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Knowing your genes: does this impact behaviour change?

Clare B. O’Donovan^{1*}, Marianne C. Walsh¹, Michael J. Gibney¹, Lorraine Brennan^{1,2} and Eileen R. Gibney¹

¹UCD School of Agriculture and Food Science, UCD Institute of Food & Health, University College Dublin, Belfield, Dublin, Ireland

²UCD Conway Institute of Biomolecular Research, UCD, Belfield, Dublin, Ireland

It is postulated that knowledge of genotype may be more powerful than other types of personalised information in terms of motivating behaviour change. However, there is also a danger that disclosure of genetic risk may promote a fatalistic attitude and demotivate individuals. The original concept of personalised nutrition (PN) focused on genotype-based tailored dietary advice; however, PN can also be delivered based on assessment of dietary intake and phenotypic measures. Whilst dietitians currently provide PN advice based on diet and phenotype, genotype-based PN advice is not so readily available. The aim of this review is to examine the evidence for genotype-based personalised information on motivating behaviour change, and factors which may affect the impact of genotype-based personalised advice. Recent findings in PN will also be discussed, with respect to a large European study, Food4Me, which investigated the impact of varying levels of PN advice on motivating behaviour change. The researchers reported that PN advice resulted in greater dietary changes compared with general healthy eating advice, but no additional benefit was observed for PN advice based on phenotype and genotype information. Within Food4Me, work from our group revealed that knowledge of *MTHFR* genotype did not significantly improve intakes of dietary folate. In general, evidence is weak with regard to genotype-based PN advice. For future work, studies should test the impact of PN advice developed on a strong nutrigenetic evidence base, ensure an appropriate study design for the research question asked, and incorporate behaviour change techniques into the intervention.

Personalised nutrition: Genotype knowledge: Behaviour change: Food4Me study

The launch of the Human Genome Project, over a quarter of a century ago, resulted in a 13-year long venture to sequence all three billion base pairs of the human genome^(1,2). The subsequent completion of this work, in 2003, was a major breakthrough in science, and many believed that it would revolutionise medicine through the identification of individuals at risk of disease⁽³⁾. From this, the concept of personalised nutrition (PN) arose, where tailored dietary advice can be delivered to individuals based on their diet and lifestyle factors⁽⁴⁾. This is in contrast to public health advice, which is

general, non-specific healthy eating advice such as the eatwell plate in the UK or food pyramid in Ireland^(5,6).

Although the original or most common concept of PN involves delivering personalised advice based on genotype, personalised nutrition can be delivered in a three-tiered concept where one tier builds on the foundations of another⁽⁷⁾. Within this concept, level 1 PN advice involves giving an individual tailored nutrition advice based on assessment of their dietary intake. Level 2 PN advice involves delivering tailored advice based on an individual’s diet and phenotypic markers such as

Abbreviations: DTC, direct-to-consumer; PN, personalised nutrition.

***Corresponding author:** C. B. O’Donovan, email clare.odonovan@ucd.ie

anthropometric measurements and blood biochemistry. Level 3 is the ultimate personalisation as tailored dietary advice is personalised based on an individual's diet, phenotype and genotype⁽⁴⁾. It should be acknowledged that dietitians provide personalised advice based on assessment of an individual's diet, anthropometric measures and blood biochemistry in clinical settings; however, personalised dietary advice based on an individual's genotype is not so readily available to the general public^(8,9). There is some evidence to support PN advice based on diet and phenotype, and for further reading on this topic, the reader is directed to the following review papers in this area^(8,10). However, the focus of the current review is on the delivery of PN advice based on genotype, and its impact on motivating behaviour change in terms of diet and lifestyle.

It has been hypothesised that information based on genotype may be more powerful in motivating behaviour, in comparison with other types of personal information, a concept referred to as genetic exceptionalism⁽¹¹⁾. This proposes that knowledge of genotype can motivate individuals to make more favourable lifestyle changes towards disease prevention⁽¹²⁾. However, there is a counter argument with the perception that disclosure of genotype risk may promote a fatalistic attitude and decreased self-efficacy⁽⁹⁾. Hollands *et al.* postulated that there are, in fact, three ways in which genetic information may impact behaviour⁽¹³⁾. Firstly, communicating disease risk may motivate behaviour change more effectively than disease risk based on other types of information. This is in line with theories of attitude change, which suggest that the more aware the individual is of their own disease risk, the greater the impact. Secondly, knowledge of genetic risk may demotivate behaviour change as diseases with a genetic cause are seen to be less controllable. Lastly, knowledge of genotype may have little or no effect on behaviour⁽¹³⁾. However, with respect to PN and other related fields, it is important to highlight that individuals may be informed that they have an at-risk genotype or no-risk genotype, which further complicates the hypothesis as depicted in Fig. 1.

