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Genetic Testing for Amelogenesis Imperfecta: Knowledge and attitudes of Paediatric Dentists

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Abstract

Introduction:

Genetic testing is increasingly applied across healthcare reflecting the value to diagnosis, clinical decision-making, service organisation and advancement of the research-informed evidence base. Patient expectations are changing. Genetic testing has not been part of dental practice. Introduction of a NHS targeted gene panel test for Amelogenesis Imperfecta (AI), a heterogeneous genetic disorder affecting enamel appearance and function, represents a paradigm shift. This impacts on specialists in paediatric dentistry and other members of the dental team delivering longitudinal care for individuals with AI.

Aim:

To evaluate the opinions of paediatric dentists on genetic testing for dental conditions using AI as the exemplar.

Method:

Two focus groups of 9 UK NHS paediatric dentists each were audio recorded (September 2016) and transcribed verbatim. Qualitative analysis was undertaken using Interpretative Phenomenological Analysis (IPA).

Results:

A wide range of views reflected existing insight and understanding. Three core concepts of justification, ownership and challenges emerged. The clinicians were generally open to involvement with genetic testing in Paediatric Dentistry, but required more support.

Conclusion:

Areas for clarification and professional development were identified as important in ensuring that genetic testing in dentistry, which is currently in its infancy, reaches translational potential and enhances patient care as this area of healthcare continues to advance rapidly.

Research in brief

- Translation of clinical genetic testing to patient care is increasing as personalised care develops, including in dentistry.
- This study provides insight into current attitudes of paediatric dentists towards genetic testing in dentistry for dental conditions.
- It demonstrates a willingness within the profession to become involved with genetic testing.
- Areas are identified where further professional development and support in dentistry are required to realise the benefits that genetic testing offers to patient care.

Introduction

Genetic testing is increasingly at the forefront of clinical care in the United Kingdom (UK) National Health Service (NHS) as highlighted in 'Generation Genome' the 2016 Report of the Chief Medical Officer for England.¹ The change reflects advances in the ability to translate genetic information to patient care as the era of 'personalised care' develops. There is added value to diagnosis, clinical decision-making, service organisation and advancement of the research-informed evidence base within a context of changing patient and public expectations. A consequence of these advances is the need for a greater number of clinicians to embed clinical genetics into their day-to-day practice. This represents a fundamental change in practice for many clinicians,² and none more so than in dentistry. We are at the start of a new era of healthcare that can be expected to develop significantly and will impact on how dentistry is practiced and oral healthcare is delivered.

Introduction of a NHS targeted 21 gene panel test for Amelogenesis Imperfecta (AI) in the summer of 2016 (UK Genetic Testing Portfolio #331),³ a heterogeneous genetic disorder affecting enamel appearance and function, represents a paradigm shift for the profession. It can be expected that further genetic testing that impacts on oral healthcare will be introduced over time.

The 21 gene AI panel test (see online supplementary information 1) has the potential to address some of the current limitations of AI care, undertaken within the challenges of multiple visits as the dentition develops and parental/guardian concerns and expectations, before transfer to adult services. The clinical burden of AI in the UK is poorly understood and this limits service planning and delivery. AI has a global prevalence of 1 in 700 to 1 in 14,000 depending on the population studied.⁴ The heterogeneous nature of AI means that different individuals have different healthcare needs. Access to specialist care can be difficult to achieve. For those with AI many activities of day-to-day living can be affected with a negative impact on self-esteem.^{5,6} The evidence base for treatment interventions for AI is weak.⁷

The classification of AI has focused on clinical phenotyping.⁸ Three main issues limit this approach. Some AI phenotypes fall outside of the classification. Post-eruptive changes to enamel can be marked and make accurate AI classification difficult. Some forms of AI are associated with other health problems, yet these can cover a wide spectrum of clinical presentations even for variants in a single gene.⁹ In AI and nephrocalcinosis the detection of AI precedes the renal calcification by many years offering an opportunity to identify affected individuals via dental examination much earlier than is currently the case.^{10,11}

The potential for genetic information to positively impact on AI care has been recognised for some time.¹² However, it is only the recent advances in clinical genetics that now allow this potential to be realised. Central to this is an ability to classify AI much more accurately and to use this insight to inform patient understanding, the genotype-phenotype relationship, multi-centre clinical trials to strengthen the evidence base for interventions and development of patient pathways within Managed Clinical Networks.

Introduction of the 21 gene AI panel test particularly impacts on specialists in paediatric dentistry, with recognition that the associated challenges will be common to other clinical areas as new tests are developed. Those providing care for AI patients did not have genetic testing included in their training and we hypothesised that they are unlikely to have subsequently acquired professional development in this area. This study aimed to evaluate the opinions of paediatric dentists about the introduction of genetic testing for dental conditions using AI as the exemplar.

