

INFORMATION FOR DOCTORS

About the D-Health Trial

The D-Health Trial is a randomised trial of vitamin D supplementation for the prevention of cancer and reduction of mortality in older adults. It is funded by the National Health and Medical Research Council. The trial is sponsored by the QIMR Berghofer Medical Research Institute (previously called the Queensland Institute of Medical Research) in collaboration with scientists and clinicians (including an endocrinologist) from around Australia. The QIMR Berghofer Human Research Ethics Committee has approved the D-Health Trial and it has been notified to the TGA.

Why do a vitamin D trial?

The role of vitamin D in diseases such as cancer and cardiovascular disease is uncertain. The vast majority of existing evidence is derived from observational studies, and for most diseases the results to date are inconsistent. The major challenge in these studies is controlling for bias and confounding. In light of the suggestive but inconclusive evidence available, several bodies (such as the International Agency for Research on Cancer and the United States Institute of Medicine) have called for large-scale trials of vitamin D. The D-Health Trial is one of several large trials taking place internationally.

Brief detail of methods

We aim to recruit 25,000 Australians aged between 60 and 84. Potential participants are selected at random from the Australian Electoral Roll or contact us to volunteer for the trial. We send a letter of invitation including an Expression-of-Interest form, which enables us to assess eligibility. Those eligible are sent more comprehensive information, a consent form and a short survey. Participants who complete the consent form and the survey enter the D-Health Trial. Volunteers who are not specifically invited can also take part.

Participants are randomised to monthly doses of 60,000 IU of vitamin D or placebo for 5 years. Health outcomes will be captured for at least 5-years beyond the intervention period through linkage with Australian health registers. Participants are sent 12 tablets at a time and we send a reminder (email, text or landline telephone) to take the tablet each month. We ask them to complete a short survey each year.

Eligibility criteria

Participants must not have a history of: sarcoidosis, hyperparathyroidism, hypercalcaemia, hypercalcaemia or osteomalacia. They must not be taking more than 500 IU vitamin D per day.

What are the risks?

The dose that we are using is safe. It is equivalent to 2000 IU/day which is half the tolerable upper limit. Using a monthly dose improves compliance, is pharmacokinetically appropriate and has been shown to be safe. Other studies are using monthly doses of 100,000 IU or higher. There are no absolute contraindications other than sarcoidosis, hyperparathyroidism, hypercalcaemia or a past history of renal calculi.

Is there a risk of vitamin D deficiency in the placebo group? The definition of deficiency is highly controversial (part of the reason that we need a trial) and current assays are unreliable, so testing everyone's 25(OH)D level is not considered appropriate. The current weight of evidence suggests a serum level of 40-50 nmol/L is sufficient for most people, and that this can be achieved with adequate safe sun exposure or a moderate supplement dose (**see Lucas and Neale, Australian Family Physician 2014; 43(3):119-122**). The current Australian recommendations are for intake of 400 IU of vitamin D per day for under 70 year olds and 600 IU per day in those over 70 *in the absence of sun exposure*. American recommendations are slightly higher (600-800 IU/day) but again this is in the complete absence of sun exposure. We are allowing participants to enter the study if they are taking up to 500 IU per day (a multivitamin or a 1000 IU dose every second day). The likelihood of deficiency among ambulatory older adults who receive some sun exposure would be low if they were taking this dose.

Our credentials

The investigator team has considerable experience in conducting large-scale population-based studies. We also carried out an NHMRC-funded pilot of D-Health (methods published in the *Journal of Clinical Endocrinology and Metabolism*, 2012; 97:4473-4480).