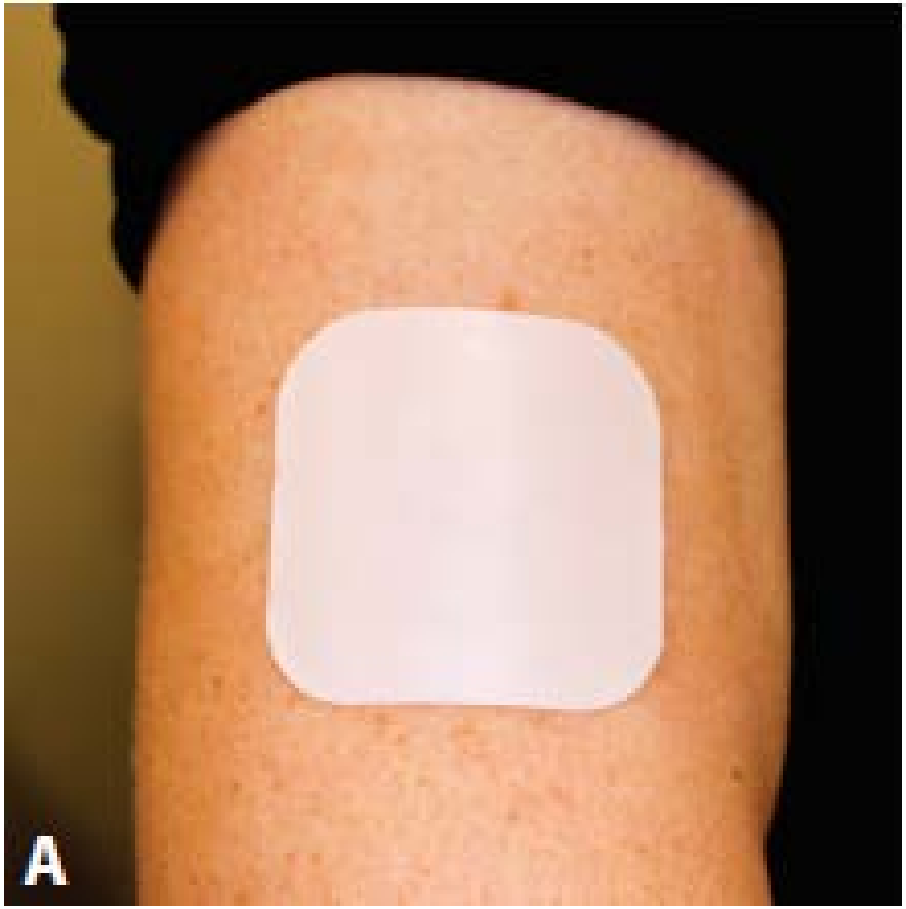
- **Progestogen:** (2nd 3rd & 4th generation)

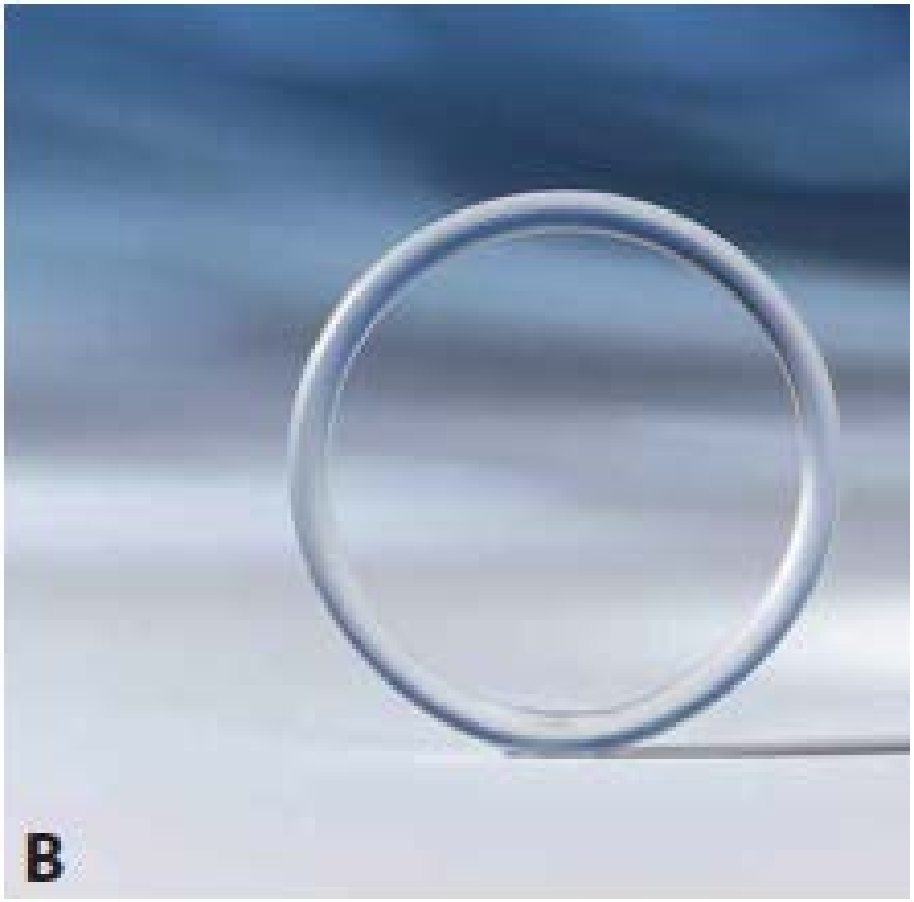
  Levonorgestrel
  Norethisterone

  Gestodene, desogestrel

  Drospirenone, dienogest

CHC patch & CHC vaginal ring





Safe prescribing refer to UKMEC

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UKMEC	Definition of category
1	Condition where there is **no restriction** for use of the contraceptive method
2	Condition where **advantages of using the method generally outweigh the theoretical or proven risks**
3	A condition where the **theoretical or proven risks generally outweigh the advantages of using the method**. Provision of a method requires **expert clinical judgement** and/or referral to a specialist contraceptive provider, since use of the method is not usually recommended unless other more appropriate methods are not available or not acceptable
4	A condition which represents an **unacceptable health risk** if the contraceptive method is used

UKMEC SUMMARY TABLE HORMONAL AND INTRAUTERINE CONTRACEPTION

Cu-IUD = Copper-bearing intrauterine device; LNG-IUS = Levonorgestrel-releasing intrauterine system; IMP = Progestogen-only implant; DMPA = Progestogen-only injectable: depot medroxyprogesterone acetate; POP = Progestogen-only pill; CHC = Combined hormonal contraception

CONDITION	Cu-IUD	LNG-IUS	IMP	DMPA	POP	CHC
	I = Initiation, C = Continuation					
PERSONAL CHARACTERISTICS AND REPRODUCTIVE HISTORY						
Pregnancy	NA	NA	NA	NA	NA	NA
Age	Menarche to <20=2, ≥20=1	Menarche to <20=2, ≥20=1	After menarche =1	Menarche to <18=2, 18-45=1, >45=2	After menarche =1	Menarche to <40=1, ≥40=2
Parity						
a) Nulliparous	1	1	1	1	1	1
b) Parous	1	1	1	1	1	1
Breastfeeding						
a) 0 to <6 weeks postpartum	See below		1	2	1	4
b) ≥6 weeks to <6 months (primarily breastfeeding)			1	1	1	2
c) ≥6 months postpartum			1	1	1	1
Postpartum (in non-breastfeeding women)						
a) 0 to <3 weeks						
(i) With other risk factors for VTE	See below		1	2	1	4
(ii) Without other risk factors			1	2	1	3
b) 3 to <6 weeks						
(i) With other risk factors for VTE	See below		1	2	1	3
(ii) Without other risk factors			1	1	1	2
c) ≥6 weeks			1	1	1	1

