Contraception in Sickle Cell Disease

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- Background
- Standards
- Evidence
- Contraception choices and effectiveness
- Recommendations

Background

- Adverse maternal and perinatal outcomes associated with SCD
- Essential that pregnancies are planned & unintended pregnancies are prevented
- Effective contraception decreases health risks

Unmet need for contraception

- SCD cohort : High rates of unintended pregnancy : 64% in 1993, 53% in 2010 (Eissa AA, Tuck et al.,2013)
- General population: 1in 6 pregnancies unplanned, 2 in 6 ambivalent and 3 in 6 planned : NATSAL- 3 survey

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- **Reasons:**

➢ Access barriers

➢ Confusion about safety of contraceptive options

➢ Patient preferences/ myths/side-effects

(O'Brien *et al.*, 2011; Whaley *et al.*, 2015, Haddad *et al.*, 2012; Smith-Whitley, 2014)

Standards

- Each woman, man or couple affected by SCD should be encouraged to have a reproductive life plan

- All women of childbearing age and all men with SCD should receive contraceptive counselling at least as part of annual review

Background evidence

- Limited number of good quality studies

- **Cochrane review** (Gomez M et al.2007) :

1 RCT (De Ceaulaer et al. 1982) DMPA v/s placebo in 25 patients, crossover design : non-significant trend towards reduced painful sickle episodes (OR 0.23;CI 0.05-1.02)

Background evidence

Systematic review (Haddad et al. 2012): 9 studies

Progestogen-only and combined hormonal contraceptives did not increase sickle cell crises & no increased risk of adverse clinical events.

Background evidence

Systematic review (Legardy & Curtis, 2006):

Progestogen-only contraceptives in SCD – no adverse clinical events, haematological or biochemical changes

Background evidence

- Other studies (de Abood et al. 1997, De Ceulaer et al 1982) :

Progestogen-only contraceptive users had less frequent & severe painful crises & improvement in biochemical & haematological parameters

Background evidence

- Lack of evidence on the risk of VTE among combined hormonal users with SCD
- No change in markers of platelet activation, thrombin generation & fibrinolysis in COC users with SCD (Yoong et al.2003)
- E & P did not reduce red cell deformability in vitro/in vivo (Yoong et al 1998, 1999)

Contraceptive choices

fpa
talking sense about sex

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Methods with no user failure – they do not depend on you remembering to take or use them

	Contraceptive injection	Implant	Intrauterine system (IUS)	Intrauterine device (IUD)	Female and male sterilisation
What is it?	• An injection of progestogen.	• A small, flexible rod put under the skin of the upper arm releases progestogen.	• A small, T-shaped, progestogen-releasing, plastic device is put into the uterus.	• A small plastic and copper device is put into the uterus.	• The fallopian tubes in women or the tubes carrying sperm in men (vas deferens) are cut, sealed or blocked.
Effectiveness	• Perfect use: over 99%. • Typical use: around 94%.	• Perfect use: over 99%. • Typical use: over 99%.	• Perfect use: over 99%. • Typical use: over 99%.	• Perfect use: over 99%. • Typical use: over 99%.	• Failure rate is about 1 in 200 or 1 in 500 for females (depending on method), and 1 in 2,000 for males.
Advantage	• Lasts for eight or 13 weeks – you don't have to think about contraception during this time.	• Works for three years but can be taken out sooner.	• Works for 3–5 years but can be taken out sooner. Periods often become lighter, shorter and less painful.	• Can stay in 5–10 years depending on type but can be taken out sooner.	• Sterilisation is permanent with no long or short-term serious side effects.
Disadvantage	• Can't be removed from the body so side effects may continue while it works and for some time afterwards.	• It requires a small procedure to fit and remove it.	• Irregular bleeding or spotting is common in the first six months.	• Periods may be heavier, longer or more painful.	• Should not be chosen if in any doubt about having children in the future.

