

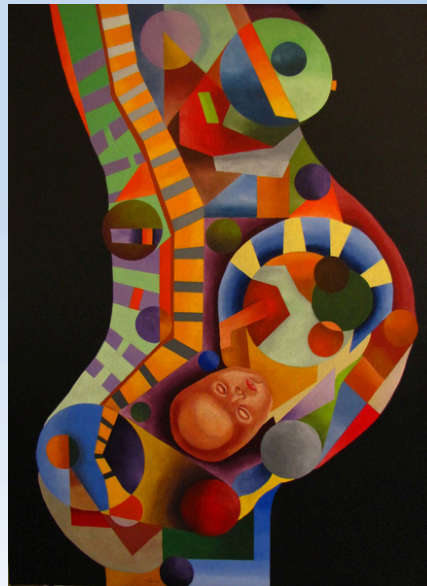
Let's Talk About Sex (No Baby)

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Overview

1. Let's really talk about sex (not just pregnancy)
2. Fertility and contraception
3. Sexually transmitted infection
4. HPV

Let's attempt to talk about sex

RENA

Sexual Contraception have C Patient Inf

Kidney Care

500 x 350

Fresenius Medical Care

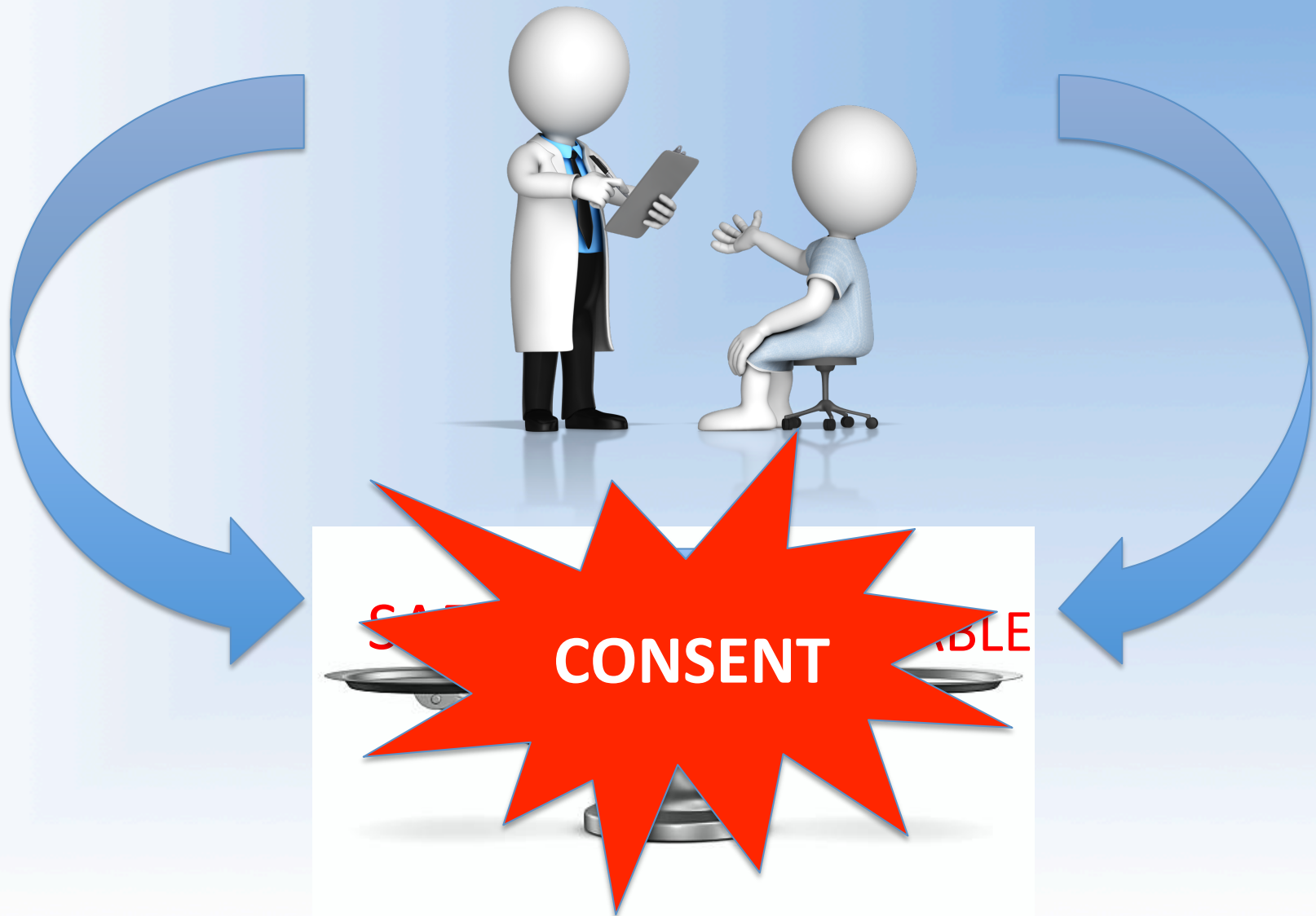
Sex Differences in Chronic Kidney Disease | FMCNA

