



Position Statement on Direct to Consumer Genomic Testing

The Royal College of General Practitioners (RCGP) and the British Society for Genetic Medicine (BSGM) recommend that health professionals should exercise caution when asked to offer, or provide, clinical expertise about the results of Direct to Consumer (DTC) genomic or genetic testing.

The analytical validity, sensitivity and clinical utility of such testing may be much lower than is popularly perceived. For certain types of DTC results, there is a very high chance of false positive or false negative results. This means that patients should be offered the NHS care which would otherwise have been offered (e.g. family history and risk assessment, healthy lifestyle advice, or referral to specialist care)¹ regardless of their DTC result.

Background

Companies that offer Direct to Consumer (DTC) genetic/genomic testing are increasing their marketing activities in the UK and over the internet and are targeting healthy people. The technology to analyse a person's [heritable] DNA (genetic code) is now fast and cheap. Exemplar types of test results from direct to consumer testing include:

1. Gene variants giving information regarding single gene conditions or predispositions: examples may be variants in breast cancer related genes (*BRCA1* or *BRCA2*), or the Cystic Fibrosis gene (*CFTR*). Results may be:
 - **False negatives:** The genes may have many different types of variation within them, yet often DTC testing only looks for a small proportion. Thus testing will miss a large proportion of these, for example in the region of 80% of known *BRCA1/2* mutations are missed by commercial companies who generally only analyse three of the many different possible mutations .
 - **False positives:** DTC tests that use a "SNP chip " [single nucleotide polymorphism] technique [used by the majority of companies in operation in 2019] are very likely to categorise rare variants wrongly². Thus 85-95% of *BRCA1/2* variants or Bowel cancer gene variants for example, will be false positives or artefacts. The impact of false positives will likely place increasing demand on the health service which will need to spend considerable time and money counselling patients and reanalysing their samples.
2. Combination of genes which indicate susceptibility to a common complex or multifactorial condition e.g. Parkinson's disease or diabetes. For these conditions there may be a combination of gene variants which individually have small effects, but in combination have additive effects that increase susceptibility to a common complex condition. These tests may have similar issues in relation to false negatives and positives as outlined above. Their predictive value (or reassurance value) even where true positive or negative may be poor.
3. Pharmacogenomic variants: gene variants which affect an individual's response to a medication, giving information predicting effectiveness of the medication or predicting an adverse drug reaction (or a suboptimal response). These tests have similar issues in relation to false negatives and positives as outlined above.

NHS patients may present to their GP or other NHS professionals requesting help with the interpretation of DTC genomic results. Care should be taken not to take these results at face value.

The ability to confidently interpret how variation within the genetic code impacts a person's health or risk of disease is often weaker than people expect. Furthermore it will often require contextual information such as clinical signs, symptoms or family history to facilitate interpretation. Within the NHS, the Genomics Test Directory lists which genetic tests accredited laboratories³ can provide if particular criteria (e.g. clinical context) are met. Confirming a clinical diagnosis through genomic testing can be very helpful, however predicting future health problems from genomic testing alone is still a vague inaccurate science. This fact can come as a surprise to patients and professionals since the discourse about genomics is often rather deterministic.

Patients should not be referred to secondary or tertiary care solely on the basis of DTC results alone. Because of the high chance of false positive or false negative results, referrals are only indicated if existing referral criteria are met.



Referral should be considered if a variant is found in a gene for which testing is offered on the NHS, or if *both* members of a couple are found to be carriers for a genetic condition. Referral should also be based on clinical signs, symptoms or family history of disease. Genomic services are generally able to provide advice where it is not clear whether a particular patient meets these referral criteria.

Recommendations

- GPs should not take at face value, or attempt to interpret, reports from non-accredited and non-kite-marked laboratories such as DTC companies.
- GPs should use clinical and family history to assess the chance of heritable disease.
- Where a patient has a medical history or family history which suggests that genomic testing is indicated, then they should be referred via appropriate pathways regardless of their DTC test results.
- If a patient who has had a DTC test is reported to have an alteration in a gene for which NHS testing is offered (e.g. *BRCA*) then you should discuss with your regional NHS genetics clinic whether referral is appropriate. Please note that majority of these results will be artefacts due to the technology used.
- If a patient wants to discuss a DTC result for which NHS genomic testing is not usually offered (e.g. paternity tests or ancestry information) then they should be signposted to the commercial DTC provider. Such predictions rarely have health implications and therefore do not fall under the auspices of the NHS
- We support educational campaigns (DH, HEE) informing patients of the limitations of DTC testing, and recommending that regulators should be asking that DTC testing companies provide clinical support as part of the models informing patients of the limitations of DTC testing.

Conclusion

In order to provide high quality, cost-efficient care in the NHS, it is important to note that many DTC results done without clinical indications may be wrong. There are significant NHS costs in confirming (or more often refuting) DTC testing results and these are not warranted unless there are clinical indications for testing.

Patients presenting with DTC results to their GP should be offered usual NHS care: family history and risk assessment, with onward referral and testing as per standard NHS pathways and protocols.

References

- 1) Horton R et al. *Direct-to-consumer genetic testing*. BMJ 2019; 367 doi: <https://doi.org/10.1136/bmj.l5688>
- 2) Weedon MN et al. *Very rare pathogenic genetic variants detected by SNP-chips are usually false positives: implications for direct-to-consumer genetic testing*. BioRxiv 696799; doi: <https://doi.org/10.1101/696799>
- 3) NHS England and Improvement. National Genomic Test Directory. 2018. <https://www.england.nhs.uk/publication/national-genomic-test-directories/>

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