Methods with user failure – you have to use and think about them regularly or each time you have sex

	Contraceptive patch	Contraceptive vaginal ring	Combined pill (COC)	Progestogen-only pill (POP)	Male condom	Female condom	Diaphragm/cap with spermicide	Natural family planning
What is it?	• A small patch stuck to the skin releases estrogen and progestogen.	• A small, flexible, plastic ring put into the vagina releases estrogen and progestogen.	• A pill containing estrogen and progestogen, taken orally.	• A pill containing progestogen, taken orally.	• A very thin latex (rubber) polyurethane (plastic) or synthetic rubber sheath, put over the erect penis.	• Soft, thin polyurethane sheath that loosely lines the vagina and covers the area just outside.	• A flexible latex (rubber) or silicone device, used with spermicide, is put into the vagina to cover the cervix.	• Fertile and infertile times of the menstrual cycle are identified by noting different fertility indicators.

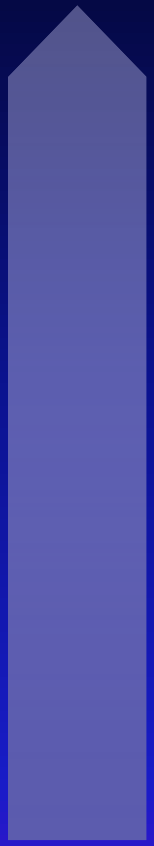
PERFECT USE MEANS USING THE METHOD CORRECTLY EVERY TIME. TYPICAL USE IS WHEN YOU DON'T ALWAYS USE THE METHOD CORRECTLY.

Effectiveness	• Perfect use: over 99%. • Typical use: around 91%.	• Perfect use: over 99%. • Typical use: around 91%.	• Perfect use: over 99%. • Typical use: around 91%.	• Perfect use: over 99%. • Typical use: around 91%.	• Perfect use: 98%. • Typical use: around 82%.	• Perfect use: 95%. • Typical use: around 79%.	• Perfect use: 92–96%. • Typical use: 71–88%.	• Perfect use: up to 99%. • Typical use: around 76%.
Advantage	• Can make bleeds regular, lighter and less painful.	• One ring stays in for three weeks – you don't have to think about contraception every day.	• Often reduces bleeding and period pain, and may help with premenstrual symptoms.	• Can be used by women who smoke and are over 35, or those who are breastfeeding.	**Condoms are the best way to help protect yourself against sexually transmitted infections.**		• Can be put in any time before sex.	• No physical side-effects, and can be used to plan as well as prevent pregnancy.
Disadvantage	• May be seen and can cause skin irritation.	• You must be comfortable with inserting and removing it.	• Missing pills, vomiting or severe diarrhoea can make it less effective.	• Late pills, vomiting or severe diarrhoea can make it less effective.	• May slip off or split if not used correctly or if wrong size or shape.	• Not as widely available as male condoms.	• You need to use the right size. If you have sex again extra spermicide is needed.	• Need to avoid sex or use a condom at fertile times of the cycle.

