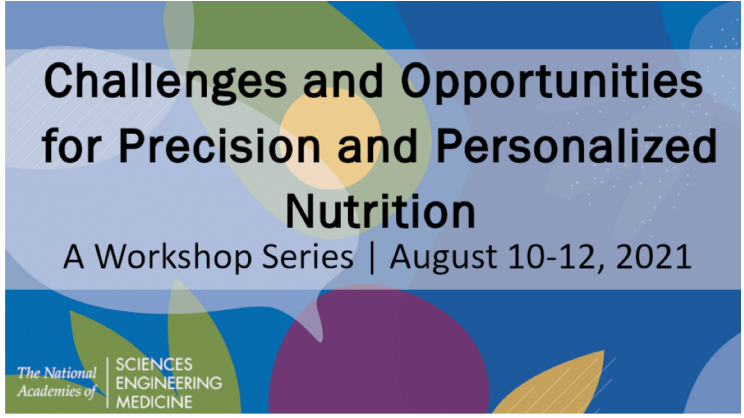

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Jim Kaput

Co-founder and Chief Scientific Officer

jkaput@vydiant.com

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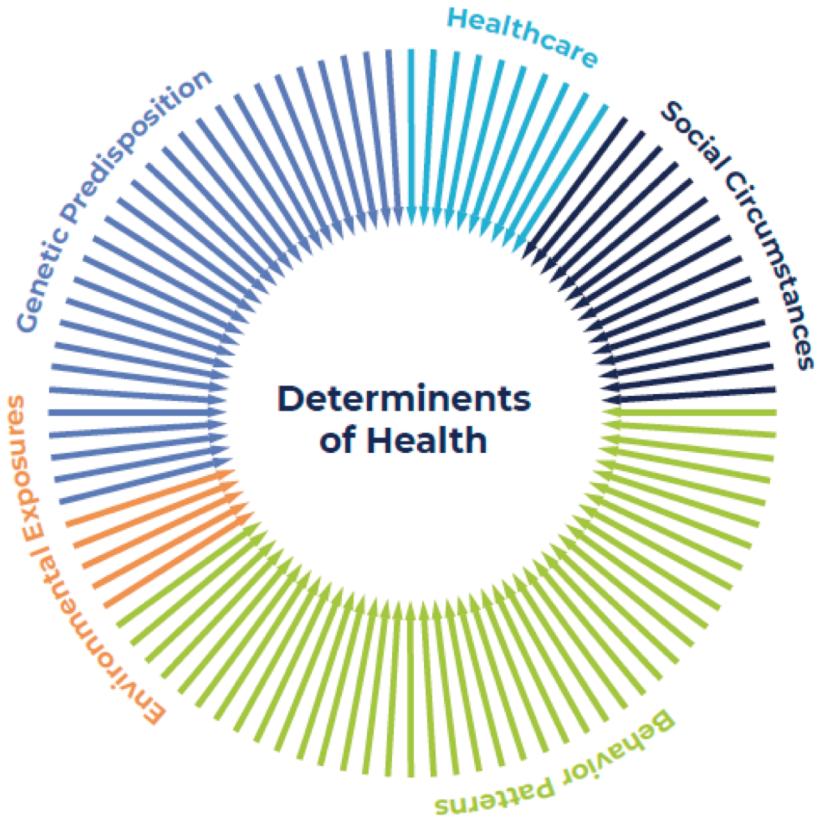
Health is Affected by Many Factors



nutrition, lifestyle, genetics

physical, mental, social, environmental determinants

physiological and molecular processes

drugs, disease conditions and co-morbidities

For this session, we focus on genetic contribution

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Genetic Makeup: Vitamin[1] Baseline and Intervention Response

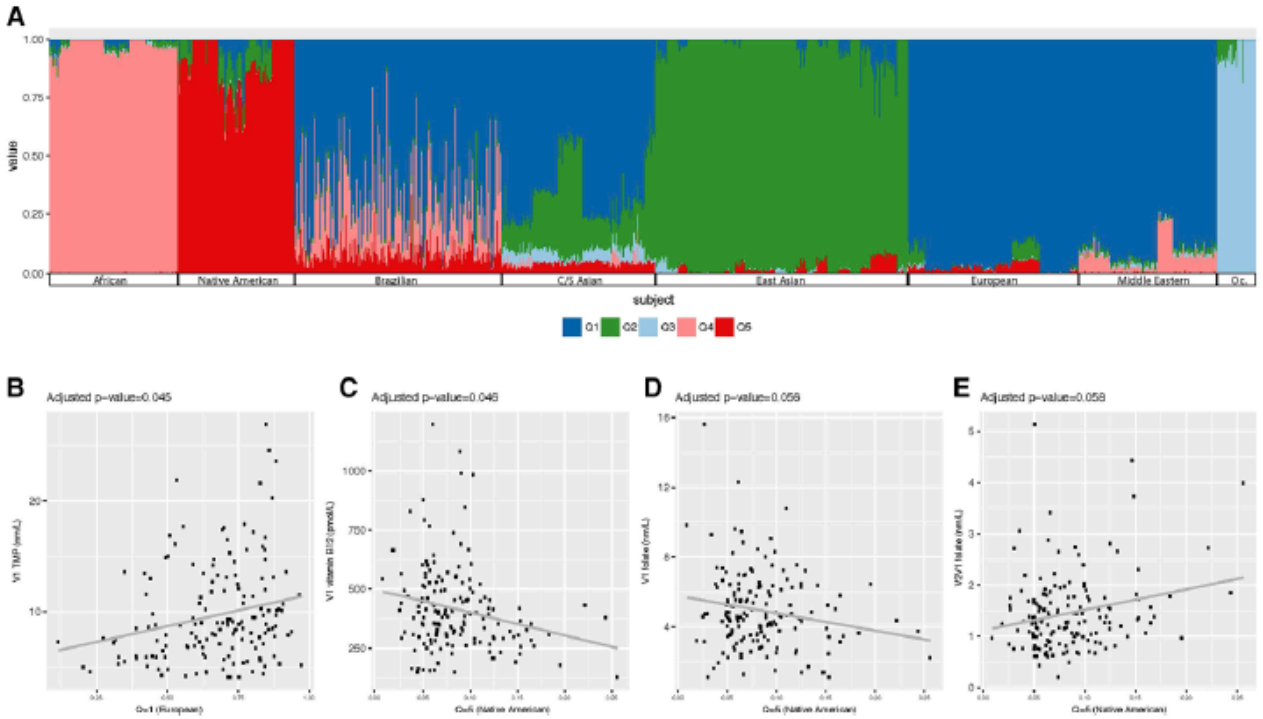

Figure 2. Admixture analysis. Influence of genetic ancestry on baseline vitamin levels. Ancestry markers from the Human Genome Diversity Project (HGDP) reference populations were used A) to identify admixture in data from unrelated participants from both years as per methods. To test whether linear regression between the ancestral components and baseline vitamin levels existed, a $k = 5$ model was used to the following covariates: trial year, sex, age, fat mass, and tanner score. Adjusted *p*-value of 0.05 was used as significance threshold. B) Baseline TMP and Q1 (Europe) with estimate of regression coefficient (ERC) 4.57, C) baseline vitamin B12 and Q5 (Native American) ECR = 186.53, D) baseline folate and Q5 (Native American) ECR = 2.13, and E) folate response as ratio of V2/V1 and k5 (Native American) with ECR = 0.77.

Primary Results

- Low baseline TMP associated with % European ancestry (Q1)
- Low baseline B12 associated with % Native Am (Q5)
- Low baseline folate associated with % Native Am (Q5)
- Folate responds to intervention (V2/V1) associated with NA (Q5)

[1] Measured 21 vitamers in plasma

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Mol Nutr Food Res. 62(6):e1700613 (2018)

Some Studies of Polygenic Risk Scores and Diet

Process	PRS	Reference
BMI	10	*NEJM* **367**, 15 (2012)
BMI	32	*BMJ* **348**, g1610 (2014)
Lipid metabolism	7	*Genes&Nutirition* **10**, 45 (2015)
T2 Diabetes	31	*AJCN* **104**, 198 (2016)
BMI	77	*BMC Med* **15**, 97 (2017)
Vitamin D	9	*Hum Genet* **138**, 1155 (2019)
Vitamin D	3	*AJCN* **108**, 1129 (2019)
Blood pressure	63	*Hypertension* **74**, 1460 (2019)

Process	PRS	Reference
Starch metabolism	9	*Diabetes* **69**, 1917 (2020)
Adiposity	159	*EJN* **60**, 249 (2021)
Lean body mass	5	*Diab Ob Metab* **22**, 2305 (2020)
CHO intake	37	*Scientific Rep* **11**, 13180 (2021)
Energy intake	44	*Scientific Rep* **11**, 13180 (2021)
Fat intake	19	*Scientific Rep* **11**, 13180 (2021)
Exercise onset	25	*Scientific Rep* **11**, 13180 (2021)
SCFA	7	*AJCN* **114**, 42 (2021)

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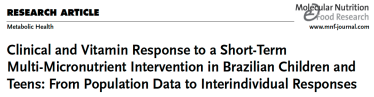
Polygenic Risk Score Catalog: https://www.pgscatalog.org/

Genetic Makeup and Vitamin Baseline and Intervention Response

Participant DNA


RESEARCH ARTICLE

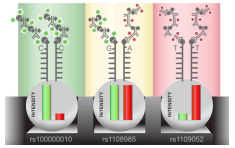
Metabolic Health

Molecular Nutrition & Food Research

www.mnf-journal.com

Clinical and Vitamin Response to a Short-Term Multi-Micronutrient Intervention in Brazilian Children and Teens: From Population Data to Interindividual Responses

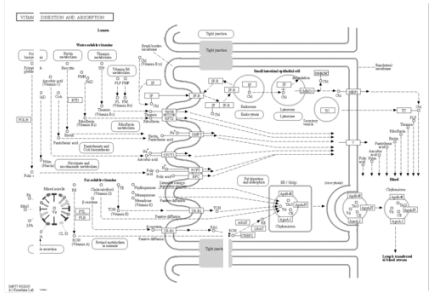
Genotype



Exome Sequencing

5 million + Exon (coverage 70 – 100x)

Vitamin B12 Metabolism



Human Genome Diversity Project

76307 SNPs

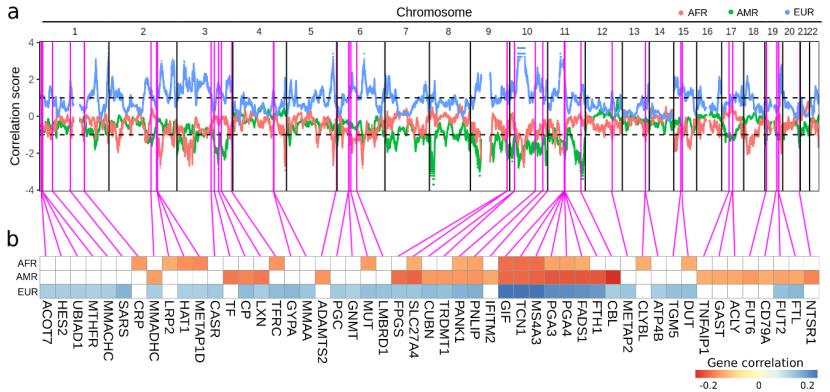
2621297 SNPs

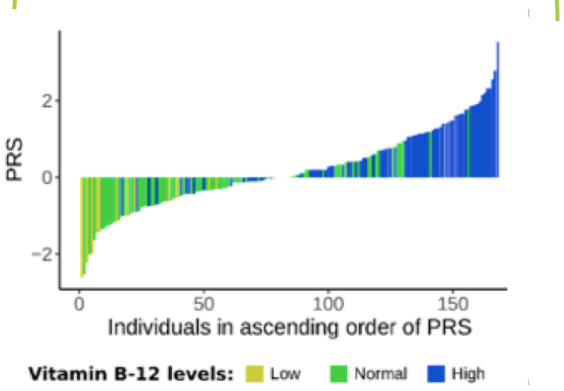
6699 B12 SNPs in 90 genes

Ancestry analyses

Map B12 genes to ancestry regions

36 SNP B12 PRS Associations





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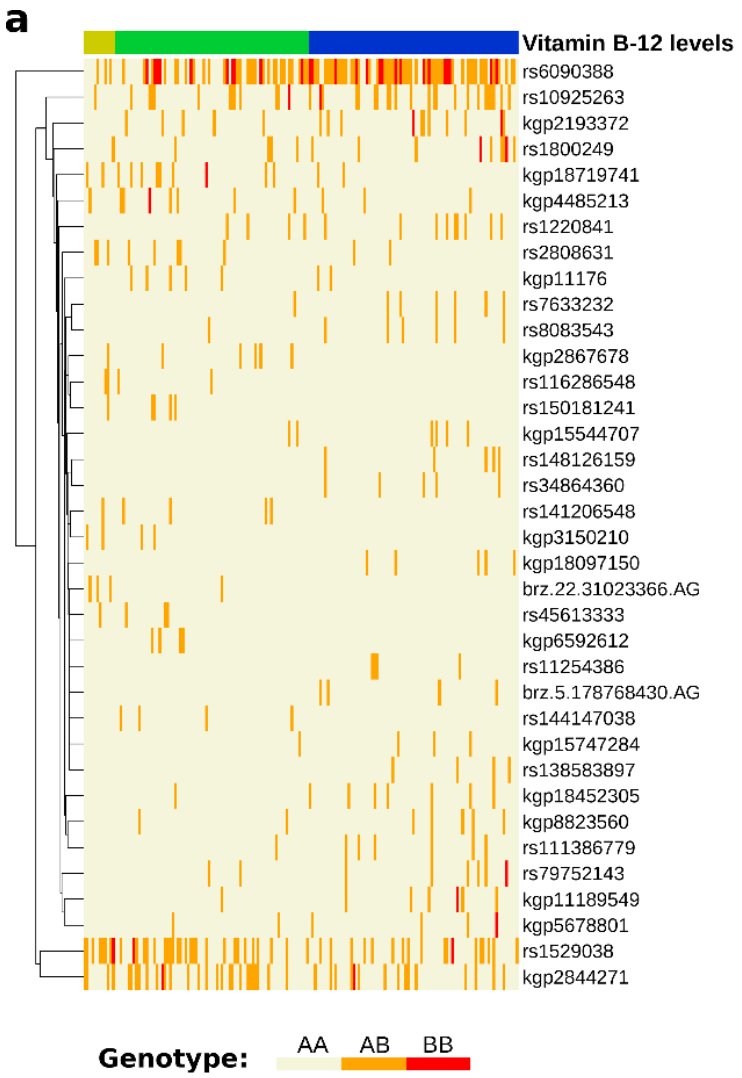
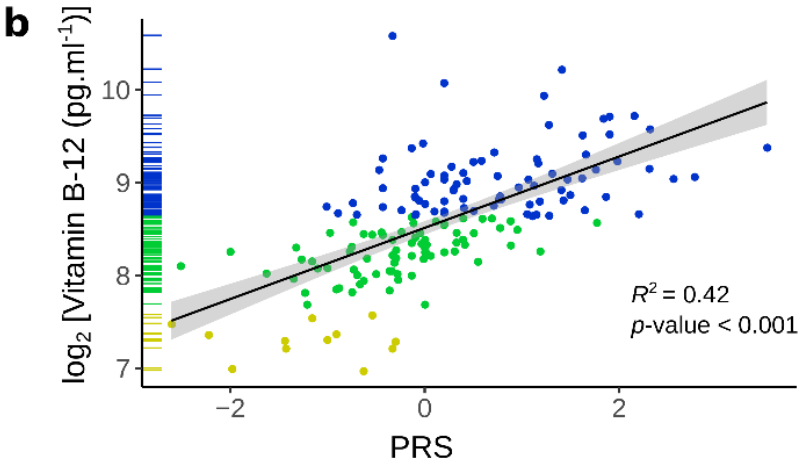
Scientific Reports 11, 11992 (2021)

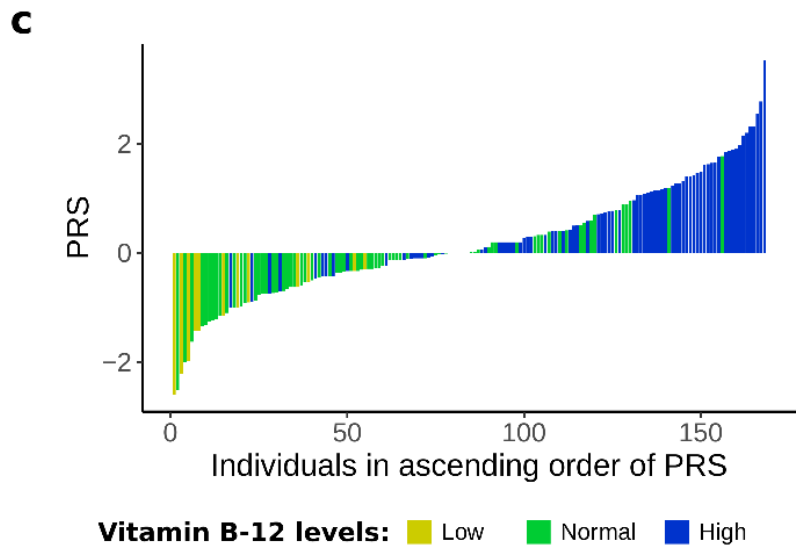
Polygenic Risk Score for B12 Levels @ Baseline

Scientific Reports 11, 11992





PRS of SNPs in 36 B12 genes explained 42% of phenotype



Individuals in ascending order of PRS versus baseline B12 levels.

Covariates: sex, BMI, age, total HEI and mean ancestry components (AFR, AMR, and EUR) per each individual.