Methods

The study was conducted following ethical approval by the Dental Research Ethics Committee at the University of Leeds on 16th August 2016, reference: 070716/FM/206. An invitation letter attached to the initial emails requesting volunteers to participate was sent. A further information letter and participant consent form were later forwarded and written consent obtained from all participants.

Participants and Recruitment

The invitation emails were sent to those registered to attend the annual British Society of Paediatric Dentistry conference in Leeds in September 2016. Only Paediatric Dentists currently working in the UK were included in the study. Two focus groups were held on consecutive days of the conference. Allocation of groups was mainly through participants indicating what day they could attend, with those who could attend both allocated to either group to ensure as balanced characteristics as possible.

Focus Groups

A topic guide was developed (see online supplementary information 2), informed by a literature review and discussion with the research team (authors of this paper). One member of the team was currently involved with genetic testing research for AI, while the others worked in a paediatric dentistry setting and had experience of referring for genetic testing and management of patients with genetic conditions. The topic guide was trialed in a pilot focus group with paediatric dentistry colleagues at the institution of the lead researcher and altered following this.

The discussions were audio recorded and mainly left to develop through the participants, with the researchers intervening to ask for clarification of any relevant points or to introduce a new topic. The topic guide was used to ensure all important areas were covered. Both groups were led by the chief researcher along with assistance from two other members of the research team. The lead researcher (FM) was a Specialty Registrar in Paediatric Dentistry. The two other researchers present were a consultant in Paediatric Dentistry (RB) and a specialist and clinical lecturer in Paediatric Dentistry (KK), with previous experience of qualitative research. The focus groups began with a member of the research team reading a prepared statement describing the context of the discussion and indicating the aim, which was to explore issues around genetic testing in Paediatric Dentistry. The recordings were transcribed verbatim (by FM) and participant information anonymised. The lead researcher reflected within 24 hours after each focus groups, with the reflection kept separate from the formal analysis.

Analysis

Analysis was carried out using Interpretative Phenomenological Analysis (IPA). The stages followed IPA best practice which is summarised in Table 1.¹³ The analysis was undertaken by FM and KK independently, who then reviewed the findings together before discussing with the rest of the research team. The transcribed audio recordings were read through many times and notes taken which included any reflections/thoughts from FM and KK on the transcriptions. The notes were then used to identify emerging themes from the transcription. Similarities were identified between themes and this was used to create sub- themes and allow core concepts to be identified.

Interpretative Phenomenological Analysis (Pietkiewicz and Smith, J. A. 2012)

**Table 1: IPA Best practice stages
(see separate document)**

Results

There were 25 positive responses from those who met the inclusion criteria to the initial invitation email. This email was sent to approximately 150 eligible individuals. Based on first come first served and each individual's availability for the 2 focus groups, ten participants were invited to attend each group. For each focus group nine invitees attended. Both groups included paediatric dentists working across the UK in different settings and in different roles including 8 consultants and 3 specialty trainees. In each group seven worked in a hospital setting with two working in a community setting. The focus groups lasted 24 and 30 minutes long.

Three core concepts emerged from the focus groups: ownership, justification and challenges concerning genetic testing. Within these three core concepts, sub-themes were identified as summarised in Figure 1. The same sub-themes were identified in both focus groups (see online supplementary information 3 and 4 for further detail). Examples of the stages used to come to final conclusions can be seen in Table 2 which is taken from the 'Justification' core concept area of the analysis.

Core concepts and sub-themes identified through both focus groups

**Figure 1: Summary of results
(See separate results)**

Example of IPA analysis concluding in the 'Justification' core concept

Table 2: Example of IPA analysis process

1. Justification

1.1. Reasons for testing

There was a significant amount of time spent discussing reasons for testing. The most common topic was the need to test at all. Some felt there may not be a valid reason for carrying out testing for conditions such as AI. Others felt families would gain further knowledge and possibly discover siblings affected by the same conditions. Concern was noted by some participants that the rest of the family unit would then need to be able to access appropriate care and the capacity for providing this.

1.2. Timing of testing

When to carry out testing on a child was discussed with reference to the risks versus the benefits. Past experiences of genetic testing for dental conditions allowed some participants to draw on the importance it could play in a child's life. Knowing about a condition in a timely manner was seen to be of benefit, but no overall consensus of when this may be reached.

