UV-irradiated mushrooms, enriched in vitamin D_2, may improve vitamin D status in individuals with *low* but not high vitamin D status: new data from an *ODIN* systematic review and meta-analysis.

There is a considerable mismatch between current intakes of vitamin D by many European populations and recommended target intakes for the vitamin [1]. While traditional fortification of milk and other dairy products remains important in tackling inadequate intake, additional strategic approaches to fortification, including biofortification, of a wider range of foods, have the potential to increase vitamin D intakes in the population [2]. Mushrooms are very rich in ergosterol, the principal sterol in fungi, and ultraviolet (UV) radiation from sunlight naturally induces the conversion to ergocalciferol (vitamin D_2) in a process resembling the cutaneous synthesis of vitamin D_3 in humans. While wild mushrooms can naturally contain high concentrations of vitamin D_2, the vitamin D_2 content of cultivated mushrooms is very low because they are cultivated indoors without the benefit of UV light [3]. Artificial UV light technology offers potential to enhance the vitamin D_2 content of commercial mushrooms and such UV-treated mushrooms are already on the market in Europe.

Data demonstrating that the vitamin D_2 in these UV-treated mushrooms can increase vitamin D status of consumers has been quite mixed, with some randomized controlled trials (RCT; the highest form of evidence) showing clear improvements [4,5], and others little, if any, effect [6,7]. Differences in study design parameters, including the way the UVB-mushrooms were processed and/or cooked in the various studies, may explain some of the divergent findings among the RCTs. However, another potentially important explanation is that under certain conditions the additional vitamin D_2 from the mushrooms while increasing serum levels of 25-hydroxyvitamin D_2 [25(OH)D_2], somehow leads to a decrease in serum levels of 25-hydroxyvitamin D_3 [25(OH)D_3]: 25(OH)D_2 plus 25(OH)D_3 (collectively termed total 25-hydroxyvitamin D [total 25(OH)D]) defines a person's overall vitamin D status. One of the aims of the ODIN project was to undertake a re-analysis of stored serum samples from one of the key RCTs [4] to get better information on these 25-hydroxy metabolites and then use this new data together with that from a number of other available RCTs to further explore whether UV-treated mushrooms can improve vitamin D status for European consumers.

The *Cork Centre for Vitamin D and Nutrition Research* used their CDC-certified liquid chromatography tandem mass spectrometry (LC-MS/MS) method to re-analyse stored serum samples from the RCT in 2011 by Dr. Paul Urbain, University Medical Centre Freiburg, Germany [4]. While this new LC-MS/MS analysis confirmed that consumption of UV-treated mushrooms increased serum total 25(OH)D in the healthy young German adults, it also showed that this increase was due to an increase in serum 25(OH)D_2 levels even despite a moderate reduction in serum 25(OH)D_3 levels [8]. Besides the Urbain *et al*. RCT [4], the ODIN systematic review, recently published in the *Journal of Nutrition* [8], identified five other RCTs [5-7,9,10] that met with our inclusion criteria. We performed a meta-analysis on the serum 25(OH)D as well as 25(OH)D_2 and 25(OH)D_3 data from these RCTs so as to try and identify what effect(s) the UV mushrooms were having overall.

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Meta-analysis of all 6 RCTs [8] showed serum total 25(OH)D was not significantly increased (P = 0.12) by UV-exposed mushrooms, but there was high heterogeneity (I^2 = 87%). Including only the 3 European-based RCTs [mean baseline 25(OH)D, 38.6 nmol/L], serum 25(OH)D was increased significantly by UV-exposed mushrooms [weighted mean difference (WMD): 15.2 nmol/L; 95% CI: 1.5, 28.8 nmol/L, P = 0.03, I^2 = 88%]. Omitting one of the European RCTs [7] in a further sub-analysis led to a much lower level of heterogeneity in the analysis (I^2 33%) and overall to an even greater increase in total serum 25(OH)D [WMD of 22.3 nmol/L; P<0.00001]. In contrast, there was no significant effect in the 3 US-based RCTs [P = 0.83; mean baseline 25(OH)D: 81.5 nmol/L].

Analysis of serum 25(OH)D_2 and serum 25(OH)D_3 (n = 5 RCTs) revealed a statistically significant increase (WMD: 20.6 nmol/L; 95% CI: 8.0, 33.3 nmol/L, P = 0.001, I^2 = 99%) and decrease (WMD: -13.3 nmol/L; 95% CI: -15.8, -10.7 nmol/L, P < 0.00001, I^2 = 0%; see **Figure 1**), respectively, after supplementation with UV-exposed mushrooms [8].

Overall, this ODIN work suggests that consumption of UV-exposed mushrooms may increase serum total 25(OH)D when baseline vitamin D status is low (less than ~50 nmol/L) via an increase in 25(OH)D_2 (+24.2 nmol/L) and despite a concomitant but relatively smaller reduction in 25(OH)D_3 (-12.6 nmol/L). This is of relevance for Europe, particularly during winter when vitamin D status is low for many in the population. When baseline vitamin D status is high the mean increase in 25(OH)D_2 (18.3 nmol/L) and a relatively similar reduction in 25(OH)D_3 (-13.6 nmol/L) may explain the lack of effect on serum total 25(OH)D.

Click on the following link to the paper describing the full study and other interesting findings: http://www.ncbi.nlm.nih.gov/pubmed/26865648

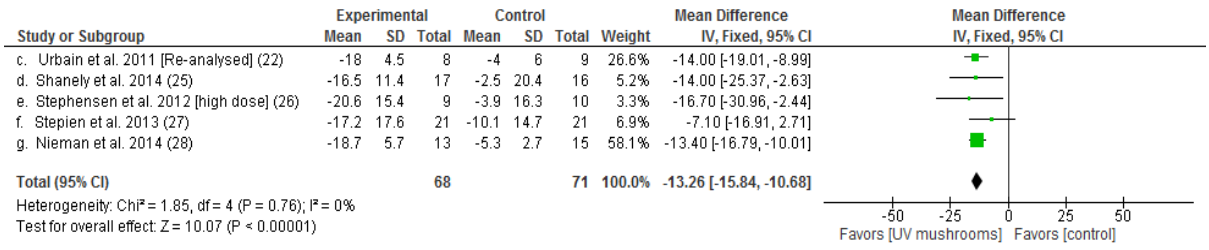

Figure 1. Forest plot: effect of UV-exposed mushroom supplementation compared to control mushrooms on serum 25-hydroxyvitamin D_3 concentration (nmol/L) from 5 randomized controlled trials of healthy individuals. Values are means (95% CI); WMD, weighted mean difference; I^2, variation in effect size attributable to heterogeneity [8].

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