Vitamin D Testing

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Instructions for Use

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Related Commercial Policy

- Preventive Care Services

Medicare Advantage Policy Guideline

- Vitamin D Testing

Coverage Rationale

Vitamin D testing is unproven and not medically necessary for routine preventive screening due to insufficient evidence of efficacy.

Vitamin D testing is proven and medically necessary for a condition or medical diagnosis associated with Vitamin D deficiency or risk of hypercalcemia; refer to the Vitamin D diagnosis codes list under Applicable Codes.

Definitions

Vitamin D: A nutrient that the body needs in small amounts to function and stay healthy. Vitamin D helps the body use calcium and phosphorus to make strong bones and teeth. It is fat-soluble (can dissolve in fats and oils) and is found in fatty fish, egg yolks, and dairy products. Skin exposed to sunshine can also make vitamin D. Not enough vitamin D can cause a bone disease called rickets. (National Cancer Institute - https://www.cancer.gov/publications/dictionaries/cancer-terms/def/vitamin-d)

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

CPT Code	Description
0038U	Vitamin D, 25 hydroxy D2 and D3, by LC-MS/MS, serum microsample, quantitative
82306	Vitamin D; 25 hydroxy, includes fraction(s), if performed
82652	Vitamin D; 1, 25 dihydroxy, includes fraction(s), if performed

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Diagnosis Codes
Vitamin D Testing: Diagnosis Code List

Description of Services

Vitamin D plays a key role in calcium absorption and mineral metabolism to maintain good bone health; it most commonly can be obtained from dietary sources or by UVB exposure in the skin. Vitamin D deficiency occurs when the body does not have enough vitamin D, and this can lead to rickets or osteomalacia. Risk factors that contribute to vitamin D deficiency include age, genetics, race, and ethnicity. While the measurement of Vitamin D is performed predominately through blood samples, it can also be measured in urine, amniotic fluid, breastmilk, and synovial fluid (Máčová and Bičíková, 2021).

Hypercalcemia is a life-threatening metabolic disorder and commonly found in patients with advanced stage cancers. It is associated with hematological malignancies, such as multiple myeloma, non-Hodgkin lymphoma, leukemias, solid cancers, as well as squamous cell carcinomas of any organ. Several mechanisms have been implicated in the development of hypercalcemia of malignancy; they include osteolytic related hypercalcemia, parathyroid hormone-related peptide (PTHrP) mediated hypercalcemia, extrarenal 1,25 dihydroxy vitamin D (calcitriol) mediated hypercalcemia and parathyroid hormone (PTH) related hypercalcemia. Early diagnosis and treatment lowering calcium levels in the blood can improve symptoms and the quality of life of these patients and avoid delays for further antitumor therapy (Asonitis et al., 2019).

Clinical Evidence

To update its 2014 recommendation, the U.S. Preventive Services Task Force (USPSTF) commissioned a systematic review on screening for vitamin D deficiency, including the benefits and harms of screening and early treatment. The conclusion was that the current evidence is insufficient to assess the balance of benefits and harms of screening for vitamin D deficiency in asymptomatic adults (USPSTF, 2021, Kahwati 2021).

Williams et al. (2021) conducted a study that aimed to assess whether supplementing the participants with Vitamin D improved their irritable bowel syndrome (IBS) symptoms. 135 people were randomized into two group; one group received a daily sublingual flavored liquid spray that delivered 3,000 IU of vitamin D3, and the other group a placebo. Vitamin D was measured as 25(OH) vitamin D2 and 25(OH) vitamin D3 using blood collected from a fingerprick; samples were obtained at baseline and again at 3 months. IBS symptoms were evaluated every two weeks throughout the trial using an IBS symptom severity questionnaire. The survey contained questions that addressed both severity and duration of abdominal pain, abdominal distension, satisfaction with bowel habits and general well-being. The authors found no benefit of vitamin D supplementation on either symptoms of IBS or the participants quality of life; however, with the prevalence of vitamin D deficiency in this population, routine screening and supplementation should be implemented for general health reasons.