Let's really talk about sex: context

- Who?
 - Alone or with partner
 - Men, women or both
- What?
 - Kissing/touching: no genitals involved
 - Genital touching (fingering/hand-jobs/masturbation): hand-genital
 - Oral sex: mouth-genital contact
 - Vaginal: vagina-genital contact
 - Anal: anus-genital contact
 - Virtual: sexually explicit communication via computer



Let's really talk about sex: aims

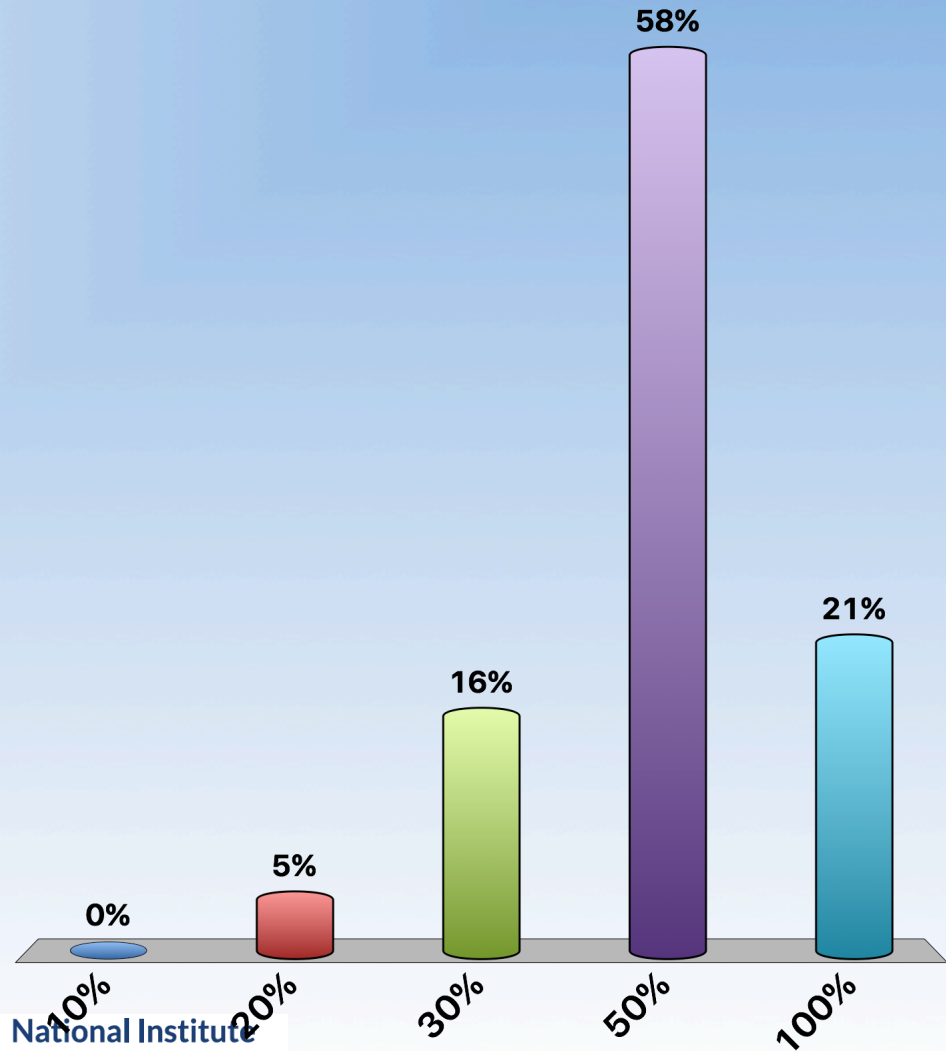


(Young) People

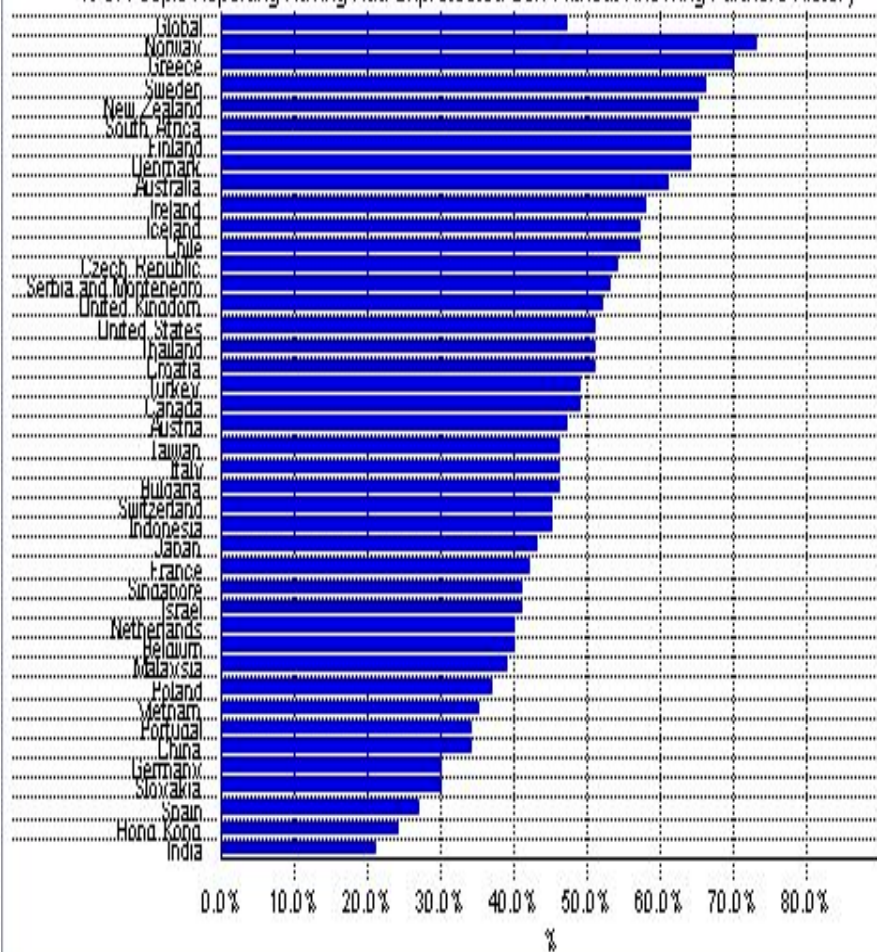
- Changing social norms
- More able to explore sexuality
- Internet exposure
- Risk of overexposed and underprepared
- Responsibility to provide reliable information
 - Communication
 - Consent
 - Intimacy
- Be prepared to ask and answer questions

What is the probability that the average UK person has had unprotected sex?

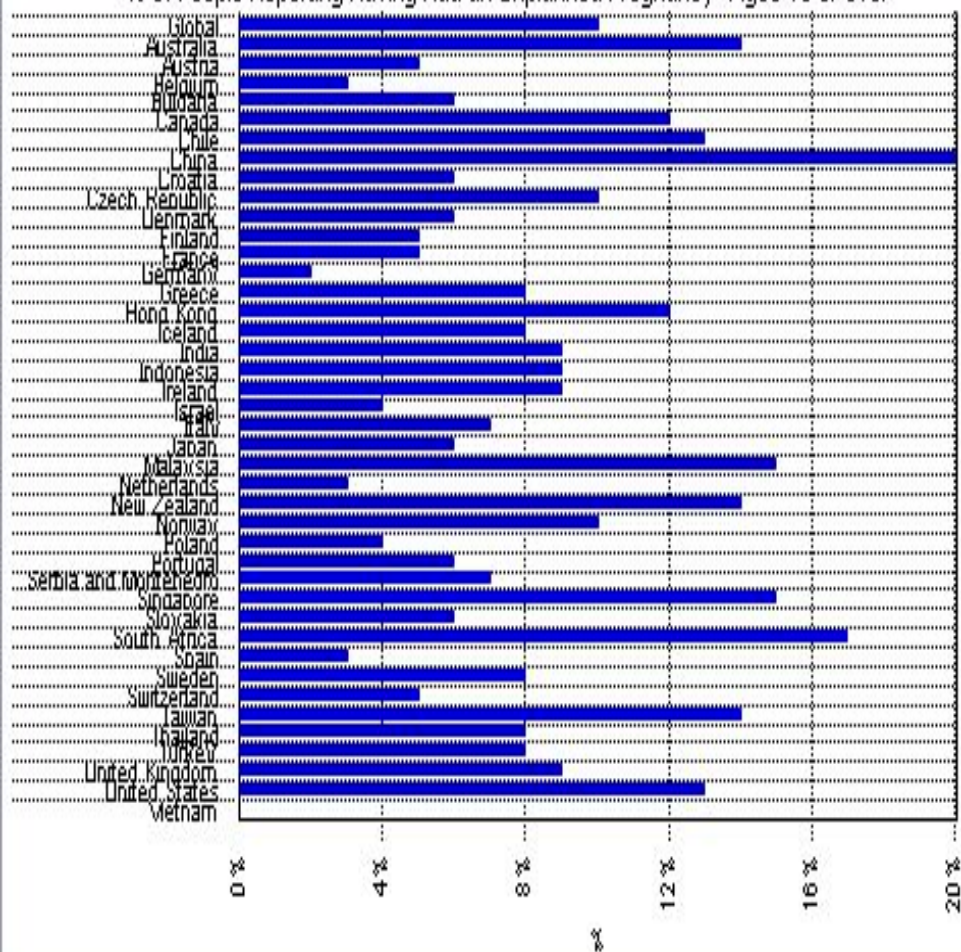
- A. 10%
- B. 20%
- C. 30%
- D. 50%
- E. 100%



% of People Reporting Having Had Unprotected Sex Without Knowing Partners History



% of People Reporting Having Had an Unplanned Pregnancy- Ages 19 or over



2005

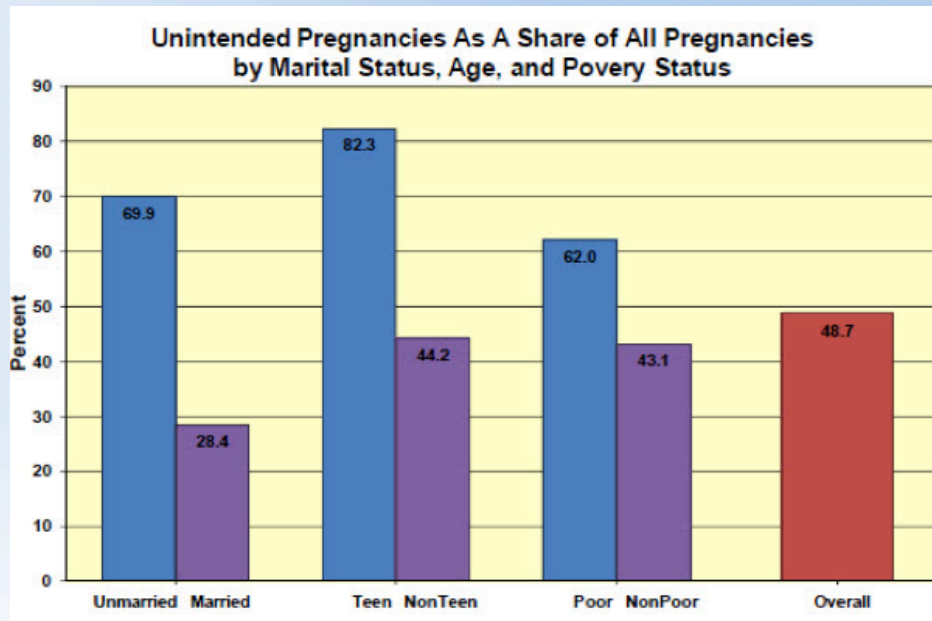
www.data360

2005

www.data360.org

Pregnancy Intention

- 2 children
- = 5 years trying/pregnant
- = 30 years of preventing pregnancy



Contraception and CKD

- Questionnaire from 1997
- 76 women with CKD
- 50% being sexually active
- 36% used contraception
- 13% had discussed sexual health

Contraception and CKD

- Abstract
- Women aged 20-47 with CKD
- 48% discussed contraception
- 45% unaware of pregnancy risks
- 39% unaware taking teratogenic medication
- 29% unplanned pregnancy (population 1 in 6)
- 53% using contraception (30% condoms)

What about transplants?

- 5-12% of transplants in women of child-bearing age
- 12-36,000 transplants in women of childbearing age in UK (20-44)

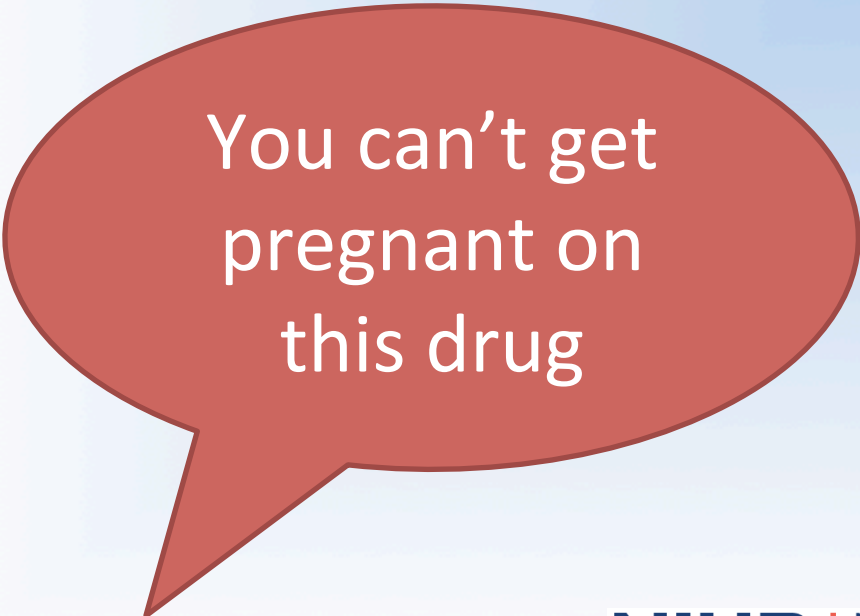
Country	Rate of unplanned pregnancy in transplant patients
UK (Braham <i>et al.</i> 2013)	33%
US (Yildirim <i>et al.</i> 2005)	50%
China (Xu <i>et al.</i> 2011)	15% (34% 2-3 unplanned pregnancies) (56% no contraception)
Brazil (Guazelli <i>et al.</i> 2008)	92.9% of pregnancies unplanned
Iran (Ghazizadeh <i>et al.</i> 2005)	29% (92% coitus interruptus)

What about dialysis?

