Vitamin B_{12} Status in Individuals Adhering to Plant-Based Diets

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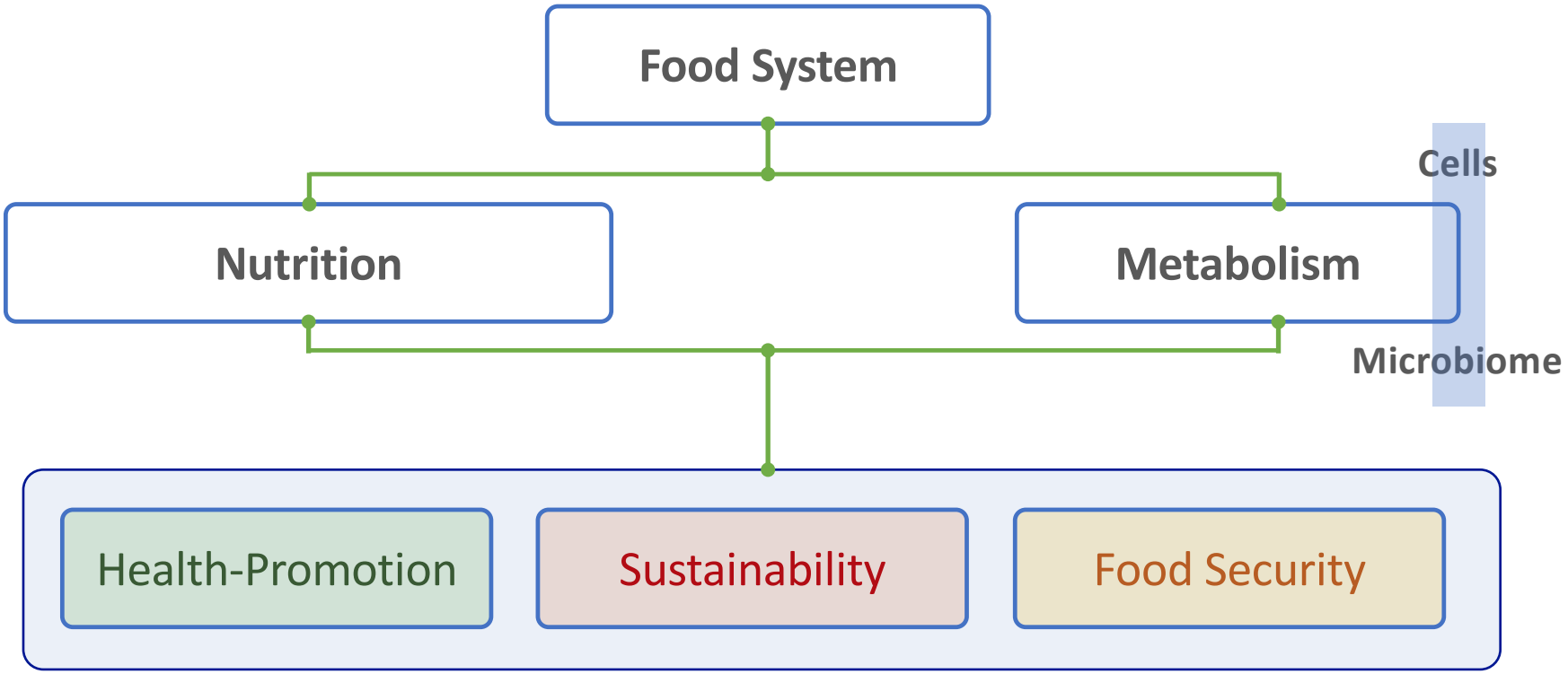
SYMPOSIUM NUTRITION AND HEALTH
Pflanzlichen Ernährung in der Pädiatrie: Braucht es Strategien zur Vorbeugung von Nährstoffmangel?
Plant-based diets in Paediatrics: Are special strategies needed to prevent nutrient deficiencies?
Thursday, November 30th, 2023

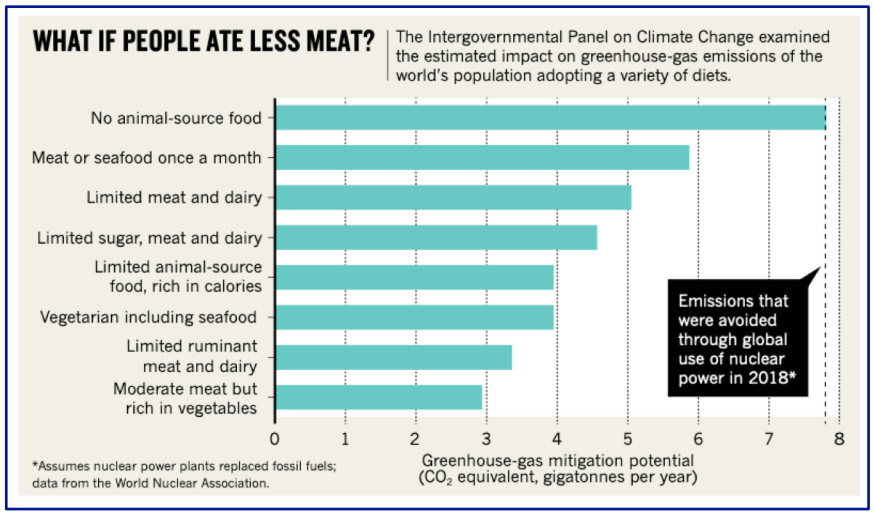
UNIVERSITÄTS KLINIKUM FREIBURG

Human Metabolism: Where do Nutrients Come from?



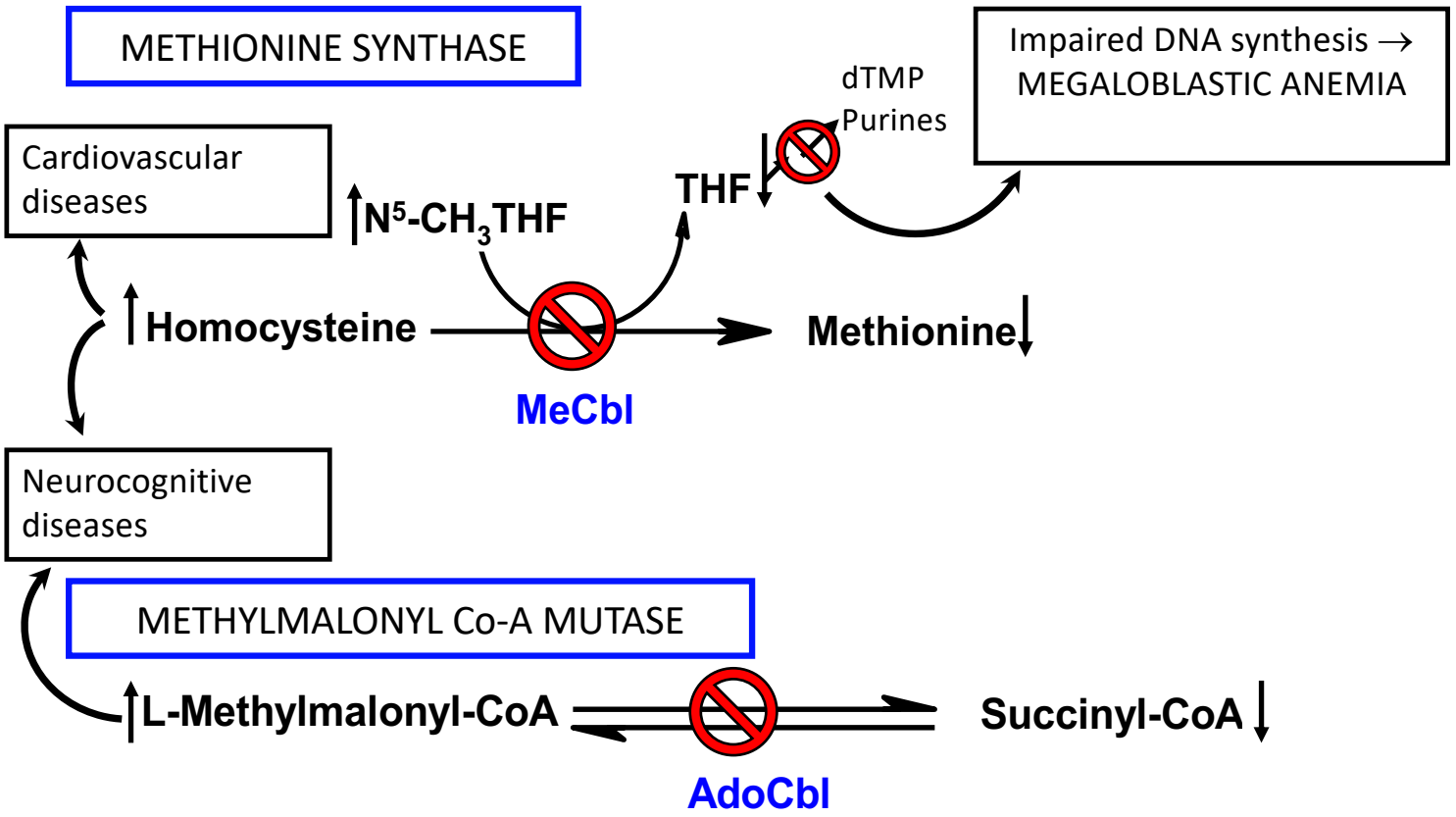
Food Systems: Plant-based Foods and Climate Change

