Journal of Infectious Diseases & Research
JIDR, 4(S1): 02
www.scitcentral.com
ISSN: 2688-6537
Abstract: Open Access

Comment re "No evidence that Vitamin D is Able to Prevent or Affect the Severity of COVID-19 in Individuals with European Ancestry: A Mendelian Randomization Study of Open Data", by Amin & Drenos

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Published May 19th, 2021

ABSTRACT

Amin et al. report no support for vitamin D supplementation to reduce Covid-19 risks from Mendelian randomisation analysis using GWAS-determined gene variant effects on serum 25-(OH)D concentrations [used as surrogates for long-term vitamin D status], from UK-biobank data on Britons with European ancestry. MRA using gene-variants for 25(OH)D is common despite well-recognised errors due to non-linearity of biological and health effect associations with 25(OH)D. Inclusion of data from the plateaus of the S-shaped associations of biological effects with 25(OH)D confounds these analyses [but was used by Amin et al.] Vitamin D efficacy is minimal along both the lower and upper plateaus, increasing from deficiency [UK definition <25nmol/l] to improving bone health at >50nmol/l, but requiring 80-100nmol/l before insulin resistance & T2DM risks fall, respectively, and with little response to supplementation once replete. GWAS effects on 25(OH)D were markedly less than the 25-50-75 nmol/l [100-200-300%] increases from deficiency such thresholds require. MRA cannot be expected to detect health benefits with small variant-related changes in 25(OH)D or in data-sets including many subjects with baseline deficiency or already replete. However, it is possible that avoiding data from associational health-effect plateaus by using datasets with baseline 25(OH)Ds between 25 -125 nmol/l, [though predicting only ~16% of final D status] might increase the value of GWAS and MRA analyses of health-effects with D status. 25-125nmol/l is suggested by the dose-wise reductions in Covid-19 risks seen prospectively with higher 25(OH)Ds measured during the year before the pandemic began in data from a large representational multi-state American cohort study. Many known mechanisms suggest that better vitamin D status should be protective against Covid-19 risks, & UK-Biobank data-analysis shows lower Covid-19 rates with pre-pandemic use of vitamin D supplements. Taken together these data suggest that MRA methodology for vitamin D status and health outcomes deserves further thought.

Keywords: COVID-19, Vitamin D, MRA methodology, Health-effect plateaus

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Citation: Boucher BJ. (2021) Comment re "No evidence that Vitamin D is Able to Prevent or Affect the Severity of COVID-19 in Individuals with European Ancestry: A Mendelian Randomization Study of Open Data", by Amin & Drenos. J Infect Dis Res, 4(S1): 02.