interLACE

International collaboration for a Life course Approach to reproductive health and Chronic disease Events.

InterLACE: **Inter**national collaboration on a **L**ife Course **A**pproach to Reproductive Health and **C**hronic Disease **E**vents

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Funded by the Australian National Health and Medical Research Council (APP1027196, APP1000986) and Australian Research Council Future fellowship (FT120100812).

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

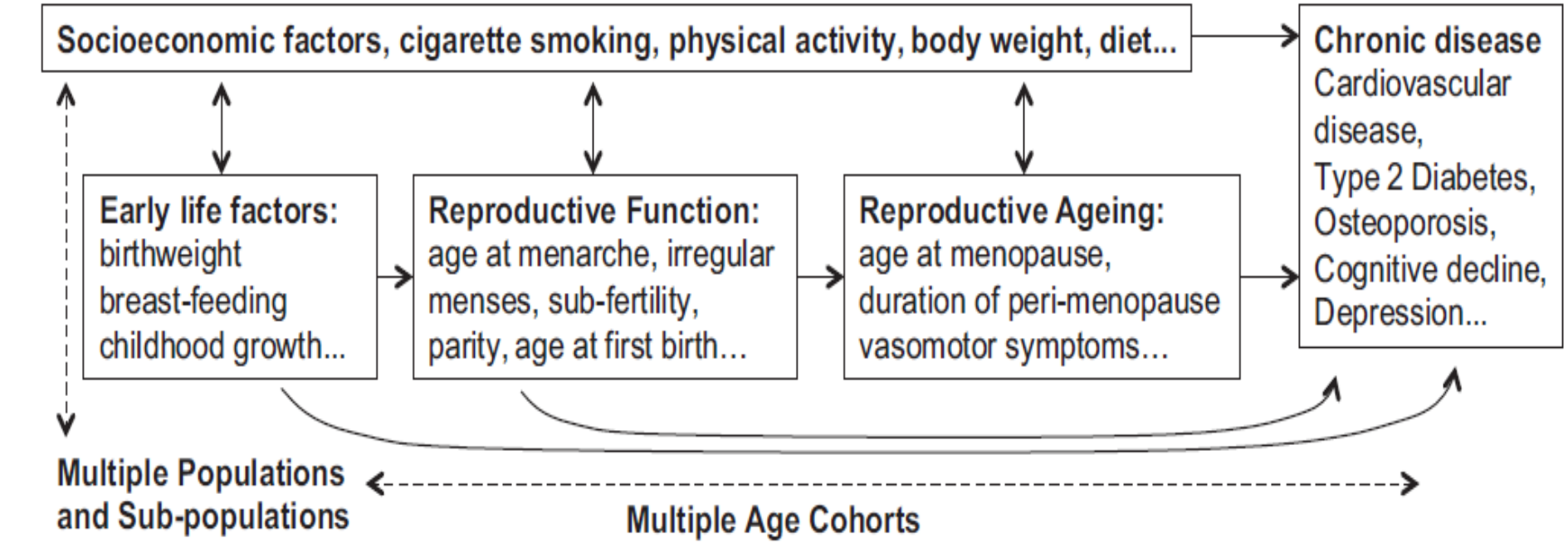
Doiron et al. Emerging Themes in Epidemiology 2013, 10:12.

