Nutrition of the future

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1 - How to quantify the nutrition and health relationship (~ biomarkers)

| Nutrient | Commonly used biomarker/indicators | Magnitude and direction of inflammation effect | Settings where used | TNO innovation for life |
|--------------|---------------------------------------|---|--------------------------------|-----------------------------------|
| Iron | Ferritin | +++ | Clinical, research, population | |
| | sTfR | + | Research, population | |
| | Hemoglobin | | Clinical | |
| | Body iron | + | Research, population | |
| | Ratio of TfR:ferritin | + | Research | |
| | TfR index | + | Research, clinical | |
| | ZPP | + | Clinical, population | |
| | Hepcidin | 0 | Research | |
| Vitamin A | Retinol | - | Clinical, research, population | |
| | RBP | _ | Research, population | |
| | Breast-milk retinol | | Research | |
| | Retinol dose response test | | Research | |
| Zinc | Serum/plasma zinc | _ | Clinical, population | |
| Folate | Erythrocyte folate | + | Clinical, population | |
| | Plasma or serum folate | _ | Clinical, population | Deiter et el INUtr 2015 |
| Vitamin B-12 | Serum/plasma total cobalamin | 0 | Clinical, population | Raiten et al, J Nutr 2015 |
| | Serum holotranscobalamin | | Research | (INSPIRE) |
| | Plasma/urine MMA | 0 | Clinical, population | |
| | Plasma total homocysteine | + | Clinical | |
| lodine | Urinary iodine | 0 | Population | |
| Vitamin D | 25(OH)D | _ | Clinical, population | |
| Vitamin B-6 | Plasma pyridoxal 5-phosphate | _ | Research, population | |
| Vitamin C | Serum ascorbic acid | - | Research, population | |

TABLE 12 Summary of key nutrient biomarkers¹

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Vitamin D genetics and 250HD levels



PLOS Medicine | DOI:10.1371/journal.pmed.1001866

Count of 250HD Decreasing Alleles

Fig 3. 25OHD level by number of 25OHD-decreasing alleles in the CaMos cohort. Here we show the box-plot of natural-log-transformed 25OHD by the count of 25OHD-decreasing alleles in the CaMos population. A count of zero represents individuals with no 25OHD-decreasing alleles (or homozygous at each loci for the 25OHD-increasing allele), and a count of six represents an individual with six 25OHD-decreasing alleles. No individuals with a count of seven or more 25OHD-decreasing alleles were observed in this cohort.

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the "bowtie" principle







Multiple micronutrients are involved in maintaining optimal inflammatory control

Each arrow represents at least one reliable published human intervention study



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alpha1-ACT



for life

Correlations between fasting micronutrient concentrations and plasma protein stress response curves PAK NOH4 RHIML ENTP3 enerav D-Ribose L-Tryptophan unknown 60 gamma tocopherol Lycopene total CHK1 alpha Carotene SIRT2 Kallikrein 4 time unknown 53 C22 1 SPM Plasmin beta Carotene total C34_2_PC Vitamin_E Hemopexin AA mean P7502 UK05 C36 1 a2 Macroglobulin Correlations vitamins with GC data Correlations vitamins with RBM data GPNMB KHA4 beta Cryptoxanthin Calpastatin VitaminA TAC Correlations vitamins with SomaLogic data **BMP1**0 25 hydroxyvitaminD3 HDGR2 ALT [U/L Correlations vitamins with clinical data L-1ra WBC-neutrophils [%] SCGF alpha Correlations vitamins with lipids data Immune status/ WBC ymphocytes [%] inflammation Correlations vitamins with vitamins Van de Broek, Genes and Nutrition 2017



Fig. 4 Overview of markers that have a different PhenFlex test response between 20 healthy male and 20 male type 2 diabetic patients. Gray = no significant differences between T2D and healthy subjects; black = significant different postprandial levels between healthy and diabetic subjects; bold black = significantly different responses to PhenFlex challenge between healthy and type 2 diabetics; asterisk = significant different fasting levels



Personalized?

Type 2 diabetes subgroups react differently on different diets



baseline and after 2 years of follow-up by IR phenotype. p<0.05 between low-fat diet (white bars) and Mediterranean diet (black bars) in each IR subgroup analysed using a univariate model adjusted for age, sex, baseline BMI and change in weight

Blanco-Rojo, Diabetologia, Oct 2015

José Lopez-Miranda



So:

- We should quantify the dynamics ("systems flexibility")
- We can optimize the dynamics by (dietary) interventions, i.e. provide the nutrients for the "flexibility machinery"
- Can we optimize system flexibility by introducing dynamics?

Beneficial effects of alternate dietary regimen on inflammation and atherosclerosis.



Wielinga, PLoSone 2011

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First Good, Then Bad

Fruits and vegetables often contain low levels of toxic chemicals that provide health benefits when consumed in modest amounts but become increasingly noxious at high levels, a process called hormesis. The disparity in effects—traced on a biphasic response curve—contrasts with mercury and other nonhormetic toxic substances that are harmful at even low amounts.



Mattson, Scientific American 2015

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Are flexibility, resilience and optimal immune system related?





Nature's Best Antibiotics ...

and how to use them!

CHALLENGING ONESELF INTERMITTENTLY TO IMPROVE HEALTH Mark P. Mattson Laboratory of Neurosciences, National Institute on Aging Intramural Research Program, Baltimore, MD. 21224.



FIGURE 1. Illustration of the simple fundamental concept that optimal health is promoted by intermittent challenges (mild stressors). Cells in the organ, in this case the brain, respond adaptively by enhancing their ability to function and resist disease.

Matson, Dose-Response 2014

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B Fungi (GABRIELA) A Bacteria (PARSIFAL) 1.0 -1.0 Living on a farm Living on a farm 0.8-0.8-0.6-0.6-Probability Probability 0.4-0.4-0.2-0.2-Asthma Asthma 0.0+ 0.0 20 40 Ó 60 8 No. of Detectable Bands No. of Detectable Taxa

Figure 3. Relationship between Microbial Exposure and the Probability of Asthma.

In both the PARSIFAL study and GABRIELA, the range of microbial exposure was inversely associated with the probability of asthma.

Ege et al, NEJM 364 (2011) 701-9

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Dosed up: could excessive prescription of antibiotics be hampering children's ability to fight disease?

Stop the killing of beneficial bacteria

Concerns about antibiotics focus on bacterial resistance - but permanent changes to our protective flora could have more serious consequences, says Martin Blaser.

TROUBLING CORRELATION

The risk of inflammatory bowel diseases in children rises with the number of courses of antibiotics taken.



Serious (Early) Life Events and Type 1 Diabetes



... we found that a Serious Life Event experienced by the child at any time during the first 14 years of life increased the risk of diagnosis of type 1 diabetes ...



Nygren, Diabetologia 2015 Li, Pediatric Diabetes 2015 Kelly, Frontiers Cellular Neuroscience 2015
 U.S. Food and Drug Administration

 Protecting and Promoting Your Health

* efsa

European Food Safety Authority



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Honey Nut

I scan a product and the App tells me if this is the right product for me, based on my preferences: Cheap / Healthy / Biological / Sustainable AND IT MAY SUGGEST AN ATERNATIVE

I don't need to look to the advertisements, health claims, suggestions, package, I don't need consumer protection, I am empowered

| have a BRAIN. | have a CHOICE. Change is UPTOME!

Consumer empowerment

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So how will nutrition look like in 10 years?



1. It is personal

- 2. The intervention or advice is based on a diagnosis, i.e. my personal health data.
- 3. A (science based) model is used to translate diagnosis into advice
- 4. The model is tailored to specific conditions and goals from a large toolbox
- 5. The toolbox is continuously and systematically updated with all relevant scientific knowledge
- 6. Exploit/use information from large numbers of personal health data

I make regular adjustments to my diet and behavior in order to stay on track





Can we make use of thousands of other personal health timelines to optimize every decision I make for my personal health ?

> Bayesian networks Artificial Intelligence

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Child Health Passport



Use this passport to record important health information. Keep it in a safe place for future reference.

Parent/Guardian Name

Phone Number

 Health Care Providers

 Public Health Office
 Phone Number

 Public Health Nurse
 Phone Number

 Doctor
 Phone Number







What data do we really have / need and what should we do with it?

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Where is our health data and how is it really useful to us?

Medical Records

Unlocking the Value of Personal Data: From Collection to Usage

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data sharing deal with drug manufacturer Genetech. The deal provides Genetech with unrestricted access to all of the de-identified data PatientsLikeMe is collecting from its users for a five-year period.

The deal represents a new monetization strategy for PatientsLikeMe, a company that has done work with pharmaceutical companies in the past, but in a different capacity. Prior to the announcement, PatientsLikeMe monetized through three business channels, all marketed to pharmaceutical companies. The first service included building disease-specific communities at the request of a drug manufacturer, so that they could study the long-term effects of the disease, and understand what aspects of the disease, and the medications used to treat it, patients were struggling with most. The second offered survey and polling services that would allow drug manufacturers to study individual patient populations within the PatientsLikeMe network. The third monetization strategy involved building predictive tools that used aggregated data from its communities to calculate individual patient outcome probabilities based on a variety of secondary risk factors.

The real value of MY health data: how can this data work for me?

Health Data Cooperative as legal entity that valorizes my own health data.

Developers





The TNO life companion and the new health economy

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Citizen based research provides evidence on lifestyle related treatments



(Do-it-Yourself) diagnosis Full health data ownership



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A new health economy provides SERVICES that I want to use



Lifestyle related health can only be optimized in a systems approach where all relevant factors are addressed.



Mozaffarian, Circulation 2016













personalized nutrion

in early life