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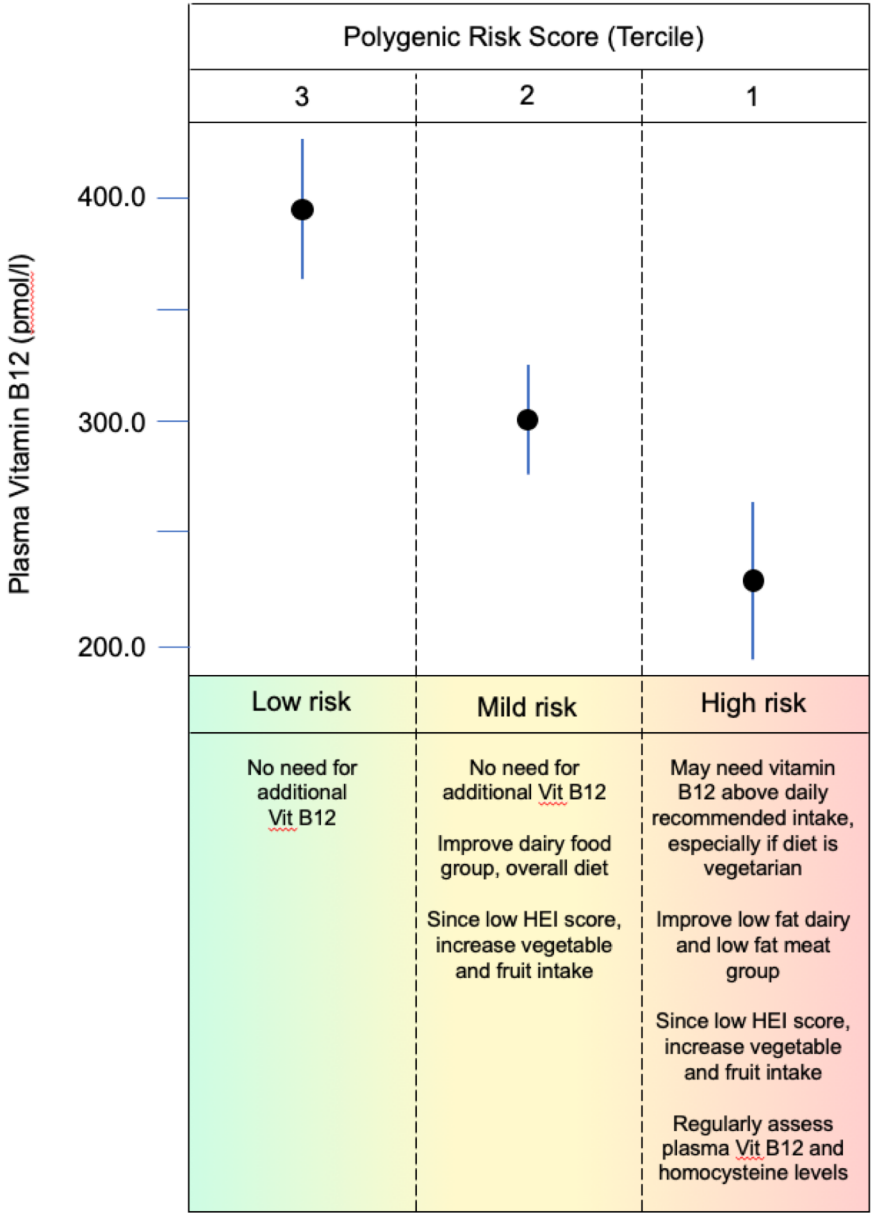
Scientific Reports 11, 11992 (2021)



Proof of Concept for Use of PRS in Personalized Diets

Individuals were stratified into terciles based on their PRS based on 36 SNPs in 26 B12 genes

Analyzed how age, sex, body mass index, total HEI, meat and milk intake (HEI components), socioeconomic status and levels of vitamin B12, homocysteine, folate, pyridoxal and riboflavin are distributed across the terciles.

Kruskal-Wallis was employed to evaluate the significance of differences among terciles within a significance level of 0.05

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Scientific Reports **11**, 11992 (2021)

Path for Assessing Genetic Contributions to Phenotype

Assessing multiple variants provides more validity than single SNP

Genetic architecture is important: we corrected for AMI, EUR, AFR ancestry

Analysis of associations corrected for factors that may influence metabolite levels

Focus on "pathway" variants allowed analysis of small population

Results need to be replicated including co-variates used in this study

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Thank You & Discussion

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Jacqueline Pontes Monterio PhD (co-principal investigator)

Clinical and Vitamin Response to a Short-Term Multi-Micronutrient Intervention in Brazilian Children and Teens: From Population Data to Interindividual Responses

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Mol Nutr Food Res. **62**(6):e1700613 (2018)

Contribution of genetic ancestry and polygenic risk score in meeting vitamin B12 needs in healthy Brazilian children and adolescents

Carlos Alessandro Fuzo[1], Fábio da Veiga Ued[2], Sofia Moco[3], Ornella Cominetti[4], Sylviane Métairon[4], Solenn Pruvost[4], Aline Charpagne[4,8], Jerome Carayol[4], Raul Torrieri[5], Wilson Araujo Silva Jr[6], Patrick Descombes[4], Jim Kaput[4,7] & Jacqueline Pontes Monteiro[2]✉

Scientific Reports **11**, 11992 (2021)

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