- ***Recommended by:*** *IPCC 2019, EAT Lancet, economists, environmentalists and health experts*
- ***Benefits:*** *reduced land use for animal agriculture, reduce expenditure of drinking water, reduced greenhouse gas emissions, reduction of chronic diseases (CVD, type 2 Diabetes, certain cancers) and with this reduction of healthcare costs, reduction and elimination of global food insecurity*
- ***Risks:*** *certain nutrient deficiencies, Se, Zn, Fe, and chiefly, vitamin* B_{12}



NATURE | VOL 572 | 15 AUGUST 2019

Physiological Role of B_{12}: Cellular Metabolism

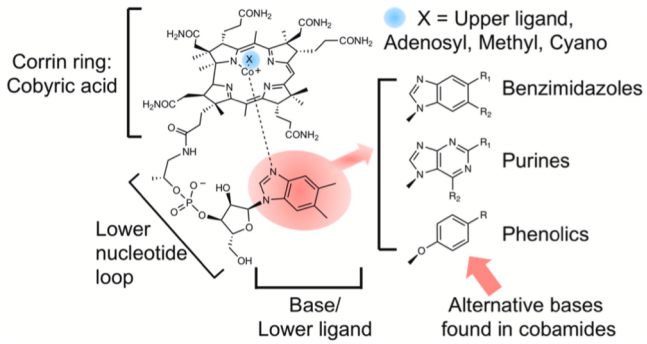


Esser, A.J. ….Hannibal, L. (2022). Versatile enzymology and heterogeneous phenotypes in cobalamin complementation type C disease. *iScience*.

Physiological Role of B_{12}: Gut Microbiome Metabolism

- *Microbial communities that produce vitamin B_{12}*
- *Microbiomal communities that use vitamin B_{12}*
- *Microbial communities that convert vitamin B_{12} into vitamin B_{12} analogues*

- **Vitamin B_{12} analogues** in human plasma: associated with **neurological disease**
  - Do microbiome-made B_{12} analogues interfere with vitamin B_{12} metabolism in human cells?
  - Can we modify the proportions of microbiome species that produce these vitamin B_{12} analogues by modifying dietary intake of B_{12}?
  - Is there specificity toward the chemical form of B_{12}, its food matrix and the dose?




> J Lab Clin Med. 1988 Jan;111(1):57-62.

Neurologic abnormalities in cobalamin deficiency are associated with higher cobalamin "analogue" values than are hematologic abnormalities

R Carmel [1], D S Karnaze, J M Weiner

Affiliations – collapse

Affiliation

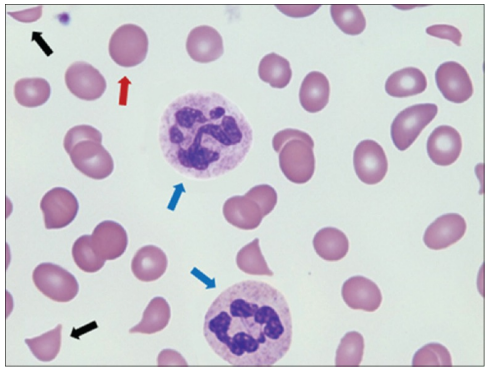
1 Department of Medicine, University of Southern California School of Medicine, Los Angeles 90033.

PMID: 3335826

"There is an urgent need to investigate the role of the gut microbiome in B_{12} metabolism and to elucidate its contribution to B_{12} depletion and analogue production" –Martin Warren

Osman, D… Warren, M. BBA - Molecular Cell Research 1868 (2021) 118896

Health Consequences of B_{12} Deficiency



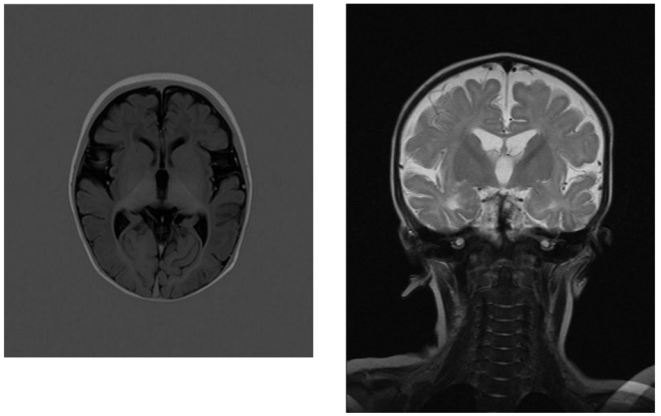
Int J Crit Illn Inj Sci. 2016 Apr-Jun; 6(2): 89–92

Hematological
Megaloblastic anaemia
Neutrophil hypersegmentation
Pancytopenia

Neurological
Paresthesia
Peripheral neuropathy
Combined degeneration of the spinal cord

Psychiatric
Irritability, personality changes, dementia, depression, psychosis

Severe B_{12} deficiency: Cerebral atrophy



Journal of Paediatrics and Child Health **49** (2013) E348–E354

- Diagnostic challenge in acquired B_{12} deficiency: long asymptomatic phase; unspecific symptoms

Esser, A.J. ….Hannibal, L. (2022). Versatile enzymology and heterogeneous phenotypes in cobalamin complementation type C disease. *iScience*.

Diagnostics: Four Biomarkers of B_{12} Status

- Homocysteine (Hcy): Blood, Urine, DBS
- Methylmalonic acid (MMA): Blood, Urine, DBS

Cellular Biomarkers

- Plasma-Cobalamin (Vitamin B_{12}): Blood
- Holo-transcobalamin: Blood

Systemic Biomarkers

Limitations:

- Hcy: influenced by other B vitamins (folate, B_9), (pyridoxal phosphate, B_6).
- MMA: increased in renal disease
- Serum Cbl: misses genetic and pharmacological disorders of metabolism.
- holo-TC: misses genetic and pharmacological disorders of metabolism.

