HRT: managing HIV through the menopause

Shema Tariq
Clinical Research Fellow & Honorary Consultant,
UCL/Mortimer Market Centre
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s.tariq@ucl.ac.uk  @Savoy__Truffle
• Epidemiology
• Menopause in the general population
• Menopause in HIV-positive women
• Management
  – HRT
  – Other considerations
NUMBER OF PEOPLE ACCESSING HIV CARE BY AGE GROUP, 2003-2013

NUMBER OF WOMEN ACCESSING HIV CARE BY AGE GROUP, 2003-2013

Source: Data provided by Graeme Rooney (Centre for Infectious Disease Surveillance and Control, Public Health England)
THE MENOPAUSE
THE MENOPAUSE

- Cessation of menstrual cycle due to loss of ovarian function
- After one year of amenorrhoea
- Spontaneous or iatrogenic
# Geographical Variation

<table>
<thead>
<tr>
<th>Region or country</th>
<th>n</th>
<th>Number of studies</th>
<th>Mean age at menopause (95% CI)</th>
<th>Heterogeneity (I-squared; %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Africa</td>
<td>1,175</td>
<td>3</td>
<td>48.4 (48.1–48.6)</td>
<td>0.0</td>
</tr>
<tr>
<td>Asia</td>
<td>39,158</td>
<td>8</td>
<td>48.8 (48.1–49.4)</td>
<td>98.9</td>
</tr>
<tr>
<td>Australia</td>
<td>9,268</td>
<td>2</td>
<td>51.3 (49.8–52.8)</td>
<td>99.1</td>
</tr>
<tr>
<td>Europe</td>
<td>18,692</td>
<td>6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Latin America</td>
<td>18,073</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Middle East</td>
<td>7,733</td>
<td>8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>United States</td>
<td>15,690</td>
<td>6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>109,789</td>
<td>36</td>
<td>48.8 (48.3–49.2)</td>
<td>99.6</td>
</tr>
</tbody>
</table>

Source: Schoenaker DA et al. (2014)
Menopausal Symptons

- 85% of women experience symptoms\(^1\)
- Median duration = 7 years\(^2\)
- Genital symptoms can be lifelong
- Negative impact on work and relationships\(^3,4\)
- Reduced quality of life\(^4\) and perceived health\(^5\)
- Menopause experience shaped by culture\(^6\)

SYMPTOMS

- Vasomotor
- Urogenital atrophy
- Musculoskeletal
- Metabolic
- Cardiovascular
- Mood and cognition
POST-MENOPAUSAL LIFE SPAN
Women can expect to live 40% of their lives post-menopause.

They may spend 10% of their lives with menopausal symptoms.
HIV & THE MENOPAUSE
HIV AND THE MENOPAUSE

- Relatively under-researched
- US studies predominate
- Symptoms misattributed\(^1,2\)
- Use of HRT $\sim 10\%^{3,4}$
- No robust data on current management or clinical need in UK

Source: 1. Johnson TM et al. (2008); 2. Cejtin HE et al. (2005); 3. Fantry LE et al. (2005); 4. Samuel M et al. (2013)
DIFFERENCES IN HIV

- Co-existing factors
- Chronic inflammation
- Chronic illness
- Opportunistic infection
- ART
- Gonadal dysfunction
AGE AT MENOPAUSE

HIV-POSITIVE

HIV-NEGATIVE
AGE AT MENOPAUSE

HIV-POSITIVE

HIV-NEGATIVE

Clark RA (2001); Fantry LE (2005); Schoenbaum EE (2005); De Pommerol M (2011); Boonyanurak P (2012); Lui-Filho JF (2013); Willems N (2013)
HIV-POSITIVE
n=1063
AGE 47

HIV-NEGATIVE
n=272
AGE 48

Cejtin H (2004)
MENOPAUSAL SYMPTOMS

- Increased vasomotor symptoms\(^1,2,3\)
- Psychological symptoms\(^3,4,5\)
- No difference in cognition\(^6\)
- No difference in sexual function\(^7,8\)

INCIDENCE OF NEW FRACTURES

Source: Sharma A et al. (2015)

OLDER AGE, WHITE RACE, PRIOR FRACTURE, HISTORY OF COCAINE OR IDU
**Immune Function & Response to ART**

- Oestrogen may inhibit HIV replication\(^1\)
- Oestrogen associated with increased CD4 T-cells\(^2\)
- CD4 lower in post-menopausal women 3 years post-seroconversion (\(p=0.09\))\(^3\)
- No difference in immunological/virological response in ART-naïve women starting ART\(^4,5\)

