

## Practitioner Dietary Supplement Reference Guide

### SuperCalcium+™

**Note:** Calcium is one of 20 known essential minerals necessary to create, develop, grow, and maintain the human structure and function. Readers are referred to the two previous sections titled “[Introduction to The Use of Health Supplements](#)” and “[Introduction to Lifelong Complete Multiple Vitamin & Mineral Supplementation](#)” in this Practitioner Dietary Supplement Reference Guide (PDSRG) for the science behind the synergy, thus necessity of consuming all 32 vitamins and essential minerals in recommended daily amounts to support development and health in all life-stages.

### Goal

To supply calcium with other supporting bone building nutrients commonly low in western diets in the amounts necessary to complement food intake in achieving the calcium Recommended Dietary Allowances (RDAs) to help build and maintain bone health throughout one's lifespan. Calcium is one of the known under-consumed essential minerals and listed as a nutrient of concern by the Dietary Guidelines for Americans (DGA).<sup>1</sup> The product is designed, including the recommendations to 1) deliver calcium in targeted amounts in combination with food intake, to reach and stay within established guidelines (1,000-1,300 mg/day) when diet falls short\*; 2) deliver the co-factors (e.g. proper forms of vitamins K, D and magnesium) required to maximize calcium's uptake into the skeletal structure, minimize resorption and avoid unhealthy deposits; 3) maintain all ingredients in a safe and recommended range when combined with diet, a multivitamin and mineral (MVM)\* or other dotFIT branded products; 4) function effectively (as claimed) as a standalone product if for some reason a user is **not** consuming a complimentary dotFIT daily multivitamin and mineral or some other branded MVM formula.

\*Calcium and potassium present the caveat to a single complete vitamin and mineral supplement (CVMS) because if they are needed, the amounts generally would not fit in an acceptable pill size along with the other known under-consumed vitamins and minerals (VMs).<sup>2,3</sup> While impossible to validate all the individual vitamin and mineral content of your foods (unless testing each food immediately before consumption), calcium and potassium food content are relatively easy to quantify given the new labeling laws. Therefore, the standard adult formula would omit these two minerals allowing persons to add separately only if needed, which a quick glance at one's diet can determine.

### Rationale

The skeleton, composed of bone mass, is similar to all human organs in that it requires nutrients to start and continue growth, development and ongoing maintenance (remodeling) until death.<sup>4</sup> Simply stated, without the bone building nutrients, there are no bones and with less than recommended intakes, we potentially create a weaker skeletal structure than if the same human was given adequate bone building nutrition, thus establishing the potential for early skeletal/bone failure.<sup>5,6</sup> Approximately 65% of bone tissue is inorganic mineral (mostly calcium and phosphorous as a salt called hydroxyapatite) and the other 35% is composed of an organic protein matrix of mainly collagen.<sup>7</sup> Genetics, diet, nutrient intake, and exercise/activity determine a person's peak bone mass.<sup>6,8</sup> Bone mass is measured and classified as bone mineral density (BMD) and peaks at ~ 30 years of age (>80% accumulated by age 16 years) at which point resorption (bone breakdown) surpasses formation, making the accrual of bone mass while able, crucial for long-term bone health.<sup>9,10,11,12,13</sup> In other words, the more bone mass acquired, starting in the womb and continuing until around age 30 years and everything else equal, the longer the human skeleton can remain healthy throughout life.<sup>9,14</sup> Therefore, although each life phase requires achieving nutrient recommendations, maximizing the intake by reaching the RDAs of the nutrients responsible for the makeup of bone tissue during these bone building years is paramount. There is virtually no bone mass catchup for missed years of ample bone nutrients and because of inadequate amounts, the human will have less bone to lose leading to early bone breakdown.<sup>9,10,11,12,13,14</sup> Figure 1 from the Pauling Institute depicts human bone development throughout a lifespan.<sup>15</sup>

Figure 1 – Bone Biology by the Pauling Institute<sup>15</sup>

### Bone Biology

#### BONE IS MADE OF

##### Type 1 Collagen

that constitutes the interior scaffolding of bone

##### Calcium and Phosphorus Crystals

that add strength to bone

##### Bone Cells

that are responsible for bone (re)modeling

#### BONE MASS OVER A LIFETIME

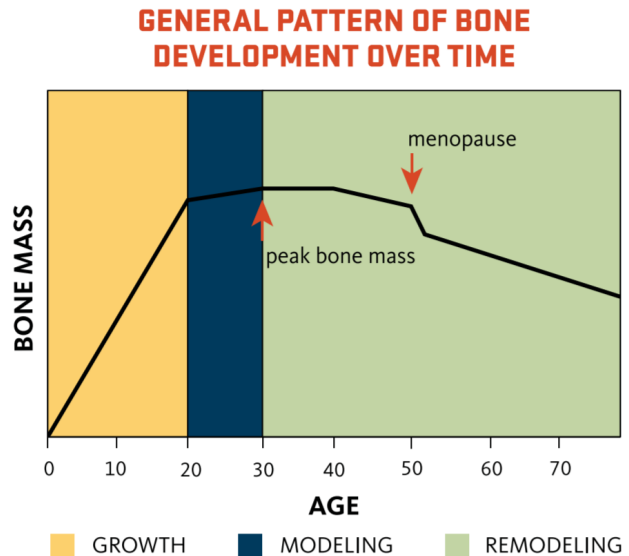
Bones grow throughout childhood, adolescence, and well into adulthood. Around age 34, there is an inevitable loss of bone mass with age, accelerated with menopause in women.

##### Modeling

During childhood and adolescence, bones grow in size and shape.

##### Remodeling

During adulthood, new bone replaces brittle bone, cracks, and deformities.



Although many vitamins and minerals (see Table 1 below from the Pauling Institute)<sup>15,16</sup> are necessary for bone formation and bone's long-term health, the primary nutrition responsible for these actions (calcium, vitamin D and magnesium) is notoriously low in the U.S. and western diets making a large portion of the population at risk for poor long-term bone health,<sup>1,2,17,18,19,20,21,22,23,24,25,26,27,28</sup> which is classified as osteomalacia (adult rickets - a failure to mineralize bone), osteopenia (precedes osteoporosis, occurring when BMD is 1.0 to 2.5 standard deviations [SD] below the average 30 year old) and osteoporosis (increased loss of bone mass classified as BMD >2.5 SD below the average 30 year old and represents the highest fracture risk<sup>24,29</sup>).<sup>30</sup> The inevitable decline of bone mass increases the risk of fractures.<sup>29</sup> Osteoporosis affects millions of people worldwide, predominantly postmenopausal women. In the United States, low bone mass is a threat for more than 53 million people.<sup>30,31</sup> The significant departure in adulthood from the use of dairy products (especially fortified cow's milk) and the warnings on sun exposure have significantly reduced the ability of the U.S. population to acquire adequate levels of calcium and vitamin D through diet alone.<sup>2,21,32,33,34,35,36,37,38,39</sup> With all this information on falling short of nutrient recommendations, it had been proposed that calcium and vitamin D supplementation could save \$12 billion in healthcare costs by 2020 according to an economic impact report commissioned by the Council of Responsible Nutrition.<sup>40</sup> A newer report from Frost & Sullivan found that use of 1,000 mg calcium plus 15 mcg (600 IU) of vitamin D supplements for the European Union population over 55 years of age, could save €19.8 billion in healthcare costs over five years, and provide a return of €3.47 in savings for every €1 spent on supplements or fortification.<sup>41</sup> Calcium (especially with vitamin D) has been an approved health intervention to reduce fracture risks.<sup>14,30,39,42,43</sup>

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**Table 1 – Micronutrients Needed for Bone Health: Recommended Intakes, Upper Limit and Average Intakes** <sup>15</sup>

Micronutrient	RDA or AI* (≥19 y)	UL (≥19 y)	Mean Intake <sup>a</sup> (≥19 y, all food sources) (25)
Calcium	Men: 1,000 mg/day (19-70y) 1,200 mg/day (>70y) Women: 1,000 mg/day (19-50y) 1,200 mg/day (>50y)	Men & Women: 2,500 mg/day (19-50y) 2,000 mg/day (>50y)	910 mg/day
Phosphorus	Men & Women: 700 mg/day (≥19y)	Men & Women: 4,000 mg/day (19-70y) 3,000 mg/day (>70y)	1,300 mg/day
Fluoride	Men: 4 mg/day* Women: 3 mg/day*	Men & Women: 10 mg/day	Not reported
Magnesium	Men: 400 mg/day (19-30y) 420 mg/day (>31y) Women: 310 mg/day (19-30y) 320 mg/day (>31y)	Men & Women: 350 mg/day <sup>b</sup>	290 mg/day
Sodium	Men & Women: 1,500 mg/day	Not determinable	Not reported
Potassium	Men: 3,400 mg/day Women: 2,600 mg/day	Not determinable	2,700 mg/day
Vitamin D	Men & Women: 15 µg (600 IU)/day (19-70y) 20 µg (800 IU)/day (>70y)	Men & Women: 100 µg (4,000 IU)/day	4.5 µg (180 IU)/day
Vitamin K	Men: 120 µg/day* Women: 90 µg/day*	Not determinable	88.2 µg/day
Vitamin A	Men: 900 µg RAE (3,000 IU)/day <sup>c</sup> Women: 700 µg RAE (2,333 IU)/day <sup>c</sup>	Men & Women: 3,000 µg RAE (10,000 IU)/day <sup>d</sup>	600 µg/day
Vitamin C	Men: 90 mg/day Women: 75 mg/day	Men & Women: 2,000 mg/day	85.4 mg/day
Vitamin B <sub>6</sub>	Men: 1.3 mg/day (19-50y) 1.7 mg/day (>50y) Women: 1.3 mg/day (19-50y) 1.5 mg/day (>50y)	Men & Women: 100 mg/day	2.0 mg/day
Folate	Men & Women: 400 µg DFE/day <sup>e</sup>	Men & Women: 1,000 µg/day <sup>f</sup>	540 µg DFE/day
Vitamin B <sub>12</sub>	Men & Women: 2.4 µg/day	Not determinable	5.2 µg/day

Abbreviations: RDA, recommended dietary allowance; AI, adequate intake; UL, tolerable upper intake level; y, years; mg, milligram; µg, microgram; IU, international units.

<sup>a</sup>Includes nutrients from enriched/fortified food

<sup>b</sup>Applies only to magnesium in supplements

<sup>c</sup>Retinol activity equivalent (RAE) is the international standard of measure that represents vitamin A activity as retinol. For example, it has been determined that 1 µg RAE would correspond to 1 µg of preformed retinol in animal products and 12 µg of β-carotene from plant-based food

<sup>d</sup>Applies only to preformed retinol

<sup>e</sup>Dietary folate equivalent (DFE) is used to reflect the higher bioavailability of folic acid found in supplements: 1 µg of food folate = 1 µg DFE; 1 µg of folic acid taken with meals = 1.7 µg DFE; and 1 µg of folic acid taken on an empty stomach = 2 µg DFE

<sup>f</sup>Applies to the synthetic form (i.e., folic acid) in fortified food and supplements

As referenced above, most Americans do not meet the recommended values of calcium, the dominant mineral in bone,<sup>1,2,44,45</sup> or the current higher recommendation of Vitamin D, necessary for calcium absorption into the body and bone, that has been associated with not just improved bone health but healthy aging in general.<sup>46,47,48,49,50,51,52,53,54,55</sup>

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Female adolescents have the lowest intake overall.<sup>52</sup> Natural food sources of Vitamin D are scarce and dependence on sun exposure present several problems including skin color, fear of skin malignancies, sunburns, etc.<sup>55,56,57,58,59,60,61</sup> Vitamin K (K1 and K2) and magnesium intakes from diet alone are also regularly below recommendations for proper bone health.<sup>1,16,18,20,23,28,62</sup> Vitamin K activates two proteins that transfer calcium to bone, help reduce bone turnover and contributes to bone strength.<sup>63,64,65,66</sup> Magnesium (Mg) is an indispensable component of the skeleton which houses over 50% of the body's total magnesium contributing to bone strength while also serving as a cofactor in enzyme systems that facilitate calcium and vitamin D regulation in both blood and bone.<sup>23,67,68</sup> Magnesium insufficiency reduces osteoblastic (bone synthesis) activity, thus decreasing bone formation.<sup>15,23,69</sup>

Therefore, the rationale for supplementation of these primary bone nutrients that work synergistically to create, grow, develop and maintain the bones of the human skeletal structure, is to correct daily food intake amounts of calcium, magnesium, vitamin D3 and Vitamin K1 and K2, which are commonly under-consumed when food (including fortified foods) alone is the delivery, to achieve the recommended levels (RDAs) that are associated with positive bone development at each life-phase and thus long-term health.<sup>1,2,5,6,9,12,14,15,21,22,23,24,29,30,32,35,38,39,40,49,55,61,62,63,65,66,67,69,</sup>

<sup>70,71,72,73</sup> Parents should be reminded in every health conversation that it is crucial their children achieve the RDA for calcium during their bone building years since there is no later makeup for this missed opportunity of supplying adequate calcium and vitamin D during this early life phase, meaning bone problems loom and not just the potential for increased youth fractures, but suboptimal BMD into adulthood sets in motion early fragility and accelerated bone aging.<sup>74</sup>

Calcium supplementation is not warranted when a person's diet contains enough daily calcium (See Table 2 for all ages;  $\geq 4$  years 1,000-1,300 mg/day), which is easy to identify with new labeling laws, and the said person is taking a complete daily multivitamin and mineral formula that contains diet complementing levels of the calcium bone building cofactors, magnesium, vitamin D3 and Vitamin K1 and K2 (see previous section titled "[Introduction to Lifelong Complete Multiple Vitamin & Mineral Supplementation](#)" for more information on vitamin and mineral synergy)".

