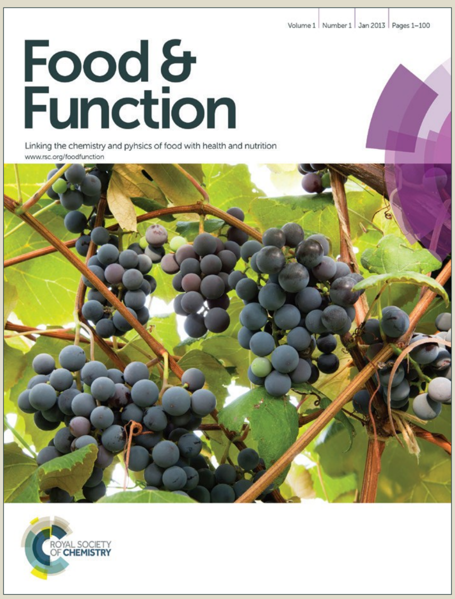
Food & Function

Accepted Manuscript



Journal Name

ARTICLE

Food Structure is Critical for Optimal Health

Mark L Wahlqvist[abc]

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

www.rsc.org/

Much nutrition policy is nutrient-based, supported by extensive nutrient science and food nutrient composition tables and recommendations for dietary evaluation. There are no comparable instruments for food structure. This constitutes a policy and practice gap since food is valued for its textural properties and not simply its chemistry. The structurally-important 'dietary fibre' at first proved of greater interest for its chemistry than its physico-chemistry even to health scientists and workers. As food chemistry became evidently complex, especially for phytonutrients, food-based dietary guidelines became an imperative and were launched by FAO and WHO in Cyprus in 1995. Food-health relationships, after weaning, are best articulated in terms of the achievement of dietary diversity, predicated partly on how intact foods are or in what way they are prepared. Cooking itself has health-promoting characteristics. Even with identical chemistry, food structure makes a major difference to biological and health outcomes. With evidence that food structure contributes to the matrix that food provides for nutrient delivery, and also to gut microbiomic profile and integrity, concern has grown about overly-processed food and health outcomes. The definition and categorisation of 'ultra-processed foods' is now a work-in-progress. Future public health nutritional and clinical nutrition developments will take account of food structure. To these ends, food composition tables will need to provide information like particle size and viscosity. Dietary recommendations will need to take account of food structure, as is the case for Brazil whose first step is "Make natural or minimally processed foods the basis of your diet".

Food systems and food structure

Much ***nutrition policy is nutrient-based***, supported by extensive nutrient science and food nutrient composition tables and recommendations about nutrient intakes for the evaluation of diets. There are virtually ***no comparable instruments for food structure***. This policy and practice gap is more obvious now than it was to our forebears who valued food for its textural properties and used terms like 'roughage', 'crumbly', 'crackling', 'runny' to describe their food.

At every step in ***the food system***, from production to transport, storage, packaging, retailing, pricing and purchase, palatability, and ultimate quality (safety and nutritional), as well as taking into account sustainability, food structure may be affected or a consideration.

Mouth feel as 'healthful' food structural sensoriness

Food systems and the health systems to which they relate are, in general, poorly connected whether in their science, training or practice. This has serious implications for food security and health.[1] Poorly studied, but obvious, is how our sense of ***well-being and mood*** changes with hunger, occasion of eating (timing, celebratory or not), food type, its availability and affordability, presentation or texture, company, location and other contextual factors. The ***social role of food*** is one of its pathways to health, presumptively intertwined with its physical characteristics. Well-being itself is recognised by the World Health Organisation (WHO) as a dimension of health, along with the absence of disease and life expectancy. Now it is also known that disorders of energy regulation, reflected in obesity, the metabolic syndrome and diabetes are also associated with depression, an affective disorder.[2] Energy regulation and its consequences can be ameliorated by a biodiverse diet which retains food structure for its component delivery matrix.[3,4] In addition, the interest in eating or appetite[5] and ability to chew[4] carry survival projections which are dependent on these dietary characteristics.

Mouth feel seems a simple concept and its appreciation elicits a range of emotional responses. Much effort has been invested into its measurement without consensus. Its perceived qualities are numerous by some accounts.[6] They include measurables like cohesiveness where food deformity before rupture is assessed and density where compactness of sample after the bite is measured. Then there are dryness, fracturability, graininess, gumminess, hardness, heaviness, moisture absorption, moisture release, mouthcoating, roughness, smoothness, uniformity of bite and chew, viscosity and wetness. But none of this has been connected with the metabolic or emotional responses which occur or their health outcomes.

