



Letters to the Editor

Data advisory with regard to NHANES serum 25-hydroxyvitamin D data

Dear Sir:

We are writing to alert readers that a data advisory with regard to serum 25-hydroxyvitamin D [25(OH)D] data from the National Health and Nutrition Examination Survey (NHANES) has recently been posted on the NHANES website (http://www.cdc.gov/nchs/nhanes/new_nhanes.htm). This advisory outlines 2 issues that all users of NHANES serum 25OHD data need to consider.

The purpose of our letter is to discuss the data advisory in relation to our recently published article that used NHANES serum 25(OH)D data (1). The first issue outlined in the data advisory is the need to adjust the serum 25(OH)D data from NHANES III to make valid comparisons with serum 25(OH)D data collected in NHANES since 2000. The exploration of this issue was one of the major objectives of our study, and the final conclusions about differences between NHANES III and NHANES 2000–2004 accounted for the methodologic difference between surveys. The first issue outlined in the data advisory was fully addressed in our article and therefore does not affect our results.

The second issue noted in the advisory describes drifts in assay comparability for the serum 25(OH)D data collected since 2000. The effect of these drifts on the population data were not fully recognized until after the publication of our article and thus was not addressed in our analyses. When we became aware of this issue, we immediately conducted an analysis to address its effect on our published results for serum 25(OH)D from NHANES 2000–2004. The analyses were repeated after the exclusion of the data of concern, and those results were compared with the results published in the Journal.

The results of these analyses are described in detail in the data advisory. Briefly, the effect of excluding the data of concern on our published results was minimal. Exclusion of the data of concern resulted in means and percentiles for NHANES 2000–2004 that were slightly lower (by 1–2 nmol/L) and estimates of the prevalence of low serum 25(OH)D values that were slightly higher (by 1–2 units) than those originally obtained when the entire 2000–2004 dataset was used. Study conclusions were not affected.

In summary, the Centers for Disease Control and Prevention (CDC) has posted a data advisory with regard to serum 25(OH)D data from the NHANES that identifies one issue, assay variability since 2000, that is relevant to our study. Our additional analyses indicate a minimal effect of this issue on our results. Work is planned by the CDC to address both issues raised in the data advisory by using the National Institute of Standards and Technology (NIST) standard reference materials (SRM) for serum 25(OH)D (2). That work will likely take many months to complete, however, and the CDC did not want to wait before informing the user community. When the NIST SRM results become available, we plan to reevaluate our published results, and we will provide an update at that time, if necessary.

None of the authors declared a conflict of interest.

Anne C Looker
David A Lacher

National Center for Health Statistics
Centers for Disease Control and Prevention
Hyattsville, MD 20782
E-mail: alooker@cdc.gov

Christine M Pfeiffer
Rosemary L Schleicher

National Center for Environmental Health
Centers for Disease Control and Prevention
Atlanta, GA 30341

Mary Frances Picciano
Elizabeth A Yetley

Office of Dietary Supplements
National Institutes of Health
Bethesda, MD 20892

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β -Carotene from rice for human nutrition?

Dear Sir:

The article by Tang et al (1) represents a valuable contribution to the discussion about the potential nutritional effect of β -carotene-containing rice. With the use of an impressive methodology, the authors provide some evidence for an uptake of β -carotene from rice in humans.

Given the enormous effort and elegance in the scientific methods used the study, however, the study fail to provide significant data for the evidence of a nutritional benefit from Golden Rice because

TABLE 3

Subject responses to a reference dose of [$^{13}\text{C}_{10}$]retinyl acetate and a Golden Rice meal with [$^2\text{H}_9$]-carotene¹

Subject no.	GR β -C	[$^{13}\text{C}_{10}$]RAc	AUC[$^2\text{H}_5$]retinol	AUC[$^{13}\text{C}_{10}$]retinol	Retinol equivalent	Conversion factor	
						By weight	By mole
	<i>mg</i>	<i>mg</i>	$\mu\text{g} \cdot d$	$\mu\text{g} \cdot d$	<i>mg</i>		
1	0.99	1.01	19.4	67.5	0.25	4	2.1
2	1.53	1.01	38.8	57.9	0.94	2.6	1.4
3	0.99	0.43	74.3	53.9	0.51	1.9	1
4	0.99	1.01	34.4	124.2	0.24	4.1	2.2
5	1.53	1.01	32.8	119.9	0.24	6.4	3.4
Mean \pm SD	1.21 \pm 0.30	0.89 \pm 0.26	39.9 \pm 20.5	84.7 \pm 34.5	0.36 \pm 0.17	3.8 \pm 1.7	2.0 \pm 0.9
SD (% of mean)	24.8	29.2	51.4	40.7	47.2	44.7	45.0
Median	0.99	1.01	34.4	67.5	0.25	4.0	2.1
Mean-median difference	0.22	-0.12	5.5	17.2	0.11	-0.2	-0.1
Mean-median difference, SD	0.73	-0.46	0.27	0.50	0.65	-0.12	-0.11

