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A Meta-Analysis of the Effects of SGLT-2 Inhibitors on Serum Electrolytes

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(*) indicates primary project advisor

(**) indicates another student who is declaring the same project as primary for SI



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Disclosures

- None

- Background: **Sodium–glucose cotransporter 2 (SGLT2) inhibitors** are a class of glucose-lowering agents indicated for the treatment of type 2 diabetes
 - Selectively inhibit renal glucose reabsorption and increase urinary glucose excretion (UGE)
- Rationale: Data on the influence of SGLT2 inhibitors on electrolyte handling in individuals with type 2 diabetes is lacking.
 - Due to increased UGE, treatment with SGLT2 inhibitors may result in osmotic diuresis, which may trigger volume depletion and dehydration affecting electrolyte levels

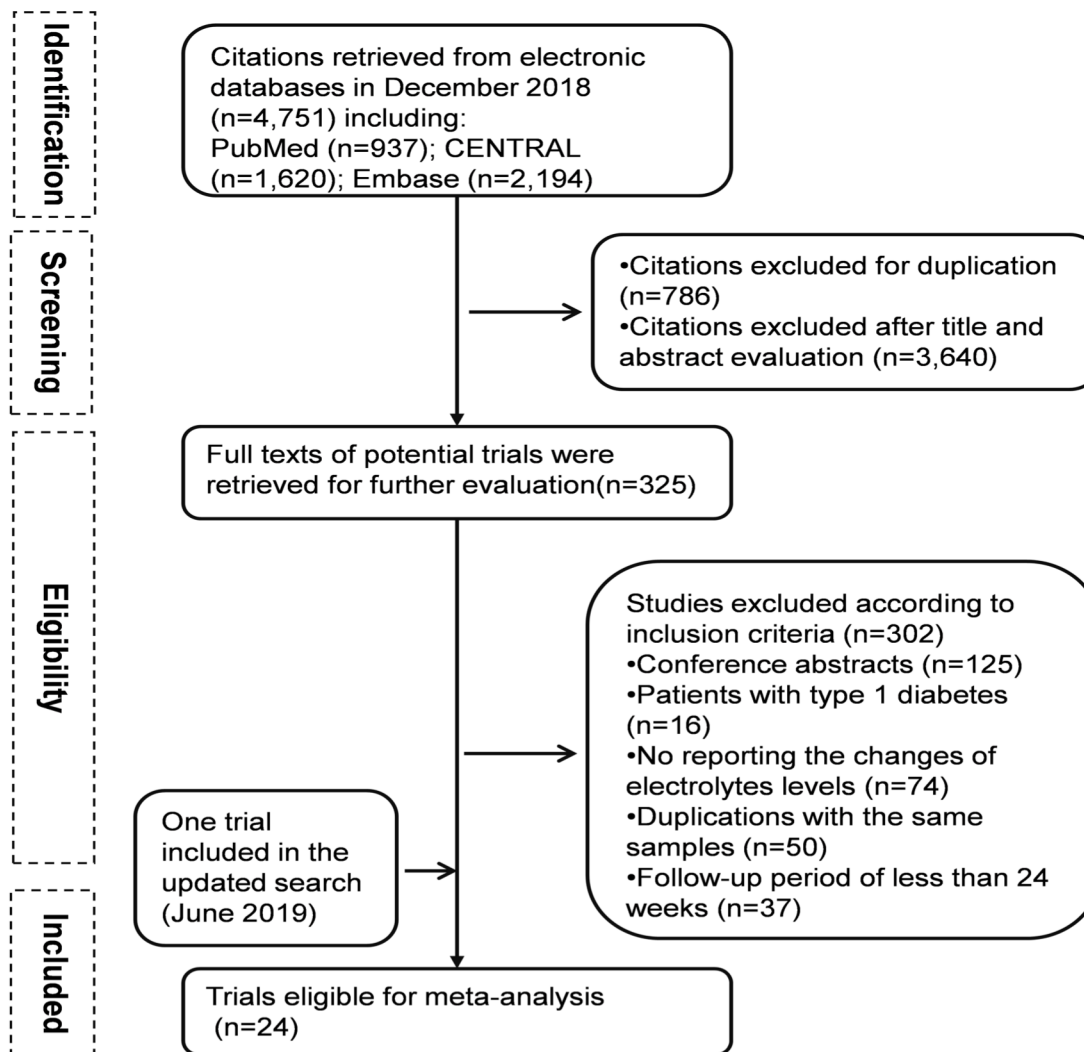
- **Why do we care? Electrolyte abnormalities can lead to serious complications and even death especially in patients with comorbidities such as DM**
 - Characterize drug class effect
 - Characterize specific drug effect
 - Investigate if effects of electrolytes can explain the renal and cardiac benefits associated with SGLT2 inhibitors in patients with T2DM
- Objectives: Meta-analysis of the available evidence to examine SGLT2 inhibitors affect on serum electrolyte levels in patients with type 2 diabetes