Recommendation: measurement of at least two biomarkers (Serum B_{12} + MMA)

Hannibal, L. et al. Front Mol Biosci. 2016; 3: 27.

Diagnostics: Four Biomarkers of B_{12} Status

Traditional Approach

- **Serum B_{12}: Single Biomarker, WHO:**

>221 pmol/L : Adequate B_{12} status

148-221 pmol/L: Low B_{12}

<148 pmol/L: B_{12} Deficiency

Allen LH. Guidelines on food fortification with micronutrients. World Health Organization. Geneva: Department of Nutrition for Health and Development, 2006.

- **Multiple Biomarkers:**

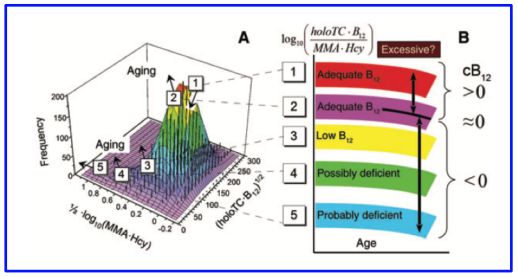
- Hcy: 5-15 µmol/L; >15 µmol/L
- MMA: 0.15-0.35 µmol/L; > 0.35 µmol/L
- B_{12}: 150-600 pmol/L; <150 pmol/L
- holo-TC: 20-125 pmol/L; >20 pmol/L

Hannibal, L. et al. Front Mol Biosci. 2016; 3: 27.

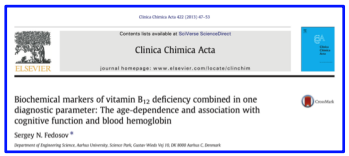
Optimized Approach

- **Combined B_{12} Index: cB_{12}**
- Accounts for: 2, 3 and 4 biomarkers
- Accounts for: Age, folate status

$$cB_{12} = \log_{10}\left(\frac{holoTC \cdot B_{12}}{MMA \cdot Hcy}\right)_{Test} - \frac{3.79}{1+\left(\frac{age}{230}\right)^{2.6}} + 1.1 \cdot e^{-\frac{folate}{3}}$$



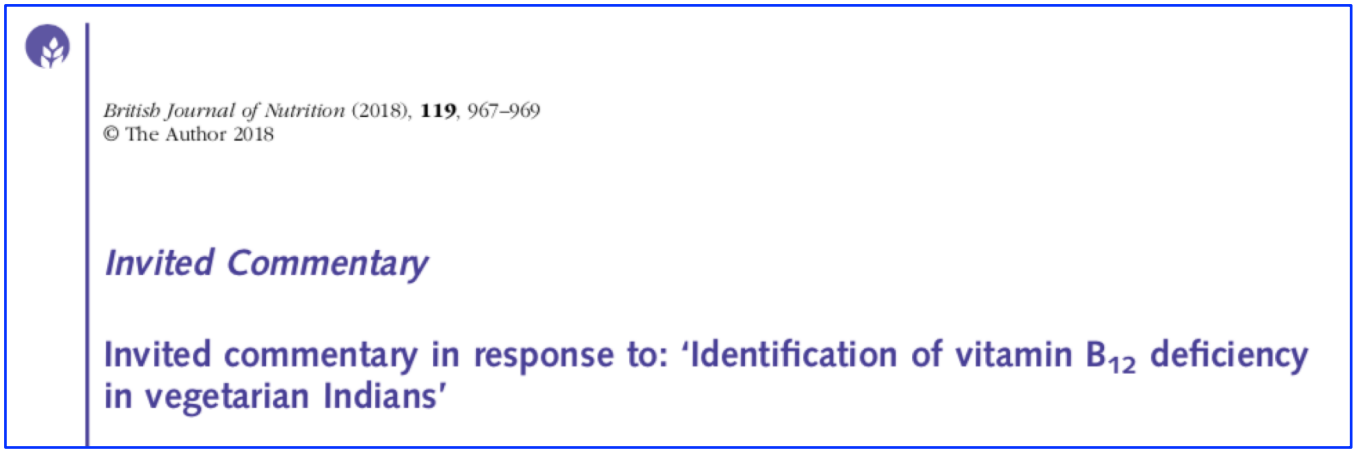
Dr. S. Fedosov



Diagnostics: Cut-offs of B_{12} Biomarkers in Vegetarians

Naik et al. propose a new set of cut-off values to improve the diagnosis of vitamin B_{12} deficiency in young vegetarian Indians. The authors propose the use of a combination of biomarkers and cut-off values of 100 and 19·6 pmol/L for plasma vitamin B_{12} and holo- TC, respectively, and values of tHcy of 17·6 and 27 µmol/L for females and males, respectively.

Source: Naik S, Mahalle N & Bhide V (2018) Identification of vitamin B_{12} deficiency in vegetarian Indians. Br J Nutr



British Journal of Nutrition (2018), **119**, 967–969
© The Author 2018

Invited Commentary

Invited commentary in response to: 'Identification of vitamin B_{12} deficiency in vegetarian Indians'

Diagnostics: B_{12} Biomarkers Upon Dietary Transition

- Healthy adults omnivores from Southwestern Germany
- Participants received education, a cook book, and weekly supervision
- Isocaloric Vegan (VD) or Meat-reach diets (MD), 4-weeks
- Run-in phase: 2 weeks; toward a homogeneous omnivore diet
- Vegan meals offered alongside a meat-based buffet at the restaurant of University Hospital Freiburg


Prof. Roman Huber

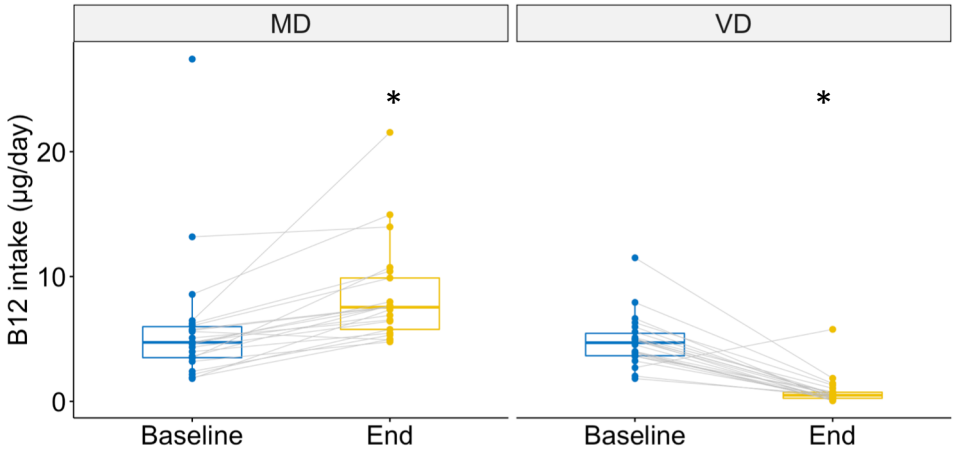

Dr. Ann-Kathrin Lederer

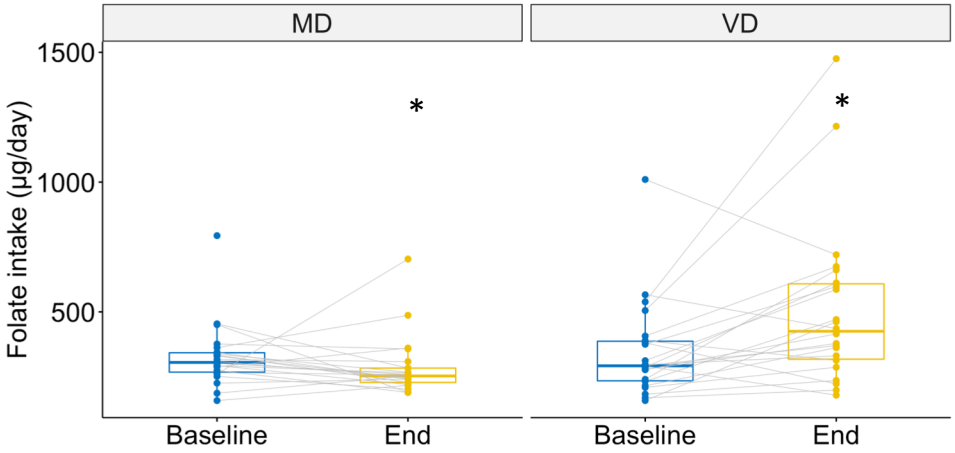
Table 1. Demographic data of participants in vegan diet group and in meat-rich group (SD = Standard deviation, *p*-value from *t*-test).

	Vegan ± SD (n = 26)	**Meat-Rich ± SD (*n* = 27)**	***p*-Value**
Age (years)	33.2 ± 11.2	29.9 ± 9.5	0.407
Baseline: Body mass index (kg/m^2)	22.9 ± 2.2	23.3 ± 2.6	0.444
End of study: Body mass index (kg/m^2)	22.7 ± 2.0	23.4 ± 2.6	0.240
Gender (male/female, %)	31/69	44/56	0.309

Vitamin B_{12} Status Upon Short-Term Intervention with a Vegan Diet-A Randomized Controlled Trial in Healthy Participants. **Lederer AK*, Hannibal L***, Hettich M, Behringer S, Spiekerkoetter U, Steinborn C, Gründemann C, Zimmermann-Klemd AM, Müller A, Simmet T, Schmiech M, Maul-Pavicic A, Samstag Y, Huber R. *Nutrients*. 2019 Nov 18;11(11):2815.

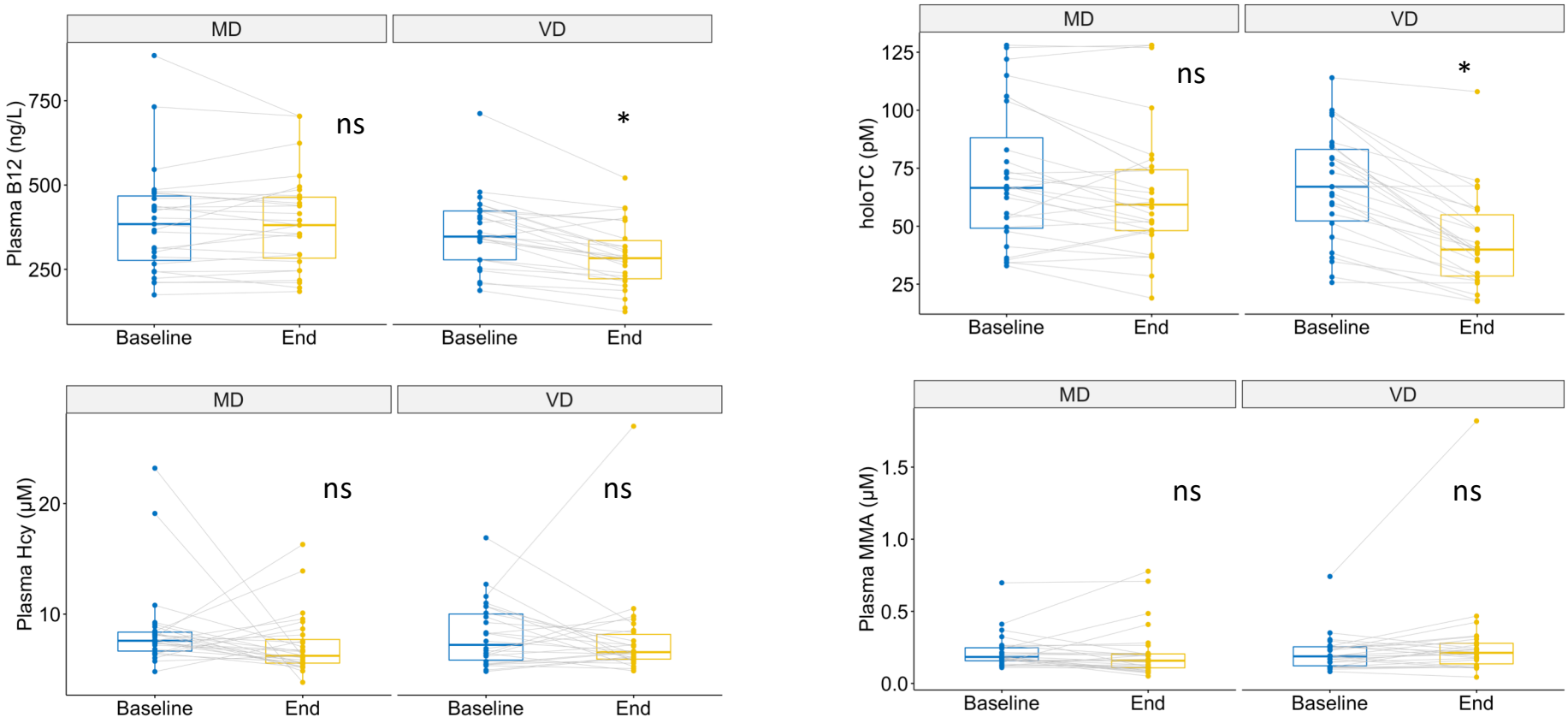
B_{12} and Folate Intakes after MD and VD Transitions





Vitamin B_{12} Status Upon Short-Term Intervention with a Vegan Diet-A Randomized Controlled Trial in Healthy Participants. **Lederer AK*, Hannibal L***, et al. *Nutrients*. 2019 Nov 18;11(11):2815. doi: 10.3390/nu11112815.

Plasma B_{12} Biomarkers after MD and VD Transitions



Vitamin B_{12} Status Upon Short-Term Intervention with a Vegan Diet-A Randomized Controlled Trial in Healthy Participants. **Lederer AK*, Hannibal L***, et al. *Nutrients*. 2019 Nov 18;11(11):2815. doi: 10.3390/nu11112815.

Conclusions: B_{12} Biomarkers Upon Dietary Transition

- A reduction in the intake of B_{12} led to 18% lower plasma B_{12} and 30% lower holo-TC concentrations in healthy subjects, in 4-weeks
- holoTC early marker of changes in B_{12} intake: possibly a fast-responding biomarker to monitor B_{12} status in vegetarians and vegans
- Hcy and MMA: did not change during the 4-week intervention

Vitamin B_{12} Status Upon Short-Term Intervention with a Vegan Diet-A Randomized Controlled Trial in Healthy Participants. **Lederer AK*, Hannibal L***, et al. *Nutrients*. 2019 Nov 18;11(11):2815. doi: 10.3390/nu11112815.

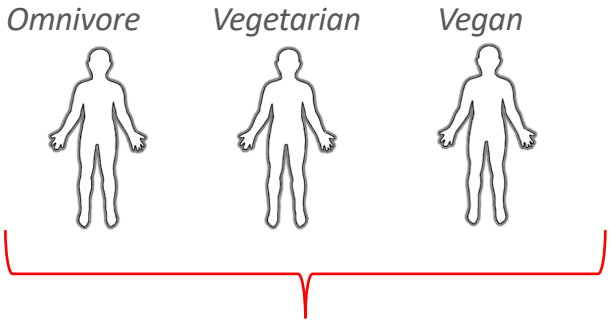
B_{12} Biomarkers in Long-Term Plant-Based Dieters

Cohort and Diet Characteristics

- Young, physically active healthy adults from Southwestern Germany
- No dietary supervision
- On diet for > 2 years
- Age- and sex-matched groups
- Diet record, supplement use record, and biospecimen sampling

Prof. Roman Huber

Dr. Max Storz



- Plasma
- Urine
- Cells
- Feces

Elevate Series

ANNALS OF MEDICINE
2023, VOL. 55, NO. 2, 2269969
https://doi.org/10.1080/07853890.2023.2269969

RESEARCH ARTICLE

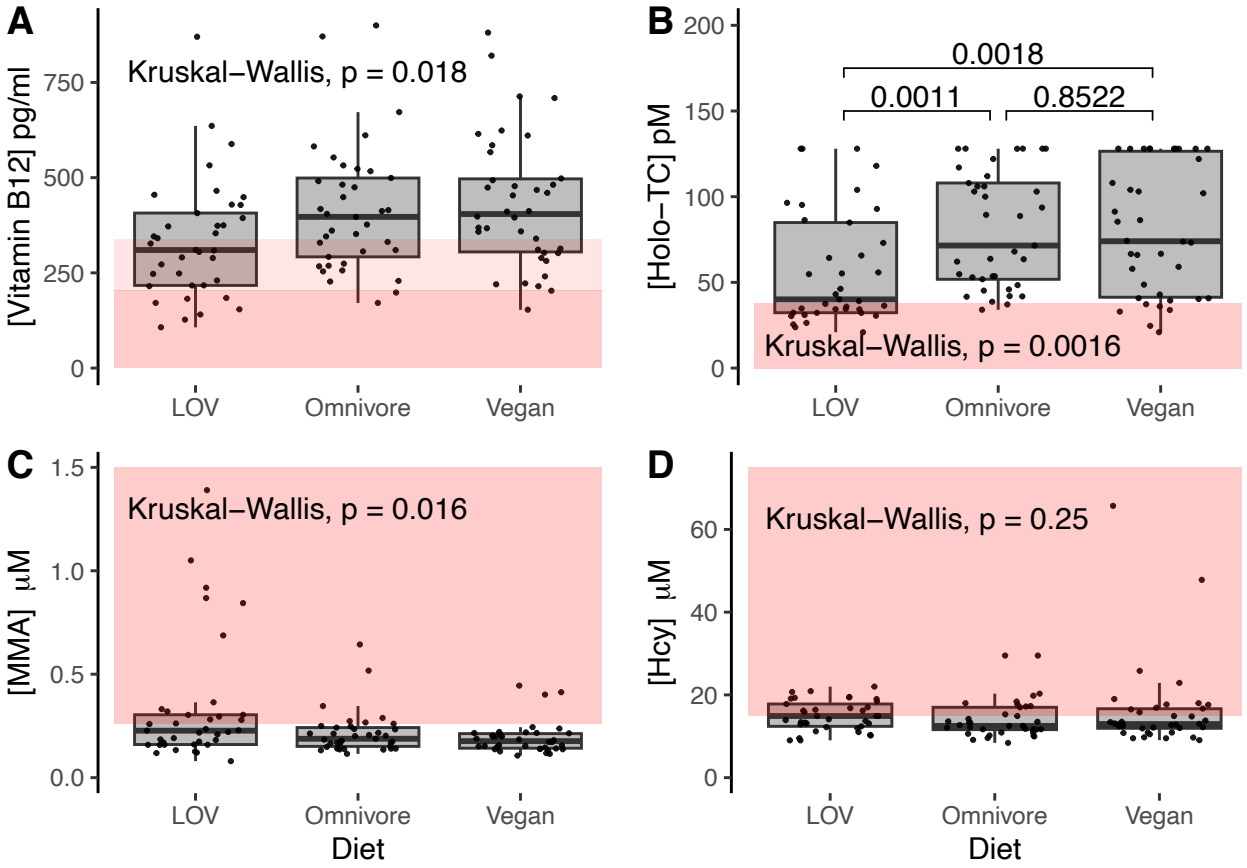
OPEN ACCESS Check for updates

A cross-sectional study of nutritional status in healthy, young, physically-active German omnivores, vegetarians and vegans reveals adequate vitamin B_{12} status in supplemented vegans

Maximilian Andreas Storz[a], Alexander Müller[a], Lisa Niederreiter[a], Amy M. Zimmermann-Klemd[a,b], Martin Suarez-Alvarez[c], Stefanie Kowarschik[a], Monique Strittmatter[a], Evelyn Schlachter[a], Cristian Pasluosta[d], Roman Huber[a] and Luciana Hannibal[c]

Storz, … Hannibal, L. Annals of Medicine 2023, 55, 2, 2269969

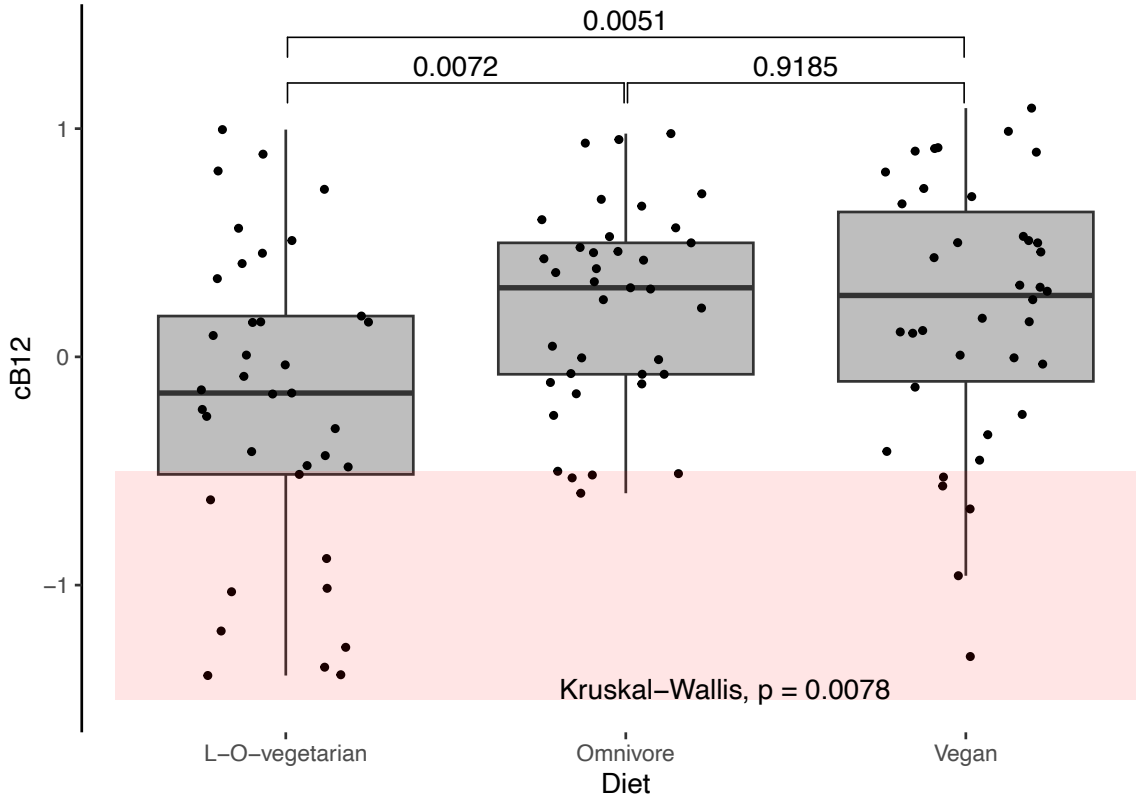
B_{12} Biomarkers in Long-Term Plant-Based Dieters



- Similar B_{12} biomarker profile in omnivores and vegans
- Lowest plasma B_{12} and holo-TC observed in ovolactovegetarians

Storz, … Hannibal, L. Annals of Medicine 2023, 55, 2, 2269969

B_{12} Biomarkers in Long-Term Plant-Based Dieters: cB_{12}



- Similar cB_{12} index in omnivores and vegans
- Lowest cB_{12} index in ovolactovegetarians, significantly different to that of omnivores and vegans

Storz, … Hannibal, L. Annals of Medicine 2023, 55, 2, 2269969

Supplement Use in Long-Term Plant-Based Dieters

	Omnivores (n=40)	Lacto-Ovo-Vegetarians (n=37)	Vegans (n=38)	p-value
Supplement intake				0.561 [a]
Yes	n = 31 (77.5%)	n = 30 (81.08%)	n = 33 (86.84%)	
No	n = 9 (22.5%)	n = 7 (18.92%)	n = 5 (13.16%)	
Multivitamin supplement intake				0.045 [a]
Yes	n = 9 (22.5%)	n = 10 (27.03%)	n = 18 (47.37%)	
No	n = 31 (77.5%)	n = 27 (72.97%)	n = 20 (52.63%)	
Vitamin B_{12} supplement intake				< 0.001 [a]
Yes	n = 11 (27.5%)	n = 19 (51.35%)	n = 34 (89.47%)	
No	n = 29 (72.5%)	n = 18 (48.65%)	n = 4 (10.53%)	
Dosage (µg)	25 (335.5)	400 (977.5)	250 (980)	0.136 [b]
Frequency (day/year)	180 (287)	40 (144)	365 (209)	0.001 [b]

Legend: [a] = based on Stata's Chi-Square Test of independence; [b] = based on Kruskal-Wallis H test

Storz, … Hannibal, L. Annals of Medicine 2023, 55, 2, 2269969

B_{12} Status and Metabolism in Long-Term Plant-Based Diets

- Plant-based diets, in particular the vegan diet, exhibited the most favorable patterns of lipid metabolism and glycemic control, but the lowest food intake of B_{12}.

- Analysis of B_{12} status (including 4c B_{12}) revealed adequacy in omnivores and vegans, and a poorer B_{12} status amongst lacto-ovo-vegetarians.

- Supplementation with B_{12} (median 250 µg B_{12}/day, over 1 year) in healthy physically-active vegans secured an adequate B_{12} status that was comparable to that of healthy omnivores.

Dietary Sources of B_{12}

- Vitamin B_{12} is exclusively synthesized by a few groups of bacteria and archaea
- Animals, including humans, are unable to make their own B_{12}
- Animals obtain B_{12} by environmental exposure, for example, to soil bacteria
- Omnivore humans obtain B_{12} by eating animals who have been previously in contact with soil or other environmental sources of B_{12}

Omnivores

- Meat, dairy, eggs
- Algae (Chlorella)

Vegetarians

- Dairy, Eggs
- Algae (Chlorella)

Vegans

- Algae (Chlorella)

Dairy and eggs provide insufficient quantities of B_{12}
Algae preparations contain variable amounts of B_{12}

Adequate Intake of B_{12}

Table 1. Recommended intake of vitamin B12 according to the Nordic Nutrition Recommendations 2012

Population*	Recommended intake (µg/d)
Infants, 6–11 months	0.5
Infants/children, 12–23 months	0.6
Children, 2–5 years	0.8
Children, 6–9 years	1.3
Adults and children from 10 years	2.0
During lactation	2.6

*No recommended intake for children <6 months.

Source: Food & Nutrition Research 2023, 67:8626

Table 1: Recommended Dietary Allowances (RDAs) for Vitamin B12 [1]

Age	Male	Female	Pregnancy	Lactation
Birth to 6 months*	0.4 mcg	0.4 mcg		
7–12 months*	0.5 mcg	0.5 mcg		
1–3 years	0.9 mcg	0.9 mcg		
4–8 years	1.2 mcg	1.2 mcg		
9–13 years	1.8 mcg	1.8 mcg		
14–18 years	2.4 mcg	2.4 mcg	2.6 mcg	2.8 mcg
19+ years	2.4 mcg	2.4 mcg	2.6 mcg	2.8 mcg

* Adequate Intake (AI)

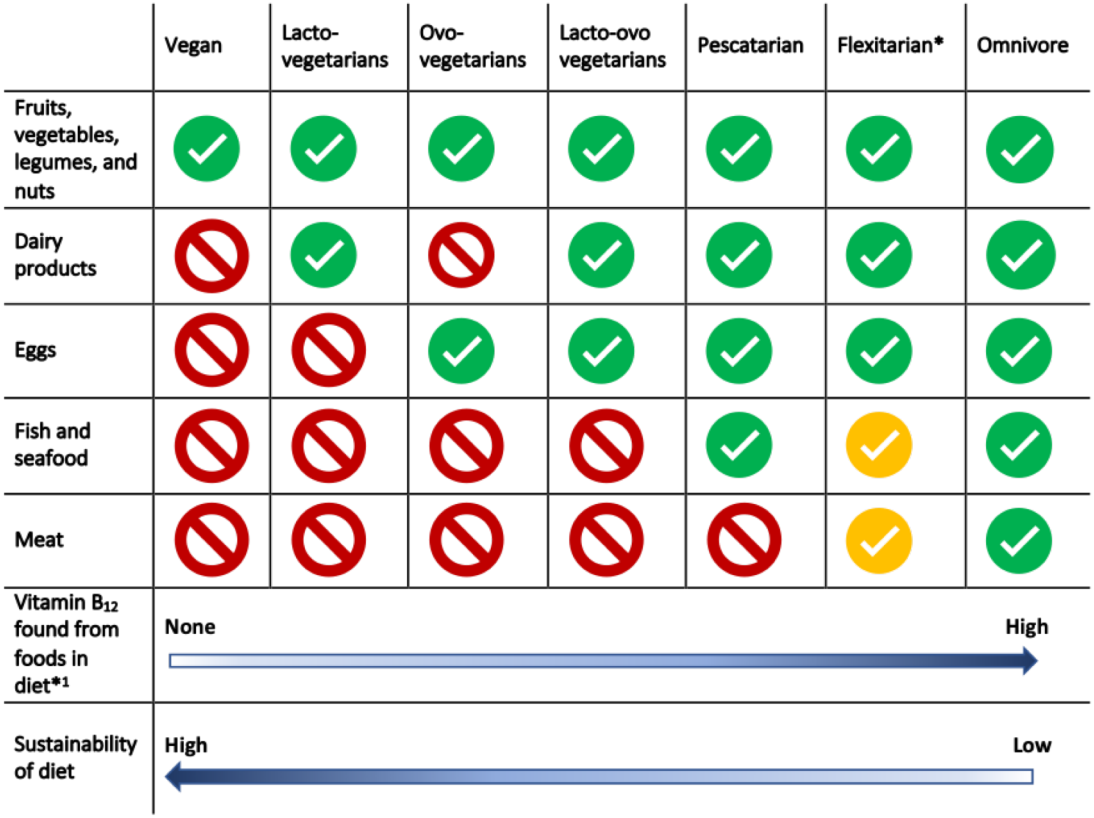
Source: National Institutes of Health (NIH), USA