UK MEC 4 and CHC

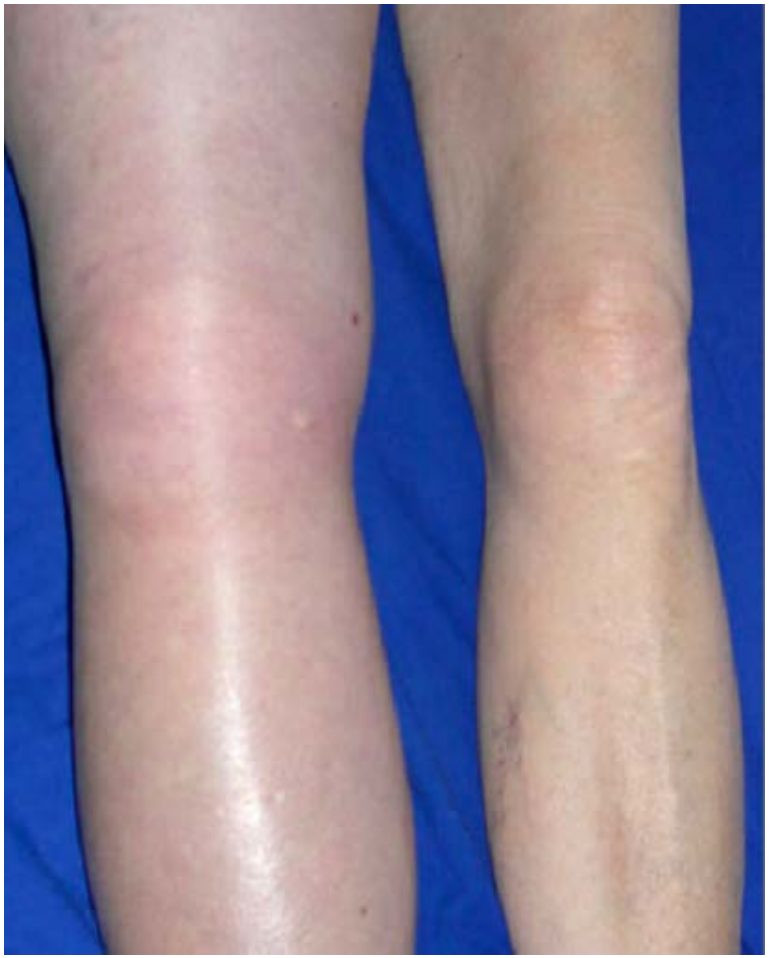
Blood pressure >160/100 mmHg
Hypertension with vascular disease
Deep vein thrombosis, current or past
Myocardial infarction, current or past
Cerebrovascular accident, current or past
Multiple serious risk factors for cardiovascular disease
Known thrombogenic mutations
Current breast cancer

VTE

- CHC increases risk DVT
- VTE rare, but potential life threatening
- CHC use common; millions globally
- *True* incidence VTE in non-users unclear
- Reported incidence non-users varies 0.5-1 vs. 5-10 per 10 000

  Heineman & Dinger 2007
- DVT can be asymptomatic or go undetected

  Scurr et al Lancet 2001



Controversial issues remain:

- Certain: **CHC use commonly identified risk factor in women with VTE**

- What is the attributable risk?
- Dose of estrogen (< 50mcg) influence risk?
- Type of estrogen?
- Type of progestogen influence risk?
- Delivery system influence risk?

Why difficult to resolve ?

- DVT rare event requires large numbers
- Databases or registries, retrospective
- Confounding factors
- BMI , family history VTE
- Active surveillance prospective studies

‘Garbage in , Garbage out’ (Grimes D)

Bias and confounding

- User may be more likely to present/ investigated/ diagnosed
- Newer formulations considered safer (prescribing bias)
- New vs established users (risk greatest commencing) *Dinger et al Contra 2007*
- Switching preparations and other methods
- Attrition bias – continue CHC with less side effects and get DVT
- Misclassification (diagnostic verification)

The two camps : Retrospective vs. Prospective

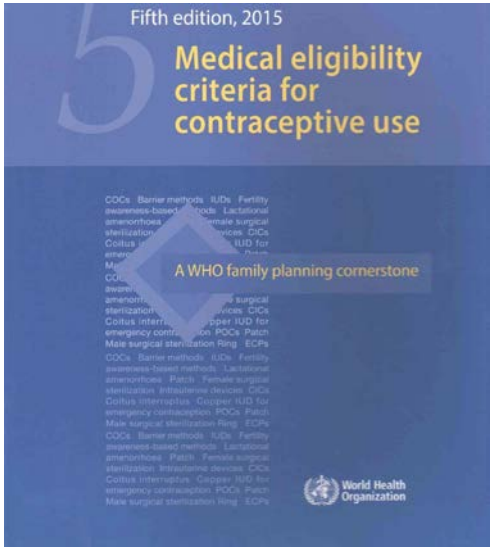
RR (95% CI)	DRSP/EE (oral)	ETN/EE (ring)
FDA-CDC Cohort 2012 (US)	1.74 (1.42-2.14)	1.56 (1.02-2.37)
Lidegaard cohort 2012 (Denmark)		1.9* (1.3-2.7)
Dinger et al 2013, 2014 (EU)	0.8 * (0.4-1.5)	0.8** (0.5-1.6)

* vs LNG/EE
** vs other contraceptives

- Retrospective cohort unable to adjust for confounders (BMI, FHx VTE)
- Prospective closer FU over time, validate diagnoses, ? Conclusions more valid

WHO MEC 2015

- All COC associated with increased risk VTE
- Studies have found differences in risk associated with COC containing different
- Current evidence suggests COC containing LNG, NET and norgestimate are associated with the lowest risk
- **The absolute differences, however, are very small**