The Vitamin D and OmegA-3 Trial (VITAL - NCT01169259) was a nationwide, randomized, placebo-controlled, 2x2 factorial trial of daily vitamin D3 and marine omega-3 fatty acids in the primary prevention of cancer and cardiovascular disease (CVD) (Manson, et al. 2020). The study included approximately 25,000 participants, including both men and woman age 50 years and older with an average mean age of 67.1 years. Participants were followed for 5 years and required to limit daily intakes of vitamin D and calcium from all supplemental sources including multivitamins. Following a 3-month placebo run-in, participants were randomized to either vitamin D, omega-3 fatty acids, both active agents, or both placebos in a 2x2 factorial design. Vitamin D3 dosage was 2000 IU/d and marine omega-3 fatty acids included 1 g/d Omacor® fish-oil capsule with 840 mg of omega-3 fatty acids, including eicosapentaenoic acid [EPA, 460 mg] + docosahexaenoic acid [DHA, 380 mg]. Participants completed questionnaires regarding clinical and lifestyle risk factors for cancer, CVD, and other conditions at baseline and again at annual follow-up; questions addressed side effects, risk factor updates, and endpoint occurrence. The authors found that taking a high daily dose of vitamin D and omega-3 did not show significant reduction in cancer incidence for CVD endpoints. Additional research is needed to determine individual benefits from vitamin D supplementation.

Bischoff-Ferrari, et al. (2020) conducted the DO-HEALTH study which investigated whether vitamin D, omega-3s and a strength training program (provided alone or in combination) improved the health outcomes of older individuals. A total of 1,075 participants were randomized into one of eight groups: 1) Vitamin D, omega-3s and strength-training exercise, 2) Vitamin D and omega-3s, 3) Vitamin D and strength-training exercise, 4) Vitamin D, 5) omega-3s and strength-training exercise, 6) omega-3s, 7) strength-training exercise and 8) placebo. Trial software was responsible for the randomization, blinding, treatment allocation

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and study labeling. Participants received 2 capsules per day which included either Vitamin D or placebo and omega-3s or placebo; all capsules had a coating to prevent unblinding. The strength exercise program which consisted of 30 minutes 3 times/week were provided by a physiotherapist not involved in the program. Primary outcomes were measured for cardiovascular, bone, muscle, brain and immune system health. Participants were followed for 3 years with annual clinical visits and telephone calls every 3 months to collect appropriate information. The overall withdrawal rate across all groups was almost 12%. After analysis, the authors concluded a treatment of vitamin D, omega-3s and strength exercise did not result in a statistically significant difference in improvement of BP, physical performance, infection rates, cognitive function or nonvertebral fractures. Study limitations included 83% of participants already engaged in a moderate to high physical exercise program thus there may have been little benefit from the added exercise, the overall improvement in cognitive function might be explained by a learning effect, 40% of participants were allowed to take an additional 800 IU/d of supplemental vitamin D outside of what was dispensed to them per current guidelines and the P value may have been too liberal given the large number of randomization groups and comparisons.

There is limited evidence showing population-based screening for vitamin D deficiency improves healthcare outcomes, but some specific interventions like the electronic health record (EHR) have been shown to help decrease unnecessary screening. Through a committee-based process, Petrilli, et al. (2018) developed a point of care advisory EHR alert system that was triggered whenever a vitamin D test was ordered. When the test was ordered, an electronic chart alert was initiated that provided reasons to the healthcare worker why the test should not be ordered and to only do so if the patient was high risk. After 3 months of implementation, a significant decline in the order of tests was observed. Over a 3-year period, both low value and appropriate tests continued to decline. The authors findings suggested that a health care system can have positive effects on reducing unnecessary testing and screening through education along with support from an EHR.

