

# Ethical, legal and social issues in nutrigenomics: The challenges of regulating service delivery and building health professional capacity

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## Abstract

Nutrigenomics, the conjunction of molecular nutrition with human genomics, is among the first publicly available applications of the human genome project. Nutrigenomics raises ethical, legal and social issues particularly with respect to how the public may access nutrigenetic tests and associated nutritional and lifestyle advice. Current regulatory controversy focuses on potential harms associated with direct-to-consumer (DTC) marketing of nutrigenetic tests and especially the need to protect consumers from unreliable tests, false claims and unproven dietary supplements. Nutrigenomics does, however, offer the potential of important health benefits for some individuals. The regulation of nutrigenomic services is slowly evolving, but there is little indication of increased professional capacity to support service delivery. Primary care physicians have minimal training in nutrition and genetics, and medical geneticists are in high demand and short supply. Dietetic practitioners are experts in nutrition science and interest in nutrigenomics is growing among members of this professional group. However, as with physicians, dietetics practitioners would require considerable training to bring nutrigenomics into their practice capacity. A downside of regulatory restrictions on direct consumer access to nutrigenomics companies is that responsible businesses may be hindered in meeting emergent public demand while health care professional groups have not yet developed capacity to provide nutrigenomics services.

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## 1. Introduction

Biomedical researchers, private sector firms, and the public are increasingly interested in the emerging field of nutrigenomics [1]. Nutrigenomics is the study of nutrient–gene interaction, and its practical applications involve the use of genetic testing for predisposition to

diseases that can be mitigated or modulated with dietary interventions in a clinical or direct-to-consumer (DTC) context [2,3]. Early entrants into the nutrigenomics market have been developing and marketing genotyping services, food products and dietary supplements said to be tailored for an individual's genetic predispositions [4]. These commercial interests are responding to an established market segment of early adopters seeking new tools to enhance health, but the regulatory environment has not kept pace [5]. Anticipated growth in nutrigenomics will require appropriate and timely regulatory responses. Safeguarding the public's interest

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while allowing business to flourish requires forthcoming nutrigenomics regulations to respond to the social impacts, and public perceptions of, links between genetics, diet and health [6].

There is growing public demand for personalized nutrition advice; one company operating in the United States has reportedly sold more than 35,000 nutrigenetic tests since 2003 [7]. While there are some applications of nutrigenomics offered directly to consumers and through health care providers, they tend to operate at the edge of regulatory environments. Consequently, health care practitioners, regulators and the nutrigenomics industry face the same challenge from different perspectives: does nutrigenomics require the bridging of existing regulations to this field, or are wholly new regulations specific to nutrigenomics required? How should regulatory development incorporate public perceptions and knowledge levels about nutrigenomics? Currently, nutrigenomics has not existed long enough for regulatory best practices to emerge. It is critical, therefore, to consider emerging ethical, legal and social issues that arise in the field of nutrigenomics [8,9].

## **2. Ethical, legal and social issues in nutrigenomic service delivery**

Nutrigenomics lies at the intersection of several fields in which ethical, legal and social issues arise – human genomics and genetics, the molecular nutritional sciences, dietary supplement research and development, medicine and dietetics. As each of these fields progress, periods of regulatory uncertainty are often encountered and emerging ethical, legal and social issues must be identified and addressed. With growing investments in human genomics research, much attention has focused on ethical and legal protections for research subjects, including concerns about study design, the collection, use, retention and exchange of biological samples and personal information, the involvement of children or other vulnerable groups, and the obligations of researchers to report results to research subjects and their family members. Nutrigenomics research arguably does not raise novel human genetic research issues, but the European Nutrigenomics Organisation (NuGO) has developed a useful bioethics guideline tool to help standardize “human genomics research ethics ... throughout the research community” [10]. This tool addresses key ethical and legal issues in genetic research, including guidelines on: obtaining informed consent from participants, both for single nutrigenomics studies as well as long-term biobanking initiatives; management of biobanks; use

and exchange of data and samples. The tool also includes links to relevant international and European domestic instruments that apply to human genetic research and associated privacy and data protection issues.

Our focus here, however, does not concern the legal and ethical issues associated with nutrigenomics research but with the current and potential issues associated with delivering nutrigenomics to the public. Castle [11] identified four models for delivering nutrigenomics services: DTC; through a health care practitioner; through multidisciplinary, integrated health care teams; in a public health model. At present, nutrigenomic services are being provided DTC and through health care providers, but are not offered to any significant extent through integrated health care providers or through public health initiatives.

