

A randomised placebo-controlled trial of the effect of hormone replacement therapy on dementia and cognitive function in post-menopausal women

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Registration date 25/10/2000	Overall study status Stopped	<input type="checkbox"/> Protocol
Last Edited 08/07/2013	Condition category Urological and Genital Diseases	<input type="checkbox"/> Statistical analysis plan
		<input type="checkbox"/> Results
		<input type="checkbox"/> Individual participant data
		<input type="checkbox"/> Record updated in last year

Plain English summary of protocol

Not provided at time of registration

Contact information

Type(s)

Scientific

Contact name

Dr Martin Prince

Contact details

Head of Section of Epidemiology
PO 060
Institute of Psychiatry
De Crespigny Park
London
United Kingdom
SE5 8AF
+44 (0)20 7848 0136
m.Hughes@iop.kcl.ac.uk

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

G9828540

Study information

Scientific Title

Acronym

WISDOM-COG

Study objectives

To investigate the association between HRT and cognitive function, specifically:

1. To investigate the efficacy of long-term HRT in lowering the incidence of late-onset dementia in post-menopausal women. This is henceforth referred to as the dementia component.
2. To investigate the efficacy of HRT in reducing cognitive decline in postmenopausal women without dementia. This is henceforth referred to as the cognitive component.

Added 19/08/09:

The WISDOM Trial

WISDOM is a long-term trial of HRT in the United Kingdom recruiting 22,000 women, aged 50-69 years, treated for a median of 10 years and followed up for a further 10 years. Participants will be recruited from among women registered with the MRCs extensive network of General Practice Research Framework (MRC GPRF) practices. Recruitment will span 1999-2002, and the trial plans to report in 2010. The trial will provide information on the relative effectiveness of oestrogen only replacement therapy (ORT), progestogen and oestrogen replacement therapy (PORT) and placebo on the principal endpoints, which are incidence of major cardiovascular disease, osteoporotic fractures and breast cancer. WISDOM-COG makes use of the opportunity provided by the WISDOM trial to test the hypotheses that HRT reduces the risk of incident dementia and cognitive decline in post-menopausal women.

Dementia component

All women recruited into WISDOM, who would reach the age of 65 before the end of the treatment period will be eligible for the dementia component sub-study. Over 12,000 eligible women will be screened by GPRF based research nurses, upon recruitment, and every two years after reaching the age of 65, using the TICS-m dementia screening test. In a three-stage dementia diagnostic assessment those scoring below a threshold on the TICS-m will receive a more detailed, cognitive, clinical and neurological assessment from one of 12 specially trained regional nurse coordinators. Final dementia diagnoses and sub-type diagnoses will be made by a consensus panel. The main outcome will be ICD-10 dementia, and the sub-study is powered (at 90%), with 36,698 women years of follow-up in the age at risk for dementia, to detect a 26% risk reduction for all cause dementia, for the PORT vs. placebo comparison.

Cognitive component

For the cognitive component, we shall recruit equal numbers (n=580) of women from four five-year age bands, 50-54, 55-59, 60-65 and 65-69 years. These women will be recruited from a subset of the larger GPRF practices. The research nurses from these practices will be specially trained to administer to them a detailed multi-domain battery of cognitive tests at entry into WISDOM, and at two and five years thereafter. In a tie in with another WISDOM sub-study, mood, wellbeing and quality of life will also be assessed in this group. This study, with 560 women in each age group, is powered to detect an effect size of 0.5 (PORT vs. placebo),

equivalent to a reduction in one word recalled on delayed recall of the 10 word CERAD list learning task.

Ethics approval required

Old ethics approval format

Ethics approval(s)

Not provided at time of registration

Study design

Randomised controlled trial

Primary study design

Interventional

Secondary study design

Randomised controlled trial

Study setting(s)

Not specified

Study type(s)

Treatment

Participant information sheet**Health condition(s) or problem(s) studied**

Obstetrics and gynaecology

Interventions

Women who have had a hysterectomy and are not already taking HRT will be randomised to oestrogen only replacement therapy (ORT), progestogen and oestrogen replacement therapy (PORT) or placebo.

Women who have not had a hysterectomy will be randomised to PORT or placebo.

The principal comparison on the principal endpoints will be HRT (PORT or ORT) versus placebo.

Updated 08/07/2013: The trial was stopped around one year after recruitment began because the very similar Women's Health Initiative trial in the USA was stopped because of a higher risk of cardiovascular events and dementia in those randomised to HRT.

Intervention Type

Other

Phase

Not Applicable

Primary outcome measure

Dementia component: The principal outcome will be onset of dementia according to ICD-10 criteria.

Cognitive component: Change of cognitive test performance on the Wechsler Logical Memory Recall.

The trial will have 90% power, at the 5% significance level, to detect an effect size, associated with randomisation to HRT, of 0.5 or greater enabling us to detect a difference of two story components recalled out of a total of 25 for Wechsler Logical Memory story recall.

Added 19/08/09: Follow up duration for primary endpoints Dementia component - 2009 (10 years) Cognitive component - Five years

Secondary outcome measures

Dementia component: The secondary outcome will be onset of the dementia sub-type diagnosis of Alzheimer's disease (AD) diagnosed according to NINCDS-ADRDA criteria (possible and probable).

Overall study start date

01/06/2000

Completion date

31/05/2010

Reason abandoned (if study stopped)

Objectives no longer viable

Eligibility

Key inclusion criteria

Age 50-69, female, post-menopausal, no contraindication to HRT.

For both components, in addition to the WISDOM trial inclusion criteria, subjects will only be recruited if they can be randomised to receive placebo, ie excluding the 21% of WISDOM recruits with a total hysterectomy who are already taking HRT.

For the dementia component sub-study only those who will reach the age of 65 years before the end of the projected follow-up period (2009) will be included.

Participant type(s)

Patient

Age group

Adult

Sex

Female

Target number of participants

Dementia component - 12,000. Cognitive component - 2,240. Total - 14240

Key exclusion criteria

Not provided at time of registration

Date of first enrolment

01/06/2000

Date of final enrolment

31/05/2010

Locations

Countries of recruitment

England

United Kingdom

Study participating centre

Head of Section of Epidemiology

London

United Kingdom

SE5 8AF

Sponsor information

Organisation

Medical Research Council (MRC) (UK)

Sponsor details

20 Park Crescent

London

United Kingdom

W1B 1AL

+44 (0)20 7636 5422

clinical.trial@headoffice.mrc.ac.uk

Sponsor type

Research council

Website

<http://www.mrc.ac.uk>

Funder(s)

Funder type

Research council

Funder Name

Medical Research Council (MRC) (UK)

Alternative Name(s)

Medical Research Council (United Kingdom), UK Medical Research Council, MRC

Funding Body Type

Government organisation

Funding Body Subtype

National government

Location

United Kingdom

Results and Publications

Publication and dissemination plan

Not provided at time of registration

Intention to publish date**Individual participant data (IPD) sharing plan****IPD sharing plan summary**

Not provided at time of registration