Shallis et al. (2017) conducted a cohort review of 54 patients, all having some type of Non-Hodkins Lymphoma but over 50% of them with diffuse large B-cell lymphoma. Hypercalcemia was defined as a value > 10.5 g/dL. Of the 54 cases, 31 blood samples collected identified serum calcitriol and 24 were for serum PTHrP level. Seven of the 31 patients had an elevated serum calcitriol level; out of 24 patients only 3 had an elevated serum PTHrP level. Approximately 30% of the original 54 patients had both the serum PTHrP and calcitriol levels measured; of these 17 patients that had measurement of both the serum calcitriol and PTHrP levels, most had neither an elevated serum calcitriol nor elevation in the serum PTHrP. The remaining 7 patients identified 5 patients with an elevated calcitriol level and 2 had an elevated PTHrP level. No patient had an elevation of both values. Upon analysis of the information, the authors concluded patients with calcitriol-mediated hypercalcemia showed a trend toward worse outcomes, suggesting that calcitriol might be a marker of high-grade lymphoma or a substitute for more advanced disease. Limitations included small sample size and retrospective review which may have contributed to bias.

Pacis et al. (2015) conducted a systematic literature review on the role vitamin D has in women undergoing assisted reproductive technology (ART) and to assess the cost-effectiveness of routine vitamin D deficiency screening prior to initiation of ART. After review of the eight articles that met the inclusion criteria, the authors concluded the outcomes from the studies were conflicting. The inconsistencies were likely caused from confounding variables and insufficient sample sizes, which further highlighted the need for future RCTs in this population.

In a 2012 health technology assessment for the Washington State Health Care Authority, it was determined no definitive conclusions can be drawn about the effectiveness of Vitamin D screening or testing. Specifically, no evidence was found that directly measured the clinical effectiveness of vitamin D screening for patients. While the evidence suggested positive effects for those with musculoskeletal issues and beneficial for general overall health, the evidence does not support vitamin D screening.

Seymour et al. (1994) evaluated two groups of patients with hypercalcemia; 16 patients had myeloma and 22 patients had non-Hodgkin lymphoma. Lab measurements included serum chemistries, parathyroid hormone, calcitriol, parathyroid hormone-related protein, and urinary electrolyte levels. The reference range for the serum calcitriol during hypercalcemia was identified as less than 42 pg/mL. Twelve of the 22 hypercalcemic patients with non-Hodgkin lymphoma had serum calcitriol levels greater than the reference range. The authors found that the serum calcitriol levels were elevated in most hypercalcemic patients with non-Hodgkin lymphoma which the authors felt connected extrarenal calcitriol production to non-Hodgkin lymphoma.

Numerous clinical trials which address vitamin D supplementation, safety and efficacy are ongoing; refer to: https://www.clinicaltrials.gov/ct2/home.

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Clinical Practice Guidelines

American Academy of Pediatrics (AAP)

For healthy adolescents, the AAP does not recommend universal screening for vitamin D deficiency. Increased dietary intake of vitamin D is recommended, and vitamin D supplementation can be considered if the recommended dietary allowance (RDA) cannot be met. For adolescents with chronic medical illnesses associated with increased fracture risk, screening for vitamin D deficiency should be performed by obtaining a serum 25-OHD level (Golden and Carey, 2016).

American College of Gynecologists (ACOG)

In a committee opinion for Vitamin D Screening, ACOG states there is insufficient evidence to support a recommendation for screening all pregnant women for vitamin D deficiency. Recommendations concerning routine vitamin D supplementation during pregnancy beyond that contained in a prenatal vitamin should await the completion of ongoing randomized clinical trials (ACOG, 2011; reaffirmed 2017).

American Academy of Family Physicians (AAFP)

The U.S. Preventive Services Task Force (USPSTF) and the AAFP have concluded there is insufficient evidence to recommend screening for vitamin D deficiency in the general population. Treating these asymptomatic individuals with identified deficiency has not been shown to improve a patient's health. (LeFevre and LeFevre, 2018)

American Geriatrics Society

In a consensus statement from the American Geriatrics Society, the overall goal for primary care practitioners is to reduce falls and fall-related injuries for the aging population. The minimum goal for older adults should be a serum 25(OH)D concentration of 30 ng/mL (75 nmol/L). The AGS states laboratory testing for serum 25(OH)D concentration is not necessary before supplementation begins and there is no need to "clinically manage" vitamin D with repeated lab tests (American Geriatrics Society (AGS), 2014).

