InterLACE: International collaboration on a Life Course Approach to Reproductive Health and Chronic Disease Events

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Overview

• The InterLACE project
• Data harmonisation
  – Process
  – Methodological challenges
• Findings
Overview of the InterLACE project

• A cross-cohort / cross-cultural collaboration that aims to provide a detailed and integrated approach to women’s reproductive health and future chronic diseases (including cardiovascular disease and type 2 diabetes)

• Results that demonstrate consistency or systematic differences across cohorts can provide evidence that is more powerful and generalizable than findings from a single study.
Benefits of harmonising and pooling research databases

- Achieve bigger sample sizes
- Improve the generalisability of results
- Help ensure the validity of comparative research
- Encourage more efficient secondary usage of existing data
- Provide opportunities for collaborative and multi-centre research

Doiron et al. Emerging Themes in Epidemiology 2013, 10:12.
Study rationale

• Sex differences in the prevalence and aetiology of chronic conditions highlight the need to understand the role of reproductive characteristics and sex hormones

• Current poor understanding of how reproductive characteristics across life combine or interact to influence health in later life
Schematic representation of reproductive health through life & chronic disease

Socioeconomic factors, cigarette smoking, physical activity, body weight, diet...

Early life factors: birthweight, breast-feeding, childhood growth...

Reproductive Function: age at menarche, irregular menses, sub-fertility, parity, age at first birth...

Reproductive Ageing: age at menopause, duration of peri-menopause, vasomotor symptoms...

Chronic disease: Cardiovascular disease, Type 2 Diabetes, Osteoporosis, Cognitive decline, Depression...

Multiple Populations and Sub-populations

Multiple Age Cohorts

The InterLACE study: Design, data harmonization and characteristics across 20 studies on women’s health

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23 participating studies from 10 countries

- Australian Longitudinal Study on Women’s Health (ALSWH; Australia)
- Healthy Ageing of Women Study (HOW; Queensland, Australia)
- Melbourne Collaborative Cohort Study (MCCS; Melbourne, Australia)
- MRC National Survey of Health and Development (NSHD; UK)
- National Child Development Study (NCDS; UK)
- English Longitudinal Study of Ageing (ELSA; England, UK)
- UK Women’s Cohort Study (UKWCS; UK)
- Whitehall II Study (Whitehall; England, UK)
- Women’s Lifestyle and Health Study (WLHS; Sweden/Norway)
- Danish Nurse Cohort Study (DNCS; Denmark)
- The Decision at Menopause Study (DAMES; Madrid, Spain; Beirut, Lebanon; Rabat, Morocco; Massachusetts, USA)
- The Study of Women’s Health Across the Nation (SWAN; USA)
- Seattle Midlife Women’s Health Study (SMWHS; Washington, USA)
- San Francisco Midlife Women’s Health Study (SFMWHS; California, USA)
- Hilo Women’s Health Study (Hilo WHS; Hawaii, USA)
- Japanese Midlife Women’s Health Study (JMWHS; Nagano, Japan)
- Japan Nurses’ Health Study (JNHS; Japan)
- Southall and Brent Revisited (SABRE; London, UK)
- UK Biobank (UK); French 3C studies (France)
Ten participating countries:
Australia, UK, USA, Demark, Sweden, Norway, Spain, Japan, Lebanon, and Morocco.
InterLACE dataset

• Socio-demographic and modifiable lifestyle factors
  – Age, birth year, race/ethnicity, marital and employment status, education level, body mass index (BMI), smoking status, alcohol consumption, physical activity, diet

• Female reproductive characteristics
  – Reproductive function (age at menarche, parity, age at first birth, timing/duration of oral contraceptive pill (OCP) and hormone replacement therapy (HRT) use)
  – Reproductive ageing (age at natural menopause, hysterectomy/oophorectomy, menopausal status, menopausal symptoms)

• Chronic disease outcomes
  – CVD (stroke, heart disease, heart attack, heart failure, angina)
  – Diabetes (Type 1 & Type 2 diabetes)
  – Data from self-reported questionnaires and linkage with national registries

• Data are available at multiple points in the longitudinal studies
Data harmonisation processes

- Study recruitment and documentation
- Harmonised variable selection and definition
- Study variable identification and harmonization potential assessment
- Data processing
- Harmonised dataset and analyses
Data processing

• Data were first checked for outliers and inconsistencies, and if present, data providers were contacted.
• Harmonization rules were documented for each variable.
• Processed study-specific data into the target (harmonised) format.
• Categorical variables were collapsed at various levels to incorporate information from as many studies as possible.
Example of data harmonisation

Race/ethnicity

12 studies had data on self-identified race/ethnicity

6 studies had data on related variables
- Country of birth or country of residency in childhood
- Language spoken at home

11 studies did not have data on self-identified race/ethnicity

5 studies did not have data on related variables
- Country of residency as a proxy

12 categories of race/ethnicity
1. Caucasian-Australian
2. Caucasian-European
3. Caucasian-American
4. Hispanic/Latin American
5. Asian-Japanese
6. Asian-Chinese
7. South Asian
8. Southeast Asian
9. Other Asian
10. Middle Eastern
11. African American/Black/Caribbean
12. Other (Aboriginal, Native American, Pacific Islander, Hawaiian, and mixed)
Example of data harmonisation

