Vitamin D analogues, mortality, and cardiovascular risk in chronic kidney disease: a systematic review and meta-analysis of randomized controlled trials

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Background

- **Kidneys play a critical role in the vitamin D metabolic pathway, thus vitamin D deficiency is highly prevalent in the chronic kidney disease (CKD) population**
- **Vitamin D deficiency is associated with all-cause and cardiovascular mortality as well as increased cardiovascular risk, and vitamin D supplementation has been shown to improve survival and cardiovascular event rates in healthy and diseased populations**
- **Current evidence for this physiological association is mainly derived from observational studies, however it is not clear whether a direct, causal relationship exists between vitamin D serum levels and all-cause or cardiovascular mortality rates**

Objective

- **To determine whether data from randomized controlled trials (RCTs) supports a direct role for vitamin D supplementation in reducing the risk of mortality and adverse cardiovascular events**
- **Further, to establish whether different vitamin D analogues provide varying degrees of risk reduction**

Methods

- **Electronic bibliographic databases (PubMed, MEDLINE, EMBASE, and Cochrane Library) nephrology journals, and conference proceedings were searched in October 2013**
- **Studies were included if following criterion were met: CKD population (GFR, <60 ml/min/1.73m^2), blinded randomization to receive oral vitamin D supplementation or placebo, mortality and/or cardiovascular serious adverse outcomes reported**
- **Pooled relative risks (RR) were calculated using a random effects model**
- **Data was further stratified by CKD stage, vitamin D analogue utilized, weekly standardized dose of vitamin D, and percentage of diabetic subjects in each trial**

Results

- **Among 4,246 studies screened, 13 RCTs were included in the meta-analysis**
- **The results suggest no significant effect of oral vitamin D supplementation on all-cause or cardiovascular mortality, or cardiovascular serious adverse events among patients with CKD regardless of stratification by a number of variables**
- **Substantial heterogeneity between trials was due to variations in dosing frequency and regimen, trial duration, and length of follow up**
- **None of the included trials were designed *a priori* to capture mortality or cardiovascular risk as an outcome in relation to vitamin D supplementation**

