Reviewer's report

Title: Serum calcium and risk of gastrointestinal cancer in the Swedish AMORIS study

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Reviewer: Dagfinn Aune

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This is an interesting study on serum calcium and gastrointestinal cancer. The study was large and had a relatively long follow-up and large number of cancer cases providing considerable statistical power to detect moderate associations. There was an increased risk of colorectal cancer with greater serum calcium concentrations after correction for albumin concentration.

Major compulsory revisions
1. One question with regard to the interpretation of the results is to what degree does serum calcium reflect dietary or total calcium intake or pathophysiological processes?

2. And what is more relevant to cancer development - serum calcium or dietary intake? It is possible that it is the calcium concentration in the intestinal lumen that is most relevant to colorectal carcinogenesis by binding secondary bile acids and ionized fatty acids and thereby reducing proliferative effects in the colonic epithelium. This should at least be mentioned as a potential limitation of the study.

3. Could the authors clarify what is the rationale for adjusting for serum albumin in the methods section? Although low or high levels can be an indicator of existing disease it could also theoretically be influenced by dietary factors including dairy products (which are high in both calcium and protein).

4. Do the authors have information on any other potential confounders (alcohol intake, smoking etc.)?

Discretionary revisions
5. It was stated that there was limited statistical power when the results for serum calcium were stratified by BMI. Were the risk estimates any different from the overall analysis? Perhaps these results could be added in a supplement?

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable
Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests