Genome-wide meta-analysis plan for menarche and menopause in ReproGen

Studies should upload data using the densest imputation reference panel (including X chromosome) they are able to share. Uploaded studies will be included in successive waves of meta-analysis which will become large in sample size and variants assayed. We ask that you analyse 5 different models (each of which should include study specific covariates to control for population structure):

1) **Age at menarche as a quantitative trait**. Self-reported and recorded in whole years.

Covariates: Birth year

Exclusions: menarche age <9 or > 17

2) **Early menarche as a binary trait -** Early (coded as 1) menarche age range 8-11 inclusive vs normal (coded 0) menarche age = 13

Exclusions: studies that do not have at least 100 early cases.

3) **Late menarche as a binary trait** - Late (coded as 1) menarche age range 15-19 inclusive vs normal (coded 0) menarche age = 13

Exclusions: studies that do not have at least 100 late cases.

4) **Age at Natural Menopause as a quantitative trait.** All women with a self-reported age at natural menopause (ANM) between 40 and 60 years inclusive. Menopause is defined as the age at the last menstrual period, after at least 12 consecutive months of amenorrhea (as derived from questionnaire data).

Exclusions:

- Hysterectomy and/or bilateral ovariectomy
- Menopause induced by radiation/chemotherapy
- HRT use before menopause

5) **Age at Natural Menopause as a binary trait.** Early menopause 20 to <45 years (coded as 1) vs menopause age ≥50 to ≤60 years (coded as 0)

Exclusions:

- Hysterectomy and/or bilateral ovariectomy
- Menopause induced by radiation/chemotherapy
- HRT use before menopause
- Studies with less than 100 cases

File upload: please contact John Perry (john.perry@mrc-epid.cam.ac.uk) or Anna Murray (A.murray@exeter.ac.uk)

Please include a README file with the following study descriptive information:

General
Contact person for each study.
Named individuals with contact details for who should be considered in future publications, including: analysts and PIs (if possible indicate their role in your study, so that we can direct any queries to the appropriate person)
Brief description of your study
Acknowledgements for your study, including funding sources

For genotypes: Genotyping QC conducted (if not part of CHARGE joint calling); Version of SNP Chip used, imputation package used.

For menarche:
Menarche question(s) administered at your study, for example: "*How old were you at the time of your first menstrual period"* and response choices

Quantitative trait analysis:
Sample size
Mean age, range of sample
Mean age at menarche, range
Birth cohort range of your sample

Dichotomous trait analysis:
Sample size, N in lower extreme, N in upper extreme
Mean age, range for lower extreme
Mean age, range for upper extreme

For menopause:
Questions use to determine age at natural menopause at your study, for example: *"Have your periods stopped for 1 year or more? Cause periods stopped? Age periods Stopped? Hysterectomy? Number of ovaries removed? Have you used hormone replacement therapy?"*

Quantitative trait analysis:
Sample size
Mean age, range of sample
Mean age at natural menopause, range
Histogram of menopause age in your population

Dichotomous trait analysis:
Sample size, N in lower extreme, N in upper extreme
Mean age, range for lower extreme; Mean age, range for upper extreme