Menopausal status

15 studies had menopausal status derived or reasons why period stopped

8 studies did not have menopausal status derived or reasons why period stopped

Use relevant variables below to define menopausal status
1. Hysterectomy and/or oophorectomy
2. Current use of HRT and/or OCP
3. Period in the last 12 months and 3 months
4. Period changed/unpredictable/irregular
   * For the longitudinal studies, once women have gone through natural menopause or surgery, the status must carry forward at subsequent surveys

6 categories of menopausal status
1. Hysterectomy/oophorectomy
2. Current use of HRT
3. Current use of OCP
4. Pre-menopause
5. Peri-menopause
6. Natural menopause
Methodological challenges

- The contributing studies varied in their sampling methods, inclusion and exclusion criteria, and modes of survey administration
  - Example 1: only recruit premenopausal women
  - Example 2: online survey or telephone interview vs. self-completed paper-based questionnaire

- Retention of participants in longitudinal studies
  - Different levels of sample attrition and missing data due to withdrawal, mortality, and other reasons for non-response
Methodological challenges

• Studies varied greatly in terms of likely representativeness of the sample with respect to the relevant national population
  – Sampling from specific professional groups

• Variations in chronic disease outcomes across studies
  – Differences in the age range of the cohort of women when they responded to the relevant survey questions
Methodological challenges

• Methodological differences in the way information was collected
  – Example: information on depressed mood was collected using different types of assessment (frequency or severity) and different recall periods (past 12 months or past 2 weeks/less). Also, the wording for depressed mood was different in each study
Socio-demographic, lifestyle and reproductive factors and the risk for premature and early natural menopause

result from 51,450 postmenopausal women from nine observation studies in the InterLACE consortium

Distribution of menarche and parity (n=51,450)

Age at menarche (years)

Number of children

Frequency (%)
AGE at MENOPAUSE

N=51,450

Frequency (%)

Age at natural menopause (years)

<40 40-44 45-49 50-51 52-53 54+

2.0 7.6 28.3 24.9 19.7 17.5
Menarche, parity, and age at final menstrual period (n=51,450)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Categories</th>
<th>Age at FMP</th>
<th></th>
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<tbody>
<tr>
<td></td>
<td></td>
<td>&lt;40</td>
<td>40–44</td>
<td>45–49</td>
<td>52–53</td>
<td>54+</td>
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<tr>
<td>Age at menarche</td>
<td>≤11</td>
<td>1.80 (1.53, 2.12)</td>
<td>1.31 (1.19, 1.44)</td>
<td>1.10 (1.00, 1.21)</td>
<td>1.07 (0.99, 1.15)</td>
<td>1.05 (0.91, 1.21)</td>
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<td>12</td>
<td>1.04 (0.87, 1.25)</td>
<td>1.05 (0.88, 1.26)</td>
<td>0.96 (0.91, 1.02)</td>
<td>0.98 (0.92, 1.05)</td>
<td>0.95 (0.88, 1.02)</td>
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<td>Reference</td>
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<tr>
<td></td>
<td>14</td>
<td>1.04 (0.79, 1.37)</td>
<td>0.99 (0.90, 1.09)</td>
<td>0.94 (0.86, 1.04)</td>
<td>0.96 (0.90, 1.02)</td>
<td>1.00 (0.95, 1.05)</td>
</tr>
<tr>
<td></td>
<td>≥15</td>
<td>1.10 (0.90, 1.33)</td>
<td>0.98 (0.88, 1.10)</td>
<td>0.94 (0.90, 0.99)</td>
<td>0.91 (0.85, 0.98)</td>
<td>1.09 (1.04, 1.15)</td>
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<tr>
<td>Parity</td>
<td>0</td>
<td>2.26 (1.84, 2.77)</td>
<td>1.32 (1.09, 1.59)</td>
<td>1.13 (1.03, 1.23)</td>
<td>0.92 (0.81, 1.04)</td>
<td>0.89 (0.76, 1.03)</td>
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<td>1.53 (1.14, 2.06)</td>
<td>1.23 (1.04, 1.45)</td>
<td>1.12 (1.05, 1.19)</td>
<td>0.94 (0.89, 0.98)</td>
<td>0.90 (0.80, 1.00)</td>
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</table>

RRR, relative risk ratio. Reference category for polytomous outcome was the FMP at age 50–51 which was the most common FMP age group. The multivariable model included study, birth year, education, marital status, smoking status, BMI, menarche and parity.
Combined exposure of menarche and parity with age at final menstrual period

*Adjusted for study cluster, birth year, education, marital status, smoking status, and BMI
Study-specific association between premature menopause (<40y) and the combined exposure of early menarche (≤11y) and nulliparity

* Adjusted for birth year, education, marital status, smoking status, and BMI
Summary of interrelationships

• Early menarche (≤11 years) and nulliparity are independently associated with premature (<40 years) and early menopause (40-44 years)

• Early monitoring of women with early menarche, especially those who have no children, for preventive health interventions, aimed at mitigating the risk associated with early menopause.
Thank you! Any questions?

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