- Few conversations (Kimmel *et al.* 2003)
- Fertility <10% of population
- Irregular cycles GFR <15ml/min
- Amenorrhoea GFR <5ml/min
- 3.3/1000 patient years
- Home haemodialysis - ? Increased fertility

Teratogens

- MMF
- Induction agents???



You can't get pregnant on this drug



...and I can recommend the following contraception

The reality from other chronic disease?

- Women with chronic disease are just as likely to have an unplanned pregnancy (20%)
- Patients want:
Information on pregnancy and conception²
- But:
Patients do not initiate conversations about reproductive health³
- And:
Documentation is sparse including 1/3 of women on teratogenic medication⁴

1. Mahadevan et al 2007

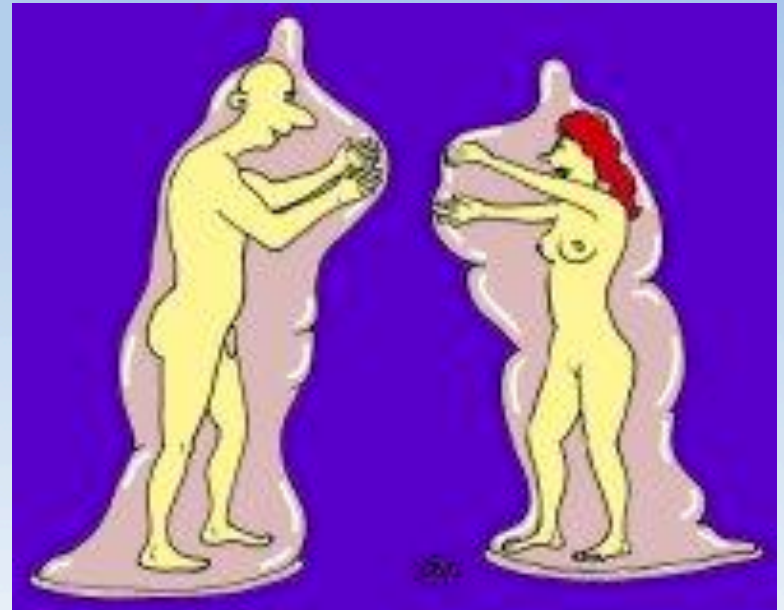
2. Marri et al 2007

3. Toomey 2013

4. Gawron 2014

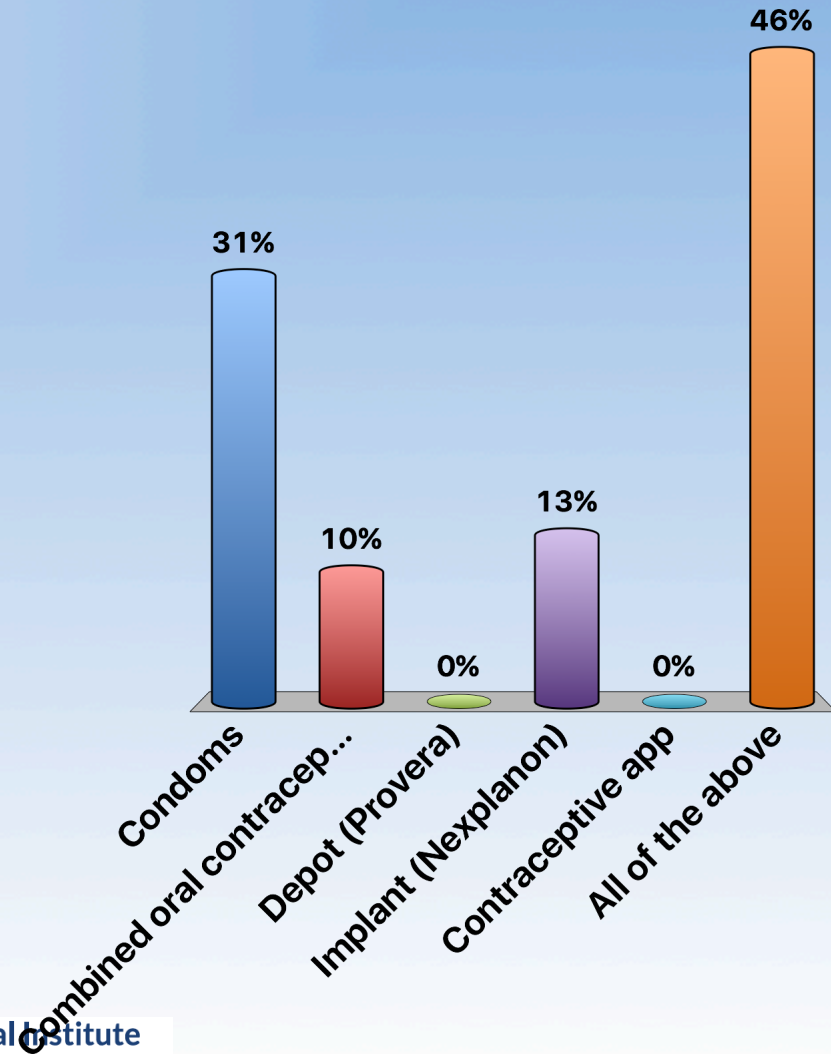


CONTRACEPTION



Which of the following are safe and effective contraception in CKD?

- A. Condoms
- B. Combined oral contraceptive
- C. Depot (Provera)
- D. Implant (Nexplanon)
- E. Contraceptive app
- F. All of the above



Which method?

Method		Failure rate with perfect use (%)	Failure rate typical use (%)
Combined oestrogen	Pill	0.3	9
	Patch	0.3	9
	Ring	0.3	9
Progesterone	Pill	0.3	9
	Depot	0.2	6
	Implant	0.05	0.05
	IUS (Mirena)	0.2	0.2
Copper IUD		0.6	0.8
Barrier	Male condom	2	18
	Female condom	5	21
	Diaphragm	6	12
	Sponge	9-20	12-14
Fertility aware		0.4-5	24
Sterilisation		0.5	0.5
No method		85	85

Is the pill safe?

- Depends which pill - **oestrogen** carries risk

- VTE:

	Risk per 10,000 women years	Risk
Baseline	3.01 ¹	1
Oestrogen contraceptive	6.29 ¹	2
SLE plus LAC		6 ²