Objectives & Hypothesis

- Research Question:
 - To what extent, if any, do SGLT2 inhibitors affect serum electrolyte levels in patients with type 2 diabetes mellitus?
- Hypothesis
 - Given that SGLT2 inhibitors induce glucosuria and osmotic diuresis, we hypothesized that increases in circulating electrolyte levels would occur with the use of these medications in type 2 diabetics

Approach & Results

- Study design: Database search and subsequent meta-analysis of included trials
- Population: Patients with Type 2 Diabetes
- Intervention: SGLT2 Inhibitors
- Comparison group: Placebo
- Outcome: Serum Mg, Phos, Ca, Na, K, Uric acid



Approach & Results

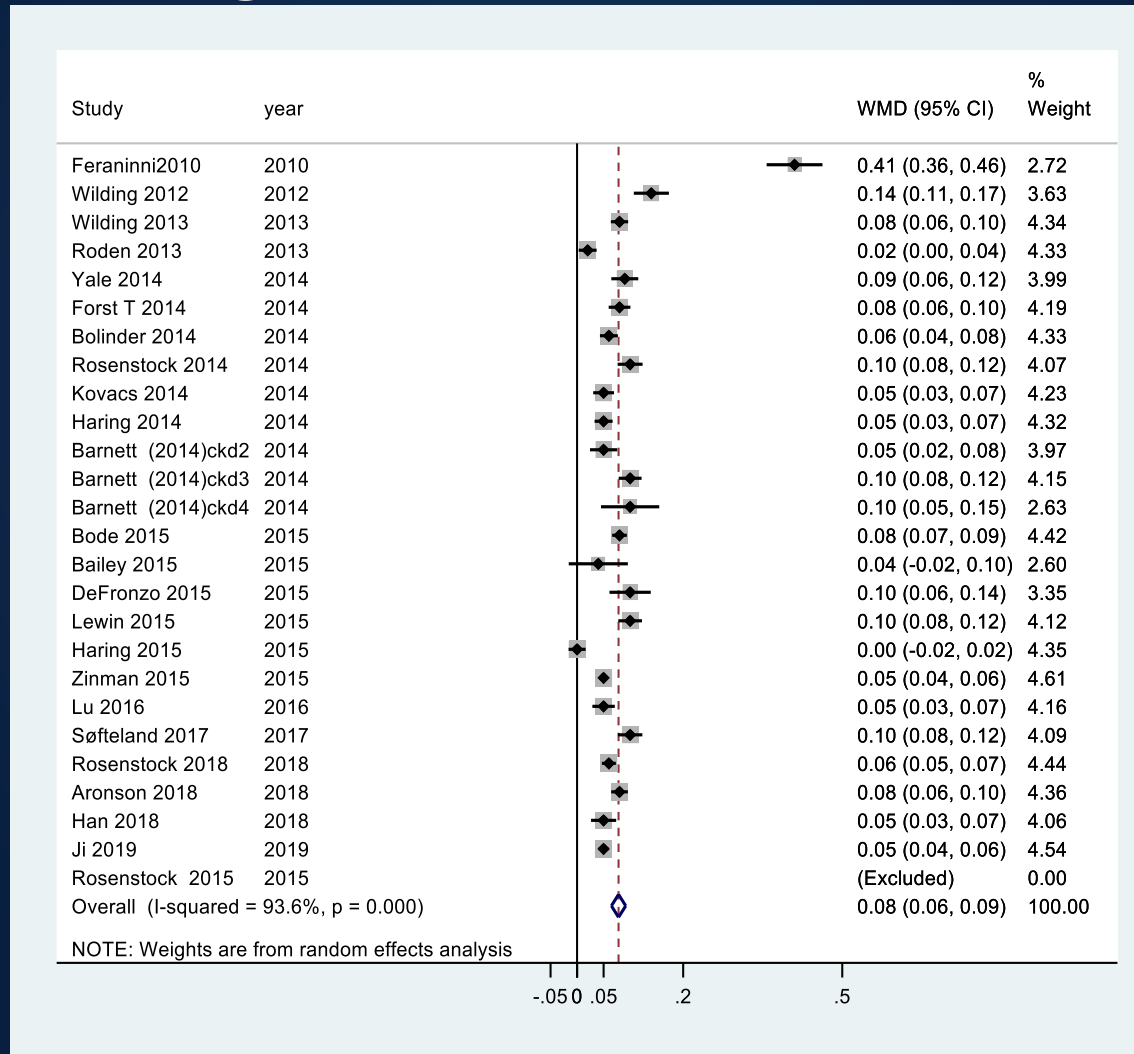
- Analysis:
 - **Weighted mean differences (WMD)** (95% CI) in serum electrolyte levels were calculated for each SGLT2 inhibitor and placebo using a random-effects model to evaluate each SGLT2 inhibitor separately and by dose
 - A **network meta-analysis** with a random-effects model was used to compare different SGLT2 medications
 - Performed with STATA v13.1

