

Mechanisms by Which Vitamin D Maintains Good Health and Reduces the Risk of Adverse Health Outcomes

Outcome	Mechanism
Autoimmune Diseases	Regulates adaptive immunity so that the body does not attack its own tissues
Bone health	Regulates calcium and phosphorus absorption and metabolism
Cancer	Reduces incidence by affecting cellular differentiation, proliferation, and apoptosis; reduces mortality by reducing angiogenesis around tumors and metastasis; many other mechanisms
Cardiovascular disease	Reduces incidence by affecting cellular differentiation, proliferation, and apoptosis; reduces mortality by reducing angiogenesis around tumors and metastasis; many other mechanisms
Infectious diseases	Induces production of antimicrobial peptides such as human cathelicidin; reduces risk of cytokine storm; Inhibits expression of proinflammatory cytokines through blocking the TNF-induced NF- B1 signaling pathway; and initiates expression of ISGs for antiviral defense program through activating the IFN- -induced Jak-STAT signaling pathway
Inflammation	Shifts production of cytokines from Th1 (proinflammatory) to Th2 (anti-inflammatory)
Insulin resistance	Maintains pancreatic-cell function; increases insulin sensitivity in insulin-responsive tissue; reduces serum concentrations of parathyroid hormone; regulates renin-angiotensin-aldosterone system; exerts positive effects on hepatic lipogenesis and gluconeogenesis; reduces formation of reactive oxygen species
Muscle health	Regulates oxygen consumption rate, maintains mitochondrial function, reduces risk of muscle atrophy
Pregnancy outcomes	Most effects mediated by calcitriol, whose concentrations increase during pregnancy. Calcitriol regulates calcium absorption from the GI tract. Calcitriol produced in the placenta acts as an autocrine/paracrine regulator of immunity at the fetal-maternal interface for acceptance of the fetal allograft; calcitriol regulates estradiol and progesterone secretion in the placenta; calcitriol downregulates FLT1 and vascular endothelial growth factor gene expression, thereby reducing risk of preeclampsia. Calcitriol regulates immune function through effects on cytokine production

FLT1 – FMS-like tyrosine kinase 1; GI – gastrointestinal; IFN – interferon alpha; ISGs – interferon-stimulated gene; TH – T-helper cell; TNF – tumor necrosis factor.