- European Food Safety Authority (EFSA):
  - Between 1.5 and 4.0 µg/day, depending on age
  - Between 4.5 and 5.0 µg/day for pregnant and lactating women

- Based on data from 13 dietary surveys in nine European Union countries:
  - Average cobalamin intake ranges across countries:
    - Infant < 1 year: 0.8–2.1 µg/day
    - Children 1 to < 3 years: 2.2–4.0 µg/day
    - Children 3 <10 years: 2.6–5.7 µg/day
    - Children 10 <18 years: 3.3–6.6 µg/day
    - Adults: 4.2–8.6 µg/day

Source: EFSA Journal 2015;13(7):4150

Plant-Based Diets and Risk of B_{12} Deficiency



- Dietary vitamin B_{12} intake decreases with a greater plant-based diet:

Estimated daily B_{12} intakes:

7.2 µg in meat-eaters
0.4 µg in vegans

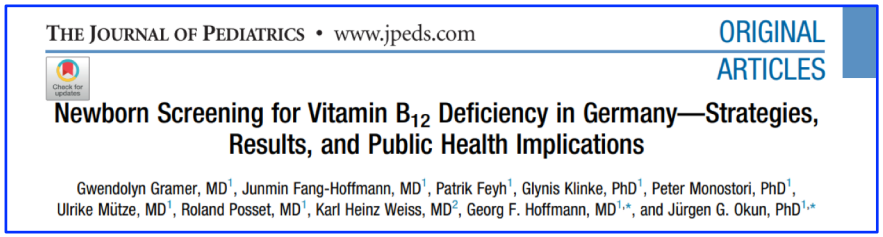
Davey GK, Spencer EA, Appleby PN et al (2003) EPIC-Oxford: Lifestyle characteristics and nutrient intakes in a cohort of 33 883 meat-eaters and 31 546 non meat-eaters in the UK. Public Health Nutr 6:259–268

The Importance of Vitamin B_{12} for Individuals Choosing Plant-Based Diets. Ali Niklewicz, (…) ,Luciana Hannibal*, Martin Warren*, P Julian Owen*, on behalf of CluB-12. *Eur J. Nutr.* 2022

Plant-Based Diets and Risk of B_{12} Deficiency

Plant-Based Diet Studies in Children

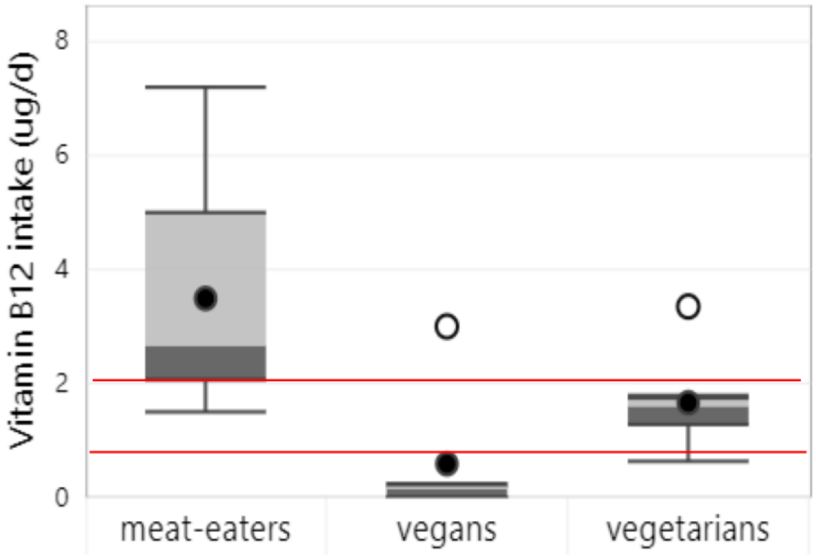
- Population of 176,702 children screened over 27 months
- 33 Children detected by NBS in whom maternal vitamin B_{12} deficiency was confirmed
- Hcy was the most sensitive marker of B_{12} deficiency, however, MMA was necessary to capture all 33 children
- 89% of Mothers adhere to a balanced omnivore diet
- 84% of Children were treated with oral vitamin B_{12} and remained without clinical symptoms
- With an incidence of 1:5355 newborns, nutritional vitamin B_{12} deficiency is more frequent than inborn errors of metabolism included in NBS panels.
- Treatment of vitamin B_{12} deficiency is easy and beneficial also for undiagnosed affected mothers



J Pediatr. 2020 Jan;216:165-172.e4. doi: 10.1016/j.jpeds.2019.07.052. Epub 2019 Oct 8.

Plant-Based Diets and Risk of B_{12} Deficiency

Plant-Dased Diet Studies in Children



Systematic review: 13 Studies reported vitamin B_{12} intake

Studies on Vitamin B_{12} Intake:

- Vegans do not the meet the estimated average requirement (EAR) of vitamin B12 according to age and sex:
  - -Meat-eaters: 3.49 µg/d
  - -Vegetarians: 1.66 µg/d
  - -Vegans: 0.59 µg/d

Studies on Vitamin B_{12} Intake + Supplements:

- Highest average vitamin B12 intake among vegans:
  - -Meat-eaters: 28.8 µg/d
  - -Vegetarians: 5.2 µg/d
  - -Vegans: 116.6 µg/d

Nutrient Intake and Status in Children and Adolescents Consuming Plant-Based Diets Compared to Meat-Eaters: A Systematic Review. Neufingerl, N and Eilander, A. Nutrients 2023, 15(20), 4341; https://doi.org/10.3390/nu15204341

Plant-Based Diets and Risk of B_{12} Deficiency

Plant-Based Diet Studies in Children

Table 2. Overview of nutrients at risk of inadequacy and nutrients of favorably high intake across dietary patterns.

Dietary Pattern	Nutrients at Risk of Inadequacy *	Nutrients of Favorably High Intake
Vegans	Vitamin B12, vitamin D Calcium, iron, zinc	PUFA, fiber Vitamin C, vitamin E, folate
Vegetarians	SAFA, PUFA **, fiber Vitamin B12, vitamin D Calcium, iron, zinc	Vitamin E, folate
Meat eaters	SAFA, PUFA, fiber Vitamin D, vitamin E, folate Calcium	Vitamin B12 Zinc

* All diet groups may be at risk of inadequate intake of iodine and EPA and DHA, but data are too limited to draw firm conclusions. ** Whereas mean PUFA intake in vegetarian children was in line with the recommendations, the mean intake inadequate in three out of seven studies.

Nutrient Intake and Status in Children and Adolescents Consuming Plant-Based Diets Compared to Meat-Eaters: A Systematic Review. Neufingerl, N and Eilander, A. Nutrients 2023, 15(20), 4341; https://doi.org/10.3390/nu15204341

Plant-Based Diets and Risk of B_{12} Deficiency

Plant-Based Diet Studies in Adults

Eur J Nutr (2017) 56:283–293
DOI 10.1007/s00394-015-1079-7

CrossMark

ORIGINAL CONTRIBUTION

Micronutrient status and intake in omnivores, vegetarians and vegans in Switzerland

R. Schüpbach[1] · R. Wegmüller[1,2] · C. Berguerand[3] · M. Bui[3] · I. Herter-Aeberli[1]

- Omnivores (n =100), vegetarians (n = 53) and vegans (n=53), aged 18-50 years old.
- All three dietary groups exhibited insufficient intake of several micronutrients
- "Vegans reported low intakes of ... vitamin B12. Despite negligible dietary vitamin B12 intake in the vegan group, deficiency of this particular vitamin was low in all groups thanks to widespread use of supplements"
- Conclusions: Despite substantial differences in intake and deficiency between groups, our results indicate that by consuming a well-balanced diet including supplements or fortified products, all three types of diet can potentially fulfill requirements for vitamin and mineral consumption.