Within the context of this hypothesis, it is important to acknowledge the type of evidence on which the genotype-based personalised advice is developed. Nutrigenetic research investigates the effect of individual genetic variability, and its effect on response to nutrients/diets in relation to health and individual nutrient requirements, and therefore, is the backbone of genotype-based PN^(14,15). The strength of evidence for genotype-based PN is a matter of much debate, with many believing that more larger-scale trials are required to justify some of the proposed dietary advice based on genetic variability⁽¹⁶⁾. However, it is likely that some genotype-based advice has a stronger evidence base compared with others, and it is important to bear this in mind whilst reviewing the evidence for the impact of genotype-based advice on motivating behaviour change.

The objective of this review is to examine the current evidence with regard to the impact of knowledge of genotype on motivating behaviour change in relation to diet and lifestyle. The evidence will be examined under

three sub-sections: (1) Studies investigating the impact of direct-to-consumer (DTC) testing; (2) Studies investigating the impact of disease genetic risk disclosure with phenotypic/familial risk presence; (3) Studies investigating the impact of genotype-based PN.

On review of the evidence, it will be investigated whether the following factors affect the impact of genetic information: the quantity of genotype information given, i.e. information regarding one gene or a number of genes and/or other personalised information based on dietary intake and phenotypic markers; the mode of delivery of the genotype information, i.e. face-to-face *v.* online delivery, DTC *v.* health professional such as genetic counsellor, doctor or dietitian; presence of familial and/or phenotypic disease risk, i.e. if there is already presence of the disease in the individual's family or whether the individual is at phenotypic risk such as overweight/obese, high blood pressure, etc.; duration of follow-up, i.e. is the impact of the genetic information on behaviour change immediate or does it have a long-term effect?

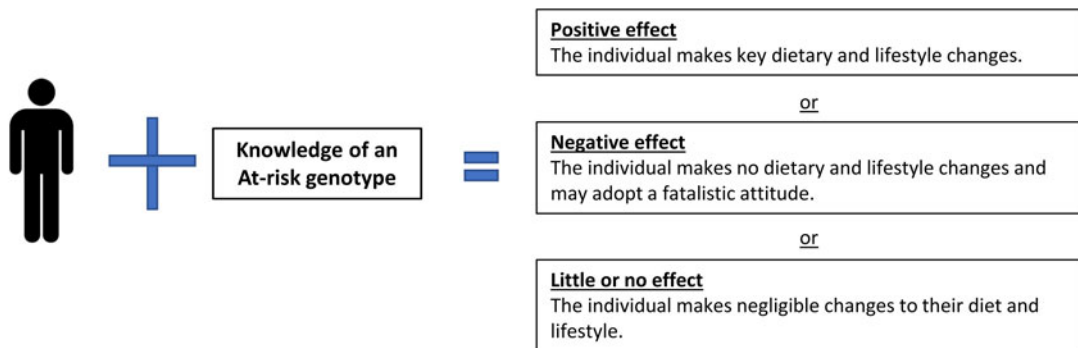
Studies investigating the impact of direct-to-consumer testing

Since the completion of the human genome sequence, many companies offering genetic testing have been established⁽¹⁷⁾. DTC testing can be defined as testing that is initiated by the individual, with the results provided directly to individuals without the involvement of a health-care provider⁽¹⁸⁾. There are some examples in the literature investigating the effect of DTC testing on behaviour change (Table 1).

Kaufman *et al.* carried out an online survey of DTC customers of 23andMe, deCODEme and Navigenics⁽¹⁹⁾. A random selection of customers were invited to take part with 33 % completing the survey (*n* 1048). As part of the questionnaire, individuals were asked information regarding demographics, health behaviours, motivations for purchasing the test, and opinions and actions taken in response to their results⁽¹⁹⁾. The investigators reported that nearly half of those surveyed had sought additional information about a health condition tested. Furthermore, 28 % of individuals had informed a health-care professional of their results, and 9 % had follow-up laboratory tests. Additionally, 16 % of respondents had made changes to their medication and/or supplement intake and one-third reported being more careful with their diet⁽¹⁹⁾. Many of these findings were significantly associated with their response to a question regarding their perceived risk of colon cancer, which suggests that those who consider themselves at high risk of cancer, were more likely to report making health behaviour changes⁽¹⁹⁾. A limitation to this survey was the lack of comparison with a control group who did not receive genetic testing. It is also important to note that only one-third of customers completed the survey, which may have biased the results.

Egglestone *et al.* conducted an online survey of individuals who had purchased a DTC genetic test (consumers, *n* 189), and these were compared with those who were thinking about purchasing a test, or who were awaiting

Scenario 1 Individual informed they have an at-risk genotype



Scenario 2 Individual informed they have a no-risk genotype

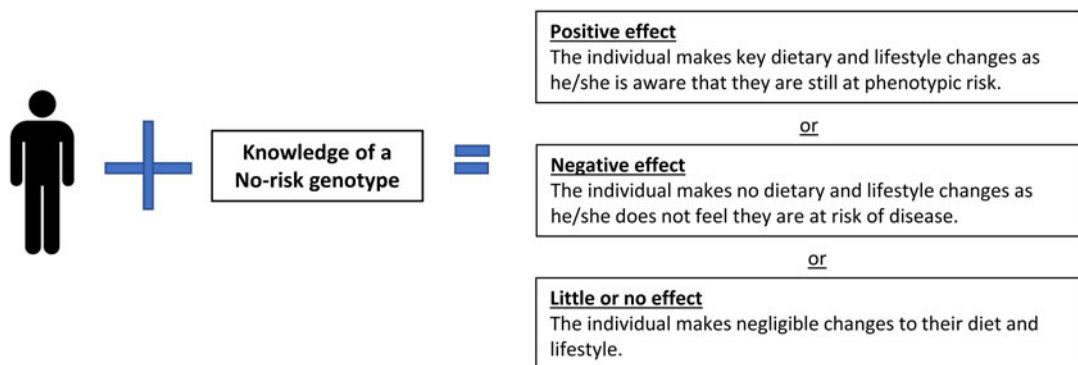


Fig. 1. (Colour online) Impact of genetic knowledge information on individual behaviour dependent on the presence of at-risk or no-risk genotypes. If individuals are informed that they have an at-risk genotype, this may promote positive dietary and lifestyle behaviour changes or the information may promote a fatalistic attitude because of the awareness of a genotypic risk for a particular disease (scenario 1). If individuals are informed that they have no genetic risk (no-risk genotype), they may still be motivated to make key lifestyle changes or the information may demotivate them from changing dietary and lifestyle habits as they are not at risk from a genetic point of view (scenario 2). In both scenarios, the genetic knowledge information may also have little or no effect on the individual, in which changes they make to their diet and lifestyle are negligible.

their results (potential consumers, $n = 86$)⁽²⁰⁾. The aim of the study was to investigate consumer perceptions of the effect of genetic risk information, obtained via DTC genetic tests, on their health behaviour and health anxiety. Individuals were contacted through social media and asked a series of open-ended and close-ended questions (forty-four questions for consumers, thirty-nine questions for non-consumers). It was found that 27.3% of consumers reported changes in their health behaviour, which were all either positive or neutral⁽²⁰⁾. Furthermore, a change in health anxiety was reported by 24.6% of consumers, of which, 85.3% were a reduction. A major strength of this survey and the one conducted by Kaufman *et al.*⁽¹⁹⁾ was the fact that they were conducted on real-life DTC consumers, rather than those who received the genetic testing free or at a reduced rate. This is in contrast to a study conducted by Bloss *et al.* who recruited employees from health and technology companies who agreed to purchase the Health Compass at a discounted rate⁽²¹⁾. Those taking part in

the study underwent health assessments at baseline and a 3-month follow-up (when they had received their genetic results) via SurveyMonkey⁽²¹⁾. Of those that completed the follow-up ($n = 2037$), no significant differences were observed between baseline and follow-up in terms of anxiety, dietary fat intake or exercise behaviour⁽²¹⁾. The investigators also re-tested these subjects at 12 months and similarly, no differences were reported in terms of anxiety, fat or exercise⁽²²⁾. Therefore, results with regard to the impact of DTC testing on changes in diet and lifestyle behaviours are mixed. It may be postulated that paying the full price for the genetic test may have a role to play in the impact of DTC testing on behaviour.

Studies investigating the impact of disease genetic risk disclosure with phenotypic/familial risk presence

Some studies have investigated the impact of genetic risk disclosure on those individuals who were already at a

Table 1. Summary of studies investigating the impact of direct-to-consumer (DTC) testing on motivating behaviour change

Author	Subjects	Design	Main findings
Kaufman <i>et al.</i> ⁽¹⁹⁾	Random sample of US DTC customers of 23and Me, deCODEme and Navigenics (<i>n</i> 1048)	Online survey of DTC consumers, including questions on demographics, perceptions of DTC results and health behaviours following DTC testing	43 % sought additional information about a health condition tested. 28 % discussed their results with a healthcare professional. 16 % changed their medication or supplement regimen. One-third reported that they were more careful with their diet
Egglestone <i>et al.</i> ⁽²⁰⁾	Individuals had purchased a DTC genetic test and received their results (consumers, <i>n</i> 189) and individuals who were awaiting test results or considering purchasing a test (potential consumers, <i>n</i> 86)	Online survey where individuals were asked if their health behaviour or health anxiety had changed after receiving their results	27.3 % of consumers claimed a change in health behaviour, all either positive or neutral. 24.6 % of consumers reported a change in health anxiety, of this, 85.3 % reported a reduction. Consumers had higher health scores than non-consumers ($P = 0.02$)
Bloss <i>et al.</i> ⁽²¹⁾	Employees who had agreed to purchase the Health Compass at a discounted rate (<i>n</i> 2037)	Web-based assessments of reported changes in anxiety, dietary fat intake, exercise behaviour, test-related distress and use of screening tests 3 months after testing	No significant differences were observed between baseline and follow-up in relation of anxiety, dietary fat intake or exercise behaviour. 90.3 % of subjects had scores indicating no test-related distress. No significant increase in the rate of screening tests observed
Bloss <i>et al.</i> ⁽²²⁾	Employees who purchased the Health Compass at a discounted rate (<i>n</i> 1325)	Follow-up of subjects 12 months after receiving genetic testing investigating changes in anxiety, dietary fat intake and exercise	Compared with baseline, no reported differences for anxiety, fat intake or exercise a year after receiving genetic testing. 96.8 % had no test-related distress. Screening test completion was significantly associated with disclosing genomic tests with a doctor (36 %, $P < 0.001$)

phenotypic and/or familial risk of a particular disease, many of which are shown in Table 2. One of the first of these studies investigated the hypothesis that confirmation of an individual's diagnosis of familial hypercholesterolaemia by the presence of genetic mutation, reduces patients' perceptions of control over the disease and adherence to risk-reducing behaviours⁽²³⁾. Individuals already diagnosed with familial hypercholesterolaemia and their first- or second-degree relatives, were randomised to receive routine clinical diagnosis or routine clinical diagnosis and genetic testing. The investigators found that those who had the mutations believed less strongly in the efficacy of diet in reducing cholesterol levels ($P = 0.02$) and demonstrated a trend in believing more strongly in the efficacy of cholesterol-lowering medication ($P = 0.06$). Therefore, the authors concluded that genetic testing does not affect the extent to which individuals believe that they have control over their health, but does affect their perceptions of how control is most effectively obtained⁽²³⁾. Hollands *et al.* investigated the effect of communicating risk assessment for Crohn's disease based on genotype on motivating smoking cessation for 24 h or longer, assessed at 6 months⁽²⁴⁾. Smokers with first-degree relatives with Crohn's disease were randomised to receive either a postal booklet detailing their risk assessment of developing Crohn's disease based on family history and smoking status, or with additional *NOD2* genotyping⁽²⁴⁾. Following receipt of the

booklet, a research counsellor contacted all participants to reiterate the information and give advice regarding smoking cessation. At 6 months, there were no differences between the groups in terms of the numbers of participants who stopped smoking for 24 h or the number of those who made an attempt to quit⁽²⁴⁾.

The effect of genetic risk information on those at an increased phenotypic risk of diabetes has also been investigated⁽²⁵⁾. Overweight individuals at phenotypic risk of diabetes were randomised to either receive genetic testing or not. For those individuals who received genetic testing, thirty-six risk alleles previously associated with type 2 diabetes were analysed and individualised genetic risk assessments were then calculated to assign participants to a higher or lower diabetes genetic risk. These individuals received a 15 min structured one-to-one genetic counselling session, explaining their results and encouragement to make certain behavioural changes to reduce overall diabetes risk⁽²⁵⁾. Following this, counselled intervention participants and untested controls took part in a diabetes prevention programme, conducted by an experienced dietitian for 12 weeks⁽²⁵⁾. There were no differences found with regard to self-reported motivation, programme attendance or weight loss when higher-risk recipients and lower-risk recipients were compared with those in the control group who received no genetic testing⁽²⁵⁾. When the higher- and lower-risk groups were compared, higher-risk result

Table 2. Studies investigating the impact of disease genetic risk disclosure with phenotypic/familial risk presence

