ARTICLE

Infrastructure

Food Insecurity Is Associated with Vitamin B12 Deficiency: The All of Us Database

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Background: **Vitamin B12 is an essential micronutrient obtained from dietary sources, but there is a paucity of information about how food security contributes to risk of vitamin B12 deficiency.**

Methods: **I used multivariable logistic regression controlling for age, sex, and metformin exposure using the multicenter, United States National Institutes of Health All of Us precision medicine database. I included all adult participants 18 to 88 years old in the All of Us database who answered the social determinants of health survey and had a vitamin B12 measurement within 1 year of the survey.**

Results: **8,989 participants with median age 65.9 years (Q1 53.0, Q3 73.7), who were predominantly female (63.2%), White-identifying (87.4%), and not Hispanic or Latino (93.4%) were included. 9.8% of participants reported experience of food insecurity, and 12.9% reported worry about food insecurity. 15.1% had metformin exposures. Vitamin B12 levels less than 300 pg/mL were associated with experiencing food insecurity (multivariable OR [mOR] 1.24, 95% CI 1.01-1.51, *P* = .037). Age (mOR 0.92 per decade), and male biological sex (mOR 1.16) were also both associated with vitamin B12 deficiency, but I did not detect an effect due to metformin exposure (mOR 1.05, 95% CI 0.88-1.25, *P* = .59).**

Conclusions: **Vitamin B12 deficiency is associated with food insecurity in United States adults enrolled in the NIH All of Us database. Future analyses designed to infer causality are warranted. (J Am Board Fam Med 2024;37:S156–S163.)**

Keywords: **ADFM/NAPCRG Research Summitt 2023, Food Insecurity, Logistic Regression, Multicenter Studies, Precision Medicine, Retrospective Studies, Social Determinants of Health, Vitamin B12, Vitamin B12 Deficiency**

Introduction

Vitamin B12 (cobalamin) is an essential, water-soluble micronutrient required for DNA synthesis, amino acid metabolism, and central nervous system functioning.[1–3] Vitamin B12 comes only from animal dietary sources and is absorbed by a multi-step molecular process.[1] Causes of vitamin B12 deficiency are manifold, but can be broadly classified into several categories: (1) inadequate dietary intake; (2) gastric or pancreatic disorders that either (a) impair intrinsic factor secretion, which is required for vitamin B12 uptake via receptor-mediated endocytosis in distal ileal enterocytes, or (b) prevent release of vitamin B12 from food and/or digestive carrier proteins; (3) intestinal disorders that impair the terminal ileum (eg, ileal resection) or microbiome; and (4) various other inherited (eg, Imerslund-Grasbeck syndrome[3]) or acquired (eg, HIV infection) disorders.[3]

Clinical signs and symptoms of B12 deficiency can be nonspecific, for example including fatigue, dizziness, paresthesias, impaired balance, irritability, mood disorders, and concentration problems.[1–3] Vitamin B12 deficiency has important implications for primary care. Complications of vitamin B12 deficiency include megaloblastic or macrocytic anemia; spinal cord degeneration; cognitive impairment and Alzheimer disease; depression;

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loss of hearing, vision, taste, or smell; infertility; and autonomic nervous system deficits, including postural hypotension, incontinence, and impotence.[1–3] The clinical manifestations of Vitamin B12 can therefore be varied and lie along a spectrum from relatively minor to quite severe symptoms, as discussed elsewhere.[2] Neurological complications of vitamin B12 deficiency can be irreversible and short-term empiric vitamin B12 supplementation, while awaiting definitive testing for deficiency, is not known to be harmful.[3] A high index of clinical suspicion thus seems warranted for vitamin B12 deficiency in primary care in at-risk individuals. To determine which individuals are at-risk epidemiologic analyses are needed to validate risk factors. Prior work has demonstrated that vitamin B12 is associated with age,[3–5] biological sex,[6–15] and metformin use.[16–19] Metformin is a common prescribed oral biguanide used to treat type 2 diabetes and may induce Vitamin B12 malabsorption by decreasing Vitamin B12-intrinisic factor complex formation, which is required for Vitamin B12 absorption in the terminal ileum.[18]

Family physicians have long recognized that health derives not just from physiologic factors, but also from environmental and social factors (sometimes called the "social determinants of health"). One determinant of health is food security, which refers to whether individuals have access to adequate, safe, nutritious, and affordable food.[20] Food insecurity is associated with malnutrition.[20] I considered that, because vitamin B12 is taken up through the diet, that vitamin B12 deficiency might be associated with food insecurity in the United States. Surprisingly, the association between serum vitamin B12 concentration and food security seems to have been inadequately explored in the existing literature. The only study I found linking vitamin B12 serum concentrations to food insecurity is a 2015 analysis of children and adult women living in Colombia wherein food insecurity was associated with a lower mean serum vitamin B12 concentration.[13]

To explore the connection between vitamin B12 deficiency and food insecurity, I performed a retrospective analysis of participants enrolled in the All of Us database. All of Us is a National Institutes of Health (NIH)-operated biorepository with the goal of accelerating precision medicine.[21] The database is particularly focused on ensuring that the participant base reflects the wide diversity of the United States population.[22] As of 2023, the database includes 4,00,000 participants nationwide spanning 25,000 distinct medication conditions, 29,000 types of drug exposures, and 16,000 laboratory measurements. Survey responses for social determinants of health are available for 117,000 participants. The All of Us database has been underutilized to accelerate primary care research, although discoveries within primary care have been slowly forthcoming.[23–26]

Methods

Datasets and Population

I used 2 datasets for the analysis. The primary dataset included all adult participants 18 to 88 years old in the All of Us database[21] (version 7) who (1) answered the social determinants of health survey, and (2) had a vitamin B12 serum concentration determined within 1 year of the survey. I used this dataset to explore the connection between vitamin B12 and food insecurity among All of Us participants. In addition, I considered an expanded dataset including All of Us[21] participants comprising all adult participants in the All of Us database (version 7) that had at least 1 vitamin B12 serum level recorded, irrespective of whether they answered the social determinants of health survey. The expanded dataset was used to quantify the prevalence of vitamin B12 deficiency.

Measures: Food Insecurity

Food insecurity was recorded in the All of Us survey using 2 questions: (1) experience of food insecurity occurring, or (2) worry that food insecurity would occur. For experience of food insecurity, the survey prompted "Within the past 12 months, the food I bought just did not last and I did not have money to get more" and gave "Never true," "Sometimes true," or "Often true" as response options. For worry about food insecurity, the survey prompted "Within the past 12 months, I worried whether our food would run out before I got money to buy more," and gave the same response options. I inferred experience of food insecurity or worry about food insecurity, respectively, if either question was answered as "Sometimes true" or "Often true." Respondents could also skip the survey question, which was interpreted instead as missing data. Surveys were administered to All of Us participants 1 time, so the date of survey participation was taken as the "index" date for each participant.

Measures: Vitamin B12 Serum Level

In the primary All of Us dataset, vitamin B12 serum levels may have been recorded multiple times for each participant. I extracted 1 vitamin B12 level for each participant, choosing the 1 that was closest to the date of their survey completion. In the expanded All of Us dataset, I again retained only 1 vitamin B12 measurement per individual, keeping the first measurement per person. Vitamin B12 is sometimes measured in pg/mL or pmol/L. Of the 1,64,461 measurements with explicit unit annotations 1,64,424 (99.98%) were in pg/mL. For the 45,296 records without explicit unit annotations, I assumed the correct units were pg/mL because that assumption was correct for virtually all records with explicit unit annotations. The typical upper-limit of normal reference interval for Vitamin B12 is approximately 1500 pg/mL.[27] From both datasets, I excluded vitamin B12 levels that were obviously erroneous (ie, more than 50-fold higher than the upper limit of normal; >75000 pg/mL).

Measures: Age and Metformin Exposure

Age was defined as age at time of vitamin B12 serum measurement. Metformin exposure was defined as any recorded prescription, administration, or other documented interaction with metformin within 12 months of vitamin B12 measurement.

Statistical Analysis

Data were prepared for statistical analysis using Python in the All of Us Researcher Workbench. All other statistical analyses were conducted using R version 4.2.2 in the All of Us Researcher Workbench. Participants were characterized using descriptive statistics. The association between food insecurity and vitamin B12 deficiency was evaluated using bivariable and multivariable logistic regression. The primary hypothesis is that experiencing food insecurity is associated with vitamin B12 deficiency. Multivariable analyses controlled for the influence of age, biological sex at birth, and metformin exposure.

There is no well-agreed level on the serum concentration that constitutes vitamin B12 deficiency, with cutoffs in the literature ranging from 135 pg/mL to 474 pg/mL.[28] I thus conducted sensitivity analyses using various cutoffs for deficiency: 300 pg/mL (primary outcome) and: 200, 300, 400, and 500 pg/mL (secondary outcomes). 300 pg/mL was chosen as the primary outcome as a value near the middle of this range, following the definition of marginal vitamin B12 level in Green *et al.*'s review[3] and in other analyses.[29–31] A lower threshold of 200 pg/mL has likely insufficient sensitivity for detection of all clinical significant deficiencies; likewise, a higher threshold, 350 pg/mL, achieves about 90% sensitivity for biochemical/clinical deficiency, but compromises specificity.[2] Thus, 300 pg/mL is a reasonable middle ground for the primary outcome.

Alternative definitions for food insecurity were also explored, including (1) experience of food insecurity (main hypothesis), (2) worry about food insecurity, and (3) a composite variable of either experience or worry about food insecurity. In summary, my overall main multivariable model was:

$$(\text{Serum vitamin B12} < 300 \text{ pg/mL}) \sim \text{Experience of food insecurity} + \text{Age} + \text{Sex} + \text{Metformin exposure}$$

Human Subjects Protection

This subject was determined by the University of [Redacted] Institutional Review Board to constitute Not Human Subjects research.

Results

Participants

Characteristics of the 8,989 participants included in the primary All of Us dataset are shown in Table 1. Briefly, the median age was 65.9 years (Q1 53.0, Q3 73.7) but participants ranged from 18 to 88 years. Participants were predominantly female (63.2%), White-identifying (87.4%), and not Hispanic or Latino (93.4%). 9.8% of participants reported experience of food insecurity, and 12.9% reported worry about food insecurity. 15.1% had metformin exposures. The expanded All of Us dataset included 68,883 participants.

Prevalence of Vitamin B12 Deficiency in the All of Us Expanded Dataset

The prevalence of vitamin B12 deficiency in the All of Us dataset depends on the deficiency cutoff specified. In the expanded All of Us dataset, the prevalence of vitamin B12 deficiency was 3.6% (2468/68891), 16.3% (11207/68891), 35.2% (24229/68891), and 53.0% (36522/68891) for the 200, 300, 400, and 500-pg/mL cutoffs, respectively.

Table 1. Characteristics of Participants

Characteristic	No. (%)
All participants	8,989 (100)
Age, median (IQR, range)	65.9 (53.0 to 73.7, 18.9 to 88.2)
Sex	
Male	3,243 (36.8)
Female	5,558 (63.2)
Missing or other	188
Race	
Asian	155 (1.9)
Black or African American	684 (8.4)
White	7,137 (87.4)
Another single population	56 (0.7)
More than one population	130 (1.6)
Declined, None, Skipped, or Not Indicated	827
Ethnicity	
Hispanic or Latino	567 (6.6)
Not Hispanic or Latino	8,040 (93.4)
Declined, None, Skipped	382
Metformin use	
Exposed	1,354 (15.1)
Not exposed	7,635 (84.9)
Food security, experienced	
Never true	8,100 (90.1)
Sometimes true	713 (7.9)
Often true	176 (2.0)
Food security, worried about	
Never true	7,827 (87.1)
Sometimes true	927 (10.3)
Often true	235 (2.6)
Food insecurity, experience and worry joint distribution	
Neither experienced or nor worried	7,728 (86.0)
Not experienced, but worried about	372 (4.1)
Not worried about, but experienced	99 (1.1)
Both worried and experienced	790 (8.8)

Prevalence of Food Insecurity in the All of Us Primary Dataset

Among individuals included in the primary dataset, most individuals neither experienced nor worried about food insecurity (86.0% n = 7,728). Some participants 4.1% (n = 372) reported only worry about food insecurity, but not experience. A few participants 1.1% (n = 99) reported only experience of food insecurity, without worry about it. Finally, 8.8% (n = 790) of participants reported both experience and worry, and 14.0% (n = 1261) reported a composite of either worry and/or experience.

Vitamin B12 Is Associated with Experience of Food Insecurity

Bivariable and multivariable logistic regression analysis revealed that the experience of food insecurity is associated with vitamin B12 levels less than 300 pg/mL (Table 2; bivariable OR [bOR] 1.31, 95% CI 1.07-1.59, $P = .007$; multivariable OR [mOR] 1.24, 95% CI 1.01-1.51, $P = .037$). Age (mOR 0.92 per decade), and male biological sex (mOR 1.16) were also both associated with vitamin B12 deficiency. Metformin exposure was not significantly associated with vitamin B12 deficiency in my analysis (mOR 1.05, 95% CI 0.88-1.25, $P = .59$). Multicollinearity was absent from the regression model (maximum variance inflation factor 1.11).

Sensitivity Analyses

Sensitivity analyses exploring alternative thresholds for vitamin B12 deficiency showed similar results at the 400 pg/mL and 500 pg/mL levels. For a threshold of 200 pg/mL only age was significantly associated with this more severe level of vitamin B12 deficiency (mOR 0.87 per decade, 95% CI 0.79-0.96). I did not find an association with vitamin B12 deficiency and only food security worry, or with a composite measure of food security experience and/or worry. The pattern of associations was largely unchanged when age was modeled as a 4-level quantized variable.

Discussion

I conducted a national, multicenter, retrospective secondary data analysis of participants in the NIH

Table 2. Regression Model for Vitamin B12 Deficiency and Experience of Food Insecurity

Variable	Bivariable or (95% CI)	Multivariable or (95% CI)
Food insecurity, experienced	1.31 (1.07-1.59; $P = .007$**)	1.24 (1.01-1.51; $P = .037$*)
Age, decades	0.93 (0.89-0.97; $P < .001$***)	0.92 (0.88-0.96; $P < .001$***)
Metformin exposed	1.06 (0.89-1.26; $P = .51$)	1.05 (0.88-1.25; $P = .59$)
Male sex	1.08 (0.95-1.23; $P = .24$)	1.16 (1.01-1.34; $P = .030$*)

All of Us database. I found that food insecurity is associated with an increased risk of vitamin B12 deficiency (bivariable OR 1.31, 95% CI 1.07-1.59, $P = .007$). This association persisted after controlling for age, biological sex, and metformin use (multivariable OR 1.24, 95% CI 1.01-1.51, $P = .037$).

The association between food insecurity and Vitamin B12 deficiency is consistent with my hypothesis. Interestingly, I found only scant evidence in the existing literature supporting a direct link between food security and Vitamin B12 serum concentration,[13] and no evidence on this link in United States populations. I believe this is the first report establishing this link among United States adults.

Moreover, a link between food insecurity and Vitamin B12 is biologically plausible. Vitamin B12 is a water-soluble, essential micronutrient that is taken up exclusively from animal dietary sources.[1] It is reasonable a priori that poor access to food – and thus micronutrients – would be a risk factor for Vitamin B12 deficiency. This is a cross-sectional analysis and can only detect associations between the experience of food insecurity and vitamin B12 deficiency; causality cannot be inferred. Nevertheless, it is now reasonable to hypothesize further that a causal link exists wherein food insecurity causes Vitamin B12 deficiency. Because Vitamin B12 deficiency can take years to develop,[1] establishing a causal relationship would require longitudinal, prospective cohort analyses that follow Vitamin B12 serum concentrations among individuals who were initially food secure, but who subsequently experienced a prolonged period of food insecurity.

Food insecurity is a major problem in the United States. In this analysis, I found that 9.9% of individuals had experienced food insecurity and 12.9% had worried about food insecurity. This is similar to the 2022 prevalence of food insecurity reported by the United States Department of Agriculture: 12.8%, representing about 17 million households.[32] Food insecurity is more common among families living in poverty and among single-mother households.[32] Primary care clinicians, especially those serving resource-limited and structurally disadvantaged communities, are likely to frequently encounter individuals with food insecurity. Toolkits to screen for essential social needs domains – such as the Health Leads toolkit[33] – often include food insecurity as a screening item. The current analysis suggests that primary care physicians should be prompted to consider the possibility of coexisting Vitamin B12 deficiency in individuals who report food insecurity in primary care.

Consistent with expectations from the literature[6–14] biological sex was associated with greater risk of vitamin B12 deficiency. The result in this analysis, that men are at greater risk of vitamin B12 deficiency than women, is concordant with many studies in adults[7,8,11,14,34] and adolescents/children.[10,12–14] Moreover, a multi-biomarker analysis of vitamin B12 status in adults participating in the NHANES 1999 to 2004 study showed better vitamin B12 status in women as compared with men.[15] Some studies, however, have demonstrated greater risk of deficiency in women in certain populations, for example woman who have undergone bariatric surgery[9], and in a study of 2507 adolescents in Turkey.[6] More complex relationships between biological sex and vitamin B12 serum concentrations clearly also exist, for example in a study of 2403 Indian adolescents, deficiency was more prevalent among rural females and urban males.[35]

Much of the extant literature indicates that there is a negative association with vitamin B12 serum concentration as age advances.[3–5] This seems to be supported by 2 main lines of argument. First, there are biologically plausible reasons that vitamin B12 levels might fall in later adulthood, most importantly the increasing incidence of atrophic gastritis and autoimmune gastritis in older adults.[2,36] In addition, data from the NHANES III[3,5] (1988 to 1994), NHANES 1999 to 2004,[15] and the Framingham Heart Study[4] (20th examination in 1988 to 1989) suggest an inverse relationship between age and vitamin B12 serum concentration. Discordant with these historic results, here I unexpectedly found a positive association between vitamin B12 serum concentration and age. Future studies specifically directed toward evaluating the relationship between Vitamin B12 deficiency and age should be pursued.

I also expected to find that metformin use is associated with an increased risk of vitamin B12 deficiency. Several meta-analyses have evaluated the effect of metformin treatment on vitamin B12 serum levels[17,18] and/or vitamin B12 deficiency[17]. Decreased serum vitamin B12 levels and increased vitamin B12 deficiency are seen in many, but not all, of the studies evaluating the relationship between vitamin B12 and metformin,[17,18] with some analyses also showing dose- and duration-dependent associations between Vitamin B12 status with metformin use.[16] In this analysis of All of Us participants, an association between vitamin B12 deficiency was not detected. This could be because the relationship between metformin and serum vitamin B12 is less certain than existing meta-analyses suggest. However, there are several factors that limit my analysis, specifically that it is cross-sectional, observational, and did not account for the dose, duration, or causal relationship of metformin exposure to serum vitamin B12 levels. Longitudinal analyses accounting for these factors – beyond the scope of this cross-sectional analysis – might (or not) detect a relationship between serum vitamin B12 levels and metformin exposure. I suggest that further prospective, randomized analyses on populations, controlling for demographics, medication use, and socioeconomic factors (such as food insecurity), should be conducted to clarify the relationship between serum vitamin B12 levels and metformin use.

This study has strengths. It analyzed a (1) large (n = 8,989), (2) multi-institutional cohort that was (3) specifically designed to capture the diversity of the United States population. These results are, thus, likely generalizable throughout the United States.

This study also has limitations. First, my analyses are necessarily limited to participants for whom I had data: those who answered the social determinants questionnaire and had a vitamin B12 level recorded. Because vitamin B12 is not routinely ordered, there is presumably a clinical justification for this test to be ordered. Therefore, the pretest probability of vitamin B12 deficiency in individuals for whom the test is ordered probably exceeds that of the general population.

Second, the epidemiology of vitamin B12 deficiency is complex and is incompletely captured by my model. Although I demonstrate that there is an *association* between food insecurity and vitamin B12 deficiency my model is not strongly *predictive* of vitamin B12 deficiency. A predictive model of vitamin B12 deficiency would be clinically useful because diagnosis requires a serum diagnostic test which is not likely to be routinely ordered without a high index of clinical suspicion. Such a model might include other laboratory observations that are not likely related to the etiology of vitamin B12 deficiency – as is my hypothesis related to food insecurity – but might be usefully predictive by detecting downstream effects of vitamin B12 deficiency. Examples of downstream variables that might be appropriate for a clinical prediction model – but not an epidemiologic model – might include hemoglobin (Hgb) level or mean corpuscular volume (MCV). Further work on the development of models that could predict the presence of vitamin B12 deficiency from a combination of demographics, commonly available laboratory values (Hgb, MCV, etc.), and environmental factors (eg, food security) would be worthwhile, but is beyond the scope of the current work.

Third, vitamin B12 values are reported as a single numeric value in the All of Us database and I cannot account for interlaboratory fixed effects in my analysis. Fourth, exposure to metformin is inferred if there was any documented exposure to metformin in the electronic medical record within 12 months of the vitamin B12 measurement. Data are insufficient to determine, in the general case, the chronicity of metformin exposure and/or whether metformin was actually taken in cases where a prescription was recorded in the All of Us database. I also did not account for the duration of metformin exposure, which might affect Vitamin B12 levels.[16] Fifth, although the All of Us database is designed to capture a wide range of diversity, the recruitment methodology is not designed to result in a randomized sample. Sixth, some possible risk factors for Vitamin B12 deficiency (eg, alternative dietary preferences, such as a vegan diet) were not interrogated by this analysis.

In summary, I demonstrate that vitamin B12 deficiency is associated with food insecurity in United States adults enrolled in the NIH All of Us database. Future analyses designed to infer causality are warranted. If a causal association with food insecurity are validated in subsequent analyses, strategies to deliver vitamin B12 supplementation or vitamin B12-enriched foods to at-risk populations may be warranted.

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References

1. Nielsen MJ, Rasmussen MR, Andersen CBF, Nexø E, Moestrup SK. Vitamin B12 transport from food to the body's cells–a sophisticated, multistep pathway. Nat Rev Gastroenterol Hepatol 2012;9:345–54.
2. Stabler SP. Clinical practice. Vitamin B12 deficiency. N Engl J Med 2013;368:149–60.

3. Green R, Allen LH, Bjørke-Monsen AL, et al. Vitamin B12 deficiency. Nat Rev Dis Primers 2017;3:17040.
4. Lindenbaum J, Rosenberg IH, Wilson PW, Stabler SP, Allen RH. Prevalence of cobalamin deficiency in the Framingham elderly population. Am J Clin Nutr 1994;60:2–11.
5. Wright JD, Bialostosky K, Gunter EW, et al. Blood folate and vitamin B12: United States, 1988-94. Vital Health Stat 11 1998;243;11:1–78.
6. Karakaş NM. The prevalence of low serum levels of vitamin D, vitamin B12, folate and ferritin in adolescents: Single center experience. Sci Prog 2021;1 04:368504211007667.
7. Yousef Khan F, Yousif AB, Suliman A, et al. Association of vitamin B12 deficiency with metformin use in patients with type 2 diabetes treated in the largest tertiary care hospital in Qatar. Qatar Med J 2021;2021:39.
8. Nandyala S, Mohamed A, Bhargava A, Chaurasia S, Senthil S, Vaddavalli PK. Vitamin B12 deficiency in a large cohort of healthcare professionals across the network of an eyecare organization in India. Indian J Ophthalmol 2022;70:1718–21.
9. Berardi G, Vitiello A, Abu-Abeid A, et al. Micronutrients deficiencies in candidates of bariatric surgery: results from a single institution over a 1-year period. Obes Surg 2023;33:212–8.
10. Saxena R, Liu X, Navas-Acien A, et al. Nutrition, one-carbon metabolism and arsenic methylation in Bangladeshi adolescents. Environ Res 2021;195: 110750.
11. Alvarez M, Sierra OR, Saavedra G, Moreno S. Vitamin B12 deficiency and diabetic neuropathy in patients taking metformin: a cross-sectional study. Endocr Connect 2019;8:1324–9.
12. Ramírez-Vélez R, Correa-Bautista JE, Martínez-Torres J, Meneses-Echávez JF, Lobelo F. Vitamin B12 concentration and its association with sociodemographic factors in Colombian children: Findings from the 2010 National Nutrition Survey. Nutrition 2016;32:255–9.
13. Herrán OF, Ward JB, Villamor E. Vitamin B12 serostatus in Colombian children and adult women: results from a nationally representative survey. Public Health Nutr 2015;18:836–43.
14. Benson J, Phillips C, Kay M, et al. Low vitamin B12 levels among newly-arrived refugees from Bhutan, Iran and Afghanistan: a multicentre Australian study. PloS One 2013;8:e57998.
15. Mineva EM, Sternberg MR, Bailey RL, Storandt RJ, Pfeiffer CM. Fewer US adults had low or transitional vitamin B12 status based on the novel combined indicator of vitamin B12 status compared with individual, conventional markers, NHANES 1999–2004. Am J Clin Nutr 2021;114:1070–9.
16. Alhaji JH. Vitamin B12 deficiency in patients with diabetes on metformin: Arab countries. Nutrients 2022;14.
17. Niafar M, Hai F, Porhomayon J, Nader ND. The role of metformin on vitamin B12 deficiency: a meta-analysis review. Intern Emerg Med 2015;10:93–102.
18. Liu Q, Li S, Quan H, Li J. Vitamin B12 status in metformin treated patients: systematic review. Pietropaolo M, ed. PLoS ONE 2014;9:e100379.
19. American Diabetes Association. 9. pharmacologic approaches to glycemic treatment: standards of medical care in diabetes—2019. Diabetes Care 2018;42:S90–S102.
20. Avery A. Food insecurity and malnutrition. Komp Nutr Diet 2021;1:41–3.
21. Denny JC, Rutter JL, Goldstein DB, All of Us Research Program Investigators, , et al. The "All of Us" research program. N Engl J Med. 2019; 381:668–76.
22. Mapes BM, Foster CS, Kusnoor SV, All of Us Research Program, , et al. Diversity and inclusion for the All of Us research program: a scoping review. PloS One 2020;15:e0234962.
23. Chandler PD, Clark CR, Zhou G, All of Us Research Program Investigators, , et al. Hypertension prevalence in the All of Us research program among groups traditionally underrepresented in medical research. Sci Rep . 2021;11:12849.
24. Devineni D, Akbarpour M, Gong Y, Wong ND. Inadequate use of newer treatments and glycemic control by cardiovascular risk and sociodemographic groups in US Adults with diabetes in the NIH Precision Medicine Initiative All of Us Research Program. Cardiovasc Drugs Ther 2022; 38:347–57. Published online November 15.
25. Nagar SD, Pemu P, Qian J, SEEC Consortium, , et al. Investigation of hypertension and type 2 diabetes as risk factors for dementia in the All of Us cohort. Sci Rep . 2022;12:19797.
26. Perry AS, Annis JS, Master H, et al. Association of longitudinal activity measures and diabetes risk: an analysis from the National Institutes of Health All of Us research program. J Clin Endocrinol Metab 2023;108:1101–9.
27. Fischbach FT, Fischbach MA. *Fischbach's a manual of laboratory and diagnostic tests*. 10th edition. LWW; 2017.
28. Aparicio-Ugarriza R, Palacios G, Alder M, González-Gross M. A review of the cut-off points for the diagnosis of vitamin B12 deficiency in the general population. Clin Chem Lab Med 2015;53:1149–59.
29. Koehler KM, Romero LJ, Stauber PM, et al. Vitamin supplementation and other variables affecting serum homocysteine and methylmalonic acid concentrations in elderly men and women. J Am Coll Nutr 1996;15:364–76.
30. Rajan S, Wallace JI, Beresford SAA, Brodkin KI, Allen RA, Stabler SP. Screening for cobalamin deficiency in geriatric outpatients: prevalence and influence of synthetic cobalamin intake. J Am Geriatr Soc 2002;50:624–30.

31. Pennypacker LC, Allen RH, Kelly JP, et al. High prevalence of cobalamin deficiency in elderly outpatients.J American Geriatrics Society 1992;40:1197–204.
32. United States Department of Agriculture. USDA ERS - Food security and nutrition assistance. USDA.gov. Accessed February 2, 2024. Available at: https://www.ers.usda.gov/data-products/ag-and-food-statistics-charting-the-essentials/food-security-and-nutrition-assistance/.
33. Health Leads. The Health Leads screening toolkit. Health Leads. Published November 30, 2022. Accessed February 2, 2024. Available at: https://healthleadsusa.org/news-resources/the-health-leads-screening-toolkit/.
34. Margalit I, Cohen E, Goldberg E, Krause I. Vitamin B12 deficiency and the role of gender: a cross-sectional study of a large cohort. Ann Nutr Metab 2018;72:265–71.
35. Chakraborty S, Chopra M, Mani K, et al. Prevalence of vitamin B12 deficiency in healthy Indian school-going adolescents from rural and urban localities and its relationship with various anthropometric indices: a cross-sectional study. J Hum Nutr Diet Off J et 2018;31:513–22.
36. Rustgi SD, Bijlani P, Shah SC. Autoimmune gastritis, with or without pernicious anemia: epidemiology, risk factors, and clinical management. Therap Adv Gastroenterol 2021;14:17562848211038771.