Fig 1. PRISMA Flow Diagram

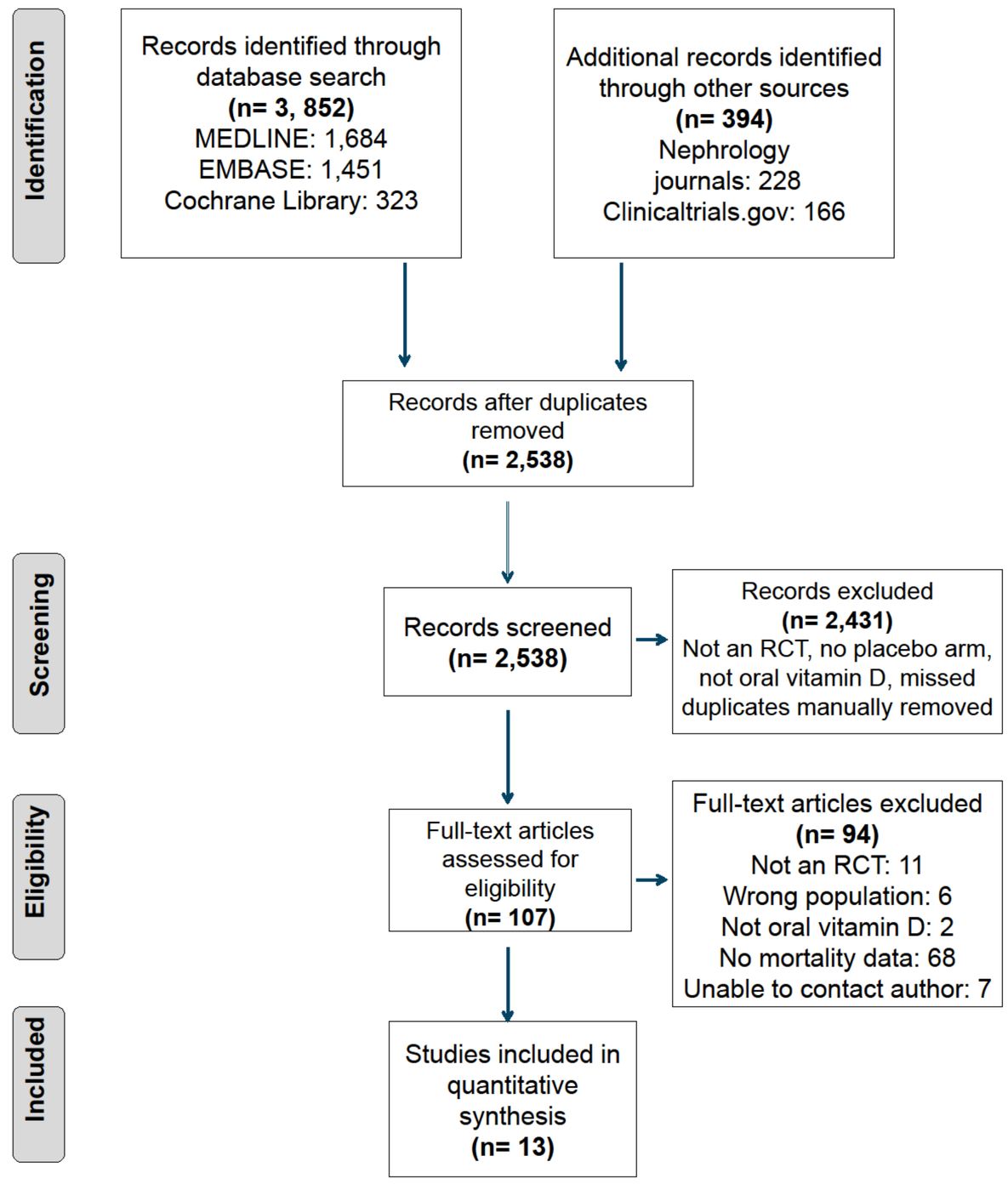
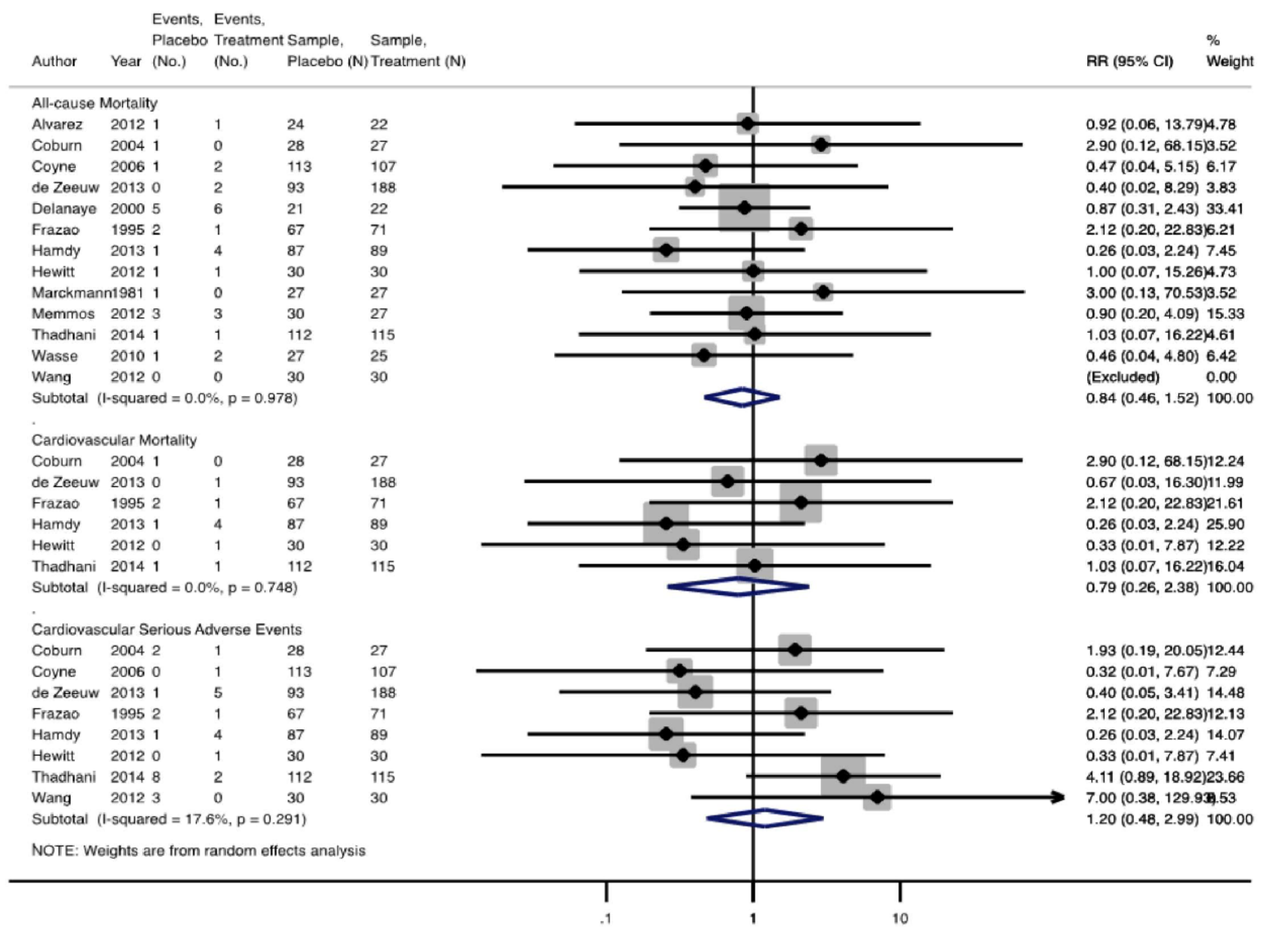


Fig 2. Pooled estimate of the effect of vitamin D on risk of all-cause mortality, cardiovascular mortality, and cardiovascular serious adverse events in CKD



Conclusion: **Current RCTs are limited and vary drastically in study design. Pooling data does not allow for interpretation of the relationship between vitamin D supplementation and all-cause mortality or cardiovascular risk within the CKD population. Additional trials investigating patient-level outcomes in relation to vitamin D supplementation are critically needed in this population.**

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H) Clinical Nephrology, Chronic Kidney Disease (CKD). H1) Lab methods, progression & risk factors for CKD 1-5, nutrition in CKD, renal diseases (except GNs and cystic diseases).
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