Women's Health: the FREDA study

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KING'S HEALTH PARTNERS

KING'S College LONDON

The FREDA Study

RaDaR
National Registry of Rare Kidney Diseases

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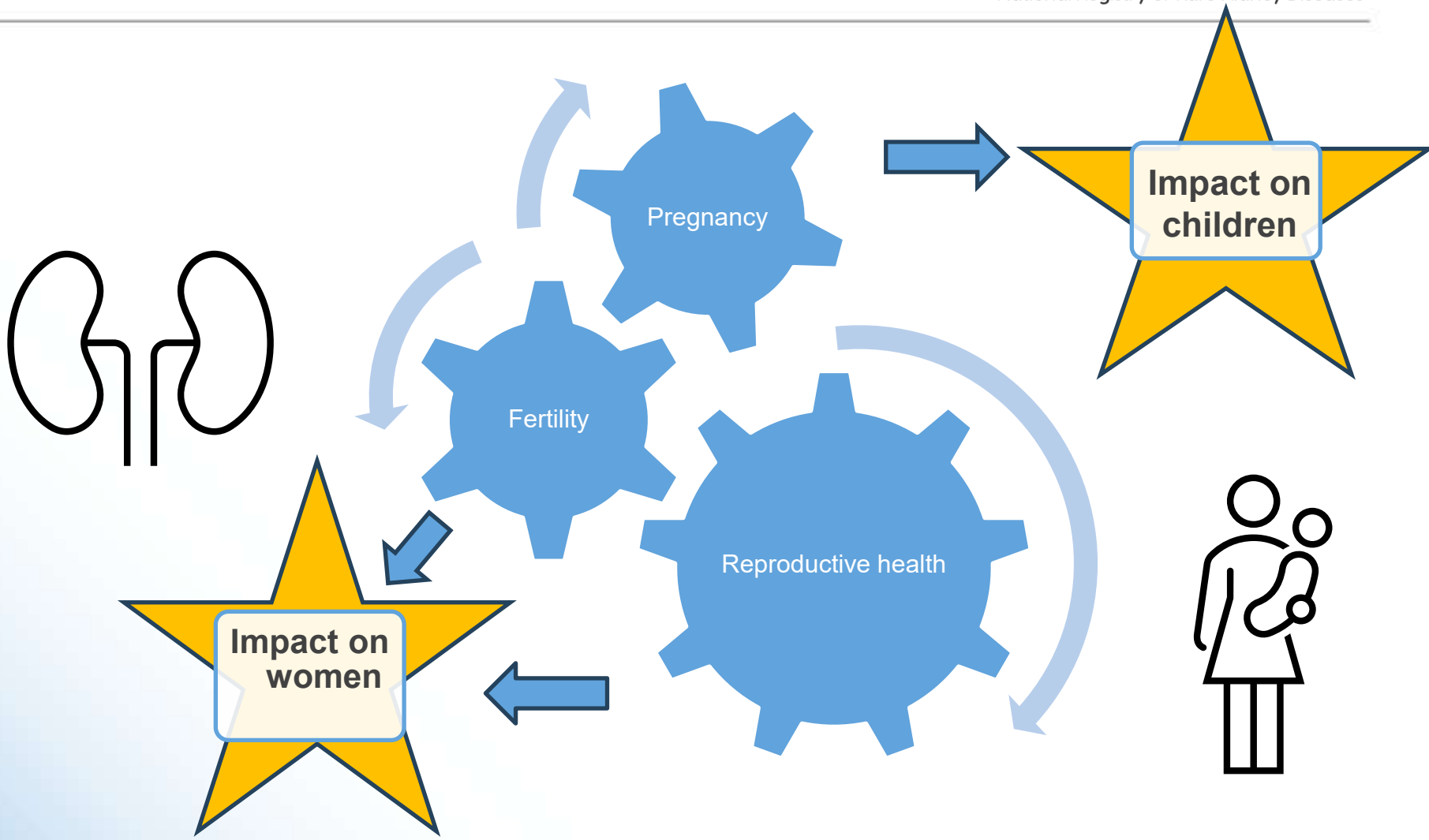


What did we do?