1.3. Dental Relevance

There was prior experience discussed regarding current practice and the genetic testing justification already practised in some areas of the country, as shown in Table 2. Other participants disputed these points by acknowledging that part of our roles is to be able to fully inform patients and allow them to make choices about information they wished to gain.

2. Ownership

2.1. Roles

Set roles, with clearly defined boundaries emerged as an important prerequisite for genetic testing to be embraced by the participants. They largely felt they should be involved in the process and that patients would expect them to have the knowledge to advise them appropriately. There was emphasis however on the dental team not leading the testing and working more as an adjunct: '*...we don't have the training so it has to be...bolted on to a service provided by the people who have been trained...*' (P 18).

There were differences noted between participants in perceptions of their involvement in a genetic testing team. Some saw their role more of as a referrer rather than part of the team:

'...that's not something that's my territory...send it and have counselling with a geneticist rather than do it myself.' (P 9). Others volunteered willingness to engage with a team under the correct circumstances.

2.2 Experience

In order to address the difference in opinions regarding roles in testing, the benefit of mirroring other specialties was discussed. Those already involved with testing in the cleft lip and palate (CLAP) setting discussed this environment, noting it felt safe, routine and a model of how genetic testing for other dental conditions could be based on: '*With cleft patients we wouldn't be terribly resistant about referring for genetic testing and it would be part of our normal procedure...*' (P 1).

2.3. Team

There was further discussion about being part of a team would allow the participants to feel comfortable with genetic testing: *'Part of the package put in place by the geneticist-the team.'* (P 7). Being an asset to the team was noted and the importance of them being part of it. *'We know the dental implications of a finding, they know how to tell the family about inheritance and further risk'* (P 18).

2.4. Child patient autonomy

Consideration was given to the rights of the child to decline testing but also the rights of parents and families to seek testing. This sub-theme was closely aligned to the justification and timing of testing concept and sub-theme. Some participants however were undecided on their opinion of this subject matter: *'...is there any benefit from doing it early or do you leave it until that person who is being tested can give consent for themselves'* (P 9). Others considered this topic more from the parent point of view: *'...it is very important for the parents to know chances of the next child going to be affected.'* (P 16).

3. Challenges

3.1 Training

All participants agreed on a need for more training on this area: *'...as paediatric dentists we will need more training to be more involved I think; but at this stage I personally wouldn't feel comfortable discussing the results of a genetic test with my patients, I don't have the training or the understanding of these things.'* (P 12). Some saw this as an essential part of having informed discussions with patients and families. Others felt it could bridge a pathway to being involved with testing. There were questions raised on the timing and setting of training and what level it should be aimed at: *'...we don't have training in genetic counselling and where would you introduce that in to curriculum, would it be at undergraduate curriculum or a paediatric dentistry specialist curriculum...'* (P 18)

3.2. Implications

Many participants reflected on negative past experiences in relation to genetic testing. Family dynamics were perceived to be affected by results of genetic tests in the sense of paternity confirmation: *'I've been in the room when.... I've been shrinking in to the corner when the geneticist has said to the dad, or to the mum actually, he is not the dad...'* (P 18). Families are also drawn in to conversations about who is responsible for a genetic condition which can be problematic: *'I've got a few families where there is actually quite a lot of internal conflict due to the diagnosis of amelo'* (P 6). Other implications seen as significant was the influence this could have over medical insurance and this could therefore be an important barrier to wanting to pursue genetic testing. Similar to the sub-theme of timing of testing when considering justification, participants considered the consent process that would need to exist with children under the age of consent. It was discussed whether it was the right approach to test those who may in the future have different views from their parents.

3.3. Clinician concerns

This sub-theme was an important area discussed in terms of how confident and willing clinicians would be to involve themselves with genetic testing. Feeling ill equipped and unsure of their own clinical capabilities was expressed. Past experiences were again drawn on to support the apprehension felt but also demonstrated the emotional involvement that can occur. *'...that was very upsetting for the parent and she came to my door with the problem and in floods of tears so and I had no experience or idea of how to deal with that'* (P 9).

Discussion

The study was conducted and interpreted according to established approaches for qualitative research involving focus groups.^{13,14} It provided insight into the opinions of dentists on genetic testing as part of oral healthcare practice, which is an area of dentistry that has not been previously reported. There are similar themes to those identified in other areas of healthcare.²

Participant recruitment to the study was based on those registered to attend a national paediatric dentistry conference. Both focus groups were concluded before all the issues raised during the discussions had been fully explored, reflecting time constrictions and the importance that the participants gave the topics. Allocation of participants to the groups was through convenience in that many participants could only attend one of the days. In another setting it would have been useful to randomly allocate groups to reduce potential bias.