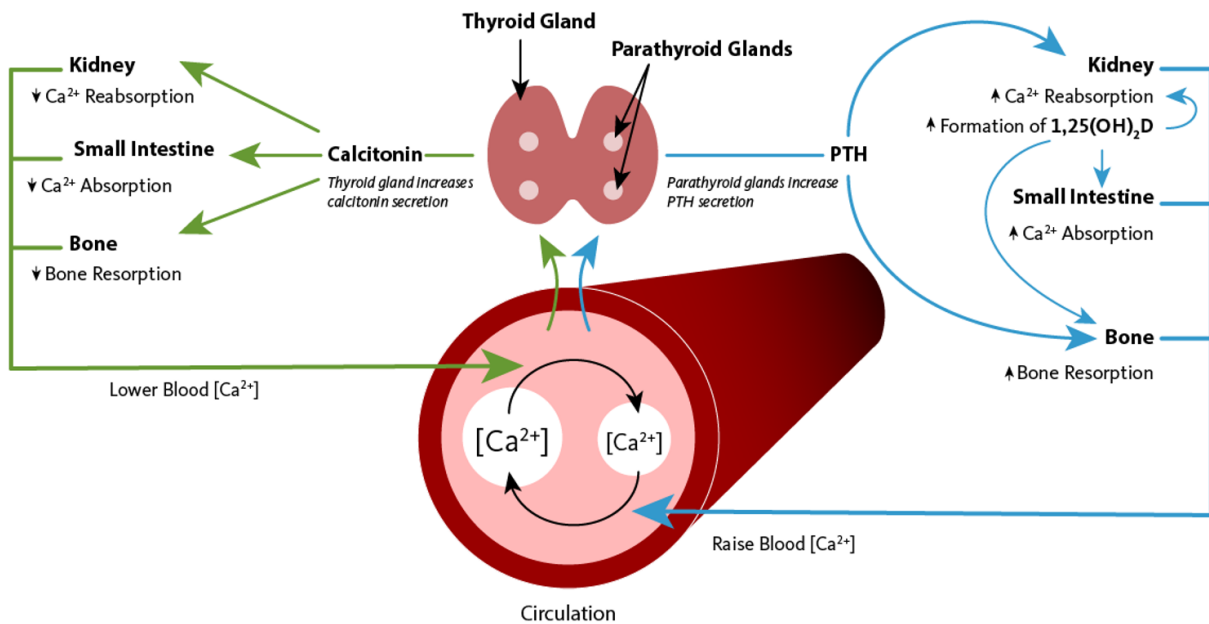
### Calcium

Calcium is one of the 20 essential minerals and like all essential minerals (EMs), calcium (Ca) has multiple indispensable biological functions that humans cannot live without and become weaker when diet does not supply adequate amounts (RDAs) to support all respective bodily functions.<sup>4,75</sup>

In the human body, Ca is the most abundant mineral because of the amount necessary to create and maintain the skeletal structure.<sup>76</sup> Ninety nine percent of all Ca stores are in bones and teeth but it is the one percent found in blood and soft tissues that is tightly regulated so that blood levels are maintained at 2.5 mmol/L<sup>24,39,75</sup> to allow Ca to perform its critical immediate life tasks such as facilitating muscle function, nerve transmission, vascular constriction, vasodilation, blood clotting and other indispensable metabolic functions.<sup>4,14,24,30,75,76,77</sup> This tight range of serum calcium preserves these physiological actions and cannot fluctuate based on inadequate dietary Ca intake and therefore, the body has evolved an elaborate system to draw Ca as needed from the skeletal structure, meaning bones act as a Ca reservoir to protect daily life at the expense of long-term bone health. When there is inadequate calcium intake (regularly below established recommendations), the parathyroid gland senses the drop in blood calcium concentration and increases secretion of parathyroid hormone (PTH) which in turn elevates levels of the active form of vitamin D to decrease calcium excretion and enhance utilization of available Ca.<sup>76,78</sup> Simultaneously, higher PTH and active vitamin D levels stimulate bone resorption (breakdown) yielding a release of Ca and other bone minerals to restore the necessary serum calcium level at which time the parathyroid gland slows PTH secretion. If Ca blood levels elevate excessively, the opposite reactions take place to maintain blood Ca within this critical tight range. This constant "cross-talk" between serum Ca and the parathyroid gland maintains life but continually compromises bone health and at an accelerated pace when Ca is regularly under-consumed as it is for most Americans, setting the stage for early bone failure and aging. Figure 2 from the Pauling Institute depicts the actions described that manage calcium homeostasis.

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**Figure 2 – Calcium Homeostasis<sup>77</sup>**



As with all essential nutrition, calcium intake recommendations are provided in the Dietary Reference Intakes (DRIs) established at the Institute of Medicine of the National Academies by the Food and Nutrition Board (FNB). Within the DRIs are the RDAs, which when established are the recommended best intakes for long term health including the amount of calcium required per day to maintain sufficient rates of calcium retention in healthy humans. Table 2 displays the calcium RDA by age, gender, and lifestyle.<sup>14,24</sup>

**Table 2 – Recommended Dietary Allowances for Calcium<sup>14,24</sup>**

Age	Male	Female	Pregnant	Lactating
0–6 months*	200 mg	200 mg		
7–12 months*	260 mg	260 mg		
1–3 years	700 mg	700 mg		
4–8 years	1,000 mg	1,000 mg		
9–13 years	1,300 mg	1,300 mg		
14–18 years	1,300 mg	1,300 mg	1,300 mg	1,300 mg
19–50 years	1,000 mg	1,000 mg	1,000 mg	1,000 mg
51–70 years	1,000 mg	1,200 mg		
71+ years	1,200 mg	1,200 mg		

\* Adequate Intake (AI)

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The RDA takes into account that not all consumed calcium is absorbed into the body.<sup>24</sup> Humans absorb roughly 30% of the calcium in foods, with plant Ca sources having significantly less absorption potential than animal (e.g. dairy) sources.<sup>24,79</sup> Additionally, life stage plays a major role in a human's ability to absorb Ca. For infants and up through much of the adolescent years, absorption may be as high as 60% of intake because of the amounts necessary for bone development.<sup>24,80</sup> In adulthood, Ca absorption from foods can plummet to 15-20% and continues to decrease with aging other than during pregnancy.<sup>14,24,79,81</sup>

The majority of the U.S. population is well below the calcium RDA when not using supplements (i.e., when using food alone including fortified foods) but of more concern is that over 50% of women and teens of both genders are below the Estimated Average Requirement (EAR), which is significantly below the RDAs. The EARs\* are by definition not a target people should shoot for and therefore we only recommend achieving RDAs since those nutrient amounts satisfy 98% of the population's nutrient health needs as compared to the 50% claimed by EARs.<sup>1,2,14,20,24,28,82,83,84</sup> On the other hand, Blumberg et al. found that with regular use of supplements, less than 10% of males and only ~ 20% of females were found to be below the calcium EAR.<sup>20</sup> It is estimated that ~43% of the U.S. population use supplements containing calcium which contributes a mean intake of 330 mg/day thus a highly recommended strategy when the diet falls short of RDAs.<sup>19,24,84</sup>

The two common forms of calcium supplements are calcium citrate and carbonate with properly prepared calcium carbonate showing superior absorption when ingested with food, which is when we recommend taking a calcium supplement – i.e. take with meals.<sup>85,86</sup> The carbonate form also has the highest content of calcium by weight allowing less expense and a smaller pill size containing more calcium than citrate and other forms.<sup>87</sup> Calcium carbonate is 40% calcium by weight while calcium citrate is only 21%.<sup>88,89</sup> Further, calcium citrate may inhibit absorption of non-heme iron while other forms including carbonate shows little to no effect.<sup>90</sup> However, calcium citrate may have a clinical application since it does not require food stimulated acids for digestion.<sup>91</sup>

\* Estimated Average Requirement (EAR): Average daily level of intake estimated to meet the requirements of approximately 50% of healthy individuals; usually used to assess the nutrient intakes of groups of people and to plan nutritionally adequate diets for them; can also be used to assess the nutrient intakes of individuals.

### Calcium Supplementation Including Controversies

As with any vitamins or essential minerals, the conclusion on any calcium intake related controversy is that humans at all life-stages should consume (diet and supplements [as necessary] combined) a daily calcium intake at the Institute of Medicine's recommendation for bone health (Table 2), but not to exceed calcium's Tolerable Upper Limit (UL) of 2,000-3,000 mg/day (depending on age) in order to protect against potential negative bone health outcomes,<sup>14,24,30,77</sup> unless advised otherwise by an individual's qualified health professional. Further, calcium like all vitamins and essential minerals work in synergy with all other VMs to create and develop life including bones,<sup>4,15,75</sup> meaning they do not work in a vacuum like a drug treating a condition and therefore, clinical study results often confuse the layman regarding the necessity of achieving recommendations. VMs are dependent on each other in their roles in constructing and maintaining human structure and therefore should not be looked as a treatment for a condition other than correcting an overt vitamin or mineral deficiency that would otherwise lead to sickness and eventual death since humans need all 32 VMs to sustain life. Instead, filling vitamin and mineral gaps including Ca, left by diet to meet scientific recommendations should be looked at as a prevention strategy and started at the beginning of life, such as the use of the prenatal multivitamin and mineral supplement and calcium (and its necessary co-factors [e.g. vitamin D, K, magnesium, etc.]) in bone building years and maintained throughout life. Further confounding calcium supplementation results would be starting supplementation too late in life when bone ailments have taken hold or looming, which we argue is more often too late to correct with any type of vitamin and mineral therapy. In summary, correcting Ca intake, whether through food or food and supplements, to meet the RDAs should be a mandatory prevention tactic along with all other VMs, and not viewed as a treatment for failing bone structure since there is no returning to the bone building years to make up the bone nutrients you missed while the body could still utilize them, as thoroughly described above. After all, a vitamin and mineral insufficiency such as calcium, vitamin D, etc. is



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generally a physically undetectable starting point that begins an insidious progression that can physically manifest as poor bone health and related issues later in life.

When vitamin and mineral supplementation studies are shown to be ineffective for a related condition, such as calcium and vitamin D for improving failing bone health, it is likely because: 1) repletion started too late since there is no “makeup”; 2) lack of long-term RDA levels of complete vitamin and mineral synergy, or 3) simply incurable conditions based on genetics or genetically programmed unmanageable cellular senescence in the targeted areas. These reasons help us understand why calcium (and other vitamin or mineral) supplementation studies often yield misleading conclusions. Please see Appendix-1 for “Why Vitamins and Minerals may Fail in Studies” from the peer reviewed referenced article titled, *“Vitamin and Mineral Supplementation in Human Health—A Case for Public Policy,”*<sup>92</sup>

The studies listed below are only to validate the safety and efficacy of using Ca supplements with food intake (with or without vitamin and mineral co-factors) when/if necessary, to meet Ca recommendations, not to prove use as a treatment. Meaning, calcium supplementation is safe, effective and recommended for filling nutrient gaps for prevention from the beginning of life, or at least before bone disease sets in when foods fail to achieve recommend intakes.<sup>14,20,30,93,94</sup>

### *Use of Supplementation and Rationale for Expert Recommendations When Diet Fails*

The previous data captured here clearly establishes the reasons to supplement calcium as needed to reach RDAs during the bone building years from the beginning of life through approximately age 30. The following data demonstrates the safe and effective use of calcium supplements later in life to help slow inevitable bone loss, thus the rationale for the current expert recommendations.

Using BMD measures as the primary endpoints, a systematic review and meta-analysis by Silk et al. on calcium supplementation with or without vitamin D in healthy males found supplementation with calcium plus vitamin D improved BMD suggesting a preventative effect.<sup>95</sup> In the same preventative vein, Gaffney-Stomberg et al. found supplementing with both calcium and vitamin D (2,000 mg and 1,000 IUs, respectively) improved BMD in young men and women during intense military training.<sup>96</sup> This also suggests that timing around exercise may be important based on the parathyroid’s role in calcium homeostasis.<sup>97</sup>

### **Older Adults**

Many randomized controlled clinical trials (RCTs) have found calcium supplementation to be moderately effective in the conservation of BMD and prevention of fracture risk in women and men 50 years of age and older. A meta-analysis of 51 RCTs found that BMD at all bone sites increased by 0.7% to 1.4% after one year and 0.8% to 1.5% after two years of calcium supplementation alone or combined with vitamin D demonstrating a reduction in aging bone loss.<sup>98</sup> In a meta-analysis of 11 RCTs including over 50,000 people, the U.S. Preventative Task Force found supplementation of calcium (500-1,200 mg/day) and vitamin D (300-1,000 IU/day) for up to seven years yielded in a 12% decrease in the risk of any new fracture.<sup>99</sup> A recent updated meta-analysis of RCTs by the National Osteoporosis Foundation (NOF) established a 30% reduction in hip fractures and 15% reduction in total fracture in older adults with calcium and vitamin D supplementation compared to placebo.<sup>39,94</sup> These and other studies have led European experts to adopt similar recommendations.<sup>100</sup>

### *Cardiovascular Health Including Vascular Calcification*

The most recent studies to date have found no connections between proper calcium supplement use (correcting food intake amounts to the RDA) and negative cardiovascular health or mortality.<sup>101,102,103,104,105,106,107,108</sup> In fact, the Academy of Nutrition and Dietetics recommends calcium supplementation as needed for hypertensive individuals.<sup>109</sup> In the Chung et al. updated systematic review and meta-analysis, researchers did not find statistically significant differences in risk for cardiovascular events or mortality between subjects using supplements of calcium or calcium plus vitamin D and those receiving placebo.<sup>110</sup> Cohort studies showed no consistent dose-response relationships

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between total (dietary or supplemental) calcium intake levels and cardiovascular mortality. The authors conclusion is that calcium intake from diet and supplements within tolerable upper intake levels (2,000 to 2,500 mg/d) is not associated with cardiovascular risk factors in generally healthy adults.<sup>110</sup> Kong et al. found in Korean women that increased dietary calcium intake was associated with a decreased risk in negative cardiovascular health, but it did not affect risk of fracture or stroke.<sup>111</sup>

Conflicting observations of calcium supplementation possibly increasing the risk of vascular calcification may have a connection to people with low overall vitamin D and K intake (see Vitamin K section below) and/or inaccuracies in totaling daily calcium intake from all sources or genetic susceptibilities.<sup>112,113</sup> Further, reviews of high calcium intakes from supplements and diet, have found a mild or non-significant reduction in blood pressure.<sup>114,115</sup> A meta-analysis of prospective cohort studies by Jayedi et al. found that higher dietary calcium intake (including one study that combined both supplements and diet), independent of adiposity and other potential blood pressure related minerals such as sodium, potassium, and magnesium, is associated with a lower risk of developing unhealthy blood pressure. Additionally, there was a dose response at each increase of 500 mg/day.<sup>116</sup>

### Current Expert Position Statement Based on the Totality of Evidence

*“The National Osteoporosis Foundation and American Society for Preventive Cardiology adopt the position that there is moderate-quality evidence (B level) that calcium with or without vitamin D intake from food or supplements has no relationship (beneficial or harmful) to the risk for cardiovascular and cerebrovascular disease, mortality, or all-cause mortality in generally healthy adults at this time. In light of the evidence available to date, calcium intake from food and supplements that does not exceed the tolerable upper level of intake (defined by the National Academy of Medicine as 2,000 to 2,500 mg/d) should be considered safe from a cardiovascular standpoint.”<sup>117</sup>* The European expert position is the same.<sup>100</sup>

### Prostate Health

Investigating the relationship between dairy products and calcium intakes to prostate cancer risk, Aune et al. found high intakes of dairy products such as milk and cheese, and total dairy calcium, but not supplemental or non-dairy calcium, may increase total prostate health risk.<sup>118</sup> While men should also stick with recommendations of total daily calcium intake of 1,000-1,200 mg/day,<sup>14,20,30,39,93,94,109</sup> studies are mixed on high calcium intake and prostate health from foods such as full fat dairy products which may have other confounders.<sup>118,119,120,121</sup> Milk consumption may increase systemic concentrations of insulin-like growth factor-1 (IGF-1), a protein involved in cell proliferation thus a possible culprit in dairy but not supplements.<sup>118,122,123</sup> However, at this point in time, men should try to reach but not exceed 1,000-1,200 mg/day from diet and supplements (if necessary) combined.<sup>124</sup> To err on the side of caution, we recommend men that need to supplement their food intake to reach 1,000-1,200 mg/day, do so by taking no more than 500 mg from supplements regardless of the dietary shortfall, unless approved by a qualified health professional.<sup>125</sup> This recommendation supports bone health but also helps protect miscalculations in actual dietary calcium consumption.

### Colorectal Health

A significant majority of studies have shown calcium intake including supplements to have a health protective effect on the human gut.<sup>126,127,128,129,130,131,132</sup> In a systematic review and meta-analysis of randomized controlled trials, Bonovas et al. found a modest preventive effect of calcium supplements against recurrent colorectal adenomas over a period of 36 to 60 months.<sup>128</sup> Veettil et al. also found a beneficial effect of calcium supplementation on the recurrence of adenomas in their later systematic review and meta-analysis of randomized controlled trials.<sup>129</sup> Another meta-analysis of observational studies by Heine-Broring et al. found a beneficial role for both multivitamins and calcium supplements on colorectal health.<sup>130</sup> One meta-analysis found little to no effect.<sup>133</sup> In an unexpected study outcome, Crocket et al. tracked outcomes of 2,000 people, aged 45 to 75, who had a history of polyps. The subjects were to consume either daily calcium supplements, daily vitamin D supplements, both, or neither



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for three or five years.<sup>134</sup> Those taking calcium alone or a combination of calcium and vitamin D were more likely to have polyps six to 10 years after the start of the study. Experts and authors warned that the “*study focused on a very specific population — patients with a history of colorectal polyps — and therefore, the study’s results are not applicable to the general population.*” But went on to recommend consumers with a history of colorectal polyps to talk with their doctors about whether calcium supplementation is appropriate.<sup>134</sup> The final analysis is that there may also be a benefit to gut health consuming the proper/recommended amount of calcium that supports bone health, which is the RDA shown in Table 1.<sup>14,24,30,80</sup>

### Kidney Stones

Because kidney stone formation (nephrolithiasis) is generally a combination of calcium phosphate and calcium oxalate, and persons with a genetic disposition along with abnormally high levels of oxalate and/or calcium (hypercalciuria) in the urine are at greater risk of this urinary system condition,<sup>135,136</sup> the intake of calcium from both diet and supplements has been investigated in relation to the incident of kidney stones.<sup>137,138,139</sup> However, as topically counterintuitive as it appears, diets high in calcium from foods (both dairy and non-dairy) and calcium supplementation alone appear to have no connection to kidney stone formation, and in fact diets high in calcium are found to be protective. Diets with a calcium content  $\geq 1,000$  mg/day (and low protein-low sodium) may be protective against the risk of stone formation in hypercalciuric stone forming adults.<sup>140,141</sup> And while calcium or vitamin D supplementation alone does not appear to impact risks either way,<sup>142,143</sup> supplementation with calcium and vitamin D in people with a history of stones has been associated with potentially increasing risk.<sup>144,145</sup> Therefore, in people predisposed to kidney stones, convincing data supports the intake of a diet high in calcium, in reducing events. Those with a history of kidney stones should consult with their health professional if supplementation is required to achieve the calcium RDA for bone health.<sup>146</sup>

### Calcium Supplementation

In summary, the vitamin and mineral RDAs have been established for best long-term bone and health outcomes. The goal for all persons throughout a lifetime, and especially within the first four decades of life, is to achieve the calcium RDA through diet unless advised otherwise by a qualified health professional. Unfortunately, the majority of the population **not supplementing** calcium is well below the RDA (and many below the EAR) throughout a lifetime, setting them up for early bone failure, which creates major clinical needs for treatments that do little other than possibly slow a generally self-inflicted accelerated progression that could likely have been mostly avoided through proper intake of bone building/maintaining nutrition (see more below) and activity at the proper levels throughout each life-phase. Therefore, proper supplementation (correction from food Ca content to RDA) is warranted when diet alone fails to supply the calcium RDA, and again, unless advised otherwise by a qualified health professional.

### Vitamin D

*Because of Vitamin D’s indispensable synergy with calcium, it should accompany calcium (unless advised otherwise by a qualified health professional) within the product formula but the amount should be complementary to the vitamin D content within a typical MVM.*<sup>55</sup>

As mentioned above, the maintenance of serum calcium levels within a narrow range is vital for normal functioning of the nervous system, as well as for bone growth and maintenance of bone density.<sup>147</sup> Vitamin D is essential for the efficient regulation and utilization of calcium by the body and is as important as calcium in building and maintaining strong bones.<sup>46,47,48,49,50,51,52,53,54,55,61,76,78,147</sup> Calcium supplementation should be accompanied with adequate amounts of Vitamin D for proper absorption and utilization.<sup>55,148,149</sup>

### Vitamin D in Calcium Homeostasis Including Bone and Connective Tissue

Classic vitamin D deficiency is characterized by rickets or osteomalacia, which is the softening and weakening of bones in growing children and/or impaired bone mineralization in children and adults.<sup>150</sup> Vitamin D’s effect on bone health is well established by the fact that left untreated, animals/humans lacking functional vitamin D receptors (VDR) or the

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CYP27B1 gene that produces the hydroxylase enzyme responsible for converting 25(OH)D, (calcidiol) to the active form of vitamin D (1,25(OH)<sub>2</sub>D), develop rickets or osteomalacia.<sup>151</sup>

Since the majority of vitamin D in humans is produced when UVB rays interact with skin, rickets became a major global problem, especially in upper latitudes, when humans moved from outdoor farming to indoor industry. Food fortification (i.e. supplementation) with Vitamin D became mandatory to stem the epidemic.<sup>152</sup> Normal growth and mineralization of bone is dependent on the adequate availability of calcium and phosphate in which Vitamin D plays a direct role.<sup>147,151</sup>

### Primary Bone Building Roles of Vitamin D

Foremost, vitamin D is essential to effectively absorb calcium and phosphorous from the gut.<sup>153</sup> Calcium is absorbed through the small intestine by two primary mechanisms: 1) a transcellular active transport process (TAT) in the duodenum and upper jejunum area; and 2) a paracellular, passive process that functions throughout the length of the intestine.<sup>154</sup> In TAT, entry through the intestinal brush border is mediated by a compound termed CaT1 and a calcium binding protein (CaBP). The biosynthesis and functions of CaBP and CaT1 are largely vitamin D-dependent. At high calcium intakes CaT1 and CaBP are downregulated because the active vitamin D metabolite is downregulated, and the inverse is true. There is also evidence that activated vitamin D can enhance paracellular calcium passive diffusion.<sup>154</sup> Secondly, insufficient vitamin D resulting in hypocalcemia (low calcium) and hypophosphatemia (low phosphate) can lead to hyperparathyroidism (also seen in a vitamin D-deficient state) and the parathyroid has its own effects on cartilage and bone.<sup>155</sup>

Finally, because of the ubiquity of VDRs, vitamin D metabolites interact in many other areas as described above,<sup>156,157</sup> including endothelial receptors,<sup>158</sup> growth hormone,<sup>159</sup> and insulin-like growth factor-1,<sup>160</sup> all of which have exclusive and synergistic bone formation effects with vitamin D. The active form of vitamin D also promotes bone resorption (necessary breakdown for bone remodeling and mineral release to blood) by increasing the activity and number of osteoclasts.<sup>161,162</sup>

*For complete current data on Vitamin D and its actions and overall recommendations, the reader is referred to the respective section in the Practitioner Dietary Supplement Reference Guide (PDSRG) maintained by the Sport and Fitness Professional Resource Center and used for practitioner education purposes only.*

### Magnesium

As with Vitamin D, magnesium is included because of its critical synergistic function with calcium in bone health.<sup>23,69</sup> Although magnesium is involved in more than 300 biochemical reactions of the body,<sup>163,164</sup> approximately 60% of the body's total magnesium is stored in the bone.<sup>164,165</sup> Low magnesium (common in humans)<sup>1,28,166,167,168</sup> leads to a decrease in: bone formation,<sup>169,170</sup> parathyroid hormone secretion (regulates calcium homeostasis including utilization),<sup>171,172</sup> and serum Vitamin D concentrations,<sup>172,173</sup> all of which contribute to low bone density and early osteoporosis.<sup>23,30,69,170</sup> Magnesium in this formula complements the typical western diet to help achieve desired magnesium levels and to work synergistically with the dotFIT multivitamin and mineral formulas which also contain magnesium, thus keeping total intake in the safe and recommended nutrient range.<sup>1,167,174,175</sup> Further, studies have shown subjects supplementing magnesium (300-400 mg/day) or with higher dietary magnesium intake (closest to the RDA ) seem to have an overall health protective effect<sup>23,69,170,176,177,178,179,180,181,182,183</sup> The magnesium in this formula is in both the oxide and citrate form for greater bioavailability compared to a single salt form.<sup>184,185</sup>

### Vitamin K1 and K2

Vitamin K1 (phylloquinone) and K2 (menaquinone) have similar and unique properties and are the two natural and essential forms of vitamin K<sup>186,187,188,189</sup> which are intricately tied to vascular and bone structure and health.<sup>62,65,190,191,192,193</sup> Insufficient vitamin K is associated with under-carboxylation of osteocalcin, osteopenia (bone thinning) and increased fracture risk, while vitamin K supplementation has been shown to reduce bone turnover and improves bone strength.<sup>64,65,66</sup> Low dietary vitamin K2 intake in children is associated with early onset of poor bone health.<sup>194</sup>

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Calcium and vitamin D from food and supplements are complemented with vitamin K2 supplementation due to its increasingly recognized role as a "calcium chaperone" (getting dietary calcium to the right places in the body) and the facilitator of vitamin K's cardiovascular system role in supporting cardiac structure and function.<sup>189,192,195,196,197,198,199,200,201,202,203,204,205,206,207</sup> The recommended daily intake of vitamin K has been established as 90 mcg for women and 120 mcg for men. However, larger amounts may be needed for complete carboxylation of osteocalcin necessary for bone building.<sup>62,64,66</sup> According to the third National Health and Nutrition Examination Survey, approximately half of the men and women in the United States consume less than the recommended amount of vitamin K, and one quarter of the population consumes less than 60 mcg/day.<sup>64</sup> In a study of hip fracture risk, women who consumed more than 109 mcg/day of vitamin K had a decreased risk of hip fractures compared to women with lower levels of vitamin K intake.<sup>208</sup> On the other hand, as to be expected, a review on vitamin K supplementation alone in post-menopausal or osteoporotic patients found no evidence that vitamin K affects bone mineral density or vertebral fractures, but may reduce clinical fractures. This is another example of starting supplementation too late (acting as a singular treatment) and without long-term synergy (lifelong RDA levels of symbiotic vitamins and minerals) with the other essential nutrients involved in bone health and maintenance.<sup>209</sup> Therefore vitamin K1 and K2 are contained in the formula to support their unique roles in bone and cardiovascular health but also to help direct the RDA daily dose of calcium's (whether from food or food and supplements) proper distribution.

### Boron

Boron is included to support overall bone health in synergy with all other ingredients especially in supporting the construction of extracellular matrix and facilitating the important role of Vitamin D.<sup>62,210,211,212</sup>

### Data Summary

Calcium (Ca) is an essential mineral not just for bone creation and maintenance but also overall health. Although 99% of the body's calcium is stored in bones, it is the ~1% found in blood and soft tissues that is tightly regulated to allow Ca to perform its critical immediate life tasks such as facilitating muscle function, nerve transmission, vascular constriction, vasodilation, blood clotting and other indispensable immediate metabolic functions. Therefore, the body has evolved an elaborate system controlled by the parathyroid gland and vitamin D to draw Ca from bone as needed to maintain this constant critical serum concentration when daily Ca intake is inadequate, as it is for most of the U.S. population when using food alone as the delivery, thus compromising long-term bone health for millions of Americans.

Genetics, diet/nutrients and exercise/activity determine a person's peak bone mass (BM), which occurs at ~30 years of age, at which point resorption (bone breakdown) surpasses formation, making the accrual of BM while you can, crucial for long-term bone health. The more BM acquired up to around age 30 years, and everything else equal, the longer the human skeleton can remain healthy throughout life. Notably, there is no making up for what you did not get during the bone building years.

Ca supplementation as needed to achieve the life-phase RDA should be viewed as a preventative measure to protect long-term bone health and not a treatment for poor bone health that has taken hold later in life. To maximize calcium's contribution to bone creation and long-term health, daily intake has been established by age and gender to be 1,000 to 1,300 mg for those four years and older (see Table 2 for all ages). If the diet cannot supply this daily amount of calcium which unlike other vitamins and minerals is now quantifiable based on food labels - the shortfall between food and the recommended daily amounts should be corrected at all ages using supplementation.

Supplementation with calcium carbonate is the more efficient/economic form when taken with food, which is when calcium and other MVM supplementation should be consumed for generally healthy individuals.

The UL for calcium is 2,000-3,000 mg/day, but using food and supplements combined, persons should not exceed the RDA unless recommended by a qualified health professional. Further, there is no established relationship between proper calcium supplementation and cardiovascular events or prostate health. However, regarding the latter, and to error on the side of caution, we recommend men use no more than 500 mg of calcium from supplements (if necessary

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based on diet shortfall), to support bone health and to help guard against miscalculations in actual dietary calcium consumption. Although diets high in calcium have demonstrated a protective effect on the formation of kidney stones, people with a history of stones and colorectal polyps should consult with their health professional if they need calcium supplementation to achieve the RDA.

The bottom line with calcium intake, as with all vitamins and essential minerals, is that humans of all ages should consume the guidelines which are the RDAs set by the Institute of Medicine. However, unlike many vitamins and other minerals, the calcium RDA can be achieved more easily from diet alone which provides rationale for the recommendation to achieve the calcium RDA from food if possible, but including a daily low dose multivitamin and mineral that does not contain calcium can: 1) complement a calcium supplement if necessary by contributing the other diet shorted bone building nutrients (e.g. vitamins D and K, magnesium, etc.) at levels that when combined with the calcium supplement and its co-factors, maintains all nutrient intake within the safe and recommended range; 2) supply other known under-consumed nutrients when food alone is the delivery because vitamins and minerals work in synergy at all levels in the human body and food alone consistently fails in delivering the amounts necessary to reach the RDAs.

### Typical Use

- For anyone not meeting the recommended intakes for calcium (1,000-1,300 mg/day) and required bone health cofactors (Vitamin D, K, magnesium) through diet (~70% of the U.S. population)
  - **Females:** Take one (1) or two (2) daily with meals.<sup>213</sup> If needed, take one with a morning meal and the second with an evening meal<sup>214</sup>
  - **Males:** Take one (1) tab only with a meal if daily dietary calcium falls short of recommendations, unless supervised by a qualified health professional<sup>118</sup>
- The formula complements the typical western diet to help achieve recommended levels of calcium, vitamin D, magnesium, boron and both forms of Vitamin K, while also remaining synergistic with any of the dotFIT multivitamin and mineral formulas, thus keeping total intake in the safe and recommended nutrient range
- Calcium supplementation is not warranted when a person's diet contains enough calcium (1,000-1,300 mg/day), which has been made easier to identify with new labeling laws, and the said person is consuming a complete daily multivitamin and mineral formula that contains diet complementing levels of the non-calcium bone building nutrients such as but not limited to, magnesium, vitamin D3 and Vitamin K1 and K2 and other known under-consumed vitamins and minerals.

***Adverse events, precautions or contraindications with calcium, vitamin D, vitamin K or boron are rare or unknown in healthy people supplementing the diet properly as described above.***

***The section below is a summary related to specific sub-populations. Qualified practitioners needing more information are referred to the [TRC Natural Medicine Data Base](#) which is continually updated with emerging evidence-based data.***<sup>215</sup>

### Precautions

Chronic calcium supplementation is considered safe at doses that combined with diet do not exceed the Tolerable Upper limit (UL) of 2,000-3,000 mg/day,<sup>216,217</sup> but based on emerging science cited above we recommend sticking with "Typical Use" described here. Large doses of calcium and iron can compete for absorption, resulting in a slightly lower absorption of iron.<sup>218</sup> However this does not affect the iron status of people with adequate iron stores.<sup>219</sup> Calcium supplements decrease absorption of bisphosphonates. Therefore, bisphosphonates should be consumed at least 30 minutes before calcium.<sup>220</sup> The bisphosphonates include alendronate (Fosamax), etidronate (Didronel), ibandronate (Boniva), risedronate (Actonel), and tiludronate (Skelid).

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People using Calcipotriene for psoriasis should not use calcium supplements unless monitored by qualified health professional.<sup>221</sup> Although diets high in calcium have demonstrated a protective effect on the formation of kidney stones, people with a history of stones and colorectal polyps should consult with their health professional if they need calcium supplementation to achieve the RDA.<sup>128,134,144,145,146</sup>

### Contraindications (also see Precautions listed above)

The use of calcium supplements by those with a history of kidney stones has varied results. Some individuals with a history of stones will benefit from the supplementation of calcium with food as it aids in the removal of oxalates. However, those with absorptive hypercalciuria may have an increased risk of stone formation although studies have found no connection with supplementation.<sup>142,222,223</sup> Supplementation with calcium and vitamin D in people with a history of stones has been associated with potentially increasing risk of stone formation.<sup>144,145</sup> Consult with a physician when a history of kidney stones or colorectal polyps exists and calcium supplementation is needed,<sup>134,146</sup> or when taking these drugs: biphosphonates,<sup>224</sup> Dolutegravir (Tivicay),<sup>225</sup> hydrogen blockers, levothyroxine,<sup>224</sup> proton pump inhibitors, quinolones<sup>226</sup> and tetracyclines.<sup>227</sup>

Excessive vitamin K does not increase the risk of blood clots, but those taking warfarin (Coumadin®) for anti-coagulation should avoid supplemental vitamin K because warfarin is a vitamin K antagonist.<sup>64,65</sup>

Oral vitamin D is well tolerated at doses significantly higher than in this formula.<sup>228,229</sup>

### Adverse Reactions

Side effects from calcium supplementation are rare, mild, and usually limited to gas, bloating and constipation.<sup>227,230</sup> There are no known adverse reactions to other ingredients in this formula when used properly at these recommended doses.<sup>65,228,229</sup> Orally, high doses of magnesium can cause gastrointestinal irritation, nausea, vomiting, and diarrhea.<sup>231</sup>

### Upper Limit/Toxicity

The National Academy of Sciences (NAS) Food and Nutrition Board (FNB) has set the upper limit for chronic calcium ingestion at 2,000-3,000 mg/day and Vitamin D at 100 mcg/day (4,000 IU).<sup>24,217</sup> The Lowest Observed Adverse Effect Level (LOAEL) is 5,000 mg/day for calcium and the No Observed Adverse Effect Level (NOAEL) is 250 mcg/day (10,000 IU) for Vitamin D.<sup>232,233</sup> The upper limit for magnesium is set at 360 mg/day from supplements only. Vitamin K has no established upper limit.<sup>24</sup>

### Summary

#### Purpose

For people not consuming their daily recommendation (Table 2) of calcium from food, known as the Recommended Dietary Allowances (RDAs). The product supplies supplemental calcium with other supporting bone building nutrients commonly low in western diets, in the amounts necessary to complement food intake to achieve the RDA of calcium to help build and support bone health throughout one's lifespan.

#### Unique Features

- Contains calcium and other primary bone building nutrients including the proper forms of vitamins K, D and magnesium required to maximize calcium's uptake into the skeletal structure, minimize resorption and avoid unhealthy deposits – i.e. enhance calcium utilization
- Calcium and magnesium are prepared in their proper salt forms designed to optimize delivery and utilization.
- Vitamin K1 and K2 support proper bone deposition of calcium.
- Boron is added to help support the role of Vitamin D in bone health
- Formula maintains all ingredients in a safe and recommended range when combined with diet, a multivitamin and mineral\* or other dotFIT branded products



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- Formula will function effectively (as claimed) as a standalone product if for some reason a user is not consuming a complimentary dotFIT daily multivitamin and mineral (MVM) or some other branded MVM formula
- NSF Certified for Sport (NSFCS), an independent third-party test which provides an additional product guarantee to ensure purity and potency for drug tested athletes. Click [here](#) for the dotFIT NSFCS section.
- Manufactured in a regularly inspected NSF certified facility, in compliance with Good Manufacturing Practices (GMPs) exclusively for dotFIT, LLC.

### Supplement Facts Panel

<b>Supplement Facts</b>				
Serving Size: 1-2 Tablets				
Servings Per Container: 60 to 120				
	Amount Per 1 tablet	%DV	Amount Per 2 tablets	%DV
Vitamin D (as cholecalciferol)	5 mcg (200 IU)	25%	10 mcg (400 IU)	50%
Vitamin K <small>(as phytonadione [Vitamin K1] and menaquinone-7 [Vitamin K2])</small>	30 mcg	25%	60 mcg	50%
Calcium <small>(from calcium carbonate)</small>	500 mg	38%	1,000 mg	77%
Magnesium <small>(from magnesium oxide and magnesium citrate)</small>	125 mg	30%	250 mg	60%
Boron <small>(from boron chelate)</small>	1 mg	*	2 mg	*
*Daily Value (DV) not established.				

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