RaDaR
National Registry of Rare Kidney Diseases

Questionnaire study

Members of RaDaR who

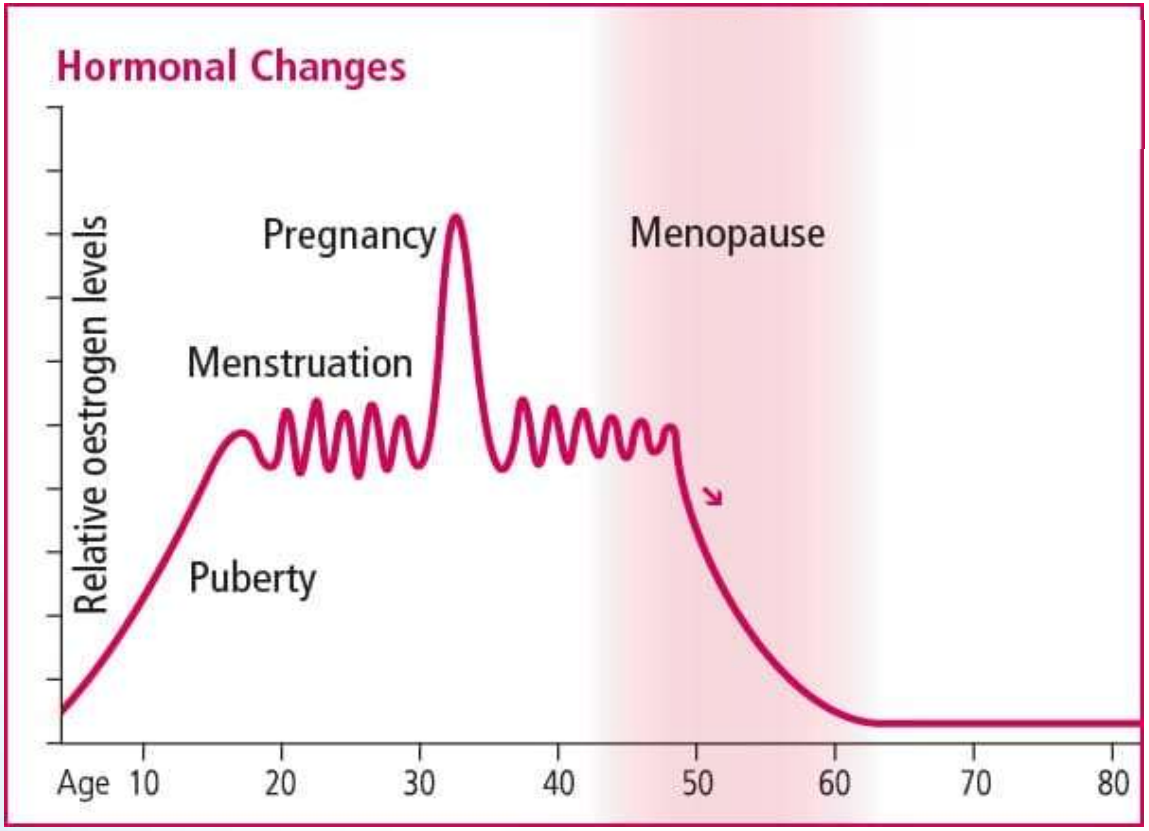
- might have a biological child between the age of 2 and 25, and/or
- may currently have periods or have had periods in the past

Questionnaire covered a wide area of women's health (periods, contraception, menopause) and pregnancies (including children)

FREDA- Over 2000 responses, THANK YOU!

