ABSTRACT

The disease centred model currently used by conventional medicine has resulted in the NHS failing to keep pace with the demands placed on it. Personal Centred Nutrition offers an alternative approach.

Key Words: nutrition, evidence based medicine, functional medicine

Introduction

The disease centred model currently used by conventional medicine has resulted in the NHS failing to keep pace with the demands placed on it. By looking at disease as a single entity rather than taking into account the person that has a given disease, biochemical, epigenetic and environmental individuality is ignored. In the functional medicine textbook¹ William Osler is quoted as saying: “It is more important to known what person has the disease than which disease the person has.”

In contrast to conventional medicine, functional medicine is essentially patient centred, rather than disease centred. One branch of this is person centred nutrition, which aims to provide individualised diet and lifestyle advice, whilst acknowledging the psychosocial elements of health. A key part of the functional medicine approach is collaboration between the health care professionals and the patient; the outcome of this being a patient-driven protocol, with increased tendency to compliance.² One of the greatest challenges in modern health care is the weakness of the evidence base. The aim of this paper is to critically analyse the current research paradigm and explore possible new methodologies to improve patient outcomes.

Evidenced Based Medicine

Evidence based medicine is the approach adopted by conventional medicine. Currently there is a deluge of wide and varied information available via the internet when searching for health solutions which can be both confusing for patients and indeed provide contradictory information. This creates a bottleneck of information, much of which is ambiguous and biased. This has lead to increased interest in evidence-based research, particularly in the arena of social sciences. This has made way for the need for organisations such as the Cochrane Collaboration. Their role is one of administration of grading schemes and thus dissemination and distilling of best evidence, supposedly making it easier to access
'good evidence'. With a more reliable evidence base, policy makers and practitioners can make better-informed decisions and this evidence base is commonly use to develop clinical practice guidelines and local disease management protocols.

Current evidence based medicines use a hierarchy that gives randomised controlled trials (RCTs) and meta-analyses supremacy The benefit of this is that clinical decision-making is objective and in theory statistical analyses helps to address problems of bias. However, in reality technological, gender, cultural and publication bias are still problematic.

From a person centred nutrition point of view, RCTs are aimed at bringing drugs to market (such as orlistat for weight loss) rather than assessing more complex health outcomes. RCTs are expensive, making them predominantly industry led. This wide adoption by the pharmaceutical industry combined with the high financial stakes has created a financial bias with increasing pressure to report positive outcomes and suppress negative outcomes. Opportunities to study clinically important questions became marginalized and this poses a threat to the reliability of the knowledge base.

**Person Centred Nutrition – The Time for a New Approach**

In person centred nutrition we want to take in to account bio-individuality, rather than adopting the one size fits all approach of conventional medicine. The problem with this is that to handle the vast amount of cellular and molecular data, mathematical models must be employed.

A number of statistical approaches are used in the modelling of this data, including using Frequentist Statistics and Bayesian Inference. To handle complex health problems involving large databases of health information, electronic health record data can be pooled together and used to explore patient outcomes. If this data can be pulled into a standardized format that is accessible in the public domain, it can be utilized in multiple ways including new hypothesis testing and biomarker discovery.

A successful example of combining these approaches is evidenced in a recent study that used a combination of Bayesian methodology and traditional frequentist approaches to look at multiple patterns of sensitization in children with atopy. An unsupervised machine learning approach was adopted to divide the participants into different classes based on atopic vulnerability. The use of Bayesian methodology enabled the authors to identify structure within the data in the form of clusters. This machine learning approach culminated in five classes in total. This five-class model was representative of a complex latent (not directly measureable) structure. Atopic vulnerability was clustered into 4 definite classes the 5th cluster indicative of no atopy (Fig 1).

They then went on to explore the affiliation between the clusters and asthma. Following this, utilization of a supervised learning approach allowed them to then pose the question of how prophetic the clusters were of developing asthma? The authors’ investigations give them the platforms to articulate to the medical profession that perhaps it is time to progress.
towards a more sophisticated definition of atopy, with a consideration of sub-classes under the atopy umbrella.

Figure 1: Graphic representation of a hidden Markov model

This strategy is also championed by Sharma and Minhas, who propose that Bayesian statistics can be employed to integrate information from RCTs and observational studies with the patient’s unique biology: “In this approach the gold standard would be the best explanatory model of the disease and the mechanism of action of the treatment”. The development of the best explanatory model is the focus of biological research; the systematic use of Bayesian methods would provide a method of testing the best explanatory theory preserving this perceived benefit of EBM while which is independent of expert opinion, thereby broadening its conception of evidence. Such a model would be applicable to any condition and would not be limited by how common the condition is. It could therefore be used as a source of evidence where none currently exists.

There are a number of challenges in the application of computer science to nutritional data. Policy change would be required in order to achieve the necessary standardization of data reporting. Furthermore, journals would have to lay down various requirements and produce information in a readable and reproducible form.
Research Approaches to Person Centred Nutrition

Genetics
An area finding increased momentum is genetic based nutrition. Joost explains that person centred nutrition is not new. Diets based on population group, life stage and disease are already common; what is new is nutrition advice based on genetic testing. He states that: “It is therefore a reasonable assumption that a knowledge of the interactions between genotype and diet (and other lifestyle factors) will be of major help when assessing disease risk and when initiating preventative measures.” In theory, the concept of personalized nutritional recommendations that are based on genetic data should help to fine-tune the prevention of nutrition-associated diseases.

The combination of genetic profiling with the measurement of disease biomarkers makes it possible to identify subjects in the pre-disease state, giving leverage in the area of prevention. As biomarkers are a dynamic entity the goal of prevention may be procured through sufficient dietary intervention. “Undoubtedly the combination of evidence based nutrition and early biomarker–based diagnostics will be mandatory to enable accurate tailor-made nutritional advice in the future.” Once refined this process could help to save resources by targeting advice, and help to improve client compliance.

However, the infancy of this type of research presents a number of problems. It is difficult to council on the basis of individual SNPs (single-nucleotide polymorphisms) because we don’t know how they will interact with each other within a given individual. Using genetic information opens the possibility of developing subpopulation specific nutrition protocols and functional foods.

We are at a stage where science has the tools to explore gene-diet-disease interactions, but more data is needed through intervention studies to confirm these findings. In addition, there are other variations in the expression of genes such as “epigenetic modifications and copy number polymorphisms” that add as extra layer of complexity.

Metabolomic Profiling (Metabolomics and Personalized Metabolic Signature)
A recent report submitted to the Parliamentary Office of Science and Technology emphasised the importance of personalized medicine. Human diversity creates the potential of genetic stratification within populations. The targeting of medical treatments based on a patient’s genotype, combined with a growing knowledge of pharmacogenetics (genetic differences in drug metabolism) and pharmacogenomics (pharmacogenetics extending to the development of drugs that have been tailored for specific genetic profiles), permits greatest patient efficacy and minimizes adverse drug reactions. This greater understanding will catalyse the development of novel drugs. Pharmacogenomics could potentially see the wane of so-called blockbuster drugs and abolition of the stance that “one size fits all.” This personalized approach can also be applied to nutrition.

Ginkgo Biloba is an example of a nutrient that can be used to alter significantly the transcription of hundreds of genes. A wide range of genes are affected by Ginkgo Biloba including those for nerve growth, differentiation, regulation and function, mitochondria, and
antioxidant protection\textsuperscript{12}.

Metabolomics is a rapidly advancing area of biology. The idea is that groups of people fitting specific metabolic profiles could be recommended more sophisticated diets than those currently recommended by the government. This concept is in its infancy but gaining momentum. Gibney et al\textsuperscript{13} proffers that this expanding field will allow people to be grouped into metabolic phenotypes so that resources would be saved by targeting advice to the relevant individual at an early stage.

\textit{Systems Biology}

Another possible avenue for improving the evidence base for person centred nutrition would be the integration of systems biology. Systems biology provides a structure for agglomerating models of biological systems; emerging applications of systems biology that are likely to be of particular importance during the decade to follow:

\begin{itemize}
\item[(a)] pathway-based biomarkers\textsuperscript{14}
\item[(b)] global genetic interaction maps\textsuperscript{14}
\item[(c)] systems approaches to identify disease genes\textsuperscript{14}
\end{itemize}

Systems biology works on a molecular level, having the capacity to give an extra dimension of information. Details of molecular mechanisms could be integrated into EBM and although in its infancy, this field has an abundant of potential going forward. 'Other studies focus on the modular organisation of the networks or the presence of network motifs. It seems that this aspect of systems biology could lead to the development of appreciable fundamental insights into the principles that underlie biology'\textsuperscript{5}. However it is worth noting that systems biology needs to take into account epigenetics\textsuperscript{4}. It is all well and good having the gene but of course if the former is silent the gene is not expressed.

\textit{Functional Medicine}

Whilst insight into genetics and biochemistry has value, the power of the individual’s case history must not be under-estimated as numerous inputs “subtly influence overall risk of disease or treatment response”\textsuperscript{11}. The functional medicine approach aims to integrate a person’s history with measures of biochemical individuality, taking into account environmental, social and psychological factors in a holistic approach to healthcare that empowers the patient.

\textit{The Future}

In summary we are developing a platform to revolutionise the evidence base for complex health issues, utilizing the best aspects of both Bayesian and Frequentist Statistics and the rapidly advancing field of machine learning. In the future, perhaps incorporation of the function medicine model making additional use of the patient’s history, psychosocial and environmental milieu will assist in generating a more advanced and bespoke patient outcome, thus in time achieving an improvement in the overall health of the population.


References


11. 'Personalised medicine', Parliamentary Office of Science and Technology, Number 329, 2009

