

SIGNIFICANCE STATEMENT

Fibroblast growth factor-23 (FGF-23) is positively associated with cardiovascular disease risk in patients with CKD, and suggested as a therapeutic target. This meta-analysis compared the associations in general, nondialyzed CKD and dialysis populations. The risk of myocardial infarction, stroke, and heart failure was consistently higher among participants in the top versus bottom third of the FGF-23 distributions. However, the size of association did not increase across these populations, despite absolute differences in FGF-23 concentration between the top and bottom thirds increasing by two orders of magnitude. Furthermore, associations were similar for cardiovascular and noncardiovascular mortality. Associations that are both nonspecific and do not exhibit an exposure–response relationship are inconsistent with cause and effect. These results do not support the hypothesis that targeting FGF-23 will reduce cardiovascular disease risk.