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



Mishra et al. Maturitas 2013; 74:235-40

InterLACE study profile

Maturitas 92 (2016) 176–185

Contents lists available at ScienceDirect

Maturitas

journal homepage: www.elsevier.com/locate/maturitas

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

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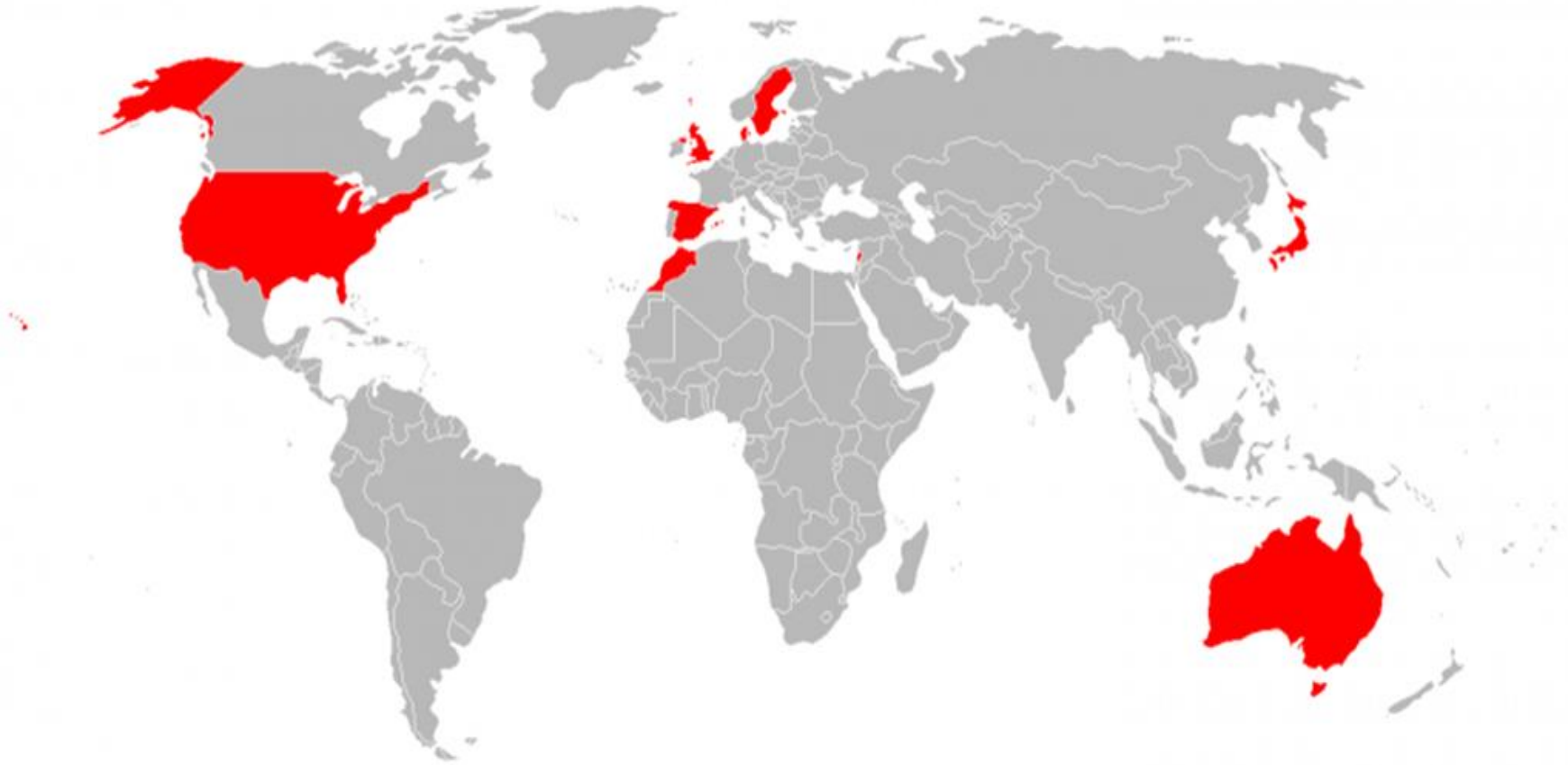
23 participating studies from 10 countries

- **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)**

InterLACE (N= 505,147)

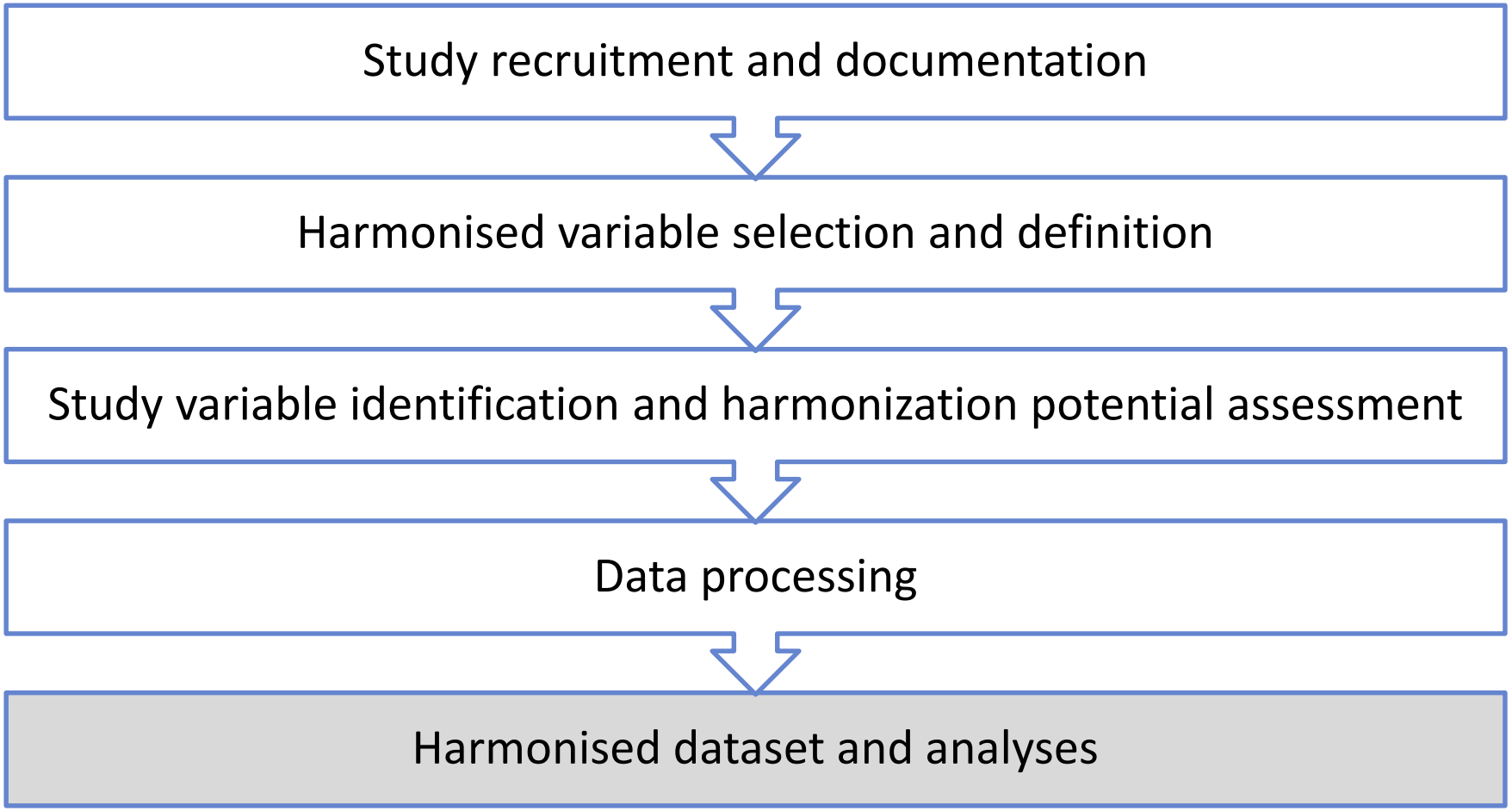


Ten participating countries:
Australia, UK, USA, Demark, Sweden, Norway, Spain, Japan, Lebanon, and Morocco.

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**

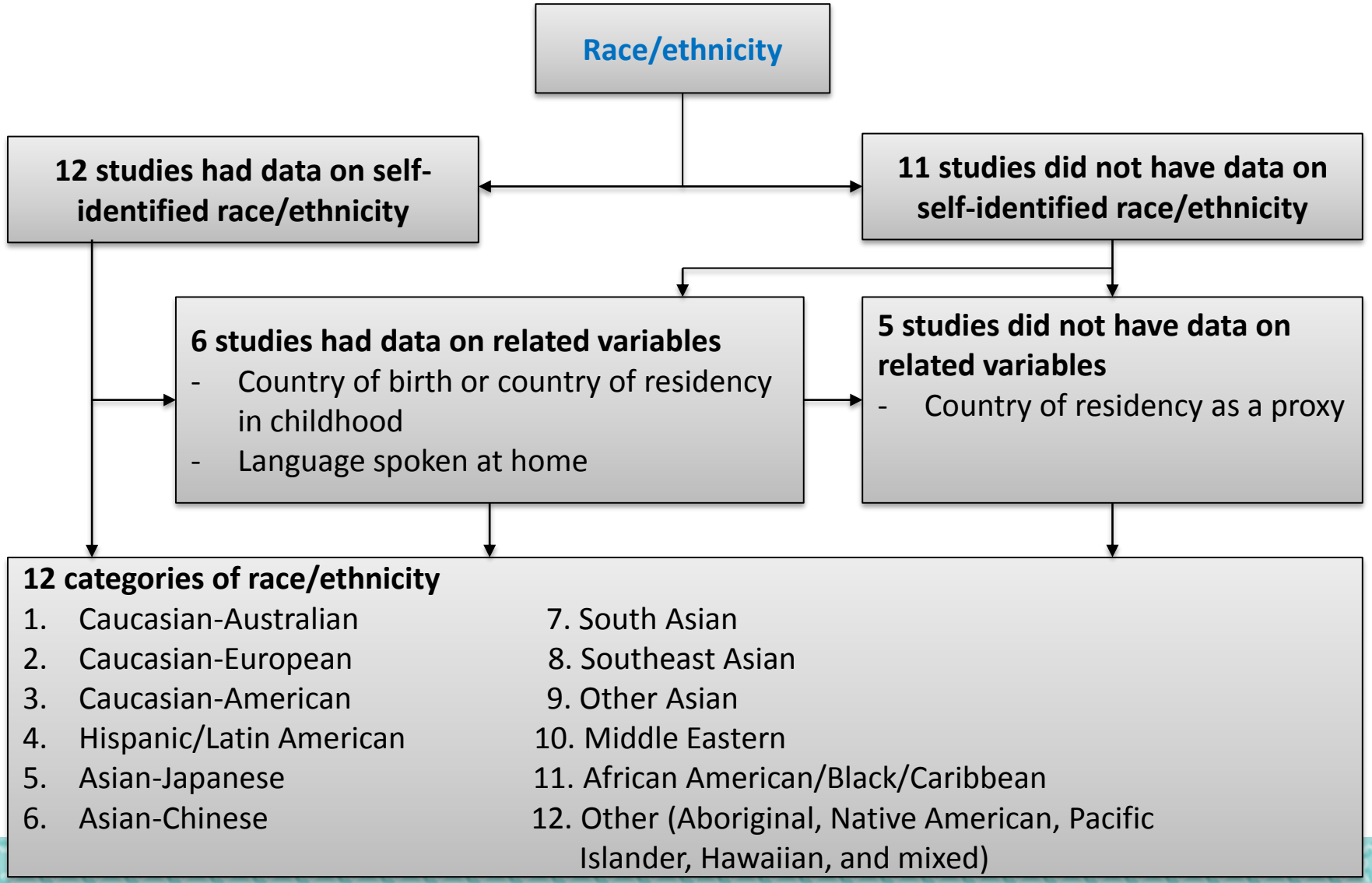
Data harmonisation processes



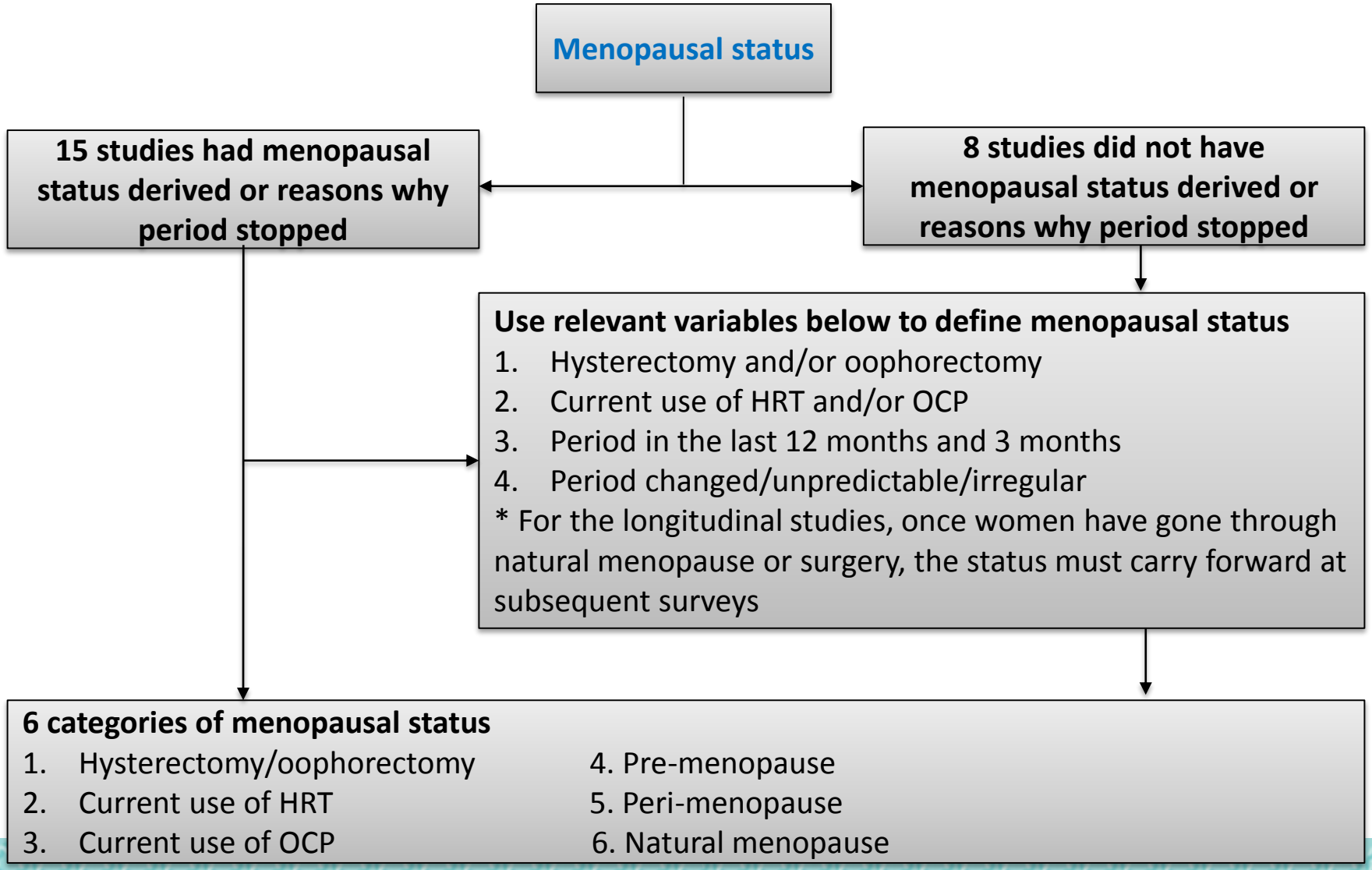
Data processing

- 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



Example of data harmonisation



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

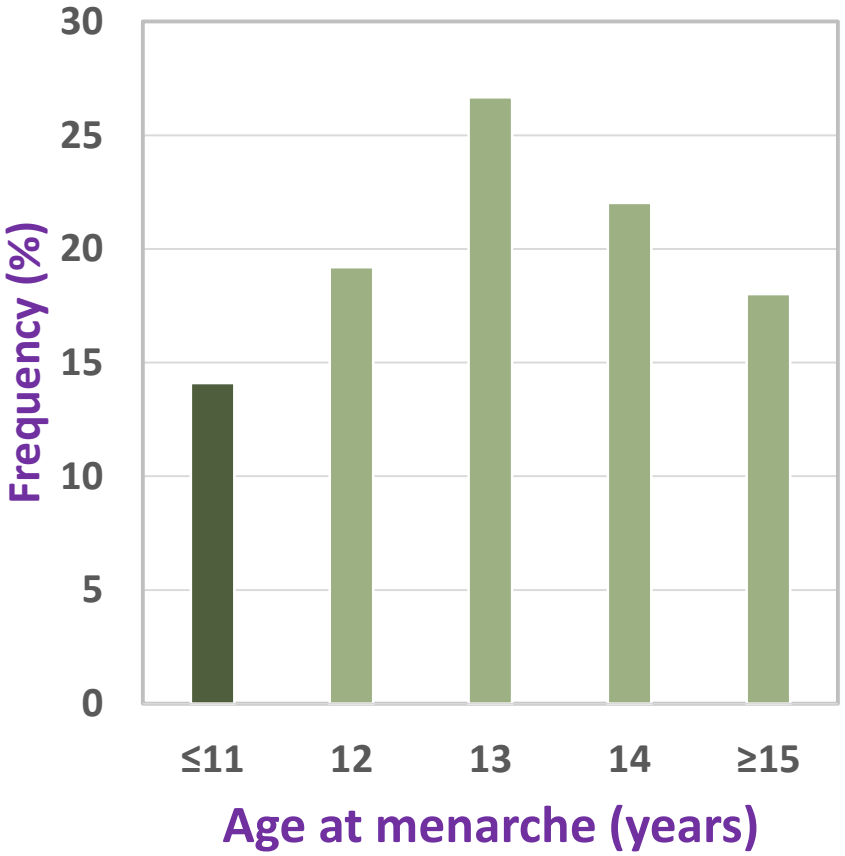
- Methodological differences in the way information was collected