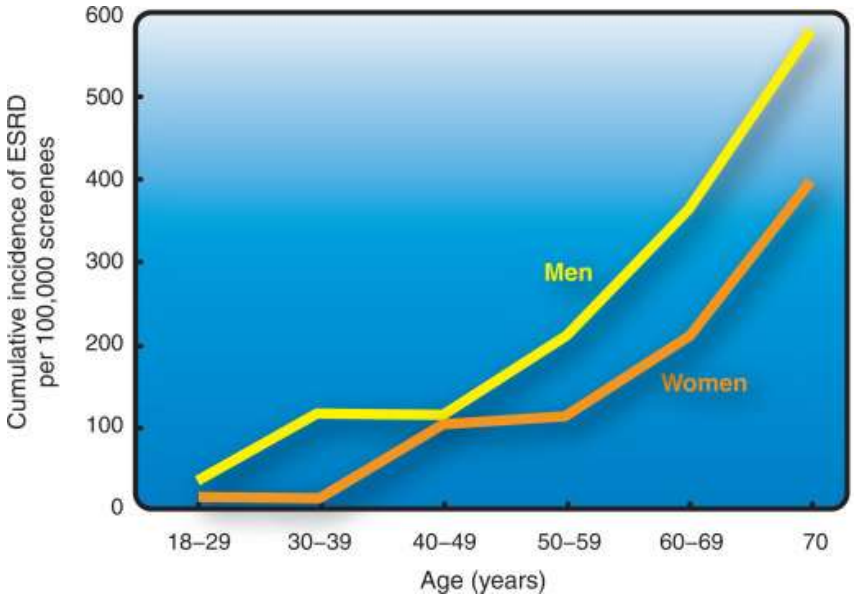
The Menopause

- The absence of periods for 12 months **and** an increase in FSH levels



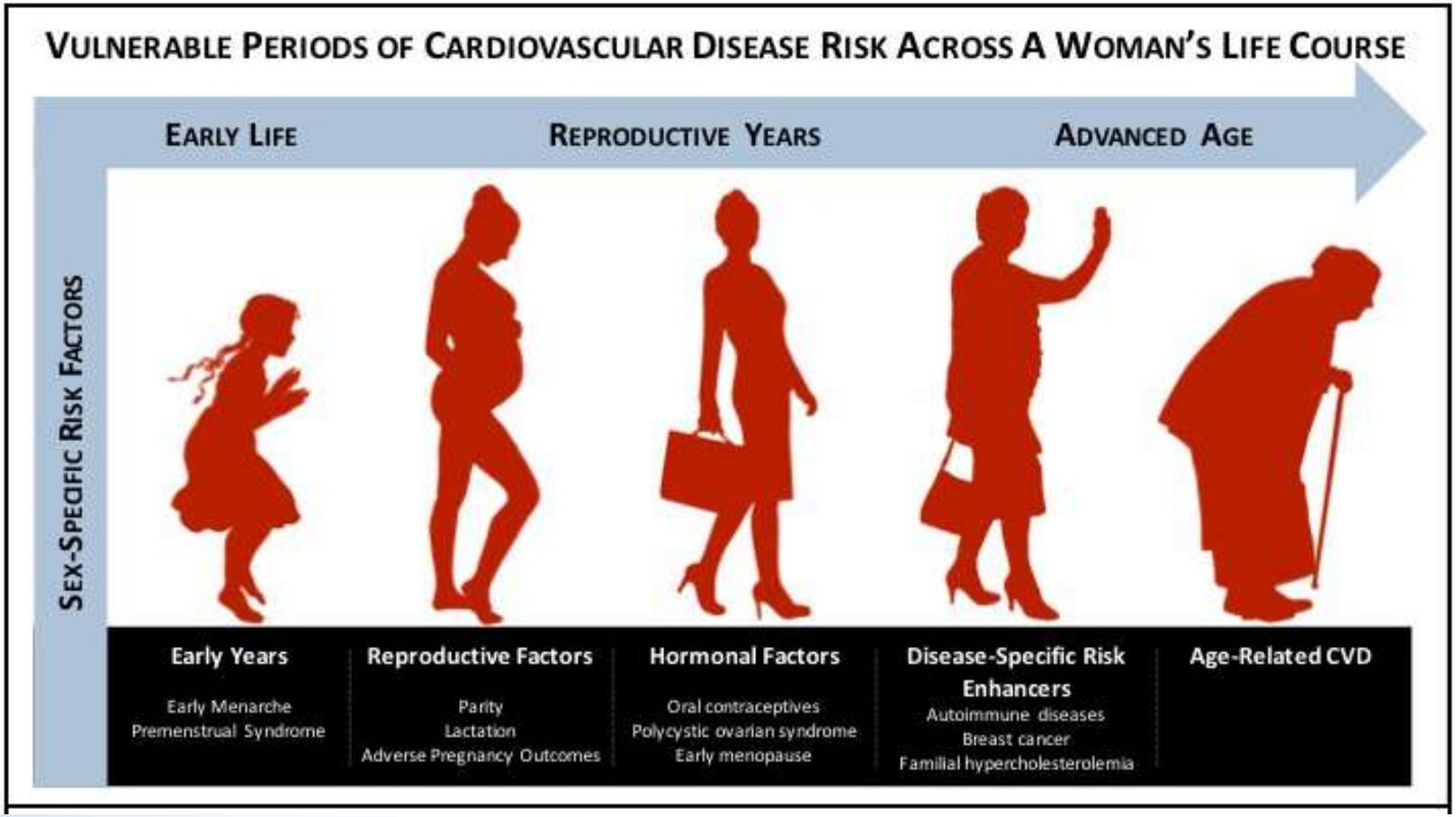
Menopause and risk

- Until menopause, women appear to have slower progression of kidney disease compared to men
- After menopause, this protective factor is lost
- Menopause is also associated with increased risk of cardiovascular disease
  - Insulin sensitivity
  - Fat distribution and
  - Blood pressure



Iseki, Kidney International 2008 74(4), p415

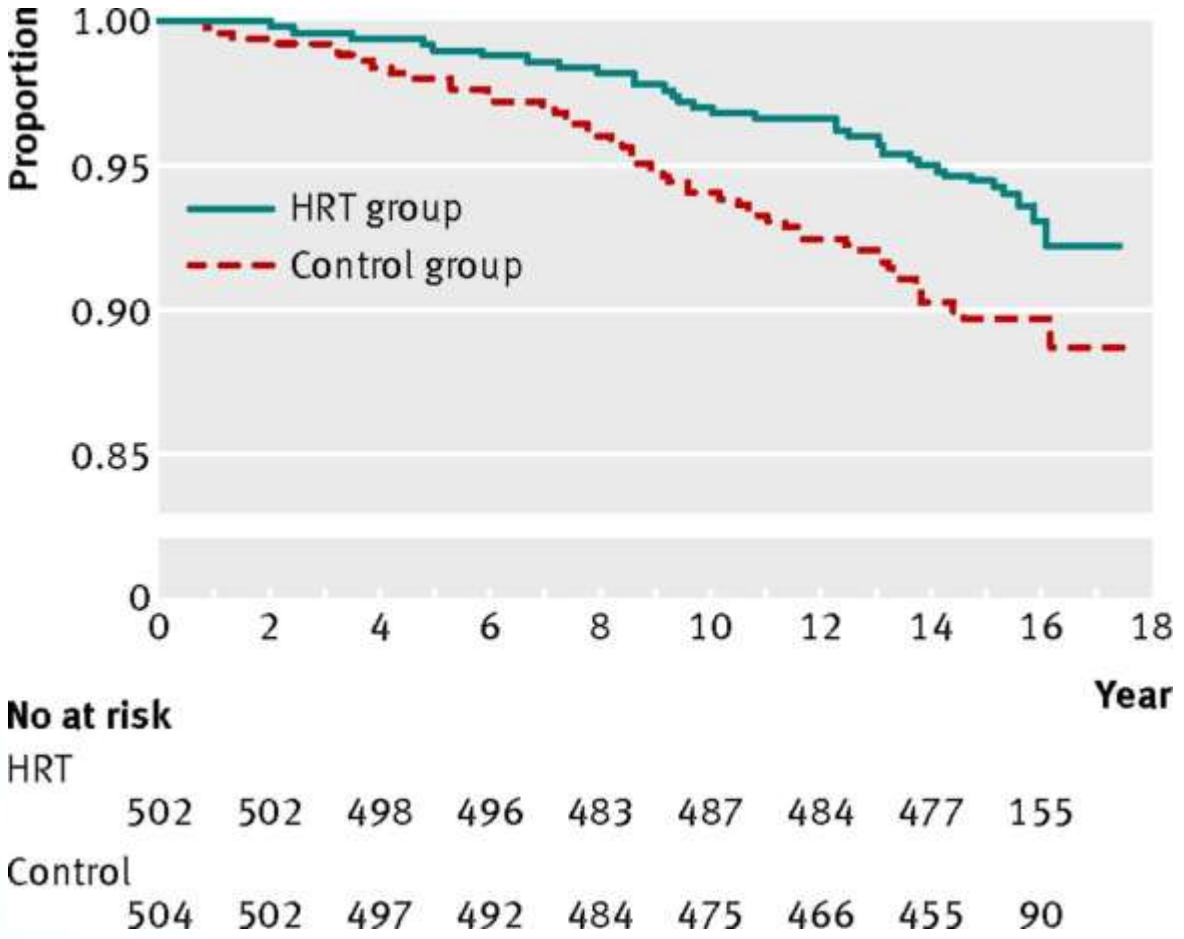
Women with Kidney disease are particularly vulnerable to cardiovascular disease



