

# The impact of seasonality and other determinants on vitamin D concentration in childhood and adulthood: still an unresolved issue

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Submitted Dec 23, 2015. Accepted for publication Dec 24, 2015.

doi: 10.3978/j.issn.2305-5839.2015.12.62

View this article at: <http://dx.doi.org/10.3978/j.issn.2305-5839.2015.12.62>

We are thankful to Zostautiene *et al.* for their comments (1) on our study about the potential association between shorter duration of daylight at birth and vitamin D metabolism later in life in a Southern European country (i.e., Italy) (2). The authors carried out a similar investigation in a Northern European country (i.e., Norway), and concluded that the month of birth had no significant relation with later serum vitamin D concentration. Indeed, some important and valuable issues were raised to explain the differences observed in the two studies. First, we definitely agree that considerable differences exist in both duration and intensity of daylight between Northern and Southern Europe, and the much greater impact of sunlight exposure in Italy may represent a crucial element for explaining our separate findings. It is also remarkable that Norway has proactively established a widespread policy of vitamin D supplementation to infants, whereas in Italy supplementation is virtually inexistent. Therefore, our epidemiological data are seemingly more robust, since the potential bias attributable to an external influence of exogenous vitamin D on the endogenous metabolism of this hormone is clearly lower. Finally, the

third issue raised by Zostautiene *et al.* about seasonality of blood collection is real. In a previous epidemiological study at our latitudes we also showed that the season of blood sampling is an important pre-analytical factor in the assessment of vitamin D status (3), wherein the frequency of subjects with vitamin D deficiency was found to be nearly double in blood samples drawn in winter and spring than in those collected in summer and autumn. Therefore, in order to rule out a potential bias due to blood sampling seasonality in our analysis about the impact of birth season on vitamin D status, we performed an additional multivariate analysis, entering serum vitamin D as dependent variable whereas age, sex, mean duration of daylight at birth and sampling season were entered as independent variables. Interestingly, age and vitamin D concentration remained unrelated, the strength of association between serum vitamin D and both gender and mean duration of daylight already found in our prior analysis was substantially confirmed, whereas a highly significant correlation was also observed between vitamin D status and season of sampling (*Table 1*).

In conclusion, an intriguing scenario emerges combining

**Table 1** Multivariate analysis obtained by entering serum vitamin D as dependent variable, whereas age, sex, mean duration of daylight at birth and season of sampling were entered as independent variables

Parameter	Coefficient	95% CI	SE	t statistic	DF	P
Age	0.00	-0.05 to 0.05	0.02	0.0	11,150	0.987
Sex	-6.60	-8.47 to -4.74	0.95	-6.9	11,150	<0.001
Daylight duration at birth	2.40	0.87 to 3.92	0.78	3.1	11,150	0.002
Season of sampling	5.32	4.64 to 6.00	0.35	15.4	11,150	<0.001

95% CI, 95% confidence interval; SE, standard error.

**Table 2** List of potential confounders of vitamin D status in epidemiological investigations

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Geographical location
Air pollution
Gender
Ethnic origin
Skin phenotype
Genetic variability
Body mass index
Dietary habits/supplementation
Alcohol intake
Medications
Comorbidities (e.g., renal function, inflammation)
Daylight duration at birth
Daylight exposure
Season of sampling
Fasting status
Physical exercise
Sample storage and transportation
Assay technology
Reference standard for measurement
Analytical interferences

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our data with those of Zostautiene *et al.* (1), in that the outcome of many epidemiological studies about vitamin D status may be dependent upon a number of pre-analytical and analytical variables (*Table 2*), which should always be considered when drawing definitive conclusions about the metabolism of this intriguing hormone in childhood and adulthood (4–6).

**Cite this article as:** Lippi G, Mattiuzzi C, Aloe R. The impact of seasonality and other determinants on vitamin D concentration in childhood and adulthood: still an unresolved issue. *Ann Transl Med* 2016;4(1):21. doi: 10.3978/j.issn.2305-5839.2015.12.62

## Acknowledgements

None.

## Footnote

*Conflicts of Interest:* The authors have no conflicts of interest to declare.

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