Approach & Results

- Results:
 - Overall, compared with placebo, SGLT2 inhibitors were **significantly associated with elevations in serum magnesium** by 0.08 mmol/L, **serum phosphate** by 0.02 mmol/L, and **serum calcium** by 0.01 mmol/L.
 - The elevated effect on magnesium was more evident for dapagliflozin compared with empagliflozin.
 - No statistically detectable differences were evident between any other two of SGLT2 inhibitors.

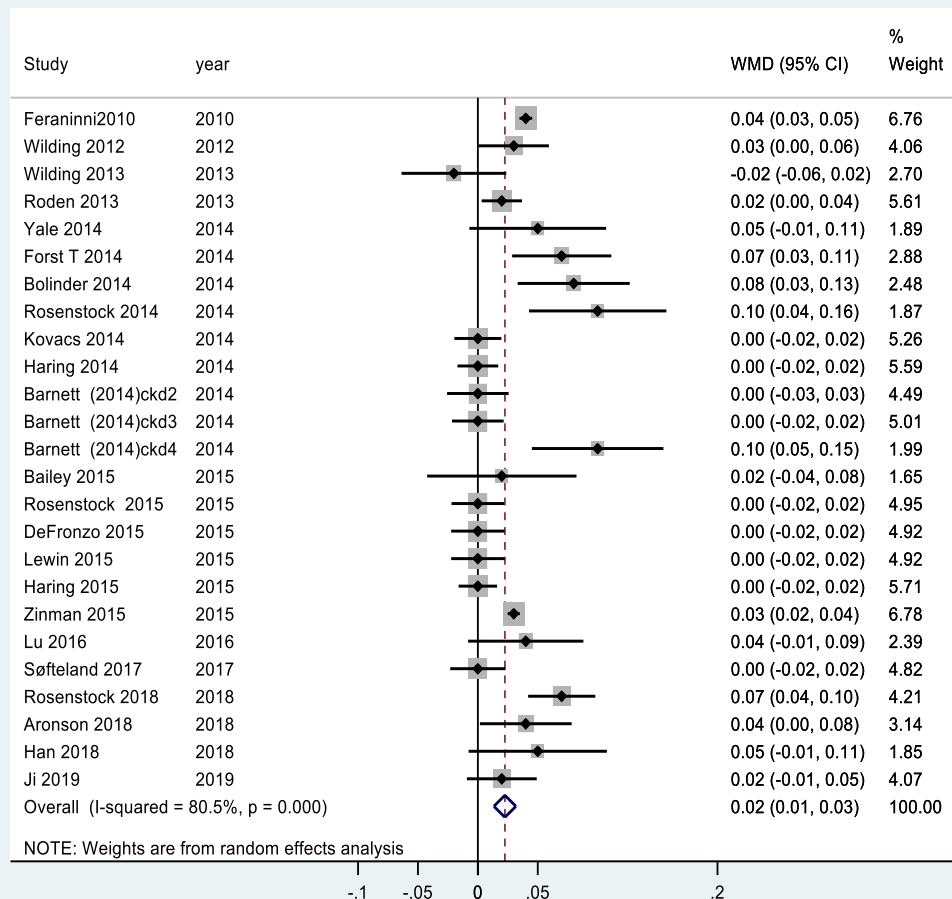
Approach & Results

- Pairwise: Magnesium Levels



