Systemic calcium homeostasis is maintained by the calcium-sensing receptor, which stimulates secretion of parathyroid hormone to promote bone resorption and convert inactive vitamin D to the active form, 1,25(OH) vitamin D, when slight increases in calcium are detected. Unfortunately, calcium signaling dysregulation can lead to the development of many adverse health outcomes such as breast cancer, which disproportionately affects African American women. Although high calcium and vitamin D deficiency have been implicated in cancer progression and metastasis, the associated cancer risk remains poorly understood. In this study, we evaluated the clinical and genetic risk of calcium and vitamin D on cancer development using de-identified electronic health records (EHRs) linked to patient DNA samples in the BioVU biorepository. First, we carried out a series of multivariable regression analyses on clinical cancer diagnoses and laboratory measurements. Using the entire EHR dataset (n = 64,459), we found that high calcium is significantly associated with an increased risk of skin cancer (OR = 1.23, p = 2.68E-14) and skin, breast, and prostate cancer.

Our results show that clinical effects of calcium and vitamin D differ from their genetic effects. There are possible ancestry-related differences in cancer development based on biomarker genetic susceptibility. Experimental follow-up studies are needed to evaluate the underlying mechanisms of these associations.

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