Pregnancy	20 ³	6
Nephrotic syndrome		8 ⁴
Post-partum	51 ³	17

Perspective: Remember risk of pregnancy

- BP: Oestradiol less BP effect than ethinyl-estradiol⁵
BP dose adjust BP Rx in 36%⁶

1. Lidegaard 2009
2. Fijnheer 1996
3. Heit 2005
4. Mahmoodi 2008
5. Pietrzak 2007
6. Grandi 2014

Oestrogen and CKD

- Arterial thrombosis:
 - X2 risk of MI and CVA ¹
 - Contraindicated in established vascular disease
 - Excess mortality in women CKD 3+ ²

Cardiovascular disease death (n=179):	N=84	N=34	N=41	N=20	
Age adjusted	1.00	0.80 (0.54 to 1.19)	1.07 (0.74 to 1.56)	1.91 (1.17 to 3.12)	0.03
Multiple adjusted	1.00	0.87 (0.58 to 1.30)	1.18 (0.80 to 1.72)	1.74 (1.05 to 2.89)	0.04

- Cervical cancer
 - X5 in renal transplant
 - Increased HPV viruses in dialysis ³
 - Efficacy of HPV vaccine unknown in RRT

1 Baillergeon 2005

2 Kurth 2009

3 Skov Dalgaard 2013

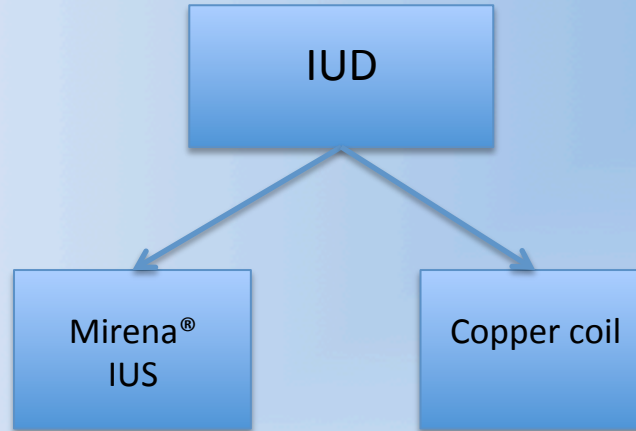
Progesterone

- Safe when oestrogen contra-indicated
- Includes:
 - VTE
 - Thrombophilia
 - Nephrosis
 - BP, smoking, obesity
- Data in lupus: effective, well-tolerated, no flare¹
- Options:
 - Pill
 - Depo-provera[®] (12 weeks)
 - Nexplanon[®] implant (3 years)
 - Mirena[®] IUS (5 years)
 - Emergency contraception

POP

- Thickens cervical mucous, ovulation not always inhibited
- Compliance limited to 3 hour window
- Except desogestrel - 24 hour window:
 - Feanolla®
 - Cerelle®
 - Cerazette®
 - Nacrez®
 - Aizea®

Intrauterine Devices



- Highly effective (0.2%-0.8% failure rate)
- Bleeding differences
- Copper coil – can be used as emergency contraception
- Can be used prior to first pregnancy

Coil and immunosuppression: Efficacy?

- Local inflammatory response in uterus
- ?attenuated by immunosuppression
- 2 failures reported with copper IUD in 1981
- But:
 - Macrophage response most important¹
 - T cell drugs – no effect
 - Steroids: activation of macrophage MIF
- No contemporary failure, none with Mirena

Coil and immunosuppression: Infection?

- Small studies
 - No infection (or pregnancy) in >3 years
- HIV data:
 - No correlation between infection and CD4¹
- Observational evidence – only if existing PID
- Consider screening in immunosuppressed²

¹ Morrison 2001

² Estes and Westhoff 2007

'Renal' Drugs & Contraception

Class of drug	Interaction	Effect on contraception	Recommendation
BP	↑ with oestrogen	None	Monitor BP
Diuretics	Possible ↓ diuresis Possible ↑K with K sparing	None	Monitor fluid balance Monitor K
Statins		Minor ↑ in some oestrogens. Significance unknown	
DM	Possible ↑BM		Monitor blood glucose
Immunesuppressants	Possible ↑ Tac/CsA	Possible ↑ some oestrogens. Significance unknown	Monitor Tac/CsA

— SEXUALLY TRANSMITTED INFECTION —



SEXUALLY TRANSMITTED INFECTION

STI: Some facts

- Anyone who has sexual contact can get an STI
- Any genital contact
- Transmission does not require penetration
- Can occur in mouth and throat with oral sex
- Risk is reduced by barrier methods
- HPV can transmit with skin-skin contact around genital area
- Females less likely to have symptoms

STI and kidney disease

- Risk of STI
 - Assumed higher than population (if immunosuppression)
 - Limited data
 - Lupus – risk of chlamydia suggested¹ and refuted^{2,3}
 - Behavioural recommendations are the same
- Screening:
 - symptoms (self or partner)
 - unprotected intercourse (emergency contraception)
 - change of partners
 - Annually?
 - Anus/mouth if sexual contact

1. Keats et al. Ann Rheum Dis 39:431, 1980

2 CostaPinto et al. Rheum Int 33:631, 2013

3. Santos et al. Lupus 5:e000293, 2018

Anal sex

- 5% females ages 16-17, 18% females aged 18-19¹
- 25% of females forced/coerced: need to discuss consent, challenge coercion²
- Higher risk with (receptive) anal sex
- Receptive (1.38%, 1 in 72) versus penetrative (0.11%, 1 in 909) for HIV³
- Water based lubricant
- Barrier use recommended for all genital contact
- Oral dam if oral/anal contact
- Can use a condom as DIY dam
- Usual advice:
 - AVOID if high dose immunosuppression
 - 6/12 after transplant
 - NO DATA

1. Herbenick et al. J Sex Med, 2010

2. Marston and Lewis, BMJ Open, 2014

3. Tan et al. AIDS 28:1509-1519, 2014.

Treatment of STI in kidney disease

STI	1 st line antibiotic	Consideration in CKD
Gonorrhoea	Ceftriaxone 1g IM	None
Chlamydia/NGU	Doxycycline 100mg bd 7/7 Azithromycin 1g	Avoid erythromycin if CNI
Trichomonas vaginalis	Metronidazole	Additional dose of tinidazole if HD
Bacterial vaginosis	Metronidazole	None
Anogenital herpes	Valaciclovir (Aciclovir) 5/7	Dose reduce of eGFR <30
Syphilis	Benzathine penicillin 2.4 MU IM	None

What **difference** has the HPV vaccine made so far?