¹ GR β -C, Golden Rice β -carotene; RAc, retinyl acetate; AUC, area under the curve.

of its biomathematical deficits. This would not be of great concern if the data were used to justify the statement that β -carotene can be absorbed from rice. Unfortunately, the data are used to advertise for the suggested benefits of the technology of genetically modified organisms in populations who may not be able to qualify the study results and conclusions drawn. Apart from this larger, principal, discussion, there are 2 critical questions regarding the data presented in the study.

In **Table 3**, the authors present their main findings. The table is reproduced here with the addition (in the lower section in bold type) of the median and the magnitude of the SD and the mean-median difference and its magnitude (calculated from the data provided by the authors in the upper lines). The means and SDs on the basis of 5 probands with large interindividual variability is a weak basis for far-reaching nutritional conclusions. The SDs of the results range from 29% to 51% of the mean in a nonnormally distributed data set. Therefore, the statement "our analysis showed a very efficient bioconversion of β -carotene to vitamin A" is based on 2 of 5 values above the median in Table 3. Even considering the limited amount of intrinsically labeled β -carotene-containing rice available—with $\approx 20 \mu\text{g}$ β -carotene/g rice—it is to be questioned why the research group did not choose a more homogenous study population at least in terms of the variables of age, sex, and nutritional and vitamin A status, at the start.

A second question concerns why the authors did not use a dietary approach more similar to the diets of the individuals who were suggested to benefit from the consumption of this β -carotene-containing rice. One of the arguments used for advertising Golden Rice is that the people at risk of vitamin A deficiency have such poor diets that other sources of β -carotene and vitamin A are not accessible to them. Because diet definitely has an effect on the bioavailability of β -carotene from any β -carotene-containing food, the choice for a study diet that included meat, oil, and nuts, which does not represent a poor diet, is of concern. Therefore, the results of the study do not much help us in preventing vitamin A deficiency in populations at risk. The argument of a better conversion rate with β -carotene-containing rice may at best be interpreted as follows: This rice is to be considered as one means of providing β -carotene besides the known vegetables and algae and in absence of animal-derived dietary sources of vitamin A. The suggested superior conversion rate alone does not solve all intrinsic nutritional, medical, and social problems of the "Golden Rice approach" in preventing vitamin A deficiency.

More research in the prevention of vitamin A deficiency is required, and animal studies in piglets may be an appropriate model

to investigate the different approaches of supplementation, fortification, natural β -carotene from the diet, and nutrient-oriented plant breeding before humans are further exposed to studies that obviously do not address potential health risks.

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Michael B Krawinkel

Institute of Nutritional Sciences
Justus-Liebig-University
Giessen
Germany

E-mail: michael.krawinkel@ernaehrung.uni-giessen.de

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Reply to MB Krawinkel

Dear Sir:

We appreciate the interest from Krawinkel in our recent publication on the vitamin A equivalency of Golden Rice (1), in which we used stable isotope methodologies and a single serving (per subject) of Golden Rice (a transgenic rice that produces β -carotene in the grain) to study β -carotene absorption and bioconversion to vitamin A in 5 healthy adult subjects in Boston, Massachusetts. We showed that Golden Rice β -carotene in the dose provided ($\approx 1 \text{ mg}$) was effectively converted to vitamin A. Although Krawinkel acknowledges that our study provides evidence for β -carotene uptake, he raises 2 concerns about the bioconversion results: one concern relating to the data analysis and the other relating to the selection of study subjects.

Krawinkel believes that the reported "effective" bioconversion efficiency of Golden Rice β -carotene to vitamin A (mean: 3.8 to 1, by weight) is questionable because 2 of 5 bioconversion values