

Review Article

The opportunities and challenges of evidence-based nutrition (EBN) in the Asia Pacific region: clinical practice and policy-setting

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Evidence-based nutrition (EBN) has gained currency as part of the growing role of evidence-based medicine (EBM) to increase the validity, utility and cost-effectiveness of both clinical practice and, increasingly, public health endeavours. Nutritionally-related disorders and diseases (NRD) account for a relatively large proportion of the burden of ill-health, disease and mortality, especially as the nexus between them and both infectious disease and so-called chronic disease is understood. As resource allocation is increasingly dependent on the evidence for preventive or therapeutic effect, the case for nutrition interventions also needs to be underpinned by evidence. However, feeding studies are not as amenable to the designs familiar to clinical trialists and dietary interventions in public health may be complex in their conduct and interpretation, making other approaches like cohort studies more attractive even if costly and long in the execution. With a number of food system changes in rapid progress or imminent, especially in the populous Asia Pacific region, along with changing demographics, changing disease patterns and concern about present and future food security, a stock-take and scenario analysis of EBN was undertaken by a panel of nutrition scientists, population scientists, agriculturalists, clinicians and policy makers together with consumer and indigenous stake-holders in Taiwan in 2007. They found that clinical practice guidelines and proposals for health and nutrition policies required greater emphasis and expertise in EBN.

Key Words: systematic reviews (SRs), clinical nutrition trials, portfolios of evidence, hierarchies of evidence, knowledge, traditional diets, evidence based health policy (EBHP)

EVIDENCE BASED HEALTH POLICY (EBHP)

In recent years, there has been much interest and activity in strategies to underpin clinical practice and, to a lesser extent, public health practice, with scientific evidence. The best examples of this are the many systematic reviews (SRs) of the literature which have been sponsored by the Cochrane collaboration, named in honour of the distinguished epidemiologist, Archie Cochrane¹ to support what has commonly been referred to as evidence based medicine (EBM). This approach requires the formulation of a question about practice or policy, searches for the best evidence, appraises it, integrates it and evaluates its effectiveness and efficiency.

The integration is of various kinds of evidence, usually laboratory, animal experimental, expert opinions, case reports, case-control studies and cohort studies. The highest order of evidence is considered to be the randomized con-trolled double-blind study. Criteria for study quality are applied and as many good studies as possible com-

bined into a meta-analysis. This work is presented and published as an SR.

THE EVIDENCE BASED NUTRITION (EBN) CONCEPT

Food and nutrition knowledge is, to a variable extent, part of the information which every person uses on a daily basis for self-preservation or in the care of dependents.² However, this information comes from various sources, tested in traditional and scientific ways, of uncertain validity, and with cultural, religious, experiential and eco

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conomic overtones, which may or may not have prospects for sustainability or optimal health.

Trichopoulos makes the point in his review of EBN³ that there are 'top-down' and 'bottom-up' approaches to nutrition evidence, the former being informed by successful food cultures and their characteristics and the latter the aggregate of pieces of scientifically-derived information which, in the synthesis, is not uncommonly faced with error in its predictive capacity.

An important difference between much of EBM⁴ and EBN is that therapeutic efficacy and effectiveness, rather than causality, is the issue. That an intervention, with a pharmaceutical agent for example, works is not evidence for causality, but of the possibility of bringing about change in a particular circumstance or population. Food habits may, in concert with other behaviours, be causally related to health outcomes and be of considerable personal, clinical and public health relevance. They cannot be 'blinded' in a clinical trial.⁵ EBM, and even Health Claims for foods⁶ appeal to *hierarchies of evidence*, with randomized double-blind clinical trials being the best or Level 1 evidence in assessing strength of evidence.

Regrettably, this does not recognize the special evidential needs in clinical and public health nutrition. For this reason, a compilation of evidence is to be preferred for EBN and this is referred to as a *portfolio approach to evidence*.⁷

The recent World Cancer Research Fund (WCRF-AICR)⁸ report on Food, Nutrition, Physical Activity and the Prevention of Cancer sets out grades of evidence which might apply to various nutritionally-related disease states. Some of the broader logic which might apply to chronic disease in general is set out by Jim Mann in an earlier publication.⁹

The WCRF report endeavours to be global in its findings about diet and cancer, by considering food patterns and cancer patterns world-wide. The limitation is that the required information is not uniformly available globally and extrapolations may be inappropriate. Much effort is needed in the Asia Pacific region to fill gaps as concluded in the Okinawan round-table on Nutrition and Cardiovascular disease (CVD) in the Asia Pacific.¹⁰ This report observed that knowledge already existent in the region

might provide for mitigation against an epidemic of nutritionally-related CVD and for the promulgation of traditionally cardio-protective food practices beyond the region.

EBN is becoming more and more active as indicated by Google listings (Table) and by numbers of SRs in the field of Diet and Nutrition (Figure). Both the American Dietetic Association¹¹ and the British Nutrition Society¹² are encouraging and facilitating SRs in nutrition and health.

The present report is mindful of the pressing need for EBN to develop in the Asia Pacific to support sustainable and economically-viable food-health options. It is based on an analysis of EBN undertaken by a panel of nutrition scientists, population scientists, agriculturalists, clinicians and policy makers together with consumer and indigenous stakeholders in Taiwan in 2007.

FOOD AND HEALTH SCENARIOS FOR EBN

A number of scenarios in food and health, which may be overlapping, can be envisaged for the Asia Pacific region

Table Evidence-based citation on Google October 23, 2007

Term Used	Number
Evidence-based	29,200,000
Evidence-based medicine	2,090,000
Evidence-based health care	227,000
Evidence-based practice	1,740,000
Evidence-based nursing	836,000
Evidence-based nutrition	38,600
Evidence-based dentistry	33,800
Evidence-based surgery	15,400
Evidence-based management	176,000
Evidence-based education	49,100
Evidence-based marketing	614
Evidence-based politics	767
Clinical practice guideline	533,000
Systematic review	1,960,000
Meta-analysis	2,100,000

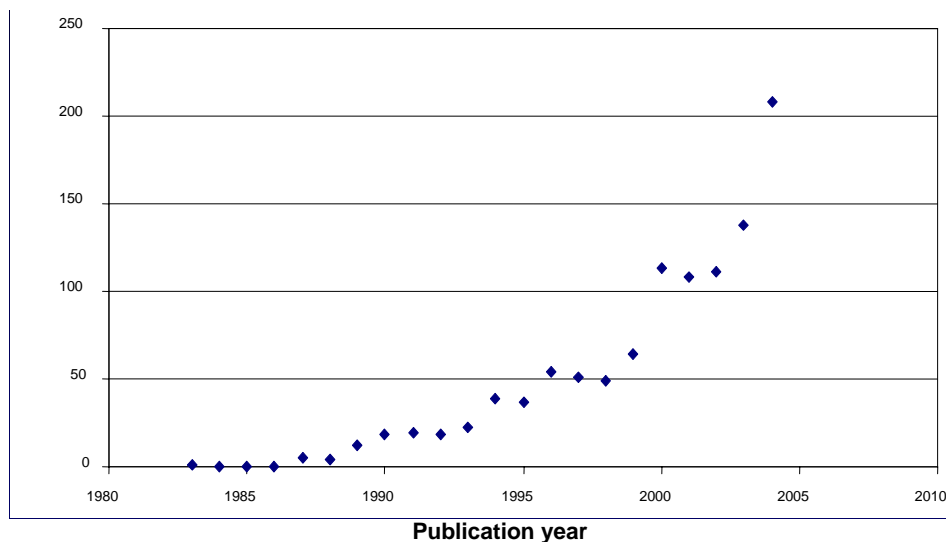


Figure Approximate number of systematic reviews / meta-analyses indexed in Medline as nutrition / diet related

and which will require forward planning and ongoing adjustment as evidence develops and changes:

1. *Increasing health care costs* where less costly non-pharmaceutical measures like diet and exercise will be sought to contain expenditure and a work-force required to implement the alternatives.
2. *Changing patterns of disease* towards whole-of-life effects of nutritional and energy balance exposures coupled with emerging pathogens as climate and ecosystems change. Such pathogens will find hosts to be of changing nutritionally-related immune status.
3. *A shrinkage in real biological food diversity* reversing recent nutritionally-related health gains attributable to biological food variety and increasing dependency on formulated foods with its apparent variety. Local food production will again be important, but difficult to achieve in some parts of the region. Climate change and energy costs will be the main drivers of these situations.
4. *Increasingly contaminated soil and water* with higher risk-benefit ratios for land crop, aquatic food and potable water safety.
5. *Health claims for traditional and designer foods.* Food regulatory agencies are endeavouring to manage a growing onslaught of health claims for food¹³ by insisting on evidence for nutrient claims, general health benefits at recommended levels of intake and high order claims that have to do with modulation of biomarker intermediates for disorder and disease or of disease and its outcomes.¹⁴

These various scenarios will push EBN more in the direction of cost and risk-benefit analysis and require close inter-sectoral collaboration between health care, food production and processing, education and information providers and economists. They are in the realm of public health evidence and, as such, will require relevant questions to be formulated, evidence to be adduced and integrated and policy to be evaluated.

CLINICAL NUTRITION PRACTICE GUIDELINES (CNPG) IN THE ASIA PACIFIC

Already new nutritionally-related disease (NRD) epidemics like obesity, diabetes, atherothrombotic cardiovascular disease, osteoarthritis, osteoporosis, and fractures, certain cancers like colorectal, prostate and breast are evident without Asia Pacific-sensitive clinical nutrition practice guidelines. To some extent this depends on a lack of food habit, food compositional, anthropometric and biogeographical information, but also on differences in historical and early life exposures. CNPGs also need to dovetail with other therapeutic modalities, especially pharmaceutical given food effects on drug bioavailability and metabolism.

Different susceptibilities to adverse drug reactions where polymorphisms and patterns of NRD differ need consideration. For example, the use of sodium-retaining, blood pressure-elevating and anti-platelet aggregation

non-steroidal anti-inflammatory drugs (NSAIDs) in certain Asian ethnic groups prone to hemorrhagic stroke, but where there are no relevant ethnically -specific trials is a case in-point. Each of these effects of NSAIDs can be modulated by diet where there may be substantial cultural difference and responsiveness

The expression of NRDs themselves may depend on the sequence of nutritional exposures as with maternal nutrition and fetal gene programming with the metabolic syndrome more likely in later life. This nutritional life-course can be difficult to discern in evidence which is adduced. Alternatively, or as well, the health significance of a NRD risk factor, itself partly nutritional, like abdominal obesity, may be dependent on various genetic polymorphisms. One such polymorphism recently described is the propensity to high fasting TG (triglycerides) in people with the ApoA5 -1131T>C allele when consuming high amounts of n6 fatty acids. But the TG response is normal for those with the wild type allele type or if those people consuming more n3 FA.¹⁵ This particular allele freq is around 13% for Caucasians. Data show the allelic frequency is 26% for Taiwanese (WH Pan, unpublished). In some reports, it is 30% for Chinese. This has implications for the expression and consequences of the metabolic syndrome in Chinese given a lower mean BMI. And lesser degrees of abdominal fatness when impaired glycaemic status is expressed.

Yet another example is the pressure, often commercial or trade. In order to decrease osteoporosis and fracture, lactose-intolerant populations were recommended to increase *calcium intake* through cow's milk or dairy products sometimes modified and fortified. Other measures may achieve the same objectives in Asian populations like reduced sodium intake to improve renal calcium retention, increased soy for its phyto-estrogen effects on the beta-receptor for estrogen in bone, or increased sunlight exposure for skin vitamin D synthesis or increased intake of vitamin D (with many other benefits which accrue from vitamin D). The dairy strategy generally ignores the bimodal relationship between calcium intakes and bone health between lower and higher calcium consumers. EBN has an obligation to be population relevant.

The review of *dietary guidelines which inform clinical and public health practice must be food-based (FBDGs)* and *dietary reference intakes or recommended dietary intakes* population specific. The problem at present in the region is the relative lack of appropriate studies.

Nevertheless, the ground work in a number of areas for EBN, like that with n-3 and n-6 fatty acids by Lau et al,¹⁶ and upper levels of intake for nutrients and related substances¹⁷ will make this effort easier in Asia. Of immediate interest here is the planned revision of Indonesian recommendations on fatty acid intakes in 2008.¹⁸

An Asia Pacific network could set out a priority list and work-plan to formulate regionally-relevant SRs as the basis for CNPGs. This list might include:

- Food patterns and NRDs
- Nutritional status and susceptibility to high risk infections, e.g. malaria, helminthiasis, tuberculosis, measles, influenza
- Nutritional and physical activity alternatives to pharmaceuticals
- Maternal nutrition and long-term health

- Critical polymorphisms in endemic NRDs, e.g. nutritional anaemia, metabolic syndrome, stroke, osteoporosis
- Food contaminants and disease syndromes, e.g. nanopollutants and respiratory disease, aquatic dioxins and endocrine-disruptive disorders
- Nutritional modulators of inflammatory phenomena and diseases, e.g. in obesity, arthritis, macrovascular disease

STRENGTHENING PUBLIC HEALTH NUTRITION POLICY IN THE ASIA PACIFIC THROUGH EBN

The *MDGs (Millennium Development Goals) of the United Nations*¹⁹ are almost all related to food and nutrition in some way with a strong emphasis on poverty alleviation and on maternal and child health. They reflect the current realization that women play a crucial role in health literacy and family food security; and that there are fetal origins of disease in later life through the nutritional effects on gene expression.

Whilst *nutrition science* must continue to play a major role in the nomenclature and definitions of the discipline, the development of specific nutrient intake reference values and dietary guidelines, preferably food-based,²⁰ with their biomedical orientation, the science required needs also to be societal and environmental.²¹ This appreciation has profound implications for the changing expectations of EBN.

An example of the pressing need for *integrative EBN* in the Asia Pacific region is the evaluation of the synergy between personal behaviours, healthy localities and chronic stress of various kinds (financial, occupational, family and more) and the epidemic of obesity. There is growing piece-meal evidence that chronic stress, mediated by neuro-hormonal pathways, including neuropeptide Y (NPY) and its receptor Y2R, has a greater propensity to cause abdominal obesity and the metabolic syndrome with certain diets.^{22, 23} The question is, what further evidence do we need, in an Asia Pacific context, to allow relevant and realistic policy initiatives?" Obtaining it and responding to that evidence will be one of the ways to strengthen regional public health nutrition policy.

Food Systems

After much controversy in food regulatory circles, and the experience of contaminants, adulteration and inappropriate animal feeding practices in some locations, it is now acknowledged that people have *a right to know the origin of their food* where they are distanced from it and have little if any way of checking its safety at source. In Taiwan in late 2007, legislation was introduced to support this quest by consumers. In Singapore, a small island and city-state, which produces virtually no food of its own, consumers are provided with information about the origin of fruits, vegetables and meats at the point of purchase and/or on labels. Food regulatory systems, like the Trans-Tasman Food Standards Australia-New Zealand (FSANZ) one address whole of food chain *food integrity*. Whilst these might be regarded as matters of ethics and human rights, they, of necessity, must be couched in reliable in-

formation and evidence of effective performance of food systems.

Demographic change

The most impressive demographic change in the Asia Pacific region is the ageing of populations with life expectancies increasing by as much as 1 year every 3 years in some countries/areas, and Asia exhibiting some of the world's best life expectancies (as in Okinawa, Japan, Hong Kong, Macau, Singapore and Australia). These are also paralleled in favourable Health Adjusted Life Expectancies (HALES). At the same time, some countries in the region, notably Indo China have poor life expectancies and others, in the Pacific, amongst the highest prevalence of chronic disease like obesity and diabetes. Australia with its exceptionally good life expectancies is blighted by the dismal health status of its indigenous population.

Migration is also very active through out the region as mothers leave their homes and children in poorer countries to look after the children of wealthier families in other countries, men leave their homes to work on construction projects in other countries, women drift to the cities from poor rural areas in search of work and end in prostitution and poverty, and the middle class gives way with rising national affluence to more poor and more rich citizens. All of this has its nutritional dimension and is not easily amenable to the prevailing methods of EBM or EBN.

It is time for novel and effective solutions to these food-health dilemmas.

Nutritionally-related disease spectrum (NRDS)

Much has been said about the "Double Burden of Nutritionally-Related Disease", which comprises a mix in the one community, family or individual of under- and over-nutrition. In reality, it is even more complex and more helpfully referred to as a spectrum of NRD.

This spectrum often, if not usually, has elements of infectious or inflammatory disease.^{24, 25} This allows a re-conceptualization of NRD processes and provides opportunities to address the problems in new ways with food and optimal energy balance. A new era of EBN can be envisaged as the mechanisms of NRD are revised.

Food security

In the past food security was predicated on good governance, avoidance of conflict, favourable seasons and communities coherent with their local eco-system.²⁶ Over-cropping, grazing or fishing, or rapid and un-regulated industrialization or excessive dependency on firewood for cooking, have often placed food supplies at risk. They have actually led to desertification with water and food too unsafe to consume.

Now, rapid climate change is upon us and there are new threats to our food supplies. It will be particularly problematic for those parts of Asia where biodiversity is most threatened, where there is a limited local food supply or where water and food sources are polluted.

EBN is thus not only relatively new in the scheme of Evidence Based Health Systems (EBHS), but needs to undergo rapid evolution to cope with these demands of climate and food system change. From here on, any

revision of dietary standards or guidelines or policy will require reference to sustainability. Its methodology will involve risk analysis and communication and the formulation of new questions about the knowledge which will allow continuing optimization of health through food.

FUTURE EBN STRATEGIES

Networking

Gathering evidence from acceptable studies and merging the information and findings through SR will continue to be important. But the evidential building blocks require re-definition. In turn, an extensive network of disciplines and professionals will need to be tapped and sensitized.

Engaging with other Disciplines

The shared interests in diverse methodologies will not always be appreciated or welcomed given the gulf in disparate training and professional experience. Bringing agriculture and health, engineering and medicine, earth, atmospheric and biomedical science, care and cure and more together will require sophisticated leadership and flexibility.

Evidence for Policy

Policy is required where the problems and answers are not evident or straightforward. In turn, policy itself requires its own evaluation and evidence for its validity.²⁷ This is a poorly developed area, not least in the field of food and nutrition policy. But when the scenarios are understood and the strategies defined, they can be subject to continual review against the projections. The German government uses a system known as ZOPP (Zielorientierte Projektplanung, or GOPP – Goal Oriented Project Planning)²⁸ whereby the agreed project is the best fit for the evidence and there is a stipulated schedule of review and adjustment of strategy and budget in relation to progress. Other such methods can be appropriated by policy makers. With socio-economic dimensions long-term cohort studies can both create evidence and enable its implementation as policy.

Food-health priorities are established by measuring the burden of disease which is NRD and to what it may be attributed. They are tempered by cost and risk-benefit analysis. However, many of the practicalities for health and other practitioners are worked through case-by-case; rather than antithetic to EBN these documented and critically-appraised experiences strengthen policy and allow the development of robust CNPGs.

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AUTHOR DISCLOSURES

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實證營養在亞太地區的機會與挑戰：臨床實踐與政策設定

實證營養(EBN)已成為實證醫學(EBM)發展中的角色的一部份，可以增進臨床實踐及公共衛生工作之效度、效用及成本效益。當營養相關失調及疾病(NRD)之間與感染性疾病及慢性疾病兩者的關係逐漸被瞭解後，它說明了一大部份的不健康、疾病及死亡的負擔。當資源分配逐漸依賴預防或治療效果的證據時，營養介入也需要證據支持。然而，餵養研究無法如同臨床試驗者熟悉的設計被檢驗。公共衛生上的膳食介入在執行與闡釋上可能更複雜，使得他如世代研究反倒較具吸引力，即便執行上昂貴且耗時。在人口眾多的亞太地區，隨著快速變化的食物系統、人口學、疾病型態及對現在及未來食物安全的考量，台灣在 2007 年，由營養、人口及農業學者、臨床醫生與決策者，連同消費者及原住民利害關係人組成專家小組，召開了一個 EBN 現況評估與情境分析。他們發現對健康及營養政策的臨床指南與計畫而言，需要對 EBN 更重視及瞭解。

關鍵字：系統性回顧(SRs)、臨床營養試驗、組合證據、層級證據、知識、傳統飲食、實證衛生政策(EBHP)。