Synopsis for Vitamin D and Longevity (VIDAL) Trial: randomised feasibility study

This is a two year randomised controlled feasibility trial on 1600 people aged 65-84 comprising two study designs:

(i) Blinded study: Participants in double-blind practices will be randomised to receive either 100,000 IU monthly (average 3300 IU/day) of oral vitamin D3 (presented as 5 ml Vigantol Oil) or double-blind placebo control (5 ml Miglyol 812 Oil) monthly for 2 years: 800 participants
(ii) Open label study: Participants in unblinded practices will be randomised to receive either 100,000 IU monthly (average 3300 IU/day) of oral vitamin D3 (5 ml Vigantol Oil) monthly for 2 years or open control (no treatment): 800 participants

Twenty GP practices will be cluster randomised to either blinded or open label study design. We will identify 10 pairs of GP practices matched on region and socioeconomic profile (deprivation score based on practice postcode) and randomly select one practice within each matched pair in which participants will be individually randomised between vitamin D and placebo, while participants in the other practices will be individually randomised between open-label vitamin D and open control.

Primary outcomes of the feasibility study

The primary aim of the feasibility study is to establish the procedures required to conduct the main trial: our target is to randomise 1,600 participants aged 65-84 through 20 GP practices.

Primary outcome measures:

1. The overall recruitment rate (the proportion of invited participants who are randomised) and comparison of recruitment rate in blinded versus open control studies.
2. The overall level of compliance with study medication and comparison of blinded medication versus open label vitamin D compliance (to evaluate whether participants taking open label vitamin D are more or less compliant than those who are unaware of IMP status). A randomized participant is defined as compliant:

(i) If allocated to vitamin D: they report taking at least 19 (79%) of the 24 monthly doses of allocated IMP, and attend the 2-year follow-up visit.
(ii) If allocated to no vitamin D (whether placebo or open control): they report taking a total of <300,000 IU of vitamin D supplements over the 2 years of the study, and attend the 2-year follow-up visit. (The current UK RDA of 400 IU/day is 292,000 IU over 2 years).

These will be combined as a single outcome measure, which is the number of people we must invite to get one person complying with allocated treatment, to demonstrate that the main trial is feasible. It equals the number invited divided by the number randomised and compliant.

Secondary outcomes of the feasibility study

(i) The overall level of attrition (failure to attend the final 2-year visit), and a comparison of attrition between open label and blinded practices.
(ii) Costs of blinded versus open label study designs.
(iii) Comparison of incidence of serious adverse events between vitamin D and control in blinded practices.
(iv) Comparison between vitamin D and control of numbers of infections, GP prescriptions and GP visits (a) in blinded practices, and (b) in open-label practices. This will provide an estimate of the bias in these measures in participants allocated to vitamin D in an open control design.
(v) Serum 25(OH)D concentration at recruitment and at 2years in relation to allocated treatment and other potential determinants of vitamin D status (self-reported sun exposure, diet and use of vitamin D supplements).
(vi) Cause-specific mortality and cancer incidence will be ascertained by flagging in the National Health Service Information Centre (NHS IC).
(vii) Hospital records will be collected by NHS number linkage with the Hospital Episode Statistics (HES) database.

Additional trial assessments

Before randomisation:

1) The GP nurse will record details of foreign holidays, sunbathing, sunbed use and use of vitamin supplements on the online Case Report Form (CRF) at the GP practice with all participants before randomisation.
2) A blood sample will also be taken, and corrected serum calcium will be assayed before randomisation to establish eligibility. Serum 25(OH)D will also be assayed. Aliquots (plasma and buffy coat) will be stored in liquid nitrogen for further analysis (subject to additional funding) including genetic studies.

At two years:

1) All 1600 participants will attend the GP practice 2 years after randomization. A further blood sample for 25(OH)D assay and responses to the same online CRF questions will be obtained to quantify differences in vitamin D status and factors that may affect it between the intervention and control groups in blinded versus open label studies.
2) Summaries of GP records for all participants will also be extracted for GP visits, prescriptions and infections for one year pre-randomisation and 2 years post-randomisation.

VIDAL Study Flowchart