The American Society for Metabolic and Bariatric Surgery (ASMBS)

For weight loss surgery (pre- and post-surgery), the ASMBS recommends nutrient screening for vitamin D and calcium however more research is needed to establish a recommendation regarding the use of vitamin D binding protein assays as an additional tool for determining vitamin D status in post-WLS patients (Parrott, 2017).

American Society for Clinical Pathology (ASCP)

The ASCP in partnership with American Board of Internal Medicine (ABIM) Foundation states many individuals do not need a vitamin D test because it does not improve treatment for the individual. While many people have low vitamin D levels, they are not seriously low and simple dietary changes are sufficient enough to get the necessary amount of vitamin D needed.

Cystic Fibrosis Foundation

A multidisciplinary committee established by the CF Foundation developed the following recommendations for Vitamin D (Tangpricha et al., 2012):

- The CF Foundation recommends that all individuals with CF have serum 25-hydroxyvitamin D measured to assess vitamin D status (consensus recommendation).
- The CF Foundation recommends against the routine measurement of PTH, osteocalcin, alkaline phosphatase, or other indirect markers to assess vitamin D status in all individuals with CF (consensus recommendation).
- The CF Foundation recommends that all individuals with CF maintain a serum 25-hydroxyvitamin D goal of at least 30 ng/ml (75 nmol/liter).
- The CF Foundation recommends that all individuals with CF have serum 25-hydroxyvitamin D levels rechecked 3 months after the dose of vitamin D3 has been changed (consensus recommendation)
- The CF Foundation recommends that all individuals with CF be treated with vitamin D3 (cholecalciferol) to achieve and maintain serum 25-hydroxyvitamin D levels of at least 30 ng/ml (75 nmol/liter) (USPSTF, grade B).
- The CF Foundation recommends that all individuals with CF who are prescribed vitamin D3 (in addition to their CF-specific vitamins) take once-daily vitamin D3 therapy or its weekly equivalent to maintain serum 25- hydroxyvitamin D levels of at least 30 ng/ml (75 nmol/liter) (consensus recommendation)

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Endocrine Society

The Endocrine Society only recommends vitamin D screening for those individuals who might be at risk for vitamin D deficiency; there is not sufficient evidence to recommend screening individuals who are not at risk (Holick, 2011).

National Institute for Health and Care Excellence (NICE)

Guidance from NICE (updated in 2017) states routine Vitamin D tests are not needed for individuals unless they have symptoms of deficiency, are considered to be at high risk for deficiency, or there is a clinical reason to do so (e.g., osteomalacia).

U.S. Food and Drug Administration (FDA)

Vitamin D screening is a laboratory test and not managed by the FDA.

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Policy History/Revision Information

Date	Summary of Changes

10/01/2022	**Applicable Codes**
	• Updated list of ICD-10 diagnosis codes to reflect annual edits:
	  ○ Added Z79.60, Z79.61, Z79.620, Z79.621, Z79.622, Z79.623, Z79.624, Z79.630, Z79.631, Z79.632, Z79.633, Z79.634, Z79.64, Z79.69, and Z79.85
	  ○ Revised description for C84.40, C84.41, C84.42, C84.43, C84.44, C84.45, C84.46, C84.47, C84.48, and C84.49
	Supporting Information
	• Archived previous policy version 2022T0631A

Instructions for Use

This Medical Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, please check the member specific benefit plan document and any applicable federal or state mandates. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Policy is provided for informational purposes. It does not constitute medical advice.

This Medical Policy may also be applied to Medicare Advantage plans in certain instances. In the absence of a Medicare National Coverage Determination (NCD), Local Coverage Determination (LCD), or other Medicare coverage guidance, CMS allows a Medicare Advantage Organization (MAO) to create its own coverage determinations, using objective evidence-based rationale relying on authoritative evidence (Medicare IOM Pub. No. 100-16, Ch. 4, §90.5).

UnitedHealthcare may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. UnitedHealthcare Medical Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

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