  - Example: information on depressed mood was collected using different types of assessment (frequency or severity) and different recall periods (past 12 months or past 2 weeks/less). Also, the wording for depressed mood was different in each study

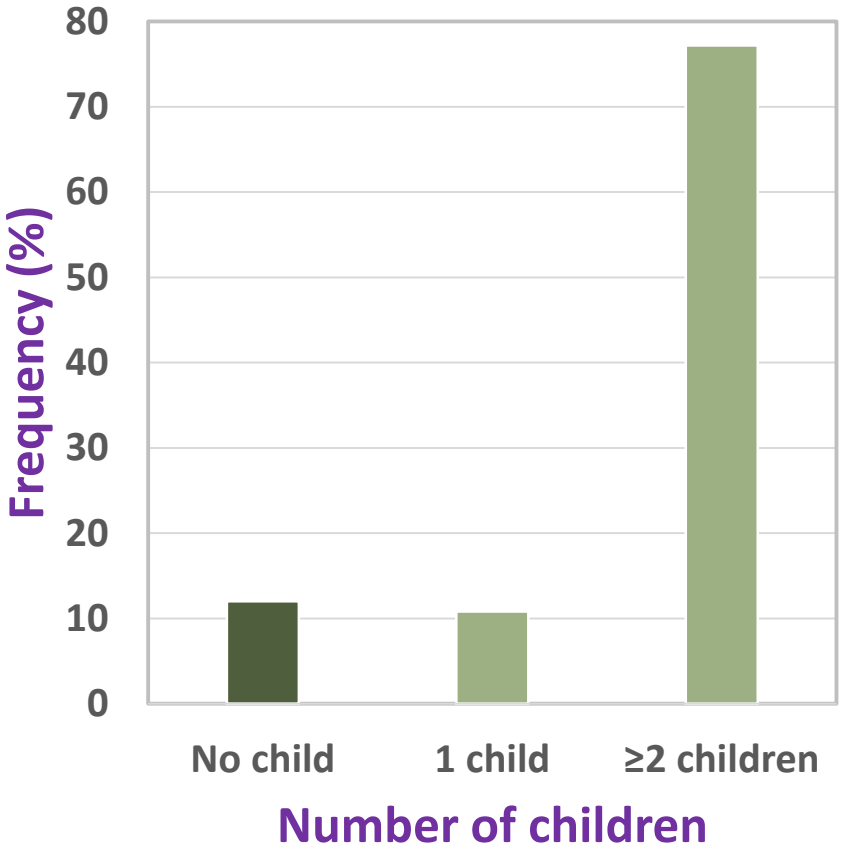
Socio-demographic, lifestyle and reproductive factors and the risk for premature and early natural menopause

