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Factors determining the integration of nutritional genomics into clinical practice by Registered Dietitians

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Conflict of Interest

MA has worked with several start-ups as a consultant in the area of nutrigenetic testing.

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Abstract

Background: Personalised nutrition has the potential to improve health, prevent disease and reduce healthcare expenditure. Whilst research hints at positive consumer attitudes towards personalized nutrition that draws upon lifestyle, phenotypic and genotypic data, little is known about the degree to which registered dietitians (RD) are engaged in the delivery of such services. This review sought to determine possible factors associated with the integration of the emerging science of Nutritional Genomics (NGx) into the clinical practice setting by practicing registered dietitians.

Scope: Search of online databases (Pubmed; National Library of Medicine; Cochrane Library; Ovid Medline) was conducted on material published from January 2000 to December 2014. Studies that sampled practicing dietitians and investigated integration or application of NGx and genetics knowledge into practice were eligible. Articles were assessed according to the American Dietetic Association Quality Criteria Checklist.

Key Findings: Application of nutritional genomics in practice has been limited. Reluctance to integrate NGx into practice is associated with low awareness of NGx, a lack of confidence in the science surrounding NGx and skepticism toward Direct to consumer (DTC) products. Successful application to practice was associated with knowledge about NGx, having confidence in the science, a positive attitude toward NGx, access to DTC products, a supportive working environment, working in the clinical setting rather than the public health domain and being in private rather than public practice.

Conclusions: There is a need to provide RGs with a supportive working environment that provides ongoing training in NGx and which is integrated with clinical practice.

Keywords: Dietitians; nutritional genomics; involvement; personalised nutrition.

Background

Since the completion of the Human Genome Project in 2003 (Venter, 2011), vast progress has been made in the field of identifying human genetic variations which may play a role in the development of obesity and chronic diseases such as diabetes, cardiovascular disease and dementia (Nielsen & El-Sohemy, 2012). With regards to modernizing healthcare, the United Kingdom (UK) government, in particular, is aiming to lead genomic research and its application within the NHS (NHS, 2015). According to the 5-Year Forward Review Report (DOH, 2014), personalized healthcare will be delivered using digital technologies and will be informed by genomic data, which is poised to revolutionize healthcare toward personalized treatment plans. Although personalized nutrition is not explicitly mentioned within the plans, diet and lifestyle play a key role in the prevention of non-communicable diseases, the European Commission (EC) has pledged make personalised diets a priority by 2050 (EC, 2014). As a consequence, nutrition is expected to become a key focus for prevention. It has been speculated that wide adoption of personalized nutrition could result in health care expenditure reduction of 13% (Marsh & McLennan, 2014).

Rapid developments in genomic research have led to the emerging field of nutritional genomics (NGx), which encompasses both nutrigenomics (the study of the impact of diet on gene expression) and nutrigenetics (which looks at how our genetic make-up affects nutrient response) (Müller & Kersten, 2003). Rosen *et al.*, (2006, p1243) defined the application of NGx as "the interpretation of genetic profile information with subsequent therapeutic prescription of an individualized dietary regimen that was tailored to the prevention or management of one or more specific diseases or conditions identified by the genetic profile". In addition, the position paper

of the Academy of Nutrition and Dietetics (AND) on NGx states "The application of NGx in clinical practice requires that healthcare professionals understand, interpret and communicate complex test results in which the actual risk of developing a disease may or may not be known" (Camp & Trujillo 2014, p299). The purpose of nutritional genomics is to enable the delivery of a personalized approach to nutrition intervention which is based on lifestyle, genotype and/or phenotype and in doing so, to prevent or mitigate the development of chronic diseases (Fenech *et al*., 2011).

The clinical utility of genetic tests designed to inform personalised nutrition plans have been widely criticized mainly because of a lack of evidence for strong gene-nutrient interactions as well as lack of effectiveness regarding (short and long term) behavior change (Ries & Castle, 2008; Fraker & Mazza, 2010; Burke, 2014; Pavlidis *et al*., 2015; Hollands *et al*., 2016). Against this, there is mounting evidence regarding the benefits of a personalized nutrition approach with regards to dietary behavior change (Arkadianos *et al*., 2007; Chao, 2008; Tierney *et al*., 2011; Nielsen & Sohemy, 2012; Nielsen & El-Sohemy, 2014; Frankwich *et al*., 2015; Celis-Morales *et al*, 2016; Fallaize *et al*., 2016; Livingstone *et al*., 2016).

The term 'personalized nutrition' has, at times, been used synonymously with 'nutritional genomics'. Personalized nutrition, however, has been defined more broadly. The Food4me project (Food4me.org) was a European-wide research effort that looked extensively into public perceptions of, attitudes towards, and preferences for delivery of different types of personalised nutrition. The potential of different business models for delivering personalized nutrition were also examined (Ronteltap *et al*., 2012; Stewart-Knox *et al*., 2013; Berezowska *et al*., 2014; Poinhos *et al*., 2014; Stewart-Knox *et al*., 2014; Fallaize *et al*., 2015; Rankin *et al*., 2016; Fischer *et al*., 2016; Berezowska *et al*., 2015). Gene-based personalized nutrition was extensively researched in previous large

studies such as LIPGENE and PREDIMED, and has already been commercialized through various avenues (Ronteltap *et al*., 2012). For the purpose of the Food4me project, personalized nutrition was defined on three levels: dietary analysis; dietary analysis + phenotypic information (eg. blood nutrient profile, anthropometry); or dietary analysis + phenotype + genotype (Celis-Morales *et al*, 2016; Fallaize *et al*., 2016; Livingstone *et al*., 2016). Results from the Food4me project results have indicated a willingness among the European public to pay for a personalized nutrition service which includes some combination of dietary, phenotypic and genotype data, at least for some groups of individuals in the population (Ries *et al*., 2010; Fischer *et al*., 2016; Stewart-Knox *et al*., 2016). Dietitians were identified as being among preferred providers of personalized nutrition (Stewart-Knox *et al*., 2013; Poínhos *et al*., 2014; Fallaize *et al*., 2015; Stewart-Knox *et al.*, 2016). Hence, RD´s may have an important role to play in being the bridge between the science and the client (Gilbride, 2007). It is crucial, therefore, to address any gaps that may exist between potential future demand and supply of practitioners adequately trained in the science at all levels. Registered Dietitians (RD´s) already provide personalized nutrition plans based on various parameters such as age, medical history as well as blood biochemical data (Nielsen & El-Sohemy, 2012; BDA, 2013). NGx adds an additional layer of personalization by including genotype information.

Debate, meanwhile, continues as to whether RD´s should be delivering gene-based service when there is only limited evidence for links between diet and genetics (Görman *et al*., 2013). Professional guidelines, therefore, do not yet explicitly recommend that nutrigenetic testing is applied in routine dietetic practice (Camp & Trujillo, 2014). Meanwhile, there is a growing expectation that RD´s should be competent in genetics (HCPC, 2013; BDA, 2013), have a basic knowledge of nutritional

genomics (Learning Outcomes for Dietitians on Nutritional Genomics, 2014) and be prepared to integrate NGx into their practice (Collins et al., 2014). There has also been an education drive for front-line healthcare practitioners to become familiar with genomics (Public Health Genomics Education, 2015). Only a few research studies, however, appear to have examined healthcare professionals' (including RD´s) engagement in the field of nutritional genomics (Lapham *et al*., 2000; Rosen *et al*., 2006; McCarthy *et al*., 2008; Whelan *et al*., 2008; Collins *et al*., 2013). With an interested potential consumer market (Stewart-Knox *et al*., 2016; Fischer *et al*., 2016), it is essential to identify and address any barriers that may affect the integration of nutrigenomic science into practice. Any lack of engagement and/or understanding of the science by nutrition providers, may impact negatively upon public perception which could have a knock-on effect on public health. The aim of this review, therefore, has been to identify and understand factors that are associated with the integration and application of NGx by registered dietitians in clinical practice. Clinical dietetic practice refers both to advising clients or patients, who may or may not have medical conditions, on nutrition (BDA, 2013). The application or integration of NGx is defined as the use of information (including genetics), to assess an individuals´ predisposition or risk of developing a disease and maintain health (Collins *et al*., 2014; Camp & Trujillo, 2014; NHS, 2014).

Method

Databases searched were: Pubmed; Ovid Medline; Nat Lib Med; Cochrane Library). Keyword strategy included a combination of Dietitian or Dietician AND Nutritional Genomics OR Nutrigenomics OR Nutrigenetics OR Diet- Gene Interaction

AND Integration OR Application OR Translation OR Involvement OR Attitude OR Clinical Practice.

All studies published between January 2000 and December 2014 were considered eligible for inclusion. Additional references were found in the bibliography of articles. Review papers, papers not in English and animal studies were excluded. Studies that looked only at dietetic students were also excluded as the purpose of this review has been to understand the perspective of registered dietitians in clinical practice ie. those already qualified. A total of 917933 records were found. After limits were applied (human studies, English and date range) 11057 articles remained. Following this step, 11048 were screened and excluded on the basis of the title or if the abstract did not meet the criteria for the review.

Figure 1 here

Data Extraction and Analysis

A total of 9 eligible studies were identified (table 1). Each study was assessed according to the American Dietetic Association Quality Criteria Checklist (ADA, 2003). This entailed answering a number of questions with the response 'yes', 'no' or 'neutral' related to each study. If most of the answers were yes, the study received a positive quality rating, if most of the answers were no, the study received a negative rating, and if most answers were not applicable, the study received a neutral rating. The evidence base is very small but mostly of positive quality as indicated in Table 1.