VTE risk

Risk of VTE in users and non-users of CHC

- 5 per 10,000 in non-pregnant non users.
- 10 per 10,0000 COCP users.
- 29–400 per 10,0000 in pregnant/postpartum.

www,fsrh.org.uk

CHC Benefits

- Treat heavy periods
- Treat irregular periods
- Manage endometriosis, fibroids
- Treat acne
- Treat hirsuitism
- Manage PMS
- Protection ovarian cancer
- Protection endometrial cancer
- Protection colon cancer

% women pregnant within 1 yr

Method	Typical use %	Perfect use %
No method	85	85
Fertility awareness-based methods	24	0.4–0.5
Male condom	18	2
Female diaphragm	12	6
Progestogen-only pill	9	0.3
Combined hormonal contraception*	9	0.3
Progestogen-only injectable	6	0.2
Cu-IUD	0.8	0.6
LNG-IUS	0.2	0.2
Progestogen-only implant	0.05	0.05
Female sterilization	0.5	0.5
Vasectomy	0.15	0.1

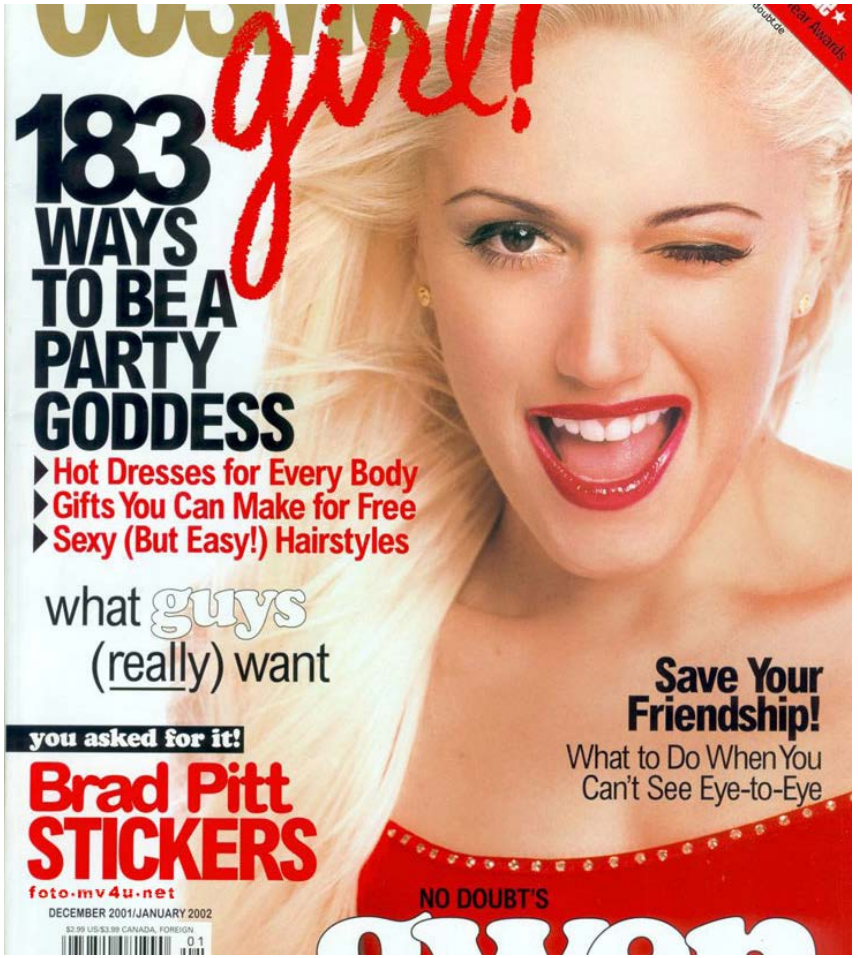
Choosing contraception

- Women should be informed about the effectiveness of contraceptive methods in particular the superior effectiveness of long acting reversible methods

Contraceptive method choice

Determinants of contraceptive method acceptability

- Personal characteristics (e.g. age).
- Fertility intentions.
- Perceptions of effectiveness.
- Perceptions of safety.
- Fear of side-effects.
- Familiarity.
- Experience of others.
- Ease of use and of access.
- Need to see a health professional.
- Intrusiveness.
- Non-contraceptive benefits.



Conclusion

- CHC increases risk VTE
- VTE risk greatest pregnancy/ postpartum
- Most effective contraceptive methods prevent most unintended pregnancies
- Intrauterine and implants most effective & are estrogen free
- Women may choose CHC (if medically eligible)
- Compliance greatest if user satisfied
- Even if it is CHC with a progestogen that may/may not slight increase absolute risk vs. others