Mehta et al. Curr Atheroscler Rep. 2020 Jul 16;22(9):46

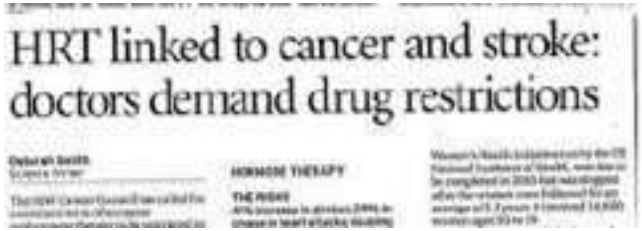
Why does this matter? Is there anything we can do to reduce cardiovascular risk?

Fig 2 Risk of death or admission to hospital due to heart failure or myocardial infarction (primary endpoint) over 16 years of follow-up including 11 years of randomised treatment.



Louise Lind Schierbeck et al. BMJ 2012;345:bmj.e6409

The headlines!



HRT linked to cancer and stroke: doctors demand drug restrictions

HORMONE THERAPY

THE RISKS

HRT pill triples risk of cancer

BBC NEWS

You are in: Health

News Front Page
World
UK
England
N Ireland
Scotland
Wales
Politics
Business
Entertainment
Science/Nature
Technology
Health
Medical notes
Education
Talking Point
Country Profiles
In Depth
Programmes

Wednesday, 10 July, 2002, 11:29 GMT 12:29 UK

HRT linked to breast cancer

The study examined estrogen and progestin

Women who take hormone replacement therapy may be at increased risk of breast cancer, heart disease and stroke, a study suggests.

Expert panel backs HRT cancer warning

Latest guidelines

- Limit HRT therapy to no more than three years
- Review its use in the treatment of osteoporosis
- Remains an appropriate short-term treatment for symptoms of menopause

'There can be risks with stopping medication suddenly without supervision'

The New York Times

New Evidence of Cancer Risk In Hormone Therapy Study

By DENISE GRADY

The New York Times

Hormone Replacement Study A Shock to the Medical System

By GINA KOLATA with MELODY PETERSEN

WALL STREET: LOSING SAVINGS—AND TRUST

IS THIS OUR FIRST ANCESTOR?

TIME

THE TRUTH ABOUT HORMONES

Hormone-replacement therapy is riskier than advertised. What's a woman to do?

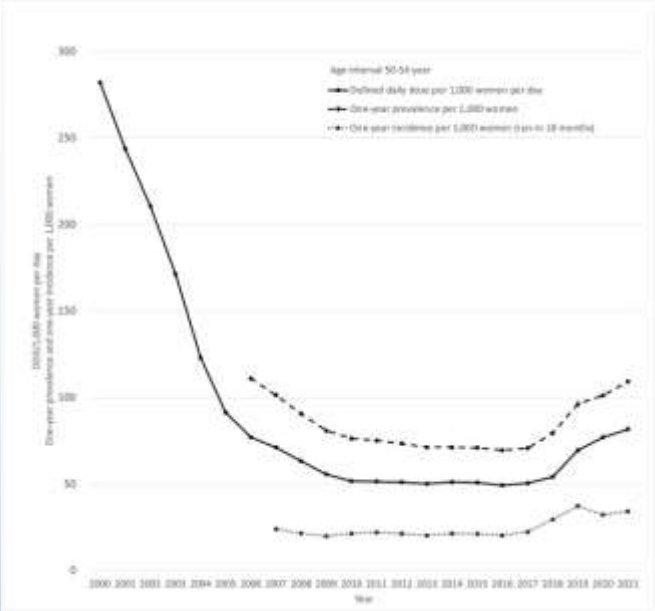
Newsweek

A New Study Raises Fears About the Risks For Millions Of Women Here's What You Should Do

Beyond Hormone Therapy

The Women's Health Initiative Study (2002)

Substantial increased risk of CHD and breast cancer



BUT…

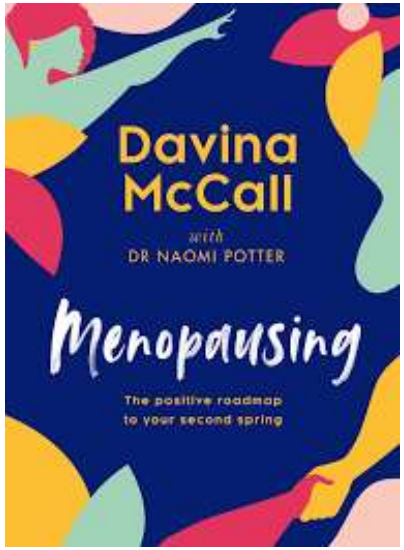
Average age 63

High rate of comorbidities

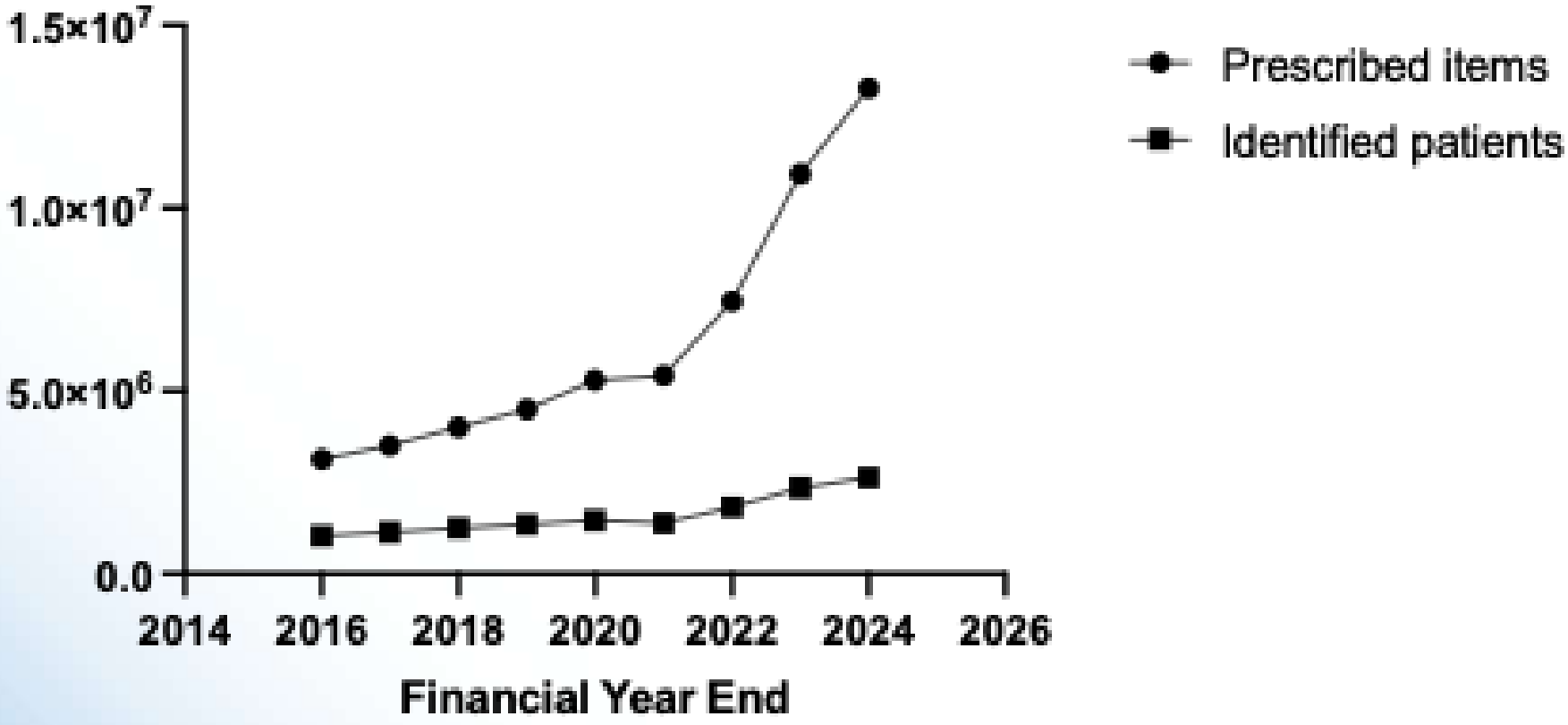
Using high dose, synthetic HRT

Thus, not representative of typical use today

More recently…

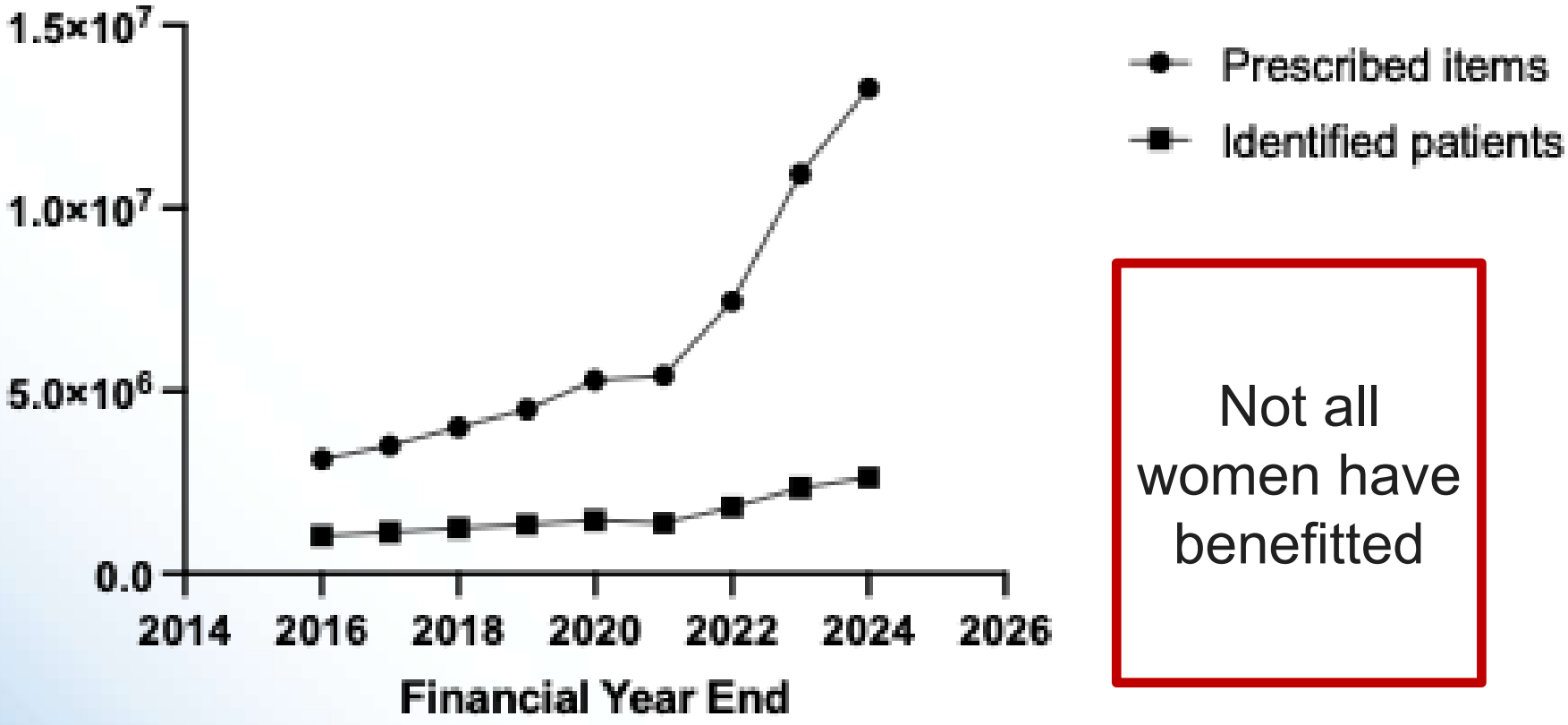


Prescriptions of HRT in England



Prescribing Data (England), Source NHSBSA

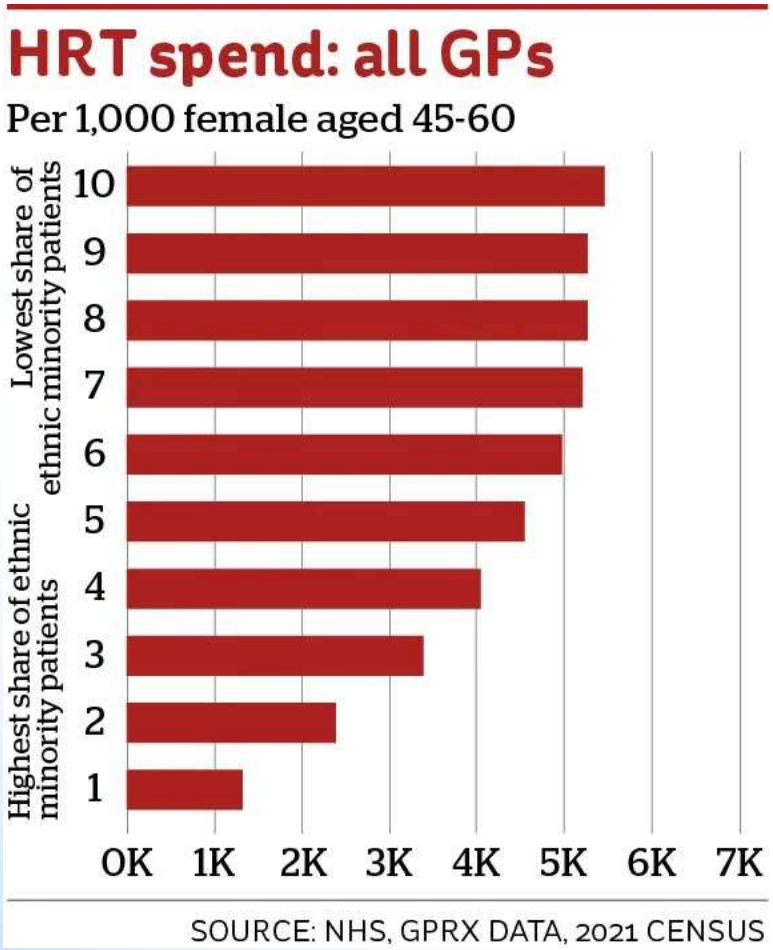
Prescriptions of HRT in England

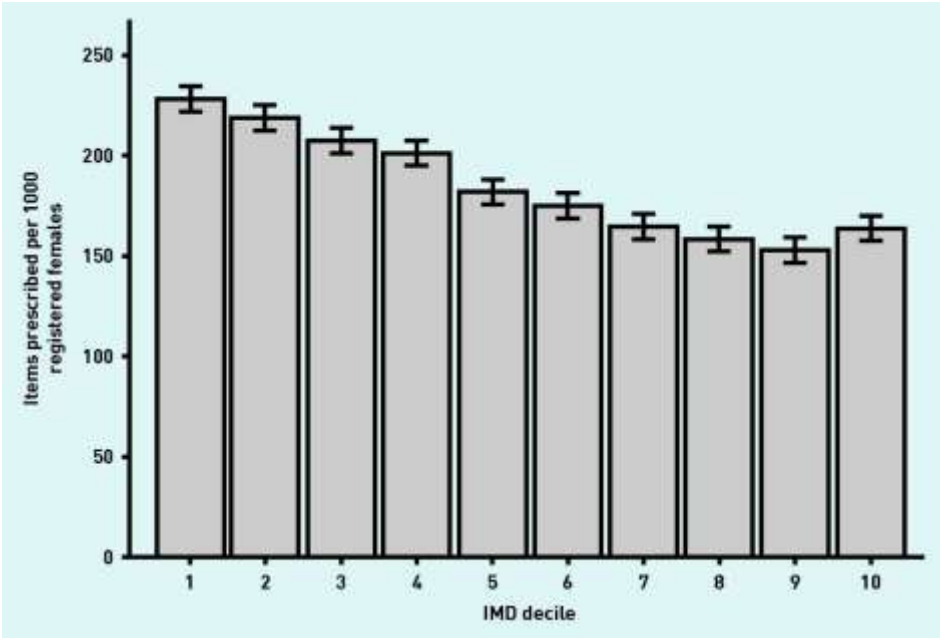


Not all women have benefitted

Prescribing Data (England), Source NHSBSA

Disparities in prescribing