Eur J Nutr. 2017 Feb;56(1):283-293. doi: 10.1007/s00394-015-1079-7. Epub 2015 Oct 26.

Plant-Based Diets and Risk of B_{12} Deficiency

Plant-Based Diet Studies in Adults

food & nutrition research

REVIEW ARTICLE

Intake of vitamin B12 in relation to vitamin B12 status in groups susceptible to deficiency: a systematic review

Linnea Bärebring[1], Christel Lamberg-Allardt[2], Birna Thorisdottir[3], Alfons Ramel[4], Fredrik Söderlund[5], Erik Kristoffer Arnesen[6], Bright I. Nwaru[7], Jutta Dierkes[8,9] and Agneta Åkesson[5]

Included populations were:

- Children (0–18 years), young adults (18–35 years), pregnant or lactating women, older adults (≥65 years) and vegans or vegetarians.
- „In conclusion, evidence is insufficient to assess if habitual B_{12} intake or an intake in line with the current Nordic RI is sufficient to maintain adequate status for all included populations. Population-based cohort studies and low-to moderate dose interventions that address this question are highly warranted.“

Food Nutr Res. 2023 Jun 30:67. doi: 10.29219/fnr.v67.8626. eCollection 2023.

National and International Recommendations

- **German Federal Institute for Risk Assessment (BfR)**

Recommendation for food supplements, and the fortification of solid foods and beverages with vitamin B_{12}:

"The German Federal Institute for Risk Assessment (BfR) recommends a maximum level of 25 micrograms (µg) of vitamin B_{12} per daily recommended dose of a food supplement (Table 1). For fortification of conventional foods, assuming a saturated market of fortified foods (30 % of daily energy intake comes from of fortified foods), a maximum level of 6 µg/100 grams (g) is recommended for solid foods and of 1.6 µg/100 millilitres (ml) for beverages (Table 1)"

Table 1: Proposed maximum levels

Food category	Maximum levels
Food supplements (per daily recommended dose of an individual product)	25 µg
Fortified solid foods (per 100 g)	6 µg
Fortified beverages (per 100 ml)	1.6 µg

Source: https://www.bfr.bund.de/de/start.html
Last published update: 18.10.2023

National and International Recommendations

- **Position of CluB-12**

European Journal of Nutrition (2023) 62:1551–1559
https://doi.org/10.1007/s00394-022-03025-4

COMMENT

Check for updates

The importance of vitamin B_{12} for individuals choosing plant-based diets

Ali Niklewicz[1] · A. David Smith[2] · Alison Smith[3] · Andre Holzer[3] · Andrew Klein[4] · Andrew McCaddon[5] · Anne M. Molloy[6] · Bruce H. R. Wolffenbuttel[7] · Ebba Nexo[8] · Helene McNulty[9] · Helga Refsum[10] · Jean-Louis Gueant[11] · Marie-Joe Dib[12] · Mary Ward[9] · Michelle Murphy[13] · Ralph Green[14] · Kourosh R. Ahmadi[1] · Luciana Hannibal[15] · Martin J. Warren[16] · P. Julian Owen[17] · on behalf of CluB-12

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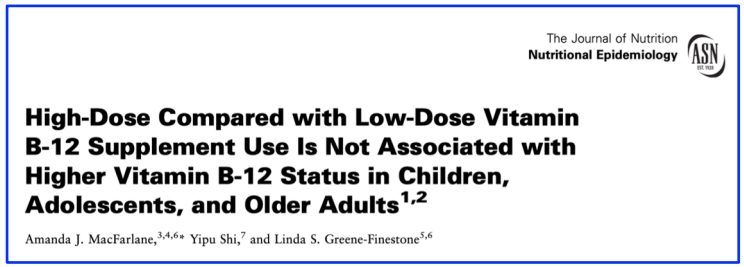
Key Recommendations to prevent vitamin B12 deficits for individuals choosing a plant-based diet:
A daily vitamin B12 supplement taken with other foods for optimal absorption.
Check food packaging labels for vitamin B12 fortified products when opting for plant-based animal alternative diets.
Be aware that vitamin B12 deficiency can occur without developing anaemia and often neurological symptoms are more commonly observed (fatigue, memory impairment, cognitive changes, and depression).
Have your blood vitamin B12 levels monitored, particularly if no B12-containing supplements have been taken in the last 3-6 months.
Seek expert advice to support planning a plant-based diet or if you are: [a] transitioning to a vegan diet, [b] planning to become pregnant, or [c] older than 60 years of age.

„ A recommendation of 4–20 µg/day is more appropriate to prevent B_{12} deficiency across the life-course.“

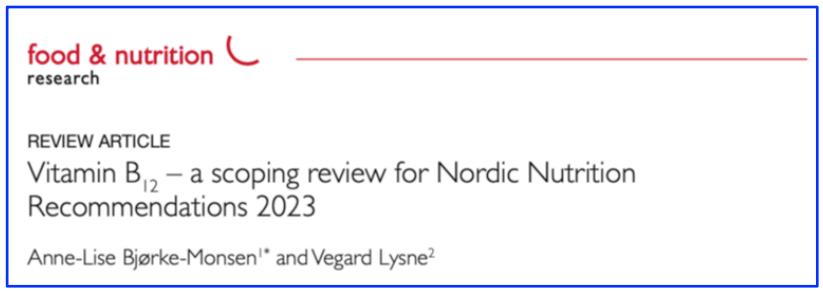
„Considering the above caution, we support well-planned plant-based diets enhanced with vitamin B_{12}, which have the ability to positively impact both human and planetary health.“

National and International Recommendations

- **Recommedations for children and adolescents from studies in Canada and Norway**



„Daily consumption of supplemental vitamin B_{12} up to 10 µg by children > 6 years old and adolescents and up to 10–25 µg by older adults is associated with higher vitamin B_{12} status.“



„A vitamin B_{12} intake from 3 to 4.9 µg/day may be adequate for younger children, whereas children >10 years may need a vitamin B_{12} intake in the range of 5.3–10 µg/day.“

Dietary Supplements Available in the Market

- B_{12} Supplements with tablets containing 50, 250, 350, 425 and 1000 µg vitamin B_{12}
- Multi-vitamin supplements with 4 and 10 µg Vitamin B_{12}
- Pre-conception, for pregnancy, and for lactation multi-vitamin supplements: 4-10 µg vitamin B_{12}

Open Questions for Further Research

- What dose and chemical form of B_{12} should be recommended to individuals on plant-based diets?
- Should a distinction be made in formulations for vegetarians and vegans?
- What set of B_{12} biomarkers should be monitored to identify subclinical B_{12} deficiencies that merit treatment initiation in plant-based dieters?
- Should clinically asymptomatic individuals in plant-based diets having elevated blood biomarkers be selected for treatment initiatiation with B_{12}?

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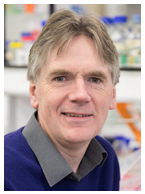

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Patient and Scientific Organisations

EHOD
European Network and Registry for Homocystinurias and Methylation Defects

CluB-12

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wörwag PHARMA

ultragenyx pharmaceutical

DFG Deutsche Forschungsgemeinschaft

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