10.5 million

doses have been given in the UK since 2008

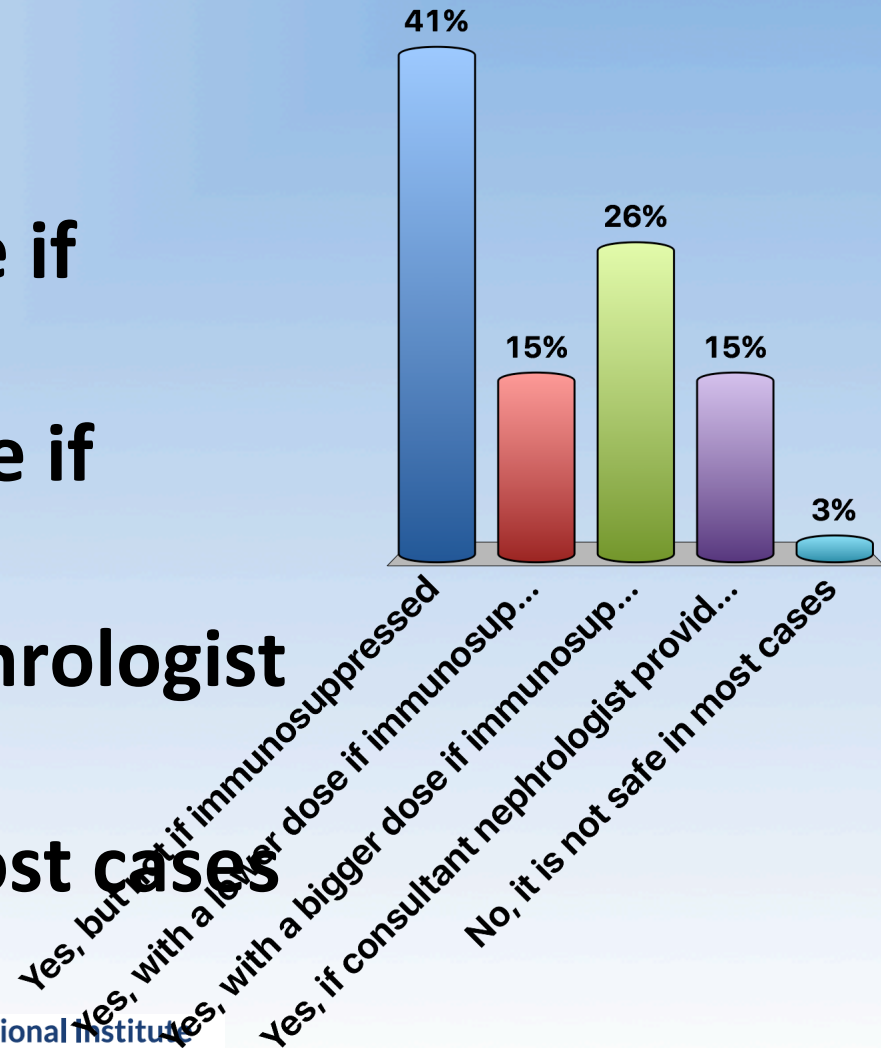


HPV vaccine reduced:

- HPV 16/18 infection by **86%** in young women
- Pre-cancerous cervical disease in women by **71%** (Scotland data)
- Diagnosis of genital warts from 2009-2017 by **90%** in 15-17yr old girls & **70%** in 15-17yr old boys

Can a young person with CKD receive the HPV vaccine?

- A. Yes, but not if immunosuppressed
- B. Yes, with a lower dose if immunosuppressed
- C. Yes, with a bigger dose if immunosuppressed
- D. Yes, if consultant nephrologist provides letter
- E. No, it is not safe in most cases



HPV in CKD

- ↑ risk HPV if immunosuppression
- HIV data:
 - ↑ high-risk DNA¹
 - >1 serotype (35-50%)²
 - ↑ viral load²
 - Persistent high-risk infection^{1,2,3,4}
- Other conditions treated with immunosuppression
 - ↑ rate cervical abnormality⁵

1. Palefsky et al. J. Natl Cancer Inst, 1999

2. Jamieson et al. AJOG, 2002

3. Adieh et al. J Infect Dis, 2001

4. Shrestha et al. BMC Infect Dis, 2010

5. Kim et al. Ann Rheum Dis, 2015

HPV Vaccine in CKD

- Subunit virus like particles, non-replicating
- No infectious component
- ↓ titre antibodies in solid organ transplants¹
- ↓ titre antibodies with MMF²
- 3 doses, not 2:
 - 0, 2 months, 6 months
 - Same as for 15 years +
- Prior to transplant
- Dialysis: 100% response to 3 doses (n=9)
- No recommendation from PHE, NKF (US): 3 doses
- Age cut off:
 - Age 26 for women (up to 45 in US)
 - Age 45 for MSM

1. Kumar et al. AJT, 2015

2. Mok et al Ann Rheum Dis, 2013

3. Nelson et al. CJASN, 2016

Erectile dysfunction CKD

- Erectile dysfunction common $\approx 40\%$ (all ages)
- Multifactorial: variable comorbidity, varies with knowledge of side effects¹
- Associated drugs:
 - Thiazides, aldosterone antagonists, beta-blockers
 - RCT: Less with nebivolol versus other BB^{2,3}
- Neutral/beneficial effect:
 - ACE, ARB, Ca channel blocker
- Sildenafil effective and safe (including dialysis⁴)

1. Silvestri et al. Eur Heart J, 2003

2. Brixius et al. Clin Exp Pharm, 2007

3. Cordero et al. Card Vasc Ther, 2010

4. Seibel et al. JASN, 2002

Summary

- Sexual health is often neglected in CKD
- Aim is for safe (pregnancy/STI) and enjoyable sex
- Evidence that counselling and advice is not optimal
- Progesterone only methods (POP, coil, implant) are safe and effective in preventing pregnancy
- Condoms should be used to prevent STI
- Includes anal sex
- Extra dose of HPV vaccine for immunosuppression and dialysis (aged <15 years)
- PHE: Vaccinate to aged 26, aged 45 in MSM
- Rationale to vaccinate all to age 45 if immunosuppressed

Thank you



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