Insert table 1 here

Results

Inclusion criteria as outlined in Table 1 were met by 9 studies. The research mostly included level 4 studies (cross-sectional, case-studies) which were conducted in mainly English-speaking countries including UK, US, Canada, Australia and South-Africa. Six out of nine studies were surveys (either mailed or online), two were mixed-method (survey and interviews or focus groups) and one was a focus group only. The study designs were mainly cross-sectional in nature, meaning it included dietitians from various clinical backgrounds and specializations, levels of post-graduate education as well as years of experience. Response rate ranged between 13% (Collins *et al*., 2013) and 65% (Whelan *et al*., 2008). The number of participants in each study ranged between 16 (Li *et al*., 2014) to 1844 (Collins *et al*., 2013). As there were a limited number of studies and methods across studies were not consistent, a narrative approach will be adopted to analyze the findings.

1. Key factors associated with the integration of NGx into practice

1.1. Involvement with NGx in the Clinical and Education Setting

Involvement in NGx has been identified as one of the key factors associated with integration into practice (Whelan *et al*., 2008; Oosthuizen, 2011; Collins *et al*., 2013). Whelan and colleagues (2008) and Collins and colleagues (2014) have broadly defined the term 'involvement' (in NGx), to refer to a various clinical (11) and educational (3) activities concerned with genetics and nutritional genomics. These included clinical activities such as "discussing the genetic and dietary basis of disease" or "providing

nutrition advice to patients which is specific to the genetic nature of their condition" as well as educational activities such as "providing training to students or other healthcare professionals on diseases that have both a dietary and genetic component". Involvement in NGx has been predominantly measured via online surveys using Likert scales (Christianson *et al*., 2005: Rosen *et al*., 2006; Whelan *et al*., 2008; Oosthuizen, 2011; Collins *et al*., 2013; Cormier *et al*., 2014). Involvement has been found to be low, such that fewer than 50% of dietitians based in the clinical setting reported engaging in activities associated with NGx (Whelan *et al.*, 2008; Oosthuizen., 2011; Collins *et al*., 2013). Activities included referring individuals for genetic counselling. The proportion was even lower in the educational setting (46.1%) where activites included being active in teaching genetics to students and other healthcare professionals (Whelan *et al*., 2008; Oosthuizen., 2011; Collins *et al*., 2013).

A multinational online survey study (N=1844) conducted by Collins *et al* (2013) in the United Kingdom (UK), Australia and the United States (US), indicated that genetics and nutritional genomics activities were not not always clearly separated, as implied in the Whelan *et al*. (2008) study. Given the study was cross-sectional in nature and that RD´s from various sub-disciplines were included in the study it was not possible to distinguish between those who were dealing with monogenetic (congenital) disorders and those with polygenetic disorders. For the purpose of statistical analysis the 'involvement' variable score was calculated from the sum of clinical and educational activities, rendering it difficult to separate out and establish the level of integration specifically into clinical dietetics practice.

1.2 Confidence in NGx Science and Technology

Confidence in the science of genetics and NGx has been identified as one of the strongest predictors of having integrated it into practice (Grimaldi, 2014). Dietitians with a moderate/high level of confidence (54%) were more likely than those with lower confidence to be involved in activities relating to genetics and NGx (Collins *et al*., 2013). Not only did the dietitians lack confidence, but it also appeared that confidence decreased with increasing years of experience (following qualification) (Collins *et al*., 2013). Rosen and colleagues reported the results of a survey (N= 995) conducted in the US in 2004 (Rosen *et al*., 2006). The results indicated that 60% of RD´s had little confidence in their ability to provide nutrition services based on NGx. According to the multinational (US; UK; and, Australia) survey conducted by Collins and colleagues (2013), confidence in NGx was associated with having engaged in education or clinical activities. Those who were involved in NGx appeared to have greater confidence in the science and in their ability to apply it to practice.

1.3 Knowledge of NGx

Lack of knowledge of the science has been identified as a reason for low integration of NGx into practice (Collins *et al.*, 2013). A survey (N=390) conducted in the UK (Whelan *et al*., 2008) and another (N=373), more recently conducted in Canada (Cormier *et al*., 2014) found that 75.9% of RD´s in the clinical nutrition (public healthcare setting) and 62.9% of RD´s working as freelance RD's in the private sector reported that they did not believe that had sufficient knowledge to incorporate NGx into their clinical practice

The notion that lack of knowledge deters the application of NGx is backed up by results of the largest (N= 1844) survey study of its kind (Collins *et al*., 2013) which

indicated that only 18.8% of RD´s knew the answer to the question "What condition is not associated with the MTHFR 677C→T defect?" At most, 33.5% could describe what the terms NGx or nutrigenetics meant. A survey (N=297) of South-African dietitians (Oosthuizen, 2011) found that higher qualifications were associated with greater knowledge and involvement in NGx. Those with postgraduate Masters and Doctoral level qualifications were more likely to be engaged in genetics and NGx related activities. This finding, however, was not borne out in the multinational study conducted by Collins et al. (2013) who found no association between knowledge of NGx and involvement. The possibility of any relationship between knowledge and level of qualification, however, was not measured. This nevertheless implies that for NGx to be applied in practice a sustainable means through which to communicate with RG's on developments in NGx science on an ongoing basis may be required. Further research may be required to determine the type of information on NGx required by practicing RD's.

1.4 Attitudes toward NGx

Relatively few studies have considered the attitudes of RG's toward NGx. A small mixed-method approach study (N=16) conducted in the UK and Australia by Li and colleagues (2014) found that 50% of dietitians in both countries surveyed did not believe that NGx played any role in informing their current practice. They also found a general reluctance among RD's to integrate the science owing to a perceived lack of evidence for its efficacy. Differences between the two countries were not measured. Another survey study (N=235) undertaken by Christianson and colleagues (2005) amongst Australian RD´s, reported that the majority (71%) attributed the lack of

integration of NGx to not having encountered patients with genetic disorders. Given genetic disorders constitute only a small part of what NGx encompasses, this suggests that many RD's have only a very limited concept of the scope of NGx comprises (ie. counselling those with monogenetic disorder) and of its potential role in the prevention and treatment of non-communicable disease in the general population. Although there were positive views on the potential role of NGx in preventing the development of chronic diseases, the majority of RD´s did not believe that NGx could improve the quality and relevance of nutritional recommendations (Cormier *et al*., 2014). This suggests a need for initiatives to inform RD's on the scope of NGx and potential for NGx in public health nutrition.

1.5 Attitudes toward Direct-to-Consumer (DTC) Nutrigenetic tests

Digital technological advances are expected to revolutionize preventative public healthcare (EC, 2014) and present an opportunity to deliver digital health technologies direct to the consumer (DTC). RD's, however, are purported to hold negative opinions of DTC testing (Weir *et al*., 2010; Cormier *et al*., 2014; Li *et al*., 2014) and appear skeptical of DTC NGx products owing to the perceived lack of scientific evidence for the efficacy of such products (Weir *et al*., 2010; Li *et al*., 2014). Negative attitudes toward DTC testing have been put forward as a possible reason for low integration of NGx into practice. RD´s have also expressed concern that the results of DTC personalized nutrition assessment if conveyed without adequate support and follow-up could cause unnecessary worry in consumers (Weir *et al*., 2010; Cormier *et al*., 2014; Li *et al*., 2014).

1.6 Job area and Healthcare Environment

Quantitative survey (N=373) conducted in Canada, has suggested that RD´s in public health/health promotion and food service management may be less likely than clinically based RD's to apply NGx in practice (Cormier *et al*., 2014). This finding echoes results of a mixed-method study reported by Li and colleagues (2014) which found that neither clinically based nor public health RD´s (UK and Australia), perceived any role for NGx in providing population level dietary advice. Whereas dietitians in public health failed to see NGx within the scope of preventative public health, those in the acute (clinical) setting saw NGx as having a preventative rather than a therapeutic role. The upshot was that neither public health nor clinical dietitians viewed NGx as relevant to their own area of practice. Other studies (Oosthuizen, 2011; Cormier *et al*., 2014), meanwhile, have indicated that those engaged in NGx related activities are most likely to be based in academia, private practice or the food industry. This implies an imperative for research to target RD's practicing in the clinical and public health sectors in an endeavor to better understand the perceived barriers encountered when seeking to engage with NGx, and to apply this understanding to the design of interventions to encourage and support them in providing personalized nutrition services.

1.7 Endorsement by Professional Organisations

A US survey (N=995) of RD´s (Rosen et al., 2006) found that 80% had never encountered NGx in practice. A possible reason for the lack of integration of NGx into practice could be the lack of priority assigned to nutrigenomics by dietetic professional associations (Li *et al*., 2014). Endorsement by professional bodies would serve to encourage RD´s to acquire knowledge of the links between genetics and diet and to

become involved in activities relating to NGx (Rosen *et al*., 2006; Oosthuizen, 2011; Collins *et al*., 2013; Li *et al*., 2014). Although Cormier and colleagues (2014) found that more than 75% (N=383) of RD´s in the Quebec-area (Canada) knew about NGx, it was not clear from the study whether this knowledge led to integration of NGx into practice. The application of NGx in practice will require leadership from professional organisations representing dietetics professionals.

Discussion

The aim of this review has been to identify barriers and enablers to the integration of NGx into dietetics practice and to pinpoint areas for research and intervention and policy to promote the application of NGx by RGs. Existing studies imply that the apparent reluctance to integrate NGx into practice is associated with low awareness of NGx and its range and scope, a lack of confidence in the science surrounding NGx and skepticism toward DTC products. Integration of NGx also appears to vary among the different dietetics domains (eg. clinical; public health) and area of practice (eg. health service; commercial). All of these factors have potential to respond to leadership by professional bodies and the introduction of core education and training initiatives.

Genetics has been designated a compulsory component of dietetics training since 2008 (ASCEND, 2011; BDA, 2013) yet, nutritional genomics remains only an optional module in undergraduate training in the UK and a module as part of MSc programs throughout the UK (BDA, 2013). RD´s involved in managing patients with inborn errors of metabolism appeared more confident in providing genetic services (Gilbride & Camp, 2004), possibly because this is covered in the undergraduate curricula. NGx in

the broadest sense, however, is not yet a part of clinical practice training, which could partly explain the apparently poor knowledge, lack of confidence and involvement in NGx activities amongst practicing RD´s (Collins *et al*., 2014).

Previous studies have demonstrated that dietitians have a preference for education and training in seminars, workshops or online courses (Busstra *et al*., 2007; Newton, 2007b; Morin, 2009). Nevertheless, even after such training, the uptake and integration of NGx can remain low (Newton, 2007b). This gap in provision of translational education has partly been solved by private companies offering continuous education to various healthcare professionals on the topic (Ronteltap *et al*., 2012). Owing to RD´s skepticism towards DTC, however, these opportunities may not be fully exploited. Digital technological advances may afford the opportunity to integrate the use of digital health technologies which includes big (omics) data on nutrition, into the dietetic curricula. Meanwhile, there may be wider issues associated with the lack of interest and involvement in updating skills in NGx despite the available educational opportunities, which require further investigation.

Confidence in the science of NGx appears to be lowest in those with more years since graduation while knowledge is highest amongst less experienced RD´s, possibly because they have had recent training on the topic at undergraduate level (Whelan *et al*., 2008; McCarthy *et al*., 2008; Oosthuizen, 2011; Collins *et al*., 2013; Cormier *et al*., 2014). This could suggest that RD´s who have been out of practice for longer should be afforded continuous education opportunities to gain experience in NGx. This apparently higher level of knowledge among recent graduates, however, does not appear to translate into clinical practice for reasons that are not entirely clear. A possible explanation could be lack of a supportive working environment (Li *et al*., 2014). Possible ways to overcome the apparent knowledge-practice gap need to be explored in

future research. Given that repetition and exposure to clinical situations can encourage learning (Banet & Nunez, 2007), the amount of genetics (and optional genomics) currently delivered through the curriculum in the UK (Dietetic Standards Health & Care Professions Council, 2013) may need to be re-evaluated. Students learn about the science but then do not receive further exposure during their clinical placement. Reviewing the curriculum to increase knowledge and enhance confidence through clinically based support and training may be necessary to address this in the future (Wright, 2014).

In view of the wide range of dietetic roles currently available, a need for change in how we train future dietitians has already been identified. The recently published paper on standards of education (BDA, 2015: p16) concluded that "the profession is ready and in need of a change of approach to student training" and that "the sole use of the one-to-one model is neither sustainable nor appropriate and similarly students who only experience NHS acute or community placements do not gain a true understanding of the breadth of dietetic practice". The profession, therefore, needs to consider RDs´ role and preparation within the 'omics' era (Wright, 2014). The core competency in the Learning Outcomes Framework on NGx for Dietitians (The UK National Genetics and Genomics Education Center, 2014: p1) stipulates that it is important to have "a broad understanding of genetics, genomics and genetic testing as it relates to common disorders seen by dietitians, in order that you are able to answer patients´ questions". Professional guidance and RD genomics education websites, however, caution that it is too early to integrate genetic testing to provide genotype-based PN advice (Camp & Trujillo., 2014). This renders involvement in NGx a difficult task, as RD´s have little exposure to NGx in the dietetic curricula.

With rapid expansion of the direct to consumer (DTC) nutrigenetic testing market (Saukko, 2013), the public are likely to seek access to qualified professionals to interpret their results (Critchley, 2015). Whilst nutrigenetic tests have been criticized for lack of clinical utility and validity (Pavlidis *et al*., 2015), strong market growth (Bloomberg, 2010) indicates market interest is growing. Yet, RD's appear to have a poor perception of direct-to consumer testing products (Bouwman *et al*., 2008; Weir *et al*., 2010; Cormier *et al*., 2014; Li *et al*., 2014). When considering DTC company websites such as Nutrigenomix (Toronto, Canada http://nutrigenomix.com) and DNAlysis (Johannesburg, South-Africa http://dnalysis.co.za), it becomes clear that a number of RD´s have started integrating NGx into practice. So why do some RD´s integrate NGx and others don´t? Although this may be explained by factors operating within the healthcare environment such as employment in public health services (Government contracted/NHS) versus private practice (Industry) within which RD´s practice, how this operates in practice is currently not clear. The use of NGx by RD working in the NHS may also be less relevant. RD´s are also concerned about cost and that DTC results could unnecessarily worry clients and that specific groups, for example, those on lower incomes, could be excluded from accessing such products (Weir *et al*., 2010; Cormier *et al*., 2014; Li *et al*., 2014). Whilst policy needs to consider the needs of the less advantaged members of society, this should not pose a barrier to RD's increasing their knowledge in preparation for responding to questions from patients and the general public.

Previous research into the integration of NGx into practice has only touched upon relevant issues in current NGx practice. A possible reason for this is that the term 'involvement' (in NGx) has been used in several papers, without it being either fully operationally defined with regard to the application of NGx or used consistently

between studies. A first step toward enabling research on the integration of NGx in dietetics practice, therefore, would be to define what the integration of NGx into practice actually means. When looking at the detail within some of the published research papers (Whelan *et al*., 2008; Collins *et al*., 2014), it is also evident that none of the activities referred to as nutritional genomics actually involved the use of a nutrigenetic test or genotypic information. Previous studies have indicated some confusion among RD's about what activities are comprised in nutritional genomics beyond the management of inherited conditions (Whelan *et al*., 2008; Collins *et al*., 2014). Future research on this topic, therefore, should provide a full definition of NGx which encompasses all of what it entails in practice going beyond medical nutritional therapy for genetic conditions such as Coeliac Disease or lactose intolerance. In defining NGx therefore, a distinction needs to be made between monogenetic disorders (such as inborn errors of metabolic disorders) and NGx which relates more to chronic diseases.

Most studies that have looked at the integration of NGx into practice have been quantitative, mainly on-line survey and cross-sectional in nature (Lapham *et al*., 2000; Christianson *et al*., 2005; Rosen *et al*., 2006; Whelan *et al*., 2008; Weir *et al*., 2010; Oosthuizen, 2011; Collins *et al*., 2013; Cormier *et al*., 2014) and a dearth of in-depth research which could assist in explaining the findings. Some of the surveys suffered from poor response rates (Oosthuizen, 2011; Collins *et al.,* 2013; Cormier *et al.*, 2014) and small sample sizes (Weir *et al*., 2010; Li *et al*., 2014), the reasons for which are unclear. Another limitation is that only certain countries have been surveyed (Australia, South-Africa, US, UK and Canada), with a relative lack of research in emerging and developing countries.

Future Directions

The perceived importance of genetics based practice among the dietetics profession appears to be associated with their level of knowledge of NGx (McCarthy *et al*., 2008; Collins *et al*., 2013). Although it is difficult to determine the direction of causation between high perceived importance and knowledge of NGx, that neither are necessarily associated with integration of NGx into practice, warrants further study.

Existing research has also suggested that RD's have ethical concerns, most especially that disadvantaged groups could be excluded from accessing products and services if they are only offered commercially (Weir *et al*., 2010; Cormier *et al*., 2014; Li *et al*., 2014). Recent research into opinions among the European public on personalised nutrition, however, has suggested that there may be two potential markets, one delivered commercially and the other through existing health services (NHS), and that under certain circumstances these types of provision should be synchronized (Stewart-Knox *et al*., 2013; Stewart-Knox *et al*., 2014; Fallaize *et al*., 2015; Fischer *et al*., 2016; Stewart-Knox *et al*., 2016). This implies a future where dietetics practitioners work alongside commercial providers of NGx and that further research is required to determine how best to encourage collaboration between DTC and clinical NGx providers.

The apparent narrow view of NGx as the management of genetic conditions rather than the promotion of dietary health could demonstrate a lack of understanding of the links between genes, diet, health and propensity for chronic disease (Gilbride, 2007), which will need to be addressed though education and training initiatives. With a low response rate of only 13% in the largest study (Collins *et al*., 2013), however, the results may not be applicable to the dietetic profession as a whole.

Given the finding that there is divided opinion on which specializations and area of practice are best place to integrate NGx, future policies will need to ensure that NGx is integrated throughout professional practice. To our knowledge no comprehensive work has been conducted to look at current provision on nutritional genomics within the dietetic curriculum. Nor do any studies appear to have looked into the attitude and perceptions of RD´s who have integrated NGx into their practice (using the classic definition of NGx) to provide gene-based PN services. The time is right, therefore, to grasp the opportunity to conduct research with 'early adopters' of NGx and enquire into traits, attitudes and perceptions that could help to determine the factors that are associated with successful integration of NGx and which can inform initiative and policies to encourage the rest of the profession to add this exciting new technology to their practitioner resources.

Insert table 2 here

Conclusions

Owing to limitations in previous research, very few conclusions can be drawn from studies of NGx integration into practice. At present, there is global variation in how NGx is integrated at the clinical practice level, with the majority of RD's abstaining. Further research should seek to understand the drivers, barriers and challenges the profession faces with regards to integration of NGx into practice. Greater clarity is needed at the strategic and policy level on how RD´s could potentially use genotype information and translate it into therapies and in dealing with client's questions. A future concern and one that policy needs to address, is the issue of equality

of access to NGx (Stewart-Knox *et al*., 2016). RD's in both private and public health provision will need enabled to deliver NGx services. Meanwhile, there appears to be a gap between what RD´s are expected to know in terms of learning outcomes and what actually happens in practice and further research is required to determine and understand the reasons why.

It is clear that action is needed to ensure that more experienced RD´s become familiar with the science, its application and the potential professional opportunities this could present. Measures also need to be taken to ensure that less experienced RD´s are encouraged to remain interested in the field once they are qualified and are afforded the opportunity to integrate NGx into their practice. How much emphasis is placed on NGx in clinical practice by educators, senior practitioners and professional organisations, therefore, could play a major role in the establishment of a confident and competent workforce that is prepared for changes the genomic revolution may bring and ready for full integration of nutrigenomics into dietetic practice (Li *et al*., 2014).

The future of modernized healthcare is likely to rely heavily on personalised health promotion and disease prevention (EC, 2014). Whilst genetic contribution of individual single nucleotide polymorphism to disease susceptibility is small 0-10% (Minihane, 2013) and between gene-environment interactions are still being unraveled, advanced skills and knowledge in genomics and systems biology may open up new opportunities in the food industry for the development of functional food, as part of digital health programs. In order to achieve this goal, educational and policy initiatives will be required to integrate NGx across all levels and domains of practice. RD's are ideally positioned to bridge the gap between suppliers and consumers. Equally, there is an opportunity to foster links between industry and academia in terms of training in

order to satisfy demand for personalized nutrition products that can mitigate disease and promote health.

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Figure 1

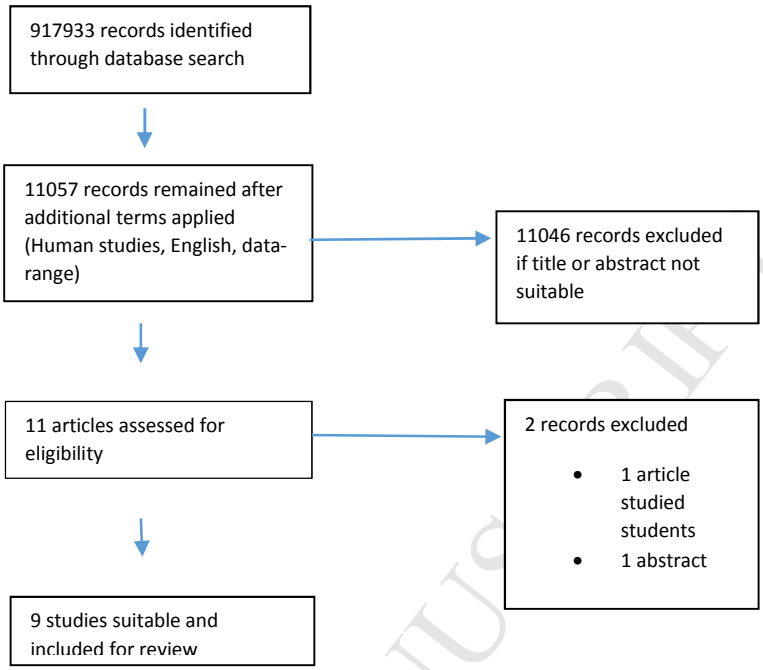

Table 1: Summary of studies that met the inclusion criteria for the critical analysis

Study, (Country)	Participants	Design	Quality criteria checklist	Factors influencing integration	Outcome of study	Result
Collins et al 2013 (UK, US, Australia)	Dietitians N=1844 (13% response rate)	Cross-sectional study using online survey	Positive	Confidence Knowledge	Knowledge of genetics & NGx Involvement and confidence in undertaking clinical or educational activities related to genetics and NGx	Strongest predictor of high involvement for clinical activities was high confidence $p<0.001$
Whelan et al 2008 (UK)	Dietitians N=390 (65% response rate)	Postal survey	Positive	Confidence Knowledge	Involvement, confidence and knowledge of dietitians in genetics and diet-gene interactions	Involvement was associated with confidence, but limited to discussing diseases with dietary and genetic component (49%) or advising patients where to access information relating to a disease with a dietary and genetic component (33%)
Cormier et al 2014 (Canada)	Dietitians N=373 (15.3% response rate)	Online survey	Positive	Experience Perception Knowledge Ethical issues Market need Job role	Current knowledge of RD´s regarding NGx to identify training needs in NGx of RD´s and to highlight the perceived limitations of the use of genetic tests in their scope of practice	Less experienced dietitians were more knowledgeable but not applying it in practice Senior dietitians were less knowledgeable and more skeptical and concerned about ethical and legal aspects associated with D-T-C tests RD´s in private practice more

						likely to integrate than RD´s in acute and food serve setting
Weir et al 2010 (Canada)	Hcp´s including Dietitians n=4, nutritionist n=1	Focus groups	Neutral	Competency Perceived benefit Attitude	Knowledge and attitude of hcp´s regarding NGx and nutrigenetic testing	High level of skepticism towards nutritional benefit. Lack of confidence and knowledge hindered integration
Christianson et al 2005 (Australia)	HCP´s including dietitians N=235 (response rate 34%)	Cross-sectional survey	Positive	Attitude	Knowledge	71% did not work with patents with genetic conditions. Lack of knowledge and understanding of the link between diet and genes
Lapham et al 2000 (US)	Dietitians N=362 (62% response rate)	Survey and focus groups	Positive	Confidence	To determine the Genetics education needs and priorities of RD´s and other hcp´s	Involvement was limited to genetic component of disease problems (67%) and counselling patients with a genetic condition (24.1%) RD´s had low confidence in applying genetics in practice
Rosen R et al 2006 (US)	Dietitians N=995 (40% response rate)	Mailed survey	Positive	Knowledge Confidence Attitude	To assess continuing education needs for RD´s regarding application of NGx	Positive attitudes were associated with greater confidence in ability to apply knowledge. Factors that hindered application included: Lack of knowledge (81%); Uncertainty about reimbursement (84%); Lack of CPD (73%);

						Lack of professional expertise (72%).
Li S et al 2014 (Australia & UK)	Dietitians N=16 (semi-structured interviews) N=7 (Focus groups)	Semi-structured interviews Online surveys Focus groups	Neutral	Confidence Knowledge Environment Perception	Low Involvement	Lack of supportive environment Limited exposure and training Lack of relevance to practice Lack of scientific evidence Too early to integrate the science into practice
Oosthuizen 2011 (South-Africa)	Dietitians N= 297 (response rate 15.2%)	Cross-sectional online and mailed survey	Positive	Knowledge Confidence	To determine involvement, knowledge and confidence in genetics and NGx	Significant positive association between involvement and confidence ($p<0.001$) Those with higher involvement had higher knowledge and were more confident

Table 2: Current gaps in our knowledge and research questions
o **How can digital technology be best used to increase knowledge, heighten interest and encourage the inclusion of NGx into the dietetic education curriculum?** o **What training is currently offered on nutritional genomics in the dietetic curriculum across the globe?** o **How has NGx been successfully integrated into clinical practice and what are the drivers, perceptions and experiences that have influenced early adopters?** o **What are the perceived barriers faced by RD's in adopting NGx into practice?** o **Has translation of the science and the barriers encountered in doing so, been consistent across countries?** o **Most research has been conducted in English speaking countries. What are the views and practices of dietitians in non-English speaking and emerging countries?**

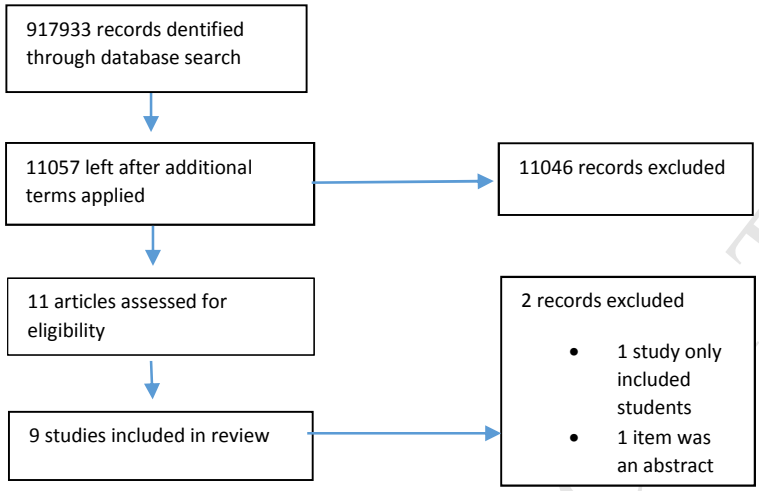

Figure 1: Literature search procedure

Highlights

- Registered Dietitians (RD's) have been identified as key healthcare professionals to translate Nutritional Genomics (NGx) into practice
- There is a lack of research conducted into the views of RD´s who have integrated NGx into practice
- Higher education curricula do not integrate genomics data into clinical practice and integration of NGx into practice is low.
- There is an opportunity to integrate DNA testing and digital health platforms into the curriculum as an innovative way to increase interest and engagement with NGx
- Leaders of dietetic organizations and academic institutions need to place nutritional genomics higher on the strategic agenda in order to progress the profession and to create new opportunities.