Hillman et al, BJGP 2020

Aims

1. To explore whether women with chronic kidney disease (CKD) experience disparities in access to HRT

2. To describe HRT preparations commonly used by women with kidney disease

3. To investigate the relationship between menopause and kidney function

Results

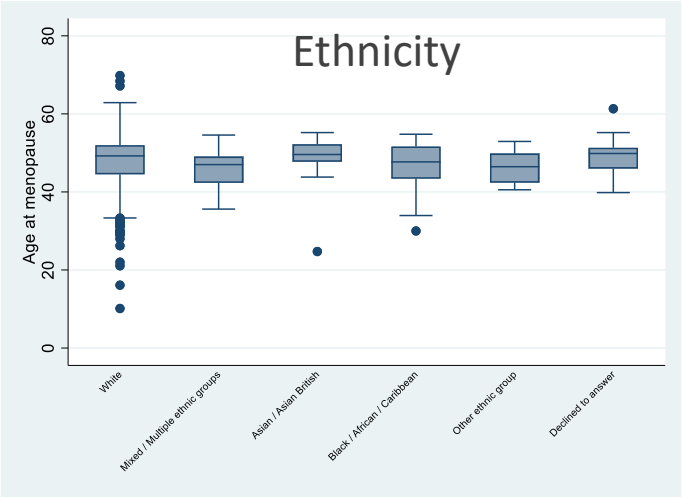
- 2096/8485 (24.7%) women completed the questionnaire.
- The median age of respondents was 54.3 years (IQR 42.0-64.7).

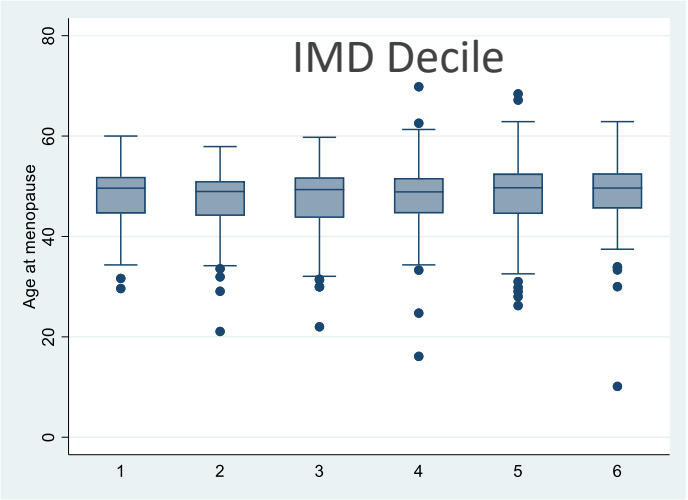
Reproductive status	N of women	Percentage (%)
Pre-menopausal	483	23
Peri-menopausal	399	19
Post-menopausal	1047	50
Unsure	167	8
TOTAL	**2096**	**100**

Results: Age at Menopause

- The median age at menopause was 49.2 years (IQR 44.5-52.0)

- 271/2082 (15%) had received cyclophosphamide as part of their treatment for kidney disease.





Results: HRT

- 514 (24.5%) had **ever** taken HRT.
  - 2024, NHS Digital, 19.6% women aged 45-55 in UK were **currently on** on HRT
  - Isaacs (2004), 50% women in the UK general population had ever taken HRT
- Amongst peri- and post-menopausal women, 478/1446 (33%) had ever used HRT.
- There was no significant difference amongst HRT uptake according to ethnicity in this cohort.

