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Precision nutrition — review of methods for point-of-care assessment of nutritional status

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Precision nutrition encompasses prevention and treatment strategies for optimizing health that consider individual variability in diet, lifestyle, environment and genes by accurately determining an individual's nutritional status. This is particularly important as malnutrition now affects a third of the global population, with most of those affected or their care providers having limited means of determining their nutritional status. Similarly, program implementers often have no way of determining the impact or success of their interventions, thus hindering their scale-up. Exciting new developments in the area of point-of-care diagnostics promise to provide improved access to nutritional status assessment, as a first step towards enabling precision nutrition and tailored interventions at both the individual and community levels. In this review, we focus on the current advances in developing portable diagnostics for assessment of nutritional status at point-of-care, along with the numerous design challenges in this process and potential solutions.

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Introduction

As per the 2016 Global Nutrition report [1], one in three people is malnourished in one form or another and monitoring nutritional status is becoming increasingly more vital both at the population and the individual level. In resource-rich settings, with increasing awareness of the importance of nutrition, dietary fads and supplements often become popular with unknown efficacy. In resource-poor settings on the other hand, many programmatic approaches such as food fortification [2], micronutrient supplementation [3] and dietary diversification [4] are being deployed to overcome nutritional deficiencies, sometimes with limited knowledge of their effectiveness. The lack of accurate methods for evaluating nutrition status at the point-of-care hampers our ability to enable precision nutrition and target interventions to those who need or respond to them, thereby limiting major improvements in public health. With advances in technology, it is now becoming possible to meet some of these diagnostic challenges to revolutionize health care at point-of-care and this is the focus of this review.

Precision nutrition

The recommended approaches [5] for nutritional screening include anthropometric indices based on body measurements, biochemical indicators (biomarkers), examination of clinical symptoms, and dietary assessment. Technology is changing our capacity to assess each of these; however, the focus of this review is on measurement of biomarkers, which often enables early diagnosis of deficiency or risk of certain diseases and provides potential opportunities for relatively simple interventions before the emergence of clinical symptoms. The Biomarkers of Nutrition for Development (BOND) program [6–8] is working to identify and harmonize the decision making process about the best uses of biomarkers in specific scenarios. A summary of various micronutrients, corresponding biomarkers and their physiological levels for determining deficiency/insufficiency, and health consequences have been summarized elsewhere [9••]. The ability to assess the health impacts of nutritional status depends on the availability of accurate and reliable biomarkers that truly reflect nutrient exposure, status and effect [10]. Precisely measuring nutritional biomarkers [11,12•,13] in biological samples can be useful to predict future events, identify individuals likely to benefit from an intervention, and help determine the efficacy and effectiveness of a nutrition program.

Conventional diagnostics for nutritional biomarkers

Numerous commercially available analyzers can be applied for quantification of nutritional biomarkers. Some examples include ADVIA Centaur XP Immunoassay System (Siemens Healthcare GmbH), IMMULITE 2000 XPi Immunoassay System (Siemens Healthcare

GmbH), ACCESS 2 Immunoassay System (Beckman Coulter, Inc.). But these analyzers are not suitable for point-of-care applications, are expensive, not portable, require cold chain, and require skilled technicians to operate them.

Microfluidics/lab-on-a-chip for nutritional biomarkers

Microfluidics-based [14] lab-on-a-chip (LOC) platforms [15,16•] handle very small volumes of test samples and can be designed to perform diagnosis and real-time monitoring of nutritional biomarkers at the point-of-care. Numerous microfluidics based analytical techniques for quantification of nutritional biomarkers have been reported in recent years, and interested readers are encouraged to refer to a summary [9••] elsewhere. LOC platforms can be designed to be disposable and also handle a wide range of clinical samples that includes blood, saliva, and urine. LOC devices can be made cost-effective by mass production, quality control, and miniaturization [17••,18]. Table 1 lists a few examples of LOC platforms applied to detection of nutritional biomarkers. Table 2 lists some of the diagnostics related considerations for nutritional biomarkers in terms of selection of appropriate biomarkers [19], type of biological samples and their storage/handling.

Real-time nutritional screening in traditional lab settings is expensive, is time-consuming and can be even more challenging with issues such as fluctuating power supply in economically poor settings with the highest burden of malnutrition. Most of these disadvantages can be overcome by applying LOC technology to develop cost-effective, portable, rapid, high-sensitivity point-of-care testing (POCT) [29–32] for nutritional biomarkers. In diagnostics, time is of the essence and POCT can provide results much faster, typically less than an hour, compared to the traditional laboratory approach. However, there is a trade-off between speed, range of parameters tested for, and portability. It is desirable for POCT to be suitable for use by minimally trained operators and reducing user error is critical to achieve the most benefit.

Table 1

Examples of lab-on-a-chip (LOC) platforms applied in detection of nutritional biomarkers

Nutritional Biomarker	Sample	Sensor	Sensitivity	Specificity	Characteristics	References
Retinol-binding protein (RBP)	Artificial serum	Impedimetric	n/a	n/a	Impedance spectroscopy to detect the binding between RBP and anti-RBP on an indium tin oxide surface.	[20]
RBP	Serum	Enzyme immunoassay	n/a	n/a	A competitive assay uses RBP adsorbed to microtest strip wells to compete with RBP in serum.	[21]
RBP4	Serum	ssDNA aptamer-based Surface plasmon resonance (SPR)	n/a	n/a	RBP4-specific aptamer immobilized on a gold chip for a label-free RBP4 detection using SPR.	[22]
Ferritin	Serum ferritin controls	Photonic crystal (PC) optical biosensor	n/a	n/a	Iron-oxide nanoparticles (IONPs) combined with a photonic crystal (PC) optical biosensor.	[23]
25-OH vitamin D (25OH-D)	Standard 25OHD solutions	SPR and electrochemical	SPR — 4.8 m ml/μg DPV — 0.020 μA ml/ng	n/a	Comparison of SPR and electrochemical methods for 25OHD detection.	[24]
Soluble transferrin receptor (sTfR)	Standard sTfR solutions	Photonic crystal (PC) optical biosensor	n/a	n/a	Iron-oxide nanoparticles (IONPs) combined with a photonic crystal (PC) optical biosensor.	[25]
Soluble transferrin receptor (sTfR)	Whole blood	Immunofluorometric assay	n/a	n/a	Immunoassay for sTfR based on the all-in-one dry-reagent assay concept and time-resolved fluorescence detection.	[26]
Ferritin, RBP and C-reactive protein (CRP)	Whole blood	Optoelectronics/lateral flow assay	Ferritin — 80.6% RBP — 75.0% CRP — 100%	Ferritin — 84.1% RBP — 62.3% CRP — 80.7%	Electronics enabled microfluidic paper-based analytical device (EE-μPAD).	[27•]
Vitamin B12	Whole blood	Lateral flow assay	87%	100%	Lateral flow assay coupled to a mobile platform.	[28•]