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

Submission date 25/10/2000	**Recruitment status** Stopped	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 25/10/2000	**Overall study status** Stopped	
Last Edited 08/07/2013	**Condition category** Urological and Genital Diseases	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
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 form 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

Study type(s)
Treatment

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(s)
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

Key secondary outcome(s))
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).

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

Healthy volunteers allowed
No

Age group
Adult

Sex
Female

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
United Kingdom

England

Study participating centre

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Sponsor information

Organisation
Medical Research Council (MRC) (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

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration