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At the CPME Board Meeting in Winchester on 24 October 2009, CPME adopted the following policy document “Vitamin D nutritional policy in Europe” (CPME 2009/179 Final EN)

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## Vitamin D nutritional policy in Europe

It is well known that vitamin D is essential for optimal bone health as severe vitamin D deficiency causes rickets or osteomalacia (depending on the age of the subject and the status of the growth plate). The introduction early in the 20th century of cod liver oil generated a “Lazarus” type of cure for rickets and virtually eliminated endemic rickets in all parts of the world. This subsequently led to the introduction of preventive strategies with a recommended (and often provided) dietary supplementation of  $\geq 100$ -400 IU of vitamin D3 (or D2) per day for infants and children. On the contrary the absence of such supplementation policies in areas of the world where general vitamin D insufficiency is still prevalent continues to cause a substantial number of cases of rickets. Indeed similar situations occur in areas where a good preventive strategy does not reach some subgroups (e.g. children of immigrants living in Western Europe).

At the end of the 20th century it became obvious that even mild or moderate vitamin D deficiency also contributes to increased risk of fractures and falls. This comes from epidemiological surveys and has been confirmed by numerous randomized intervention trials with vitamin D with or without calcium to reduce fractures and falls, dealing with more than 50,000 (mostly elderly) subjects. Several peer reviewed detailed meta-analyses evaluated all these studies and coherently conclude that a vitamin D (600-800 IU of vitamin D3/d) and a good calcium intake (about or above 1 g/d) can reduce hip and non-vertebral fractures and falls by about 20%. Although this reduction may not at first look that significant it could nevertheless have major health benefits if the correct and safe prevention therapy would be widely applied to millions of the “target” population. Such a preventative therapy (600-800 IU of vitamin D3/per day) would increase the prevailing 25OHD concentration (this is the major metabolite of vitamin D as it circulates in blood and is the best known marker for vitamin D status) by about 8 ng/ml (or 20 nmol/L) and would increase 25OHD levels above 20 ng/ml or 50 nmol/L in nearly all subjects. This is in sharp contrast with the overall 25OHD status around the world which is estimated at a mean level of 21 ng /ml, based on a compilation of all published literature – implying that approximately 50% of the population is deficient and in some cases severely deficient. In case of osteoporosis, vitamin D and calcium are



an important part of treatment but should be complemented by more powerful anti-osteoporosis drugs (e.g. Biphosphonates).

It is now also known that the vitamin D endocrine system is not only important for bone and muscle health but also influences many other tissues such as the immune system, the cardiovascular/ metabolic system, cell proliferation and cancer. This is based on well documented biochemical, cellular and animal data generated in many research laboratories around the world. The human data is principally based on cross-sectional and/or observational data linking many and in fact nearly all major human diseases and preventable conditions to the body's vitamin D status. Overall the highest risk of cancer (especially colon cancer), infections, several major autoimmune diseases such as multiple sclerosis, type 1 diabetes and inflammatory diseases, cardiovascular risk factors and the metabolic syndrome (including hypertension and type 2 diabetes) are more prevalent or more severe in subjects with the poorest vitamin D status (25OHD levels < 20 ng/ml or 50 nmol/L). There is even a noticeable trend for lower risk for all such diseases and conditions in subjects with 25OHD levels above 20 ng/ml. However good the basic, preclinical and epidemiologic data suggest the causality between vitamin D status and all these major diseases, true randomised clinical trials for "non bone/muscle" end points are still not available – apart from a few negative studies (probably related to their design or low vitamin D dose) or preliminary studies (due to lack of power). Therefore no reliable threshold level for 25OHD for minimising these non-calcaemic endpoints can yet be defined, however for individual subjects the combined data and evidence needs to be considered in making any recommendation.

There are different possible strategies to improve the vitamin D status in the major target groups around the world and no single strategy has been nor probably will be beneficial for all subgroups. The vitamin D status could be improved by advocating a greater exposure to natural sunlight (e.g. an extra 10 – 20 minutes exposure of arms and legs to sunlight at an optimal time of the day depending on latitude, environmental conditions and cultural and religious habits), but the risk of lifelong accumulation of photo damage and skin cancer deters such strategy. Increased intake of vitamin D rich natural food such as fatty fish would also help to improve the vitamin D status but is unlikely to be really effective because of cultural habits and above all there is probably not sufficient fatty fish in the oceans to propose that as a strategy. Therefore as a consequence, only vitamin D supplements or vitamin D enriched food products are in reality truly strategic and viable options for optimising the vitamin D status. The practical implementation of these options depends largely on medical, social, cultural, legal and financial aspects.



## Conclusions

The greatest risk for bone and several major human diseases and preventable human health conditions are associated with 25OHD levels below 20 ng/ml (or 50 nmol/l).

Several authoritative meta-analyses indicate that a daily dietary vitamin D supplementation (600-800 IU D3) plus calcium reduces the risk of fractures and falls. Such vitamin D dose is likely to increase mean 25OHD levels by 6-16 ng/ml (15-40 nmol/l) and bring serum 25OHD to  $\geq 20$  ng/ml ( $> 50$  nmol/l) in most subjects.

The mean or median level of 25OHD around the world hardly exceeds 20 ng/ml (50 nmol/l) with slightly higher levels in US Caucasians (NHANES data). An estimated number of at least 1 billion (and probably many more) people around the world have 25OHD levels  $< 20$  ng/ml, so that their bone health and maybe even their global health could be improved by vitamin D supplements that bring their 25OHD level above 20 ng/ml.

It is not unlikely that even higher vitamin D supplements, bringing 25OHD levels to over 30 ng/ml may convey further benefits without creating additional risk. This would however require vitamin D supplements  $\geq 2000$  IU D3 per day for millions, if not billions of people, and until the completion of long term large scale RCTs the efficacy and safety of such interventions cannot be assured for the general population.

Vitamin D supplementation (600-800 IU D3) plus calcium should be considered for elderly people (older than 75 years) with an increased fracture and/or fall risk, in particular people living in nursing homes.