WHO Decision Aid on Contraceptive Effectiveness

Most Effective

≤1 pregnancy per 100 women in 1 year



~30 pregnancies per 100 women in 1 year

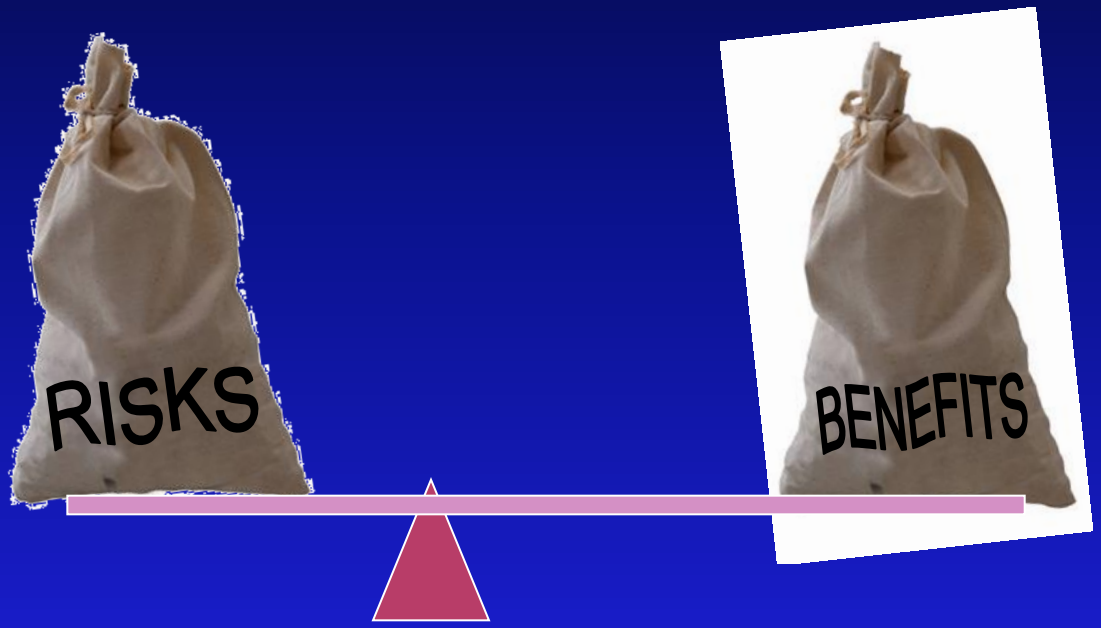
Least Effective

- Implants, Female Sterilization, Vasectomy, IUD/IU
- Injectables
- Pills, Patch, Vaginal Ring
- Lactational Amenorrhea Method
- Male condoms
- Diaphragm
- Cervical Cap, Sponge, Female Condoms
- Withdrawal, Fertility Awareness-based
- Spermicides

Adapted from World Health Organization. 2006.

UK Medical Eligibility Criteria for Contraceptive Use 2016

https://www.fsrh.org/standards-and-guidance/external/ukmec-2016-digital-version/



UK Medical Eligibility Criteria

- **Most** contraceptive users medically fit & can safely use any available contraceptive method
- **Some** conditions may pose risks
- Knowledge of these will remove unnecessary medical barriers
- Defines conditions and allocates medical eligibility categories 1- 4

UKMEC Categories

- UKMEC 1 — No restriction
- UKMEC 2 — Advantages generally outweigh risks
- UKMEC 3 — Theoretical/proven risks usually outweigh advantages
- UKMEC 4 — Unacceptable health risk

UKMEC in Sickle cell disease

Progestogen-only contraception: UKMEC 1

- Subdermal Implant (Nexplanon®) : 3 years
- Injectable: DMPA IM or subcut (Sayana-Press®) : 13 week intervals
- LNG-IUS (eg. Jaydess®, Mirena®, Kyleena®), : 3 - 5 years
- P-only pills (eg. Cerazette®) : 1 pill daily

Advantages:

- Lower risk of VTE compared to combined hormonal contraception
- Possible reduction in acute painful events

Side-effects : unpredictable vaginal bleeding

Combined Hormonal contraception Estrogen+Progestogen

UKMEC 2 for SCD

- COC pill (eg.Microgynon®) : taken every day with or without pill free break
- Combined transdermal patches (Evra®) - changed every week
- Combined vaginal ring (NuvaRing®) - changed every 21 days

Combined hormonal contraception(CHC)

- **Benefits**: predictable bleeds, ↓menstrual flow & pain
- **Risks**: ↑ risk of VTE (RR of about 2 compared to non-users); Absolute risk 9-10 events/10,000 users/year
- Differences in risk of VTE with COCs containing different progestogens
- COCs with levonorgestrel, norethisterone and norgestimate have the lowest risk

Other co-existing medical conditions must be considered – eg. h/o stroke or other cardiovascular conditions will contraindicate CHC

Copper IUD

UKMEC 2 for SCD

- Limited evidence from studies in SCD
- No theoretical safety concerns
- Side-effects: ↑ menstrual blood loss

- IUS may be preferable due to ↓menstrual loss

Emergency contraception

Preventing pregnancy after unprotected sexual intercourse (UPSI)

- Copper IUD (most effective): (within 120 hrs of UPSI or 5 days of expected ovulation)
- Levonorgestrel 1.5 mg (Levonelle®) - (within 72 hrs of UPSI)
- Ulipristal acetate 30 mg (ellaOne®)(within 120 hours of UPSI)

Information to give to women

Counselling is KEY

- Efficacy of method
- How the method works
- Duration of use
- Safety
- Risk and possible side effects
- Non-contraceptive benefits
- Any potential drug interactions
- The procedures for initiation and discontinuation
- When to seek help

LARC methods

- **More effective than pills (NICE, 2005)**

- Administered less than once per cycle or month
- Three progestogen-only methods
  - intrauterine system
  - injectables
  - implants.
- The copper intrauterine device (non-hormonal)