Author	Subjects	Design	Main findings
Vassy <i>et al.</i> ⁽²⁶⁾	Young adults (<i>n</i> 521)	Individuals were given scenarios of receiving genetic susceptibility results for heart disease, type 2 DM and stroke. Responses were analysed by the presence of established disease-risk factors	Respondents with high phenotypic diabetes risk reported increased likelihood of improving their diet and physical activity in response to high-risk results compared with those with low diabetes risk, OR 1.82 (95% CI 1.03, 3.21) for diet and OR 2.64 (95% CI 1.24, 5.64) for physical activity
Grant <i>et al.</i> ⁽²⁵⁾	Patients at phenotypic risk of type 2 DM	Randomised to receive either genetic testing or not. Both groups attended a 12-week DM prevention programme	No differences were found between the groups in terms of self-reported motivation, programme attendance or weight loss
Marteau <i>et al.</i> ⁽²³⁾	Adults diagnosed with familial hypercholesterolaemia and their first- and second-degree relatives (<i>n</i> 341)	Randomised to routine clinical diagnosis or routine clinical diagnosis and genetic testing	Having the risk genotype did not affect perceptions of control over disease, adherence to medications, diet, physical activity and smoking
Alamian <i>et al.</i> ⁽⁴⁴⁾	Women at high risk of hereditary breast and ovarian cancer (<i>n</i> 303)	Examined use of supplements 12 months post <i>BRCA1/2</i> test result disclosure	51 % of participants reported using a dietary supplement
Vernarelli <i>et al.</i> ⁽²⁷⁾	Unaffected relatives of patients with Alzheimer's disease (<i>n</i> 272)	Examined effect of <i>APOE</i> genotype disclosure on health behaviour changes	Those individuals with one copy of risk variant were more likely to report change in supplement use. There were no significant differences between <i>APOE</i> E4+ and E4- participants in changes in overall diet, exercise or medications
Hollands <i>et al.</i> ⁽²⁴⁾	Smokers who were first-degree relatives of patients with Crohn's disease (<i>n</i> 497)	Risk assessment based on family history and smoking status, or with additional <i>NOD2</i> testing	Smoking cessation did not differ between the groups

DM, diabetes mellitus.

recipients more often reported that the genetic counselling made them more motivated to participate in the 12-week programme ($P = 0.003$) and make lifestyle changes ($P = 0.008$); however, programme attendance and weight loss were not statistically different between these two groups⁽²⁵⁾. In contrast to this, Vassy *et al.* conducted a nationally representative survey of young adults, who were given hypothetical scenarios of receiving genetic susceptibility results for heart disease, type 2 diabetes and stroke⁽²⁶⁾. These individuals were asked about their interest in such testing, anticipated likelihood of improving diet and physical activity with high- or low-risk test results and readiness to change. Responses were analysed based on the presence of established disease-risk factors⁽²⁶⁾. The investigators reported that those individuals with high phenotypic risk reported increased likelihood of improving their diet and physical activity in response to high-risk results, compared with those with low diabetes risk for diet and physical activity (Table 2). Furthermore, Vernarelli *et al.*⁽²⁷⁾ reported that individuals who were informed that they had at least one copy of the risk increasing (E4+) gene, had 4.75 times the odds of reporting a change in dietary supplement use than those with less risky genotype (E4-)⁽²⁸⁾. However, there were no differences found in terms of changes in overall diet, exercise or medications.

Therefore, evidence is mixed with respect to impact of genetic testing on behaviour change in the presence of

familial or phenotypic disease risk. It can be postulated that the particular disease risk is likely to have an effect on the impact of genetic knowledge, i.e. the perceived seriousness of the disease may affect motivation to change.

Studies investigating the impact of genotype-based personalised nutrition

Studies investigating the hypothesis of delivering genotype-based PN advice on motivating key behaviour changes such as diet, lifestyle and physical activity are presented in Table 3. One of the first studies to test this concept was by Arkadianos *et al.* in a weight loss clinic in Greece⁽²⁹⁾. Patients with a history of weight loss failures were offered a nutrigenetic test examining twenty-four variants in nineteen genes involved in metabolism (*ACE*, *APOC3*, *CBS*, *CETP*, *COLIA1*, *GSTMI*, *GSTPI*, *GSTT1*, *IL6*, *LPL*, *MTRR*, *MTHFR*, *MTR*, *NOS3*, *PPARG*, *SOD2*, *SOD3*, *TNFA* and *VDR*), using the Sciona MyCellf kit. These individuals were then matched for age, sex, starting BMI and number of times they had visited the clinic with patients who had not taken the test. Both groups followed a low glycaemic index Mediterranean diet, recommended exercise routines and regular follow-up visits to the clinic. For those in the nutrigenetic group, the diet and exercise programme was modified based on the individual genetic

Table 3. Studies investigating the impact of genotype-based personalised nutrition