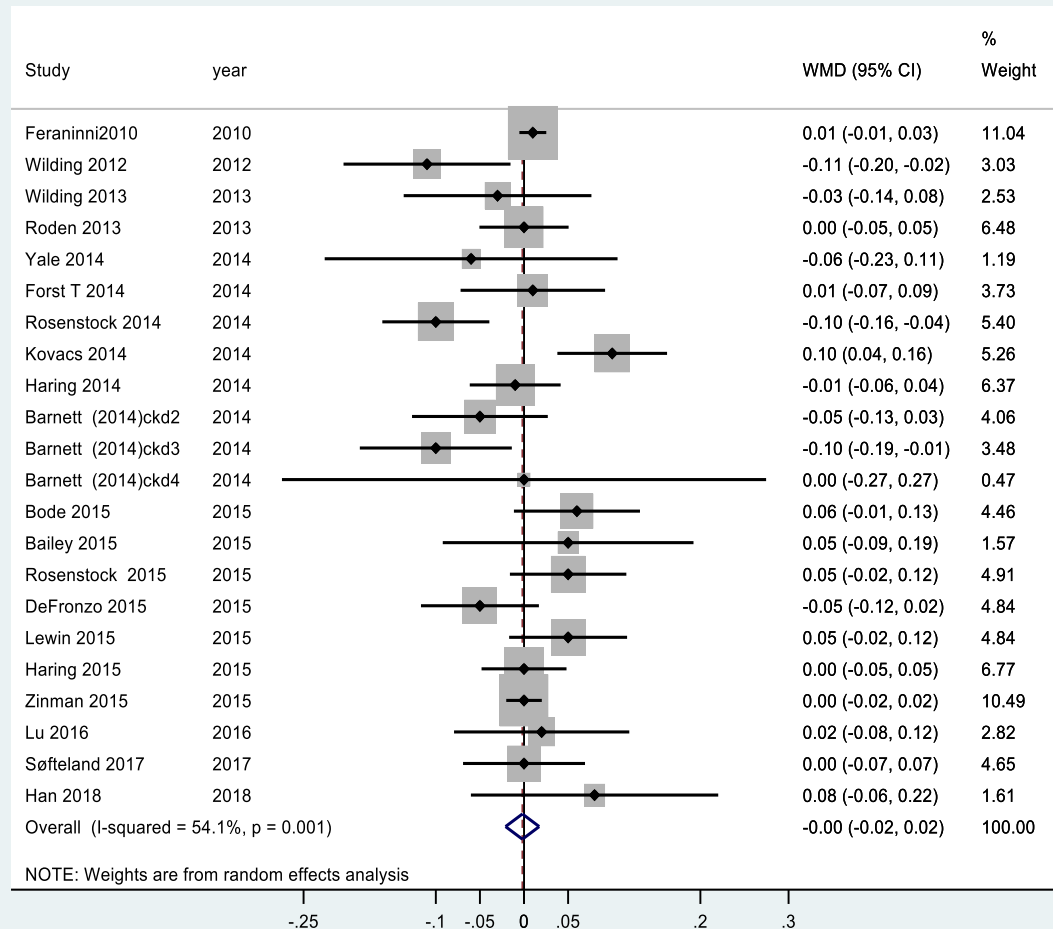
Approach & Results

- Pairwise: Phosphate Levels



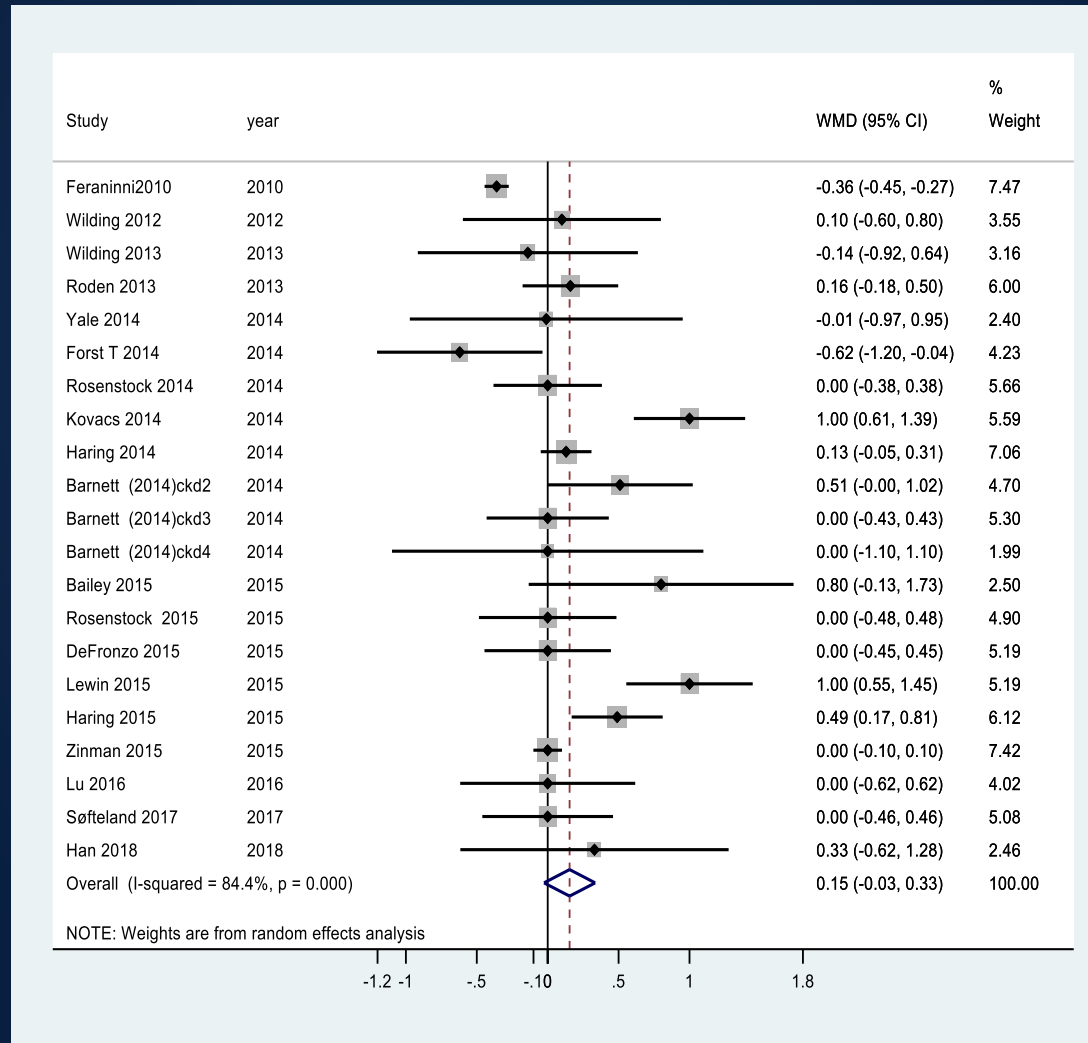
Approach & Results

- Pairwise: Potassium Levels



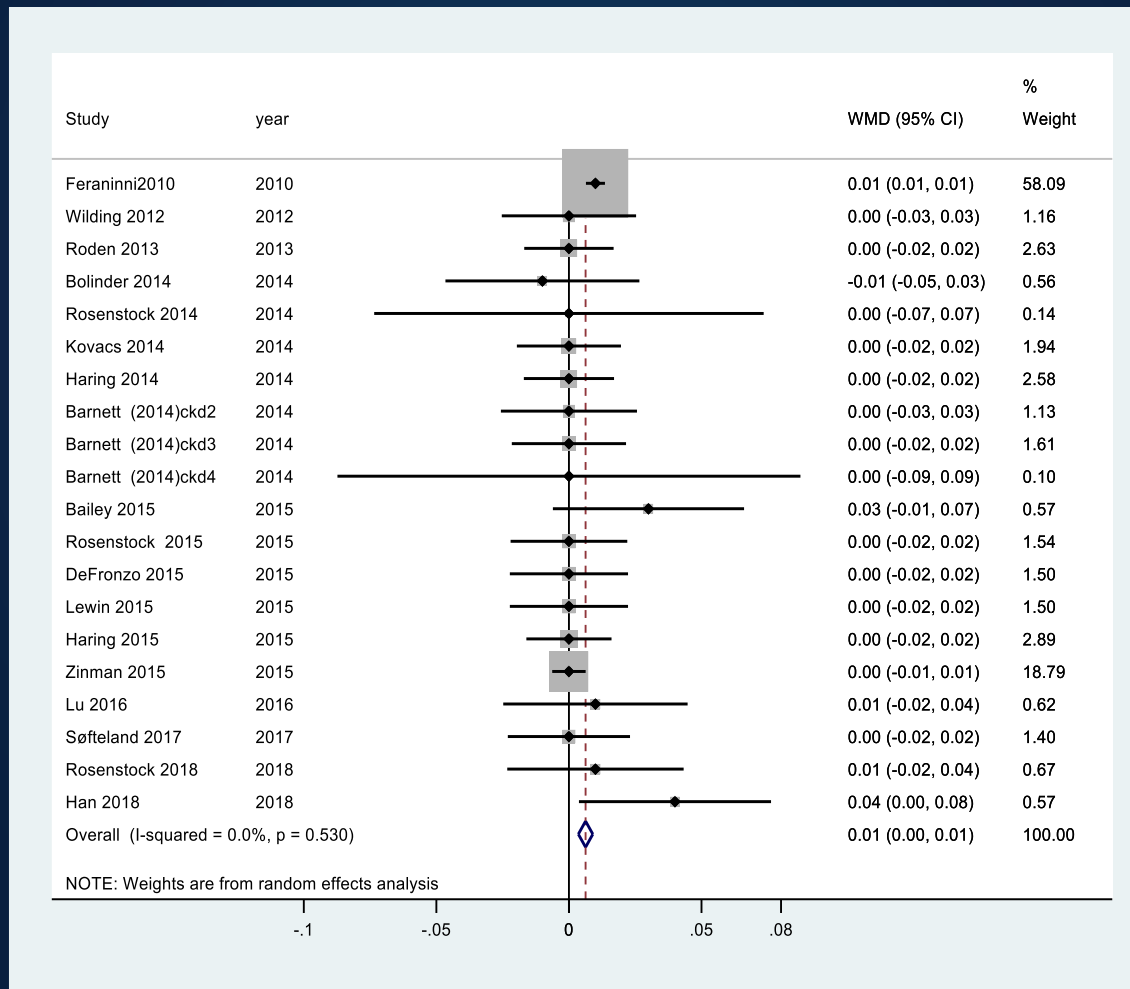
Approach & Results

- Pairwise: Sodium Levels