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

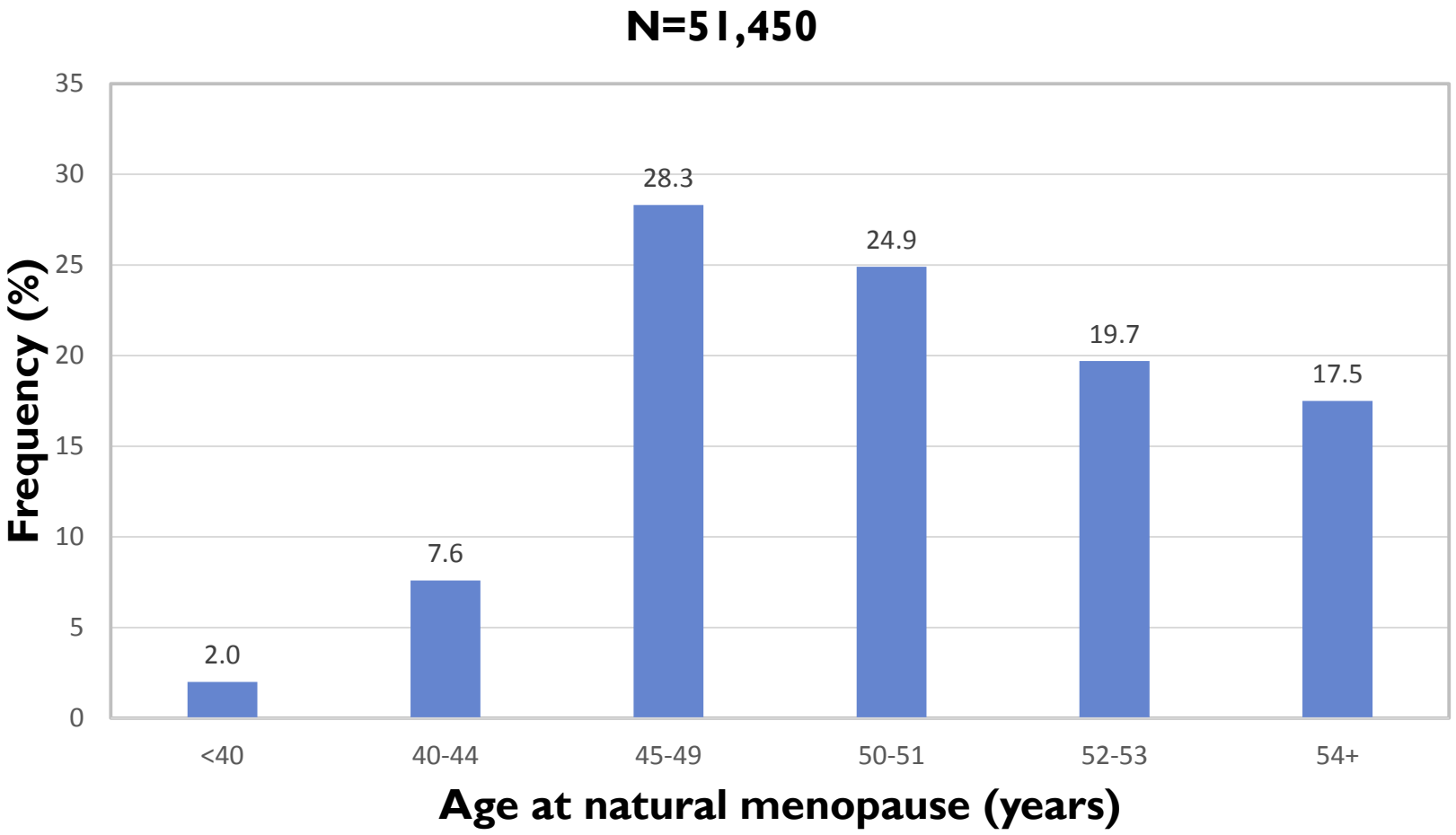
Mishra GD et al (2017) Early menarche, nulliparity and the risk for premature and early natural menopause. Human Reproduction 32(3): 679-686. doi:10.1093/humrep/dew350