[a] *Fuli Institute, Zhejiang University, 866 Yuhangtang Road, Hangzhou, China 310058.*
[b] *National Health Research Institutes, Taiwan.*
[c] *Monash Asia Institute, Monash University, Australia.*
Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/x0xx00000x

Beyond the eyes, ears, nose and mouth , from where the initial sensory inputs by food come, with their dependency on a wide range of food characteristics, food activates receptors and neuroendocrine pathways distal to and seemingly unrelated to these sense organs. For example, ***food memory*** located in the brain's amygdala compiles extensive information which allows differentiation of foods by way of touch colour, smell, texture and taste.[7] Other memories are primed by the supra-nasal olfactory apparatus with its capacity to distinguish billions of olfactant combinations***. Tastant receptors*** are to be found not only in the gut, but, along with other food component receptors, throughout the body.[8-10] That said, this description is bereft of the potential modification of this physiology by food excipients, as would obtain with medication and pathophysiology. Myriads of food structural possibilities are described.[11] Thus, if food is simplified to a set of nutrients with negligible structure, it is inevitable that ***an enormous collection of food and ecological information will be in deficit.*** As yet, we are only at the earliest understanding of what this means for human health and survival. At the same time, we are often challenged clinically to provide what we know to be the least nutritional constituents compatible with life in the short to medium term, notwithstanding ***what may be required for optimal nutrition in patients unable to eat normally.***

There may be rather subtle changes taking place in ***the potential of foods to be health protective.*** In breeding food plants to be more palatable, they have been made less bitter, a taste which we used to learn to appreciate in the safety of our traditional diets. But this means less of compounds and their structural associations which have been health protectants.[12]

Food structure–its biological relevance

It is somewhat curious how long into *the 'nutrient era' of nutrition science* that food structure was seen to be vital to human health. People talked about 'roughage' as being both a judgement of 'cheap food' and 'healthy' depending on a host of socio-cultural considerations. But by the latter half of the 20th century ***'dietary fibre'***, initially from plantain (a woody banana) in Uganda and, later, from other plant-based foods, especially grains and other seeds, it came to be accepted as important for bowel health. Its absence then became an indicator of dietary patterns that predisposed to so-called chronic disease including obesity, cardiovascular disease, diabetes and certain cancers. Yet even the structurally-important 'dietary fibre' proved of greater interest for its chemistry than its physico-chemistry during its early interest to health scientists and workers. This had a commercial attraction inasmuch as it could be isolated from intrinsically 'healthy' foods and added as ingredient to others perceived to be less healthy. Some of its more immediate properties like satiety and laxation could be transferred as ingredients, but more long-term benefits of the food supplementation or fortification approach were not so promising- and some even detrimental, particularly with large bowel cancer.[13] Energy regulation by physical activity, background diet, food component interactions and gender have proven more important.[14] What ***a food or meal*** does or is subject to as a whole is of greater physiological or pathophysiological interest than any one component. This applies to the particular gut functions with which food structure is involved, particularly mastication, swallowing, the matrix that food provides for nutrient and other bioactive food component delivery and gut microbiomic profile and integrity.

In regard to the immediate effects of a meal, it is of interest that a culinary herb like turmeric in an amount akin to customary usage (1 g) can improve working memory, without the risk and cost that might attend the use of extracted curcumin.[15] This points to the safety features of food structure - and food science risk management.

Even with ***identical chemistry***, food structure can make a major difference to biological and health outcome. Differences in macronutrient handling by the gut for ***peanuts*** of different physical form were found with less fat absorbed from nuts than the butter or oil.[16] The same was found for insulin and glycaemic responses to ***fruit*** in different forms.[17] In due course, it became clear that, while almost any fruit was protective against diabetes when eaten intact, fruit juice increased the risk.[18] Thus, the food matrix can play a substantial role in nutritionally-related health.

Serial publications on ***Kiwi fruit and constipation*** indicate how researchers progressively tackle a food-health issue for better or worse.[19-21] Reasonably good evidence was first provided about the laxative effects of the fruit. Then an active component was postulated to be responsible and studied without finding convincing effects. Why do this? After all, it is the structured form of the fruit which has the health benefit. Perhaps new cultivars might be bred to retain an active principle and the overall health value. Or is it just a matter of intellectual property and the commercial marketing potential for an isolate and specific effect rather than an available, affordable, sustainable and healthful fruit? Food structure and processing science and technology is beset with these questions.

Major advances in our understanding of how food intake affects the ***human gut microbiome*** also indicate the importance of food structure. While we may each have one of a few characteristic core gut microbiomes, these can be profoundly and rapidly perturbed by diet. Gut microbiomic profile changes within days with the introduction of a plant-based or animal-based diet.[22] Theses profiles are now known to be relevant to a wide range of health outcomes from energy regulation to brain function.[23] The food matrix now assumes more human health significance than heretofore conceived.

Food-based Dietary Guidelines (FBDGs)

As food chemistry revealed overwhelming component complexity, especially that of phytonutrients, it became an imperative to develop food-based dietary guidelines, which were launched by FAO and WHO in Cyprus in 1995. Food-health relationships, after weaning, could be best articulated in terms of the achievement of dietary diversity, which itself was predicated on how intact the foods scored were or in what way they were prepared.[24]

Food structure and health

The contributions of food structure to pathophysiology are ***not simply to do with a particular foodstuff and occasion of eating***, although such acute or short-term evaluations have been instructive in the understanding of mechanisms. What also matters is how meal-type and background diet alters responsiveness, how this can be adaptive, accumulative or more detrimental with time, and how a disease state may itself alter the effects of a given food structure.

These points can be illustrated by the development of the current approaches to the ***dietary management of diabetes***. In the late 1970s, a series of publications changed the thinking about food and nutrition science and the approach to the nutritional prevention and management of diabetes, especially type 2 diabetes (T2DM). In 1976, 2 groups showed that dietary fibre isolates improved glycaemic status in those with diabetes.[25,26] This was followed by confirmatory studies published in 1977 and 1978.[27,28] The ***glycaemic index (GI) concept*** was advanced in 1981.[29] In 1977, Haber et al reported that, for apples (whole, pureed and juice), food structure itself, attributed to dietary fibre in cell walls, was responsible in part for the degree of glucose and related insulin response in healthy people.[17] In 1978, Wahlqvist et al published findings in health and diabetes to show that saccharide chain length (mono-, di-, penta- and poly-) made no measurable difference to the glucose, insulin or other metabolic responses to carbohydrate load.[30] This was in contradistinction to the view which had prevailed since the 1920s that chain length accounted for so-called fast and slow carbohydrates and which had underpinned faulty dietary advice to people with diabetes. It was now clear that ***the avoidance of unrefined plant foods in diabetes was not justified*** and that these could improve the nutritional status of patients.

However, there was now a dichotomy or combination of 2 approaches to nutrition and diabetes – the ***use of dietary fibre as a food ingredient or supplement and an emphasis on relatively intact or unrefined plant foods***. There were also those who still insisted on limited and fixed portions of carbohydrate, whatever its matrix, meal or dietary pattern context, usually with higher fat intakes than optimal. Studies slowly emerged to show that certain foods like beans (legumes) had a particular merit in diabetes management[31,32] and, later in survival in populations at large.[33,34] ***The effects of foods were also not the same in health as in diabetes***.[35,36] Cooking affected the metabolic responses.[36] It took almost 3 weeks for the full benefits of a higher unrefined plant food diet to be fully realised and this was dependent on reduced nocturnal gluconeogenesis.[37]

There have been ***few long-term studies*** to show whether a lower glycaemic load from low GI foods is associated with less complication of diabetes. In Da Qing, China , microvascular complications have been reduced with a combination of exercise and diet over 6years .The dietary approach included an increase vegetable intake , but also attention to sugar and alcohol intakes and to weight management.[38] As the ***spectrum of diabetes complications*** became more evident, especially with the inclusion of ***neurodegeneration*** (dementia, Parkinson's disease, affective disorders),[2,39,40] the evidence has grown that nutritional management must also take advantage of the energy regulatory role which food structure can provide through increased satiety[41] and without compromise in physical performance.[42] A biodiverse diet where food structure has natural characteristics remains important not only in the prevention of diabetes, but also in its management to prolong disability-free survival.[3] Although the excess mortality in diabetes relates to its complications, there are some pathways which merit particular attention. One is cognitive function, itself a contributor to the reduced disability-free survival in diabetes, but which association is minimised by dietary diversity.[43] Another is the accentuated mortality risk when hyperhomocysteinaemia is found in diabetes, possibly attributable to the increased risk of a complex cardiomyopathy.[44] Unfortunately, while ***mortality risk in diabetes is less with dietary diversity***, the advent of homocysteinaemia seems to preclude this which demonstrates the persistent ***barriers to effective nutritional management of diabetes***.[3,44] These limitations to some extent reflect the limited approach which a continuing macronutrient-centred, particularly carbohydrate, approach lacking in food science sophistication and in socio-cultural context encourages.[45,46]

Clinical needs for modified food structure

With compromised gut function or altered nutritional needs in disorder and disease, food structure may need to be tailored accordingly. In an increasing number of food regulatory jurisdictions, ***Foods for Special Medical Purposes (FSMP)*** are being scheduled. Since risk and benefit need to be individualised, clinical supervision and support is usually expected.

Examples of FSMP where food structure or texture is modified include:

- Nutrient or other food component Bioavailabity
- Energy regulation where impaired as in body compositional disorders
- Glycaemic index & load /Insulin resistance
- Chewing difficulty
- Dysphagia (textures are often standardised through speech therapy societies as in Australia)
- Gut motility disorders (eg autonomic neuropathy such as gastroparesis)
- Enteral feeding

Dysphagia (swallowing disorders) is found in the following clinical settings:

- Presbyphagia (age-related swallowing difficulty)
- Nervous system disorders, such as Parkinson's disease and cerebral palsy
- Problems with the oesophagus, including GERD (gastroesophageal reflux disease)
- Stroke
- Head or spinal cord injury
- Cancer of the head, neck, or oesphagus

Cooking

Cooking up to 5 times per week has been shown to be a predictor of survival in later life.[47,48] Its ***health-promoting characteristics*** are probably complex requiring organisational, mental and physical skills as well as resources. But it does underscore the value of personal control over one's food preparation and the opportunity to retain food structural features otherwise lost.

Processed food

Please do not adjust margins

There is growing evidence that the degree of food processing is related to health outcomes, with the most processed being linked to the current patterns of so-called chronic disease (which may have a rapid course) including energy and metabolic dysregulation(obesity, diabetes) cardiovascular, cerebrovascular, neoplastic, osteoporotic, other musculo-skeletal, neurodegenerative and mental health.

In order to identify, monitor and address this problem, ***three food processing categories*** have been proposed:[49-51]

Group 1 being minimally processed (including traditional cooking)

Group 2 lightly processed, and

Group 3 'ultra-processed.'

(Includes "sugared soft drinks, cakes and pastries, burgers, pizza, and potato chips")

The Brazilian dietary guidelines now recommend avoidance of ultra-processed foods and other food authorities are likely to follow suit. The first step to a healthy diet in the Brazilian guidelines is "Make natural or minimally processed foods the basis of your diet".[52]

An example of the ramifications of this appreciation of the health risks of ultra-processing is what it means for the promotion of preferred dietary patterns like that of the Mediterranean[53] should they be more processed.[54]

The definition and categorisation of 'ultra-processed foods' is now a work-in-progress of In Foods at FAO along with measures of food biodiversity.[55]

Microstructural contaminants and additives

Adventitious microparticles may include ***microplastic*** and pesticide or other residues (co-aggregated and transported with microplastic).[56] Plastic particles can account for various adverse biological phenomena including immunotoxicology, altered gene expression and apoptosis through both chemical and particle stress.[57] While most microplastic is 1-5 mm, it also exists as ***nanoplastic*** which can accumulate in various tissues including brain with long half-lives and can cross the placenta into the fetus.

Nanonutrients are appearing in the market place with little or no reference to safety considerations. The limited work in animal models is well short of what is needed to address human effects.[58] Preliminary and cautionary positons have been taken by regulatory bodies in some jurisdictions.[59] This position is illustrated by the case of excessive delivery of iron in supplementary form and its association with increased mortality from overwhelming malarial infection in infants and demonstrates the logic for food as a delivery system as preferred in the ***Harvest Plus biofortification program.***[60]

There are potential benefits to be had from nanotechnology applied to foodstuffs. These include shelf-life, reduced energy density (eg by a decrease in the fat: water ratio), improved food component density where only limited quantities of food may be eaten, and palatability (although this may enable food to be eaten when otherwise compromised, it may be accompanied by the loss of healthful food components as with ***bitter components***, as reported by Marta Zaraska in 2015).[12] ***The risks*** are inappropriate bioavailability (as in the example given of excess iron),[60] untoward and ill-defined interactions in biological transport and destination tissue ,and long-half-lives, tissue accumulation & toxicity (as evidenced with nanoplastic).[56,57]

Future Food

- Future ***public health nutrition***, particularly dietary guidelines, and ***clinical nutrition*** developments should be required to take account of food structure.
- To these ends, ***food composition tables*** will need to provide information like degree of processing, texture, particle size and viscosity.[55]
- The ***health system will need to be food system conscious*** and understand the econutritional basis of disease.[61]

The risk of inappropriate food processing with adverse health outcomes is increasing on account of a narrowness in food and nutrition science education, the misrepresentation of value-addedness of foods for health advantage when profit is the over-arching motive, size-of-population pressure, and poor food and health literacy in the community.

The International Science Council (ICSU) and the United Nations Standing Committee on Nutrition (UN-SCN), through their constituencies like IUFoST (International Union of Food Science and Technology), IUNS (International Union of Nutritional Sciences), FAO (Food and Agricultural Organisation) and WHO (World Health Organisation), could establish working parties charged with the responsibility to enable and ensure that food structure is reflected in their science and policy.

Since the food system throughout is reflected in the ultimate structure and other characteristics of food for consumption, it can sub-serve the ***UN (United Nations) Global Goals*** promulgated in September 2015 to do with food security, including availability, affordability and sustainability.

Notes and references

1 M. L. Wahlqvist, J. D. Keatinge, C. D. Butler, S. Friel, J. McKay, W. Easdown, K. N. Kuo, C. J. Huang, W. H. Pan, R. Y. Yang, M. S. Lee, H. Y. Chang, Y. W. Chiu, D. Jaron, M. Krawinkel, S. Barlow, G. Walsh, T. L. Chiang, P. C. Huang and D. Li, *Asia Pac J Clin Nutr*, 2009, **18**, 688-702.
2 M. L. Wahlqvist, M. S. Lee, S. Y. Chuang, C. C. Hsu, H. N. Tsai, S. H. Yu and H. Y. Chang, *BMC Med*, 2012, **10**, 150.
3 M. S. Lee, Y. C. Huang, H. H. Su, M. Z. Lee and M. L. Wahlqvist, *J Nutr Health Aging*, 2011, **15**, 815-821.
4 M. S. Lee, Y. C. Huang and M. L. Wahlqvist, *J Am Geriatr Soc*, 2010, **58**, 1072-1080.
5 Y. C. Huang, M. L. Wahlqvist and M. S. Lee, *Appetite*, 2014, **83**, 89-96.
6 Wikipedia, Mouthfeel, https://en.wikipedia.org/wiki/Mouthfeel, (accessed 19th October, 2015).
7 H. Nishijo and T. Ono, *Asia Pac J Clin Nutr*, 1992, **1**, 3-12.
8 D. E. Cummings, *Am J Clin Nutr*, 2015, **102**, 717-718.
9 S. Janssen and I. Depoortere, *Trends Endocrinol Metab*, 2013, **24**, 92-100.
10 M. van Avesaat, F. J. Troost and D. Ripken, 2015, **102**, 729-735.
11 I. Heertje, *Food Structure*, 2014, **1**, 3-23.
12 M. Zaraska, *New Scientist*, 2015, 26-30.
13 C. S. Fuchs, E. L. Giovannucci, G. A. Colditz, D. J. Hunter, M. J. Stampfer, B. Rosner, F. E. Speizer and W. C. Willett, *N Engl J Med*, 1999, **340**, 169-176.

14 WCRF, Colorectal cancer, http://www.dietandcancerreport.org/cup/current_progress/colorectal_cancer.php, (accessed 20th October, 2015).
15 M. S. Lee, M. L. Wahlqvist, Y. C. Chou, W. H. Fang, J. T. Lee, J. C. Kuan, H. Y. Liu, T. M. Lu, L. Xiu, C. C. Hsu, Z. B. Andrews and W. H. Pan, *Asia Pac J Clin Nutr*, 2014, **23**, 581-591.
16 A. S. Levine and S. E. Silvis, *N Engl J Med*, 1980, **303**, 917-918.
17 G. B. Haber, K. W. Heaton, D. Murphy and L. F. Burroughs, *Lancet*, 1977, **2**, 679-682.
18 I. Muraki, F. Imamura, J. E. Manson, F. B. Hu, W. C. Willett, R. M. van Dam and Q. Sun, *BMJ*, 2013, **347**, f5001.
19 C. C. Chang, Y. T. Lin, Y. T. Lu, Y. S. Liu and J. F. Liu, *Asia Pac J Clin Nutr*, 2010, **19**, 451-457.
20 S. Kindleysides, B. Kuhn-Sherlock, W. Yip and S. D. Poppitt, *Asia Pac J Clin Nutr*, 2015, **24**, 421-429.
21 E. C. Rush, M. Patel, L. D. Plank and L. R. Ferguson, *Asia Pac J Clin Nutr*, 2002, **11**, 164-168.
22 L. A. David, C. F. Maurice, R. N. Carmody, D. B. Gootenberg, J. E. Button, B. E. Wolfe, A. V. Ling, A. S. Devlin, Y. Varma, M. A. Fischbach, S. B. Biddinger, R. J. Dutton and P. J. Turnbaugh, *Nature*, 2014, **505**, 559-563.
23 E. A. Mayer, *Nat Rev Neurosci*, 2011, **12**, 453-466.
24 M. L. Wahlqvist, *Ecol Food Nutr*, 2009, **48**, 457-481.
25 D. J. Jenkins, D. V. Goff, A. R. Leeds, K. G. Alberti, T. M. Wolever, M. A. Gassull and T. D. Hockaday, *Lancet*, 1976, **2**, 172-174.
26 T. G. Kiehm, J. W. Anderson and K. Ward, *Am J Clin Nutr*, 1976, **29**, 895-899.
27 D. J. Jenkins, T. M. Wolever, T. D. Hockaday, A. R. Leeds, R. Howarth, S. Bacon, E. C. Apling and J. Dilawari, *Lancet*, 1977, **2**, 779-780.
28 D. J. Jenkins, T. M. Wolever, A. R. Leeds, M. A. Gassull, P. Haisman, J. Dilawari, D. V. Goff, G. L. Metz and K. G. Alberti, *BMJ*, 1978, **1**, 1392-1394.
29 D. J. Jenkins, T. M. Wolever, R. H. Taylor, H. Barker, H. Fielden, J. M. Baldwin, A. C. Bowling, H. C. Newman, A. L. Jenkins and D. V. Goff, *Am J Clin Nutr*, 1981, **34**, 362-366.
30 M. L. Wahlqvist, E. G. Wilmshurst and E. N. Richardson, *Am J Clin Nutr*, 1978, **31**, 1998-2001.
31 H. C. Simpson, R. W. Simpson, S. Lousley, R. D. Carter, M. Geekie, T. D. Hockaday and J. I. Mann, *Lancet*, 1981, **1**, 1-5.
32 B. J. Venn and J. I. Mann, *Eur J Clin Nutr*, 2004, **58**, 1443-1461.
33 W. C. Chang, M. L. Wahlqvist, H. Y. Chang, C. C. Hsu, M. S. Lee, W. S. Wang and C. A. Hsiung, *Public Health Nutr*, 2012, **15**, 663-672.
34 I. Darmadi-Blackberry, M. L. Wahlqvist, A. Kouris-Blazos, B. Steen, W. Lukito, Y. Horie and K. Horie, *Asia Pac J Clin Nutr*, 2004, **13**, 217-220.
35 R. W. Simpson, J. McDonald, M. L. Wahlqvist, L. Atley and K. Outch, *Am J Clin Nutr*, 1985, **42**, 449-453.
36 R. W. Simpson, J. McDonald, M. L. Wahlqvist, L. Atley and K. Outch, *Am J Clin Nutr*, 1985, **42**, 462-469.
37 R. W. Simpson, J. McDonald, M. L. Wahlqvist, N. Balasz, M. Sissons and L. Atley, *Am J Clin Nutr*, 1988, **48**, 104-109.
38 Q. Gong, E. W. Gregg, J. Wang, Y. An, P. Zhang, W. Yang, H. Li, H. Li, Y. Jiang, Y. Shuai, B. Zhang, J. Zhang, R. B. Gerzoff, G. Roglic, Y. Hu, G. Li and P. H. Bennett, *Diabetologia*, 2011, **54**, 300-307.
39 C. C. Hsu, M. L. Wahlqvist, M. S. Lee and H. N. Tsai, *J Alzheimers Dis*, 2011, **24**, 485-493.
40 M. L. Wahlqvist, M. S. Lee, C. C. Hsu, S. Y. Chuang, J. T. Lee and H. N. Tsai, *Parkinsonism Relat Disord*, 2012, **18**, 753-758.
41 D. S. Grimes and C. Gordon, *Lancet*, 1978, **2**, 106.
42 M. J. Sparks, S. S. Selig and M. A. Febbraio, *Med Sci Sports Exerc*, 1998, **30**, 844-849.
43 R. C. Chen, Y. H. Chang, M. S. Lee and M. L. Wahlqvist, *Food Nutr Res*, 2011, **55**.
44 M. Wahlqvist, L. Xiu, M. Lee, R. Chen, K. Chen and D. Li, *Asia Pac J Clin Nutr*, In press.
45 L. S. Gross, L. Li, E. S. Ford and S. Liu, *Am J Clin Nutr*, 2004, **79**, 774-779.
46 J. Tay, N. D. Luscombe-Marsh, C. H. Thompson, M. Noakes, J. D. Buckley, G. A. Wittert, W. S. Yancy, Jr. and G. D. Brinkworth, *Am J Clin Nutr*, 2015, **102**, 780-790.
47 R. C. Chen, M. S. Lee, Y. H. Chang and M. L. Wahlqvist, *Public Health Nutr*, 2012, **15**, 1142-1149.
48 R. Erlich, A. Yngve and M. L. Wahlqvist, *Public Health Nutr*, 2012, **15**, 1139-1140.
49 C. Monteiro and G. Cannon, *World Nutrition*, 2012, **3**, 406-434.
50 C. A. Monteiro, R. B. Levy, R. M. Claro, I. R. de Castro and G. Cannon, *Public Health Nutr*, 2011, **14**, 5-13.
51 J. C. Moubarac, A. P. Martins, R. M. Claro, R. B. Levy, G. Cannon and C. A. Monteiro, *Public Health Nutr*, 2013, **16**, 2240-2248.
52 R. Sichieri, S. E. Chiuve, R. A. Pereira, A. C. Lopes and W. C. Willett, *Cad Saude Publica*, 2010, **26**, 2050-2058.
53 A. Trichopoulou, A. Kouris-Blazos, M. L. Wahlqvist, C. Gnardellis, P. Lagiou, E. Polychronopoulos, T. Vassilakou, L. Lipworth and D. Trichopoulos, *BMJ*, 1995, **311**, 1457-1460.
54 R. Hoffman and M. Gerber, *Nutrients*, 2015, **7**, 7925-7964.
55 FAO/INFOODS., *FAO/INFOODS Analytical Food Composition Database Version 1.0 –AnFooD1.0*, FAO, Rome, 2012.
56 R. C. Thompson, C. J. Moore, F. S. vom Saal and S. H. Swan, *Philos Trans R Soc Lond B Biol Sci*, 2009, **364**, 2153-2166.
57 N. Seltenrich, *Environmental Health Perspectives*, 2015, **123**, A35-A41.
58 F. Sawosz, L. Pineda, A. Hotowy, S. Jaworski, M. Prasek, E. Sawosz and A. Chwalibog, *Arch Anim Nutr*, 2013, **67**, 347-355.
59 A. Schäfer, Nanomaterials in food contact materials -EU Regulatory issues, http://www.ilsi.org/Europe/Documents/PMWS2012/S2.7%20WSPM12%20Schaefer.pdf, (accessed 19th October, 2015).
60 Harvest Plus., Iron and malaria: addressing potential risks from food-based approaches to alleviate iron deficiency among children less than two years of age exposed to malaria, http://www.harvestplus.org/sites/default/files/H+%20Iron%20and%20malaria%20position%20paper_11.23.10.pdf, (accessed 19th October 2015).
61 M. L. Wahlqvist, *Asia Pac J Clin Nutr*, 2014, **23**, 1-15.