Health and wellbeing

- Quality of life
- Engagement in care
- Adherence
Quality of life

Engagement in care

Adherence
• Biological plausibility that menopause may be different in HIV
• May be associated with earlier menopause
• Possibly increased symptoms
• Likely increased complications e.g. osteoporosis
• Very little is known about impact on wellbeing
THE PRIME STUDY: POSITIVE TRANSITIONS THROUGH THE MENOPAUSE
THE PRIME STUDY: POSITIVE TRANSITIONS THROUGH THE MENOPAUSE

PRIME Study

1500 HIV+ WOMEN AGED 45-60
15 CENTRES ACROSS UK
QUESTIONNAIRES AND INTERVIEWS
LONGITUDINAL FOLLOW-UP
To explore the impact of the menopause on HIV-positive women’s wellbeing and engagement with HIV care
MANAGEMENT
HRT

• Synthetic oestrogens +/- progestogen
• Large body of evidence that HRT reduces vasomotor and mood symptoms
• Improves quality of life
• Reduces risk of fragility fractures
• Oral vs. transdermal vs. topical
• Lowest effective dose for shortest duration possible
THE HRT CONTROVERSY: 2002

HRT DANGER FOR WOMEN

'Huge increase' in killer disease risk

CARDIOVASCULAR DISEASE
BREAST CANCER
ENDOMETRIAL CANCER
## Breast Cancer Risk

<table>
<thead>
<tr>
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<th>Relative risk of breast cancer</th>
<th>No. of extra (or less) cases/1000 over 5 years</th>
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<tr>
<td>No HRT</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Combined HRT</td>
<td>1.26</td>
<td></td>
</tr>
<tr>
<td>Oestrogen-only HRT</td>
<td>0.73</td>
<td></td>
</tr>
<tr>
<td>BMI &gt; 35</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>≥ 2 units alcohol/day</td>
<td>1.5-2</td>
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Source: Ayres J et al. (2013)
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<td>1.5 - 2</td>
<td>8 - 15</td>
</tr>
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</table>

Source: Ayres J et al. (2013)
IF STARTING HRT <10 YEARS AFTER MENOPAUSE...

- Breast cancer: 0
- Ovarian cancer: + 1/1000
- Thrombosis: + 5/1000
- Stroke: + 4/1000
- Coronary artery disease: - 8/1000
- Death: - 6/1000
NICE GUIDELINES (Nov 2015)

- Discuss and inform
- Offer HRT:
  - menopause age <40
  - hysterectomy/oophorectomy
  - for symptoms (age <60)
  - transdermal if VTE risk
- Other options: lifestyle, SSRIs, CBT, lubricants, herbal
Contra-indications:

- Age >60
- Oestrogen dependent tumour
- Undiagnosed vaginal bleeding/breast lump
- Active/recent VTE
- Acute liver disease
- Pregnancy
- Contra-indications
HRT in HIV

- Probably underused
- Drug interactions between HRT and ART
  - absence of data
  - ↓ oestrogen (PIs/NNRTIs)
  - ↑ progestogen exposure?
- Risk of CVD, VTE or malignancy in HIV?
- Improved outcomes e.g. osteoporosis, QoL, mood?
MANAGEMENT OF HIV+ WOMEN IN MIDLIFE

1. Ask
   - menstrual history (clinical diagnosis)
   - symptoms

2. Inform
   - symptoms
   - treatment options

3. Assess and address
   - risk of comorbidity (CVD, osteoporosis, CIs to HRT)
   - drug interactions
4. Advise
   - lifestyle modification (exercise, alcohol, smoking)
   - contraception
   - breast and cervical screening

5. Offer support

6. Liaise with GP
   - symptoms
   - is patient interested in HRT?
   - transdermal?
in partnership with...

The British Menopause Society

Norfolk & Norwich University Hospital

WELCOME
the leading site for tailored menopausal advice provided by experts

A unique opportunity for you to get menopausal advice from experts in post reproductive health that is specific to your needs.

We hope you find the ‘Manage my Menopause’ questionnaire, ‘MmM advice for you’ lifestyle advice and the Manage my Menopause handbook useful.

Our aim is to highlight the changes you are going through at this time of your life, how these changes may impact on your long-term health and suggest small changes in your lifestyle. This should help to help manage your symptoms and reduce the risk of developing certain diseases in the future.

www.managemymenopause.co.uk
It would be good to hear this earlier, then we would start noticing it in our bodies. It would be a thing that we know. Not a kind of shock. I ran time after time to my doctor asking:

‘What is this? What is this?’

You don’t know what is happening to you.

Come and teach us. Tell us more.
CONCLUSIONS

• Increasing numbers of older women living with HIV
• Menopause can have physical and psychological consequences
• Under-recognised in HIV+ women
• Paucity of data on symptoms, morbidity and management
• Need for awareness and support
Acknowledgements:
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