Author	Subjects	Design	Main findings
Arkadianos <i>et al.</i> ⁽²⁹⁾	Patients with a history of weight loss failures were offered nutrigenetic test (<i>n</i> 50) and compared with patients, of similar characteristics, attending the clinic who did not undergo genetic testing (<i>n</i> 43)	Patients were given dietary advice based on their genetic results and compared with patients attending the clinic who received the usual care dietary advice	At 12 months, individuals who received nutrigenetic advice were more likely to have maintained some weight loss (73 %) than those in the comparison group (32 %). Average BMI reduction in the nutrigenetic group was 1.93 kg/m ² compared with an average BMI gain of 0.51 kg/m ² (2.2 % gain) (<i>P</i> < 0.0023)
Nielsen & El-Soehy ⁽³²⁾	Healthy men and women aged 20–35 years (<i>n</i> 138)	Participants were randomised to receive either personalised DNA-based dietary advice or general dietary advice with no genetic information for 12 months	Compared with the control group, no significant dietary changes were observed at 3 months. At 12 months, those with the risk version of <i>ACE</i> gene had significantly lower intakes of sodium compared with the control group (<i>P</i> = 0.008)
Hietaranta-Luoma <i>et al.</i> ⁽³¹⁾	Healthy adults aged 20–67 years (<i>n</i> 107)	Single-blinded intervention where participants were randomised into either control group (<i>n</i> 61) or intervention group (<i>n</i> 61) who received health message based on their <i>APOE</i> genotype	Dietary fat quality improved in the E4+ group compared with the E4– and control groups (<i>P</i> < 0.05), but only for a short time
Frankwich <i>et al.</i> ⁽³⁰⁾	Obese or overweight US veterans on a weight management programme (the MOVE! Programme) (<i>n</i> 51)	Participants were randomly assigned to either a nutrigenetic-guided diet or a standard balanced diet	No significant difference in the percentage of participants on the balanced diet compared with the nutrigenetic-guided diet who lost 5 % of their body weight at 8 weeks or at 24 weeks

results. For example, if an individual had a variation in *MTHFR*, *MTRR*, *MTR* or *CBS*, they were advised to take a supplement containing 800 µg folic acid, 15 mg vitamin B₆ and 20 µg vitamin B₁₂⁽²⁹⁾. The investigators reported that after 6 months the two groups performed the same in terms of weight loss⁽²⁹⁾. However, at 12 months, the nutrigenetic group were more likely to maintain some weight loss compared with the control group, with an average BMI loss of 1.93 kg/m² in the nutrigenetic group compared with an average BMI gain of 0.86 kg/m² in the control group (*P* < 0.023). It is important to note that the individuals were put on altered diets based on their individual genetic results and therefore, this study design cannot distinguish between whether knowledge of genotype-motivated individuals to make appropriate dietary and lifestyle changes or whether the particular diet chosen for each individual promoted a better biological response, which resulted in sustained weight loss compared with the control group.

In contrast to these positive findings, a US research group investigated the effect of genetic-guided weight loss advice in comparison with a standard weight loss diet⁽³⁰⁾. The investigators randomised fifty-one obese or overweight US veterans to either a nutrigenetic-guided diet (balanced, low-carbohydrate, low-fat or Mediterranean) based on seven genes (*APOA2*, *ADIPOQ*, *FTO*, *KCTD10*, *LIPC*, *MMAB* and *PPARG*) or standard balanced diet for 6 months. No differences were observed in the percentage of participants who lost 5 % of their body weight at 2 or 6 months between the groups⁽³⁰⁾.

As secondary analysis, the researchers also investigated the role of adherence in the participants' weight loss and found that, within the nutrigenetic-guided group, there was a significant relationship between adherence and weight loss (*P* = 0.002) and those in the top quartile had lost a significant amount of weight compared with the lowest quartile (*P* = 0.03)⁽³⁰⁾. This may suggest that genotype-based PN advice may be of benefit to those who are most adherent to their recommended diet plan⁽³⁰⁾. Similar to the study conducted by Arkadianos *et al.*⁽²⁹⁾, this study does not test the hypothesis of the impact of genotype-based personalised advice on motivating behaviour change but rather the potential biological response to a nutrigenetic-guided weight loss diet.

Hietaranta-Luoma *et al.* investigated the effect of *APOE* genotype information on behavioural changes related to diet, including fat quality, vegetable and fruit consumption, alcohol consumption and exercise levels in a 12-month intervention study⁽³¹⁾. Participants were randomised to either the control group who received general information or intervention group who were tested for the *APOE* genotype and given a tailored health message related to their *APOE* genotype, its effect on CVD risk and importance of dietary and lifestyle changes based on the extended parallel process model⁽³¹⁾. Dietary changes were assessed at baseline, 10 weeks, 6 months and 12 months. Those with the *APOE* E4+ genotype reported better dietary fat quality compared with those in the E4– group and control group (*P* < 0.05) at 10 weeks and 6 months; however, this was not observed

at 12 months⁽³¹⁾. Nielsen *et al.* also reported changes in sodium intake following disclosure of the *ACE* genotype⁽³²⁾. Here, the investigators recruited healthy individuals to take part in an online randomised controlled trial, where individuals were randomised to receive either genotype-based PN advice or general healthy eating advice. Those in the intervention group were genotyped for five dietary-related genes including *CYP1A2*, *GSTT1*, *GSTM1*, *TAS1R2* and *ACE*. The investigators reported no differences between the groups at 3 months, but at 12 months, those with the risk version of the *ACE* gene reported significantly lower dietary sodium intakes compared with those with the non-risk *ACE* genotype or control group ($P = 0.008$). However, no differences were observed in terms of any of the other dietary markers associated with the genes investigated⁽³²⁾.