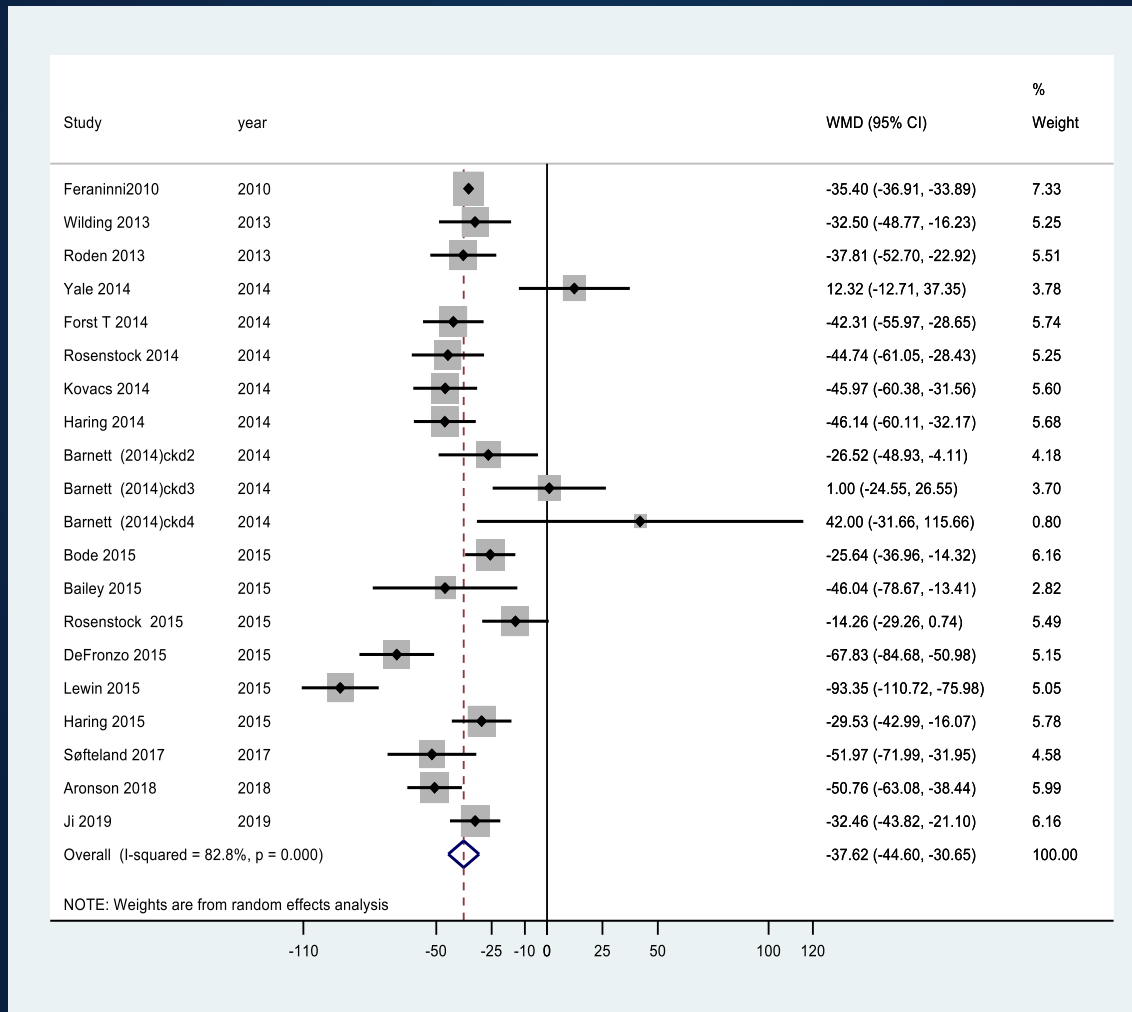
Approach & Results

- Pairwise: Calcium Levels



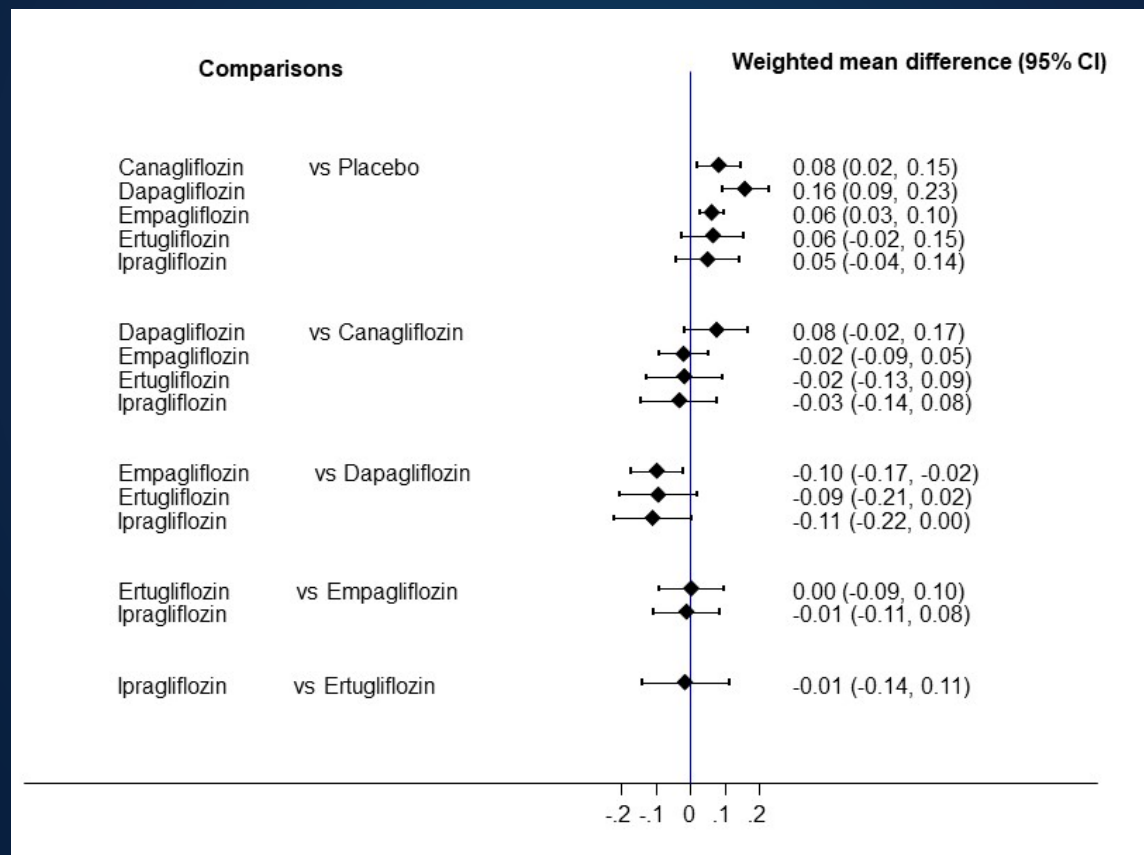
Approach & Results

- Pairwise: Urate Levels



Approach & Results

- Network Analysis: Magnesium



Conclusions

- This study suggests that use of SGLT2 inhibitors increase electrolyte levels to varying degrees, with discernible effects on magnesium, phosphate, and calcium
- Future investigation is required to assess clinical consequences of these effects in T2D patients

Future Directions

- Currently updating to include all trials through December 2020
 - Increase power of study and improve network analysis for comparison between SGLT2 inhibitors
- Study does not take into account other medications taken by patients with T2DM

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