Do/Did you take any of the following types of systemic hormone treatment?		
Oestrogen as a patch, gel or spray (for example Evorel, Estradot, Sandrena, Oestrogel, Lenzetto)	258	51%
Oestrogen as a tablet (for example Premarin, oestradiol, + as above)	81	16%
Combination oestrogen and progesterone patch (for example Evorel Conti, Evorel Sequi, Elleste Duet)	84	17%
Combination oestrogen and progesterone tablet (for example Bijuve, Femoston, Kliovance, Indivina)	53	11%
Progesterone as an oral capsule (for example, Utrogestan, Gepretix)	72	14%
Another type of progesterone tablet (for example, Norethisterone, Noriday, Provera)	20	4%
Vaginal progesterone (for example, vaginal Utrogestan/ Gepretix, Cyclogest pessaries, Lutigest pessaries)	25	5%
Mirena or other type of hormonal coil (such as Kyleena, Jaydess).	82	16%
Tibolone	13	3%
Testosterone gel or cream (for example, Testogel, Androgel, Testim)	32	6%
Testosterone subcutaneous implants	4	1%
Compounded ('bioidentical') hormones (these are hormone formulations that are only prescribed by some private healthcare providers and have been manufactured in an independent pharmacy).	3	1%
Other – please specify	33	7%
None	43	9%

Results: Renal Function

- Renal function was significantly lower in postmenopausal than premenopausal women:

	Pre-menopausal	Post-menopausal	P Value
Mean eGFR (ml/min/1.73m^2)	82.6 (SD±32.7)	52.0 (SD±26.4)	**P <0.0001*** **

- Postmenopausal women who had taken HRT had a significantly higher current mean eGFR compared with those who had never taken HRT:

	Ever taken HRT	Never taken HRT	P Value
Mean eGFR (ml/min/1.73m^2)	55.0 (SD±26.2)	47.9 (SD±25.7)	**P = 0.004** **

Results

- In a linear regression model, current eGFR in postmenopausal women was significantly associated with age, disease type and HRT use

	Coefficient	95% CI		p-value
HRT=No	0.			
HRT=Yes	8.08	3.413707	12.74177	**0.001****
Ethnicity	-2.35	-6.053842	1.345071	0.212
IMD Quintile	-0.4	-1.991118	1.196662	0.625
Cohort=Cystic	-12.87	-17.56238	-8.171792	**0.000*****
Cohort=Metabolic	-10.38	-28.84642	8.089857	0.270
Cohort=Tubular	25.38	1.072082	49.6853	0.041
Cohort=Other	-6.52	-21.54462	8.510714	0.395
Age (Nov 2024)	-0.77	-1.026977	-.5063445	**0.000*****
Intercept	104.81	86.75066	122.8598	**0.000*****

Results

- In **170 people** with data pre and post menopause (16.2%) , there was no significant difference in eGFR slope pre and post menopause (-2.9 vs -3.0ml/min/1.73m2/year, p=0.96),

	Pre-menopausal	Post-menopausal	P Value
Mean eGFR slope (ml/min/1.73m^2)	-2.9	-3.0	P = 0.96

- However, there was a significant drop in eGFR between pre-menopausal and post-menopausal values (4.7ml/min/1.73m2, p-value <0.0001).

Qualitative work: Menopause

"my experience [of menopause] has been one of hell", "I never felt supported by the renal teams".

"My kidney disease was masked by my menopausal symptoms"

"Then after my transplant, my body returned to normal and my menopause continued, with more side effects than previous."

"I think my perimenopause period went on for 3-4 years-It felt a long time with symptoms, I was quite emotional and anxious about my kidney health during that period and was referred to a renal psychologist who mostly asked me about my home situation- however looking back now, I was just going through the menopause process, but it wasn't mentioned. At one point, I thought I was just depressed

"I had my kidney transplant in December 2022 and my perimenopause symptoms hit quickly from March 2023, it seemed to me that the transplant or medication might have brought them on"

"I would be interested to know if my CKD contributed to the 9 year menopausal time frame"

Conclusion

- Only 33% of peri-/post-menopausal women had **ever** used HRT
  - Difficulties in accessing HRT?
  - Concerns about prescribing safety?
  - Different symptom profiles in women with kidney disease?
- No ethnic disparities were identified.
- We identified a significant post-menopause decline in renal function.
- We found HRT use was associated with higher current eGFR in post-menopausal women

Conclusion

- Post menopausal women with kidney disease face real challenges in accessing help and support for menopause symptoms
- Partly due to the interplay and overlap between menopause and kidney disease
- But also due to a lack of awareness amongst health professionals
- More work is needed to establish
  - Effects of hormones on kidney function and cardiovascular health with women with kidney disease
  - Effects of kidney disease on menopause and post-reproductive health
  - Safety of HRT in women with kidney disease
  - Identifying challenges and reducing inequities of access for women with kidney disease

Future Work

- To complete analysis of survey responses
  - Menopause
  - Children's outcomes
  - Qualitative work on all aspects of women's health
- To try and improve access to HRT for women with kidney disease through
  - Development of UKKA guidelines on Menopause/ HRT for WKD
  - Education and outreach
  - Future clinical trials to establish potential benefit

Acknowledgements

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Dr Zoe Plummer
Mr David Pitcher

Thank you for listening

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