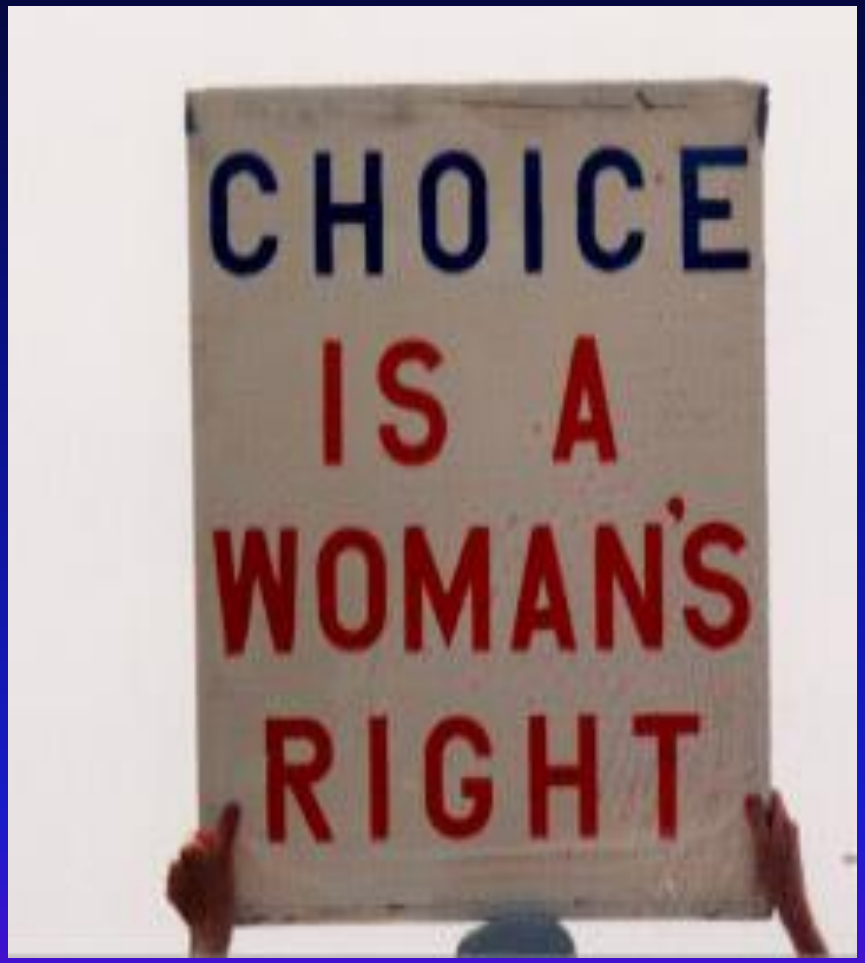

Mirena
Levonorgestrel 20µg/24h
SCHERING


Depo Provera


1 applicator containing 1 subdermal implant
NDC 0052-0274-01
Nexplanon®
(etonogestrel implant) 68 mg
Radiopaque
Subdermal Use Only
Rx only
This product is intended to prevent pregnancy. It does not protect against HIV infection (AIDS) and other sexually transmitted diseases.

Why does LARC matter?

- Very effective
- Safe
- Reversible
- Less user dependant
- Health benefits
- Suitable for most women



Recommendations - Summary

- No restrictions for use of Progestogen-only contraceptives(POP, injectables, implants, IUS) and barrier methods in SCD

- Advantages of use of CHC(pills, patches & rings) and IUDs outweigh risks

Recommendations - Summary

- Lack of evidence on whether increased VTE risk with CHC increases further in SCD

- Other co-morbidities may contraindicate use of a contraceptive method – Refer to UKMEC guidance

Recommendations - Summary

- LARC methods to be recommended as highly reliable and effective compared to pills and barrier methods
- Access to specialist contraceptive advice should be available

Recommendations - Summary

- Potential teratogenic effect of Hydroxycarbamide:

➢ Sexually active couples should use contraception if one person is using Hydroxycarbamide

➢ Hydroxycarbamide should be stopped prior to conception

https://www.fpa.org.uk/resources/leaflet-and-booklet-downloads

Thank you