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Prevalence of cervical disease at age 20 after immunisation with bivalent HPV vaccine at age 12-13 in Scotland: retrospective population study

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Scotland's public health campaigns to improve vitamin D nutriture occurred within the same timeframe as HPV vaccination

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In April 2019, Palmer et al [1] published a retrospective population study crediting vaccination against human papilloma virus (HPV) with reduction in HPV prevalence in Scotland, and the authors attributed a reduction in HPV prevalence among unvaccinated women with “herd protection.” However the authors did not mention Scotland’s population-wide public health campaigns to address endemic vitamin D deficiency. The Scottish Government recognized the high prevalence of vitamin D deficiency in its population and began recommending vitamin D supplementation not later than 2006. Vitamin D deficiency results in impaired mucosal and immune defenses and correlates in a dose-dependent manner with increased cervicovaginal HPV infection [2]. By 2009, coincident with the start of the HPV vaccination campaign in 2008, numerous vitamin D supplementation (and sun exposure) campaigns were being implemented throughout Scotland to combat the documented population-wide problem of vitamin D deficiency.

13 April 2019

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Scotland's public health campaigns to improve vitamin D nutriture occurred within the same timeframe as HVP vaccination

In April 2019, Palmer et al [1] published a retrospective population study crediting vaccination against human papilloma virus (HPV) with reduction in HPV prevalence in Scotland, and the authors attributed a reduction in HPV prevalence among unvaccinated women with “herd protection.” However the authors did not mention Scotland’s population-wide public health campaigns to address endemic vitamin D deficiency. The Scottish Government recognized the high prevalence of vitamin D deficiency in its population and began recommending vitamin D supplementation not later than 2006. Vitamin D deficiency results in impaired mucosal and immune defenses and correlates in a dose-dependent manner with increased cervicovaginal HPV infection [2]. By 2009, coincident with the start of the HPV vaccination campaign in 2008, numerous vitamin D supplementation (and sun exposure) campaigns were being implemented throughout Scotland to combat the documented population-wide problem of vitamin D deficiency.

Our views of vitamin D experienced a paradigm shift in the early part of this century with landmark publications such as Vieth’s authoritative documentation of safety in 1999 [3], Zittermann’s “Vitamin D in

preventive medicine” in British Journal of Nutrition in 2003 [4], and Vasquez’s “Clinical importance of vitamin D (cholecalciferol): a paradigm shift with implications for all healthcare providers” in 2004 [5] followed by an important partial summary of vitamin D usage guidelines in British Medical Journal in 2005 [6]. These and similarly themed articles have contributed to increased awareness of vitamin D’s safety and roles in preventive medicine and public health, including reducing the burden of infectious diseases such as viral infections and various types of cancer. Consistent with this evidence of safety and benefit, along with evidence that the human daily requirement is an order of magnitude greater than previously believed [7], use of vitamin D supplementation began to increase slowly and then exponentially in the United States [8] and other countries, especially English-speaking societies, most notably the United Kingdom. Indeed, according to the Scottish Health Survey 2003 [9], use of dietary supplements such as vitamins (including vitamin D), fish oils (a source of vitamin D) and minerals (magnesium supplementation improves vitamin D status and is necessary for vitamin D activation, binding, transport, metabolism, and gene expression [10]) had already begun to increase between 1998 and 2003. Certainly not later than 2006, the Scottish Government was already recommending widespread use of vitamin D supplements to combat the high prevalence of vitamin D deficiency in Scotland [11].

Widespread vitamin D deficiency in Scotland was followed by widespread recommendations for vitamin D supplementation starting in 2006 and 2009. In 2006, Burleigh and Potter published in Scottish Medical Journal [12] stating that, “The prevalence of vitamin D deficiency is high in older outpatients in this geographical area.” In 2007, Hyppönen and Power [13] showed that among British adults “Prevalence of hypovitaminosis D in the general population was alarmingly high during the winter and spring, which warrants action at a population level rather than at a risk group level.” In 2008, Rhein [14] further specified that “Vitamin D deficiency is widespread in Scotland.” In 2009, the Scottish Government acknowledged the need to educate its population about the importance of vitamin D3 supplementation [15]. From that time until the present, the Scottish Government, United Kingdom National Health Services, and various advocacy groups and programs (e.g., ScotsNeedVitaminD.com[16], Healthy Start, which provides vitamin D supplements to all children and pregnant women in Scotland [17]) continue assertive public health campaigns recommending vitamin D supplementation and increased vitamin D production via sun exposure via the “Shine on Scotland” program initiated in 2009 [18] for all of its citizens [19-23].

Vitamin D supplementation has been the subject of many clinical trials documenting anti-inflammatory, antiviral, and anticancer benefits. Correction of vitamin D deficiency has significant anti-inflammatory [24] and immunomodulatory [25] benefits. Vitamin D and its direct metabolites promote production of antimicrobial peptides which have antibacterial and antiviral properties, while also reducing viral replication by inhibiting the NF-kappaB pathway. Consistent with these immunomodulatory and antiviral mechanisms, data from several placebo-controlled trials shows that vitamin D provides benefit in a variety of infectious conditions including human immunodeficiency virus (HIV) [26], hepatitis C virus [27-29] and upper respiratory infections [30-31]. Vitamin D administration displays impressive clinical effectiveness against dermal HPV as shown in case reports, clinical series, and placebo-controlled trials, with remarkable safety, high efficacy, and a consistent trend toward complete resolution of lesions [32-36]. In 2014, Schulte-Uebbing et al [37] published “Chronical cervical infections and dysplasia (cervical intraepithelial neoplasia [CIN] 1-2): vaginal vitamin D treatment” showing that among 200 women with cervical dysplasia, vitamin D vaginal suppositories (12,500 IU, 3 nights per week, for 6 weeks) provided “very good anti-inflammatory effects” and “good antidysplastic effects” in women with CIN 1. In 2017, Vahedpoor and colleagues [38] published a double-blind placebo-controlled trial of vitamin D in women with HPV, in which they found that vitamin D3 administration for 6 months among women with CIN1 resulted in its regression and had beneficial effects on markers of insulin metabolism and antioxidant status. In 2018, Vahedpoor and colleagues [39] published a

double-blind placebo-controlled trial of vitamin D in women with HPV, in which they observed, "The recurrence rate of CIN1/2/3 was 18.5 and 48.1% in the vitamin D and placebo groups respectively", thereby clearly favoring treatment with vitamin D over placebo.

In Scotland, programs advocating HPV vaccination (started in 2008) and vitamin D supplementation (started not later than 2006 and again in 2009) occurred in close chronologic proximity. Crediting the reduction in HPV-related disease solely to vaccination via retrospective population study is potentially invalid and misleading, especially when the authors make no account whatsoever of the national program for vitamin D supplementation which started in the same timeframe. Numerous studies have shown that vitamin D provides immunomodulatory, anti-inflammatory, microbiome-modifying, antiviral and anti-HPV benefits with high safety, good efficacy, low cost, wide availability, and clinically important collateral benefits.

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Competing interests: Dr Alex Vasquez is a lecturer and author of numerous articles, letters, and books related to topics of nutrition, clinical medicine, neuroinflammation, and the human microbiome. Dr Vasquez has served as a consultant to Biotics Research Corporation.

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