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





AGE at MENOPAUSE



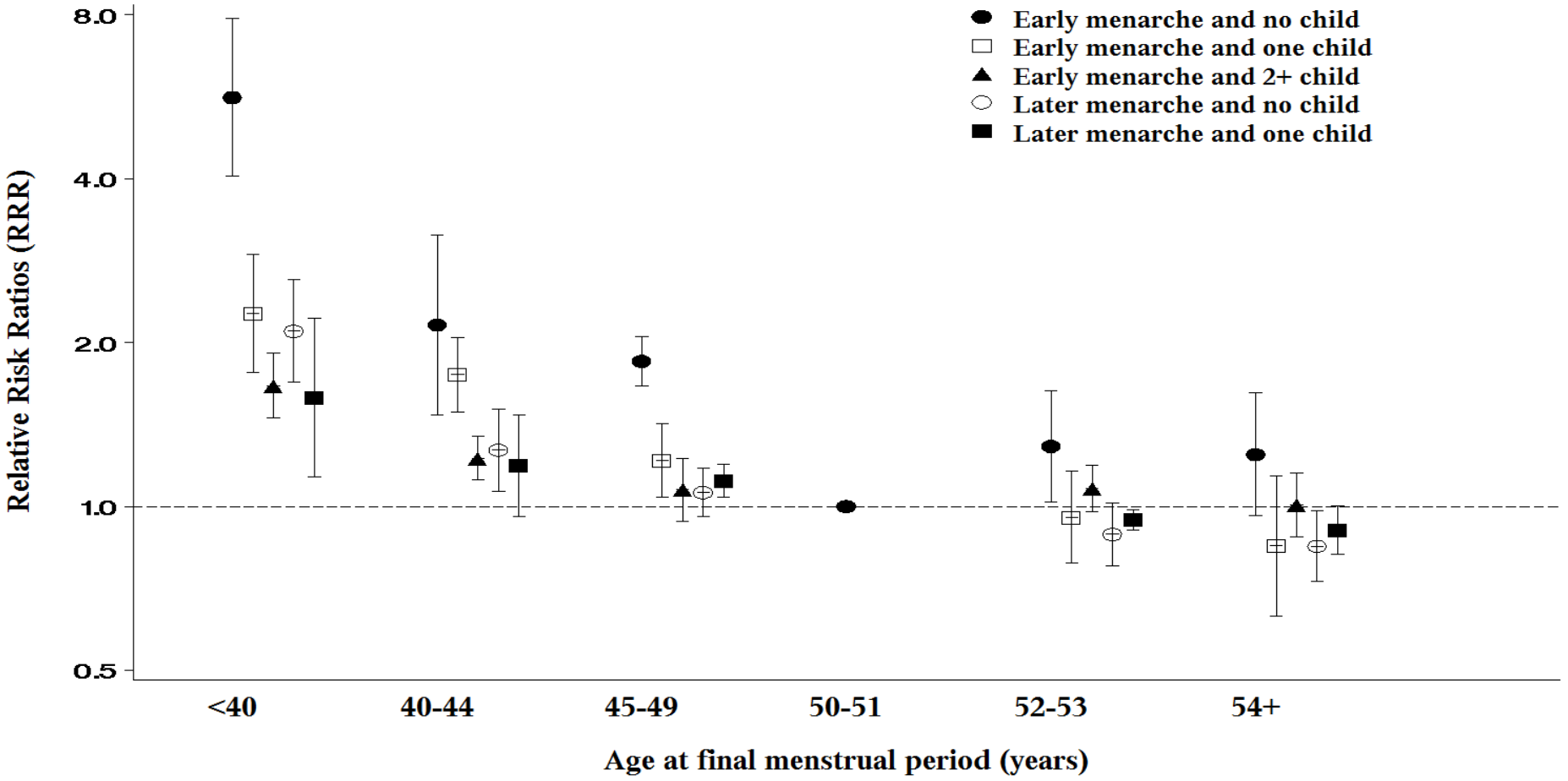
Menarche, parity, and age at final menstrual period (n=51,450)

Table IV Multivariable adjusted RRR and their two-sided 95% CI of reproductive characteristics and their association with age at FMP using multinomial logistic regression.

		Age at FMP				
		<40	40–44	45–49	52–53	54+
Variable	Categories	RRR (95% CI)	RRR (95% CI)	RRR (95% CI)	RRR (95% CI)	RRR (95% CI)
Age at menarche	≤11	1.80 (1.53, 2.12)	1.31 (1.19, 1.44)	1.10 (1.00, 1.21)	1.07 (0.99, 1.15)	1.05 (0.91, 1.21)
	12	1.04 (0.87, 1.25)	1.05 (0.88, 1.26)	0.96 (0.91, 1.02)	0.98 (0.92, 1.05)	0.95 (0.88, 1.02)
	13	Reference	Reference	Reference	Reference	Reference
	14	1.04 (0.79, 1.37)	0.99 (0.90, 1.09)	0.94 (0.86, 1.04)	0.96 (0.90, 1.02)	1.00 (0.95, 1.05)
	≥15	1.10 (0.90, 1.33)	0.98 (0.88, 1.10)	0.94 (0.90, 0.99)	0.91 (0.85, 0.98)	1.09 (1.04, 1.15)
Parity	0	2.26 (1.84, 2.77)	1.32 (1.09, 1.59)	1.13 (1.03, 1.23)	0.92 (0.81, 1.04)	0.89 (0.76, 1.03)
	1	1.53 (1.14, 2.06)	1.23 (1.04, 1.45)	1.12 (1.05, 1.19)	0.94 (0.89, 0.98)	0.90 (0.80, 1.00)
	≥2	Reference	Reference	Reference	Reference	Reference

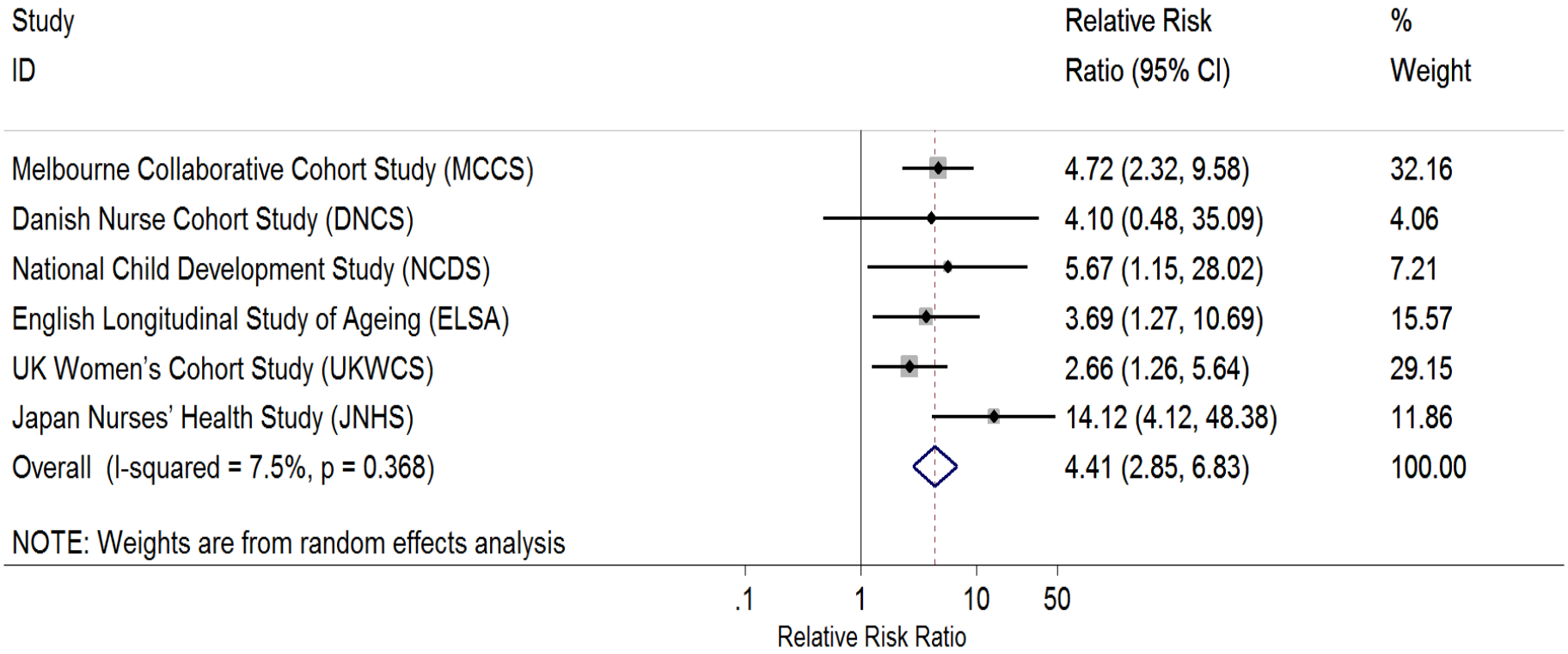
RRR, relative risk ratio. Reference category for polytomous outcome was the FMP at age 50–51 which was the most common FMP age group. The multivariable model included study, birth year, education, marital status, smoking status, BMI, menarche and parity.

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?

Acknowledgements

The data on which this research is based were drawn from several global longitudinal studies including: Australian Longitudinal Study on Women's Health (ALSWH) (funded by the Department of Health), Healthy Ageing of Women Study (HOW), Melbourne Collaborative Cohort Study (MCC), Danish Nurse Cohort Study (DNC), Women's Lifestyle and Health Study (WLH), MRC National Survey of Health and Development (1946) (NSHD), The National Child Development Study (NCDS), English Longitudinal Study of Ageing (ELSA), UK Women's Cohort Study (UKWCS), Whitehall II, Hilo Women's Health Study (HILO), San Francisco Midlife Women's Health Study (SFM), Study of Women's Health across the Nation (SWAN), Japanese Midlife Health Study (JMHS), Japan Nurses' Health Study (JNHS), Decisions at Menopause Study (DAMES), and Seattle Midlife Women's Health Study (SM). The Study of Women's Health Across the Nation (SWAN) has grant support from the National Institutes of Health (NIH), DHHS, through the National Institute on Aging (NIA), the National Institute of Nursing Research (NINR) and the NIH Office of Research on Women's Health (ORWH) (Grants U01NR004061; U01AG012505, U01AG012535, U01AG012531, U01AG012539, U01AG012546, U01AG012553, U01AG012554, U01AG012495). All studies would like to thank the participants for volunteering their time to be involved in the respective studies. The content of this manuscript is solely the responsibility of the authors and does not necessarily represent the official views of the NIA, NINR, ORWH or the NIH. The findings and views in this talk are not those of the original studies or their respective funding agencies.

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