DTC services have become the standard delivery model in nutrigenomics. The service typically involves internet-based advertising and sales. Individuals purchase a test kit online, or through a retail outlet, collect a buccal swab, then send it, along with personal and lifestyle information to the nutrigenomics company. The company analyses the biological sample to search for genetic polymorphisms associated with nutrient metabolism, and compares these findings with the personal and lifestyle information. The company will provide a report back to the consumer with results and recommendations that may include a summary of genes that were tested, polymorphisms that were identified, descriptions about nutrient–gene associations thought to elevate risk for disease susceptibility and dietary recommendations to off-set risk and mitigate disease susceptibility. Nutritional recommendations may include whole foods, but more often counsel supplementation, sometimes with products sold by the same company. As we discuss below, these same services can also be offered through a health care practitioner who, acting as an intermediary between the client/patient and the company that does the nutrigenetic analysis, interprets results of the genetic screen, claims about disease risk and dietary recommendations.

Nutrigenomic services have three main components: (1) the genetic test and its interpretation; (2) the assessment of disease susceptibility based on the test results; (3) formulation of dietary recommendations. Each component raises serious ethical and legal issues regardless of how the service is provided. DTC genetic tests tend to be a lightning rod for criticism about hazards of under-regulating genetic tests [12,13]. While demands for greater regulation of DTC tests are often

well-founded, proposals for stiffened regulations tend to ignore the fact that there are few health care practitioners who can provide either genetic or nutritional counselling, let alone nutrigenomic counseling. If laws restrict DTC delivery of nutrigenetic tests, those wishing to take advantage of such testing and associated nutritional counseling may find themselves in a void where they cannot seek services from companies with purported expertise, nor can they likely find a health care professional with specialized knowledge in nutritional genomics. Nutrigenomic tests might be available, but only through care providers ill-equipped to interpret them.

### 2.1. *Genetic tests and the DTC controversy*

Much current controversy about delivery of nutrigenomic services focuses on regulation of DTC genetic tests. One position is that direct access to testing services allows greater self-direction in one's health. This position is based tacitly on the view that personalization, and possibly the results of a genetic test, contributes to greater degrees of compliance with recommended diets and improved outcomes. A corollary is that tests offered DTC may protect privacy since test results are not recorded in medical records. Insurance companies, particularly those operating in conjunction with conditions of employment in the United States, may have a future interest in risk rating based on genetic information. Early introduction of DTC tests could be lauded for offering a service, and perhaps a foothold for future services, where individuals can access their genetic information prior to insurance companies using genetic information to risk rate their clients. At the same time, however, under-regulation of DTC services opens avenues through which consumers may be misled or harmed by unscrupulous companies marketing tests no more informative than a pedigree analysis, and particularly companies linking test results to the sale of unproven or over-priced supplement regimens.

Concern over DTC marketing of nutrigenetic tests was emphasized in a 2006 United States Government Accountability Office (GAO) report. In an attempt to assess the scientific legitimacy and consumer benefit of such tests, the GAO sent genetic samples and lifestyle information for 14 "fictitious consumers" to four nutrigenomic companies that market their services over the internet. The GAO concluded that the "results we received from all the tests we purchased mislead the consumer by making health-related predictions that are medically unproven and so ambiguous that they do not provide meaningful information to consumers" [7].

The report also criticizes two of the companies that sell "costly supplements that they claim are developed according to an individual's unique DNA. In reality, the pills are not unique in any way, make unproven medical claims, and are potentially harmful" [7].

While drawing attention to potentially important consumer protection issues, the GAO report has some serious methodological flaws that undermine many, if not all of its criticisms. For example, the report is premised on an incorrectly deterministic view of genetics. Where the same DNA sample is submitted to a company, but accompanied by different personal and lifestyle information, the report suggests that the counseling results should be identical. This fails to take account of the important role of environmental exposures in the gene–environment interactions that nutrigenomics addresses. In other words, the different results actually support company claims that genetic tests generate individualized results, as they should if genetic polymorphisms unique to individuals are being assayed. Equally, it has not escaped the attention of many that the GAO actually submitted DNA of one of the study author's nine-month-old child, perhaps suggesting the GAO believed inaccurately that child and adult DNA are structurally different.

There is a misperception that nutrigenomic services are not regulated at all [14], but in truth the problem is far more complicated. The GAO report targeted the United States Food and Drug Administration (FDA) which is already considering how best to regulate genetic tests. In a recent guidance document [15], the FDA has attempted to extend its regulatory purview without new legislation to tighten regulation of analyte specific reagents used in genetic tests and the associated algorithms used to interpret the physical data generated by these tests. The net effect is that companies offering DTC genetic tests will now have to comply with the Clinical Laboratory Improvement Amendments (CLIA) [16], which establish quality standards to ensure accuracy and reliability of laboratory tests. In the wake of the FDA action, there is now uncertainty about whether algorithms used to interpret those results will be regulated as medical devices. Raising the bar on the approval process for tests would be a market entrance barrier. While based solely on guidance documents at this point, the general direction of the FDA is likely to receive support from professional organizations with vested interests in the regulation of DTC genetic tests. Among these, one notable advocate of tighter regulations is the American College of Medical Genetics which has called for prohibitions on DTC marketing and argues that genetic tests should only be available through a health care professional [17].

## 2.2. Genetic and nutritional counseling: Capacities and limitations

There are good reasons for thinking that nutrigenomics will offer significant health benefits to some individuals [18,19]. Nevertheless, there are concerns that unregulated, or under-regulated, DTC nutrigenomic testing services might undermine the development and transfer of beneficial technologies. To achieve consumer protection while allowing legitimate commercial development in this field, regulatory criteria should focus on separating bogus DTC marketing from genuine applications of nutrigenomic science. One regulatory approach would restrict DTC genetic tests and channel service delivery through health care practitioners, a model that assumes dietetic or medical professionals have pre-existing expertise to advise patients on nutrigenomics, or that professional capacity in this area will grow along with nutritional genomic science. Unfortunately, both assumptions have significant shortcomings.

Health care practitioners' lack of appropriate education in genetics and nutrition has been identified as one of the major barriers in offering nutrigenomic services to the public. Practitioners need to know how to understand and communicate susceptibility information [20], and how to use this information in combination with nutrition information to advise patients about dietary modification. Yet effective communication about disease susceptibility based on nutrient–gene association demands knowledge about genetics and nutrition and evidence shows health care practitioners lack adequate training in these areas.

With respect to genetics, most health care practitioners do not have expertise in clinical genetics and molecular testing, and their training provides, at best, basic information on genetics, probability and risk [21]. For example, of U.S. doctors now in practice, very few would have been in one of the 45 medical genetic residencies available in that country, and while there are 2000 genetic counselors in practice, only 160 counselors and 50 clinical geneticists are trained per year [22]. In Canada, a recent report on the gap between genetic research and clinical needs observes that “legions of patients are in limbo because of long wait times for consultations with clinical geneticists [23].” Queues to see a genetics specialist exceed two years in some regions and “the number of training positions has not kept pace with demand and the pool of patients is growing as researchers are discovering more about the genetic component of conditions that develop in adults [23].” Other countries face similar health human resource challenges.

To counsel patients on nutrigenomics, health care providers need to understand and communicate complex, probabilistic information including how to quantify risk, how to frame test outcomes, and how to deal with false negative and false positive test results [24]. Because understanding and interpreting predictive tests requires a fairly sophisticated understanding of genetics, these tests are highly susceptible to misinterpretation, even by medical professionals. One study that examined the use of a commercial genetic test for a mutation in a colon cancer gene found that physicians incorrectly assessed the test results in 31.6% of cases studied [22]. When asked, primary care practitioners identify lack of genetics education as one of the greatest deficits in their professional training, one which will require systematic training to overcome [25]. A recent, comprehensive review of health care professionals' training needs in genetics and genomics states that although, medical schools continue to increase genetics content of the undergraduate curriculum, studies in the United States and the European Union alike shows that current educational approaches do not prepare students to practise in a health-care environment that will be increasingly influenced by genetics and genomics [25]. Further, deficiencies in genetics knowledge among medical personnel are not limited to students and practitioners [25]; health insurance plan officials are similarly disadvantaged, which may impede integration of genetic services into public and private health benefit schemes.

With respect to nutrition, health care practitioners often lack sufficient nutritional science knowledge that would be required to interpret a nutrigenomic test. This is particularly true of physicians, who lack confidence in their nutrition knowledge, and are generally reluctant to give nutritional advice to patients [26]. A recent in-depth analysis of the role of nutrition education in medical schools and postgraduate training programs showed a large deficit in practical nutrition knowledge [27]. This gap in training persists, despite the fact that there is evidence the public thinks medical professionals have greater knowledge about nutrition and place it high among the factors important to the maintenance of health and the management of disease [27].

Physicians in general practice face daily pressure to manage heavy workloads and the limited time available with each patient focuses predominantly on acute health concerns, not counselling for health promotion and disease prevention. American physicians in one study spent less than a minute on average discussing nutrition with their patients [34]. In another study, the time spent in

nutrition counselling in primary care settings is usually less than 5 min per patient, with the average time being 1 min, during an average office visit lasting only 10–16 min [35]. Overall, general medical practitioners give low priority to nutrition counseling, except with specific patient groups, such as paediatric, geriatric and maternity patients [28].

When genetics and nutrition are combined, the results are dismal. Strikingly, one international conference on nutrition and medical practice in the late 1990s found that physicians from 11 countries with well-developed medical institutions were only vaguely aware of a link between proper diet and health [29]. In contrast, another study of nutrition interventions by primary care practitioners in the United States concluded that levels of basic nutritional knowledge were fairly good [30]. In addition to, at best, variable or, at worst, low levels of knowledge about nutrition, other barriers prevent primary care practitioners from providing dietary counseling. They include lack of time, lack of patient compliance, inadequate teaching materials, lack of nutritional knowledge and insufficient reimbursement [31]. When the complexities of emerging nutrigenomic science are added to this already long list of challenges, the prospects for timely and constructive integration of nutrigenomic services into existing health care practice situations seem dim. We have emphasized here the limits of physicians' capacity and discuss below the role of dietetics professionals in nutrigenomics.

### 3. Moving forward

A fledgling science like nutrigenomics would offer the most benefits and fewest risks were it offered with the greatest scientific pedigree, the highest quality genetic tests and most robust dietary intake assessments, with comprehensive genetic and nutritional counseling to help inform behaviour modification and produce healthier outcomes. This, obviously, is the best-case scenario. While there will be continuous tussles in the scientific literature about what constitutes the best of nutrigenomic science and how to move forward with applications, there are positive steps that can be taken to address the major ethical and legal issues arising in the current situation. Requiring the genetic tests to meet the highest standards of laboratory validity is desirable. In the United States, for example, it is appropriate that in-house or out-sourced laboratories meet CLIA certification standards. Ultimately, one might seek other FDA approvals for tests, particularly where specific claims about risk or health outcomes are involved.

Shortcomings in the human resources capacity to cope with mainstream nutrigenomics will be more difficult to overcome and present longer term challenges than regulatory reform. While it would be foolhardy to revamp curricula in anticipation of each new development in applied human genomics, the evidence for deficiencies in physicians' genetic and nutritional knowledge is alarming. When one considers that nutrigenomics is not a fiction but is now being offered to the public, albeit on a small scale, the question of capacity to support nutrigenomics becomes more pressing.

Dietetic practitioners arguably stand to gain the most by developing competency in nutritional genomics. They already have competency in nutrition and professional skills in patient counseling regarding diet and health. As with physicians, financial and other barriers limit comprehensive genetics training in dietetic education and dietetic practitioners face similar pressures in daily practice that will slow uptake of genetics into their practice [32]. Yet, some advocate for expanded education in genetics for dietetic practitioners, and possibly even nutrigenomics [33,34]. As De Busk comments:

The dietetics profession has an exciting opportunity that if seized and properly executed could enhance the scientific foundation of clinical practice, improve therapeutic outcomes and significantly expand career and economic opportunities for practitioners. The future of dietetics is unquestionably intertwined with nutritional genomics [35].

While it may be true that nutrigenomics represents the future for dietetic practice, professional inertia [36] will certainly slow the transition from genetics-competent dietetic practitioners to nutrigenomics professionals. Anticipating that regulations around genetic tests will be in place well before there is professional competency to support nutrigenomics creates a complex scenario for the future. If DTC tests are heavily restricted or prohibited, consumers will likely lose the benefit of timely access and the privacy advantages of DTC tests if access is only available through health care practitioners. The current, practical limits on health professionals' training and time to integrate nutrigenomics into practice do not lead necessarily to the conclusion that DTC delivery is the most appropriate model as real concerns exist about consumer protection in the DTC model. Ideally, dual efforts are required to support greater nutrigenomics education for health care professionals and better means to protect consumers from disreputable companies while allowing responsible businesses to help meet the antic-

ipated growth in demand for access to nutrigenomic services.

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