It is interesting to note the differences in the duration of follow-up within these studies, as the effect of genotype-based personalised advice was observed at 12 months in studies conducted by Arkadianos *et al.*⁽²⁹⁾ and Nielsen & El-Sohemy⁽³²⁾, but not reported in those studies of shorter duration⁽³⁰⁾. However, Hietaranta-Luoma *et al.* reported positive changes early on in the intervention, but these were no longer evident at 12 months⁽³¹⁾. At present, the evidence for the benefit of genotype-based PN is not strong, and more studies are warranted before any clear conclusions can be deduced on personalised advice based on genotype and motivating behaviour change.

Recent findings in personalised nutrition: the Food4Me study

In the previous section, studies investigating the effect of genotype-based personalised advice on motivating behaviour change were examined. However, PN advice is not exclusive to genotype information, and in fact, PN advice can be delivered using dietary intake information as well as phenotypic markers and genotype⁽⁴⁾. Therefore, the Food4Me proof-of-principle study set out to investigate the effect of varying levels of PN advice on health outcomes in comparison with general healthy eating advice⁽³³⁾. Individuals were recruited across seven centres in Europe to take part in a 6-month online PN intervention study where participants were randomised into one of four groups: control group who received general healthy eating guidelines; level 1 group who received PN advice based on dietary intake; level 2 group who received PN advice based on diet and phenotypic; level 3 group who received PN advice based on diet, phenotype and genotype information.

This study was designed to emulate existing PN services, and therefore, all data were self-collected and self-reported by the participants⁽³³⁾. To facilitate this, participants were sent instructions and equipment via post. Online videos were also available demonstrating how to perform the measurements. Dietary information was collected using an online FFQ, specifically designed for the purposes of the study^(34,35). Anthropometric measurements, including BMI, waist, hip and thigh circumferences were self-collected by the volunteers. Participants collected dry blood spots and posted them

back to their local research centre. These dry blood spot cards were analysed for cholesterol, glucose, a range of fatty acids and carotenoids⁽³³⁾. Each participant also collected a sample of their DNA using a buccal swab and a panel of thirty-three SNP were analysed⁽³³⁾. Participants received tailored feedback reports appropriate to their intervention level (as above) at months 0, 3 and 6, using decision trees for a systematic approach across seven research centres in line with behaviour change techniques⁽³³⁾. Level 3 participants received feedback on five dietary-related SNP, including *FTO*, *TCFL2*, *APOE*, *FADS1* and *MTHFR*.

The investigators reported that following a 6-month intervention participants who were randomised to personalised groups (levels 1, 2 and 3), were more motivated to make positive changes to their diet, compared with those who were given healthy eating guidelines⁽³⁶⁾. More specifically, those in the personalised groups, consumed significantly less red meat (-5.48 g (95% CI -10.8 , -0.09), $P = 0.046$), salt (-0.65 g (95% CI -1.1 , -0.25), $P = 0.002$) and saturated fat (-1.14 % of energy (95% CI -1.6 , -0.67), $P < 0.0001$)⁽³⁶⁾. Furthermore, levels 1, 2 and 3 personalised groups significantly increased their folate intake and had higher Healthy Eating Index scores, than those in the control group. However, the researchers concluded that there was no additional benefit of phenotypic or phenotypic and genotype-based personalised advice, i.e. no difference across the levels of personalisation⁽³⁶⁾.

Within Food4Me, the impact of genotype-based PN advice has been investigated further in relation to *APOE* and *MTHFR* genotypes to date^(37,38). Fallaize *et al.* investigated the impact of knowledge of *APOE* genotype on dietary fat changes⁽³⁷⁾. The researchers reported significantly higher total cholesterol concentrations in those with the risk E4+ genotype, compared with those with the non-risk E4- genotype ($P < 0.05$)⁽³⁷⁾. Both *APOE* risk and non-risk groups significantly reduced their saturated fat intakes compared with baseline values; however, no differences were observed between the risk and non-risk groups⁽³⁷⁾. Moreover, those participants who were told that they had the non-risk *APOE* genotype (E4-), had a smaller reduction in their saturated fat intake compared with participants who did not receive genotype-based personalised advice (level 2 participants), suggesting that knowledge of 'less risky' genotypes may actually demotivate individuals from making key dietary and lifestyle changes as previously postulated⁽³⁷⁾.

The impact of *MTHFR* risk knowledge within the Food4Me cohort was also investigated⁽³⁸⁾. In Food4Me, participants randomised to level 3 group were informed whether they had the risk version (CT or TT genotypes) or non-risk version (CC genotype) of the *MTHFR* 677CT gene. To examine the impact of knowledge of *MTHFR* risk, level 3 participants were split into those with the risk version and those with the non-risk version and dietary intakes of folate were compared with those who received general healthy eating advice (control group)⁽³⁸⁾. Overall, no differences were observed between the *MTHFR* risk, non-risk and control



groups for changes in total dietary folate intake from baseline to month 6. Similarly, no differences were observed between the groups in terms of changes in gram intakes of food groups that contain folate such as liver, green leafy vegetables and fortified cereals⁽³⁸⁾. Further analysis was conducted investigating the differences between the *MTHFR* risk, *MTHFR* non-risk and participants in levels 1 and 2 who received non-genotype-based personalised advice, but no differences were observed. This suggests that *MTHFR* genotype-based PN advice did not have a more significant impact on increasing dietary folate intakes, compared with general healthy eating advice or non-genotype-based PN advice. It could be postulated that perhaps the effect of genotype-based PN advice could not be observed in this study as *MTHFR* genotype is not as well-known from a public health point of view compared with *APOE* genotype and its impact on saturated fat⁽³⁸⁾.

Conclusion

In this review the impact of genotype-based personalised advice on individuals' behaviour was investigated. We reviewed the current evidence under three sub-sections: impact of DTC testing, impact of disease genetic risk disclosure in the presence of associated familial and/or phenotypic risk, and the impact of genotype-based personalised advice. The current evidence does not appear to provide strong support for genotype-based personalised advice with respect to motivating behaviour change. Furthermore, there is some evidence to suggest that genetic knowledge could have a negative effect on individuals in terms of demotivation or increase in anxiety. These findings are in line with those reported from two Cochrane reviews^(13,39). However, more work in this field is required to investigate this hypothesis further.

It should be noted that study designs within existing publications in this area vary greatly and it is difficult to deduce if any one study correctly tests the hypothesis of the impact of genetic knowledge on behaviour change. Using *FTO* genotype and weight loss as an example, in theory, the population studied should be divided into those with the at-risk genotype and those with the no-risk genotype. To correctly test impact of knowledge of genotype on motivational change, within the *FTO* at-risk genotype group, half of the individuals should be informed that they have the at-risk genotype and the other half informed that they have the no-risk genotype and the same approach in the no-risk group. This study design could then distinguish between the issue of genotype-based advice motivating behaviour change or whether the right diet given per genotype results in a positive phenotypic change, i.e. weight loss. Whilst ideal, this would be challenging from an ethical point of view. For future work in this area, it is important to consider carefully the appropriate study design in light of the research question asked, i.e. is it motivation that causes the change or biological response to the genotype.

Another issue to consider is the strength of evidence with regard to the genotype-based personalised advice

based on nutrigenetic research. It is important to remember that this is still an area in its infancy and whilst promising, there is a lack of substantial evidence for the majority of SNP identified, with few exceptions⁽¹⁶⁾. The majority of the evidence in this area is based on observational studies and few diet–gene interactions have been tested for causality in human intervention trials⁽⁴⁰⁾. Therefore, more evidence is required before the impact of genotype-based personalised advice can truly be assessed⁽⁴¹⁾. Furthermore, when considering motivating individuals to change their diet, behaviour change techniques are necessary. In the Food4Me study, the intervention was designed in line with behaviour change techniques adapted from the work by Michie *et al.* on smoking cessation and dietary change behaviour^(42,43). However, the vast majority of the studies reviewed did not mention the inclusion of behaviour change techniques within their study design, and as such, interpretation of their results in the context of success of behavioural change is then challenging.

In conclusion, current evidence does not seem to support the hypothesis that genotype-based personalised advice motivates behaviour change. However, more research in this area is warranted, and future work needs careful consideration with regard to the study design, selection of SNP used for the development of PN advice, and the inclusion of behaviour change techniques.

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Conflict of Interest

None.

Authorship

C. B. O. D. drafted the outline of the manuscript, conducted the literature search and drafted the manuscript. M. C. W., M. J. G., E. R. G. and L. B. were responsible for critically reviewing the manuscript. All authors read and approved the final manuscript before submission.

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