There were some differences in the topics raised by each focus group. The first group discussed testing in the medical specialties and participants reflected on the counseling side of testing associated with sharing test results. This group also discussed patient knowledge, the complexity of testing and support that would be required for implementation. Group Two included discussion on public perception in terms of increased awareness of genetic testing and how this affects clinical care. This group also had different levels of experience and background to draw from. One participant was part of a multi-disciplinary genetic testing team in a dental setting and relevant experiences were shared. Group Two discussed the lack of scope in the dental curricula for further genetic training. Concern was expressed on the financial impact of testing on local services. Some differences between the 2 focus groups reflect the current complexity of UK-wide NHS provision within local arrangements coupled with differing service pressures and challenges. These differences however emerged as part of the same overall sub-themes and core-concepts. This attached validity to the results of the study with the two groups reaching common conclusions via different routes.

This study revealed a number of areas that should be considered in implementation of genetic testing for AI as part of clinical care. Many of the sub themes were inter-connected with the three core-concepts of ownership, justification and challenges summing the wide breadth of information gained.

There was recognition that genetic testing has an important role and is part of the development of personalised care. However, concerns were expressed about the introduction of genetic testing as a new aspect of care in dentistry. Some of the potential barriers raised may reflect nothing more than the natural suspicion associated with new and unfamiliar tests. Other concerns were more specific to the impact on day-to-day clinical practice. Identifying how testing should be offered was a primary focus of discussions, with no clear conclusion reached by the participants. This demonstrates the need for better information on what AI genetic testing can achieve coupled with clarity on its limitations.

For a named condition such as AI, genetic testing can be undertaken in 3 main ways with increasing costs linked to technical and clinical complexity: targeted gene panel; whole exome sequencing (WES) and whole genome sequencing (WGS). NHS AI genetic testing is currently available only via a targeted 21-gene panel in which variants are known to cause AI. This approach is the most likely to give a negative result (i.e. no relevant genetic variants found) reflecting that not all genes that cause AI have yet been identified.¹⁵ Despite this limitation, this test can identify many relevant AI gene variants and do not carry the same risks of recognition of coincidental pathological gene variants (e.g. predisposing to cancer) that can be a feature of WES and WGS.

It was recognised that patients and families have changing expectations and will be increasingly aware of the options available to them. Participants agreed there should be access to support for patients and families throughout the process if genetic testing is pursued. There were variations in opinion as to how this can be best achieved. Personal experiences greatly affected the opinions of the clinicians. Emotive language was used in many of the shared experiences.

Concerns were raised regarding the involvement of dental professionals in genetic testing where traditionally clinical geneticists and clinical genetic counselors have led on care. Some participants felt that it was not their responsibility to take on new roles in this area. Negative experiences of being involved in genetic testing with feelings of being out of their depth were implied by some of the participants. Some negative experiences of focus group members were historical and before the ongoing healthcare-wide initiatives towards greater use of genetic testing to inform personalised care. However, these views continue to carry weight and should inform future planning.

Positive experiences were also shared. For example, personal stories were recounted by those with direct experience of genetic testing, for example in a cleft lip and palate setting. Those clinicians with prior positive experiences have a potentially invaluable role in successful implementation of genetic testing in oral healthcare, including for those with AI.

It is important to recognise that genetic testing will not be part of care for all with AI and as with any investigation, it should only be included as part of care after consideration of the potential benefits and risks.

There was broad agreement that clinicians require support, professional development, up to date resources and clear mechanisms to access support to deliver the benefits of testing effectively and appropriately within changing clinical practices across healthcare. The focus group discussions confirmed that more needs to be done to prepare the dental workforce for the introduction of genetic testing more widely to healthcare. There is an immediate implication for the specialty-training curriculum in paediatric dentistry, which is currently under review alongside all the General Dental Council specialty curricula. There is also a need to iteratively support professional development of specialists in paediatric dentistry in this area of practice.

Participants discussed the possible cost implications of genetic testing within the context of current service pressures and limited funding. It was recognised that justification is required for genetic testing so that it is clear how testing will influence clinical decision-making, inform better care and make best use of resources. This highlights the need for a strategic approach to service organisation to improve equity and quality of care in parallel with an improving intervention evidence base. AI care development fits well with a Managed Clinical Network approach. AI genetic testing has the potential to underpin these much needed initiatives and inform detailed economic modelling linked to patient outcomes. Some of these developments will take time and translation of genetic information to oral healthcare is in its infancy. However, the need to translate this emerging area to improve patient oral healthcare is clear. This study has highlighted the need to develop the dental workforce to meet this challenge.

Conclusion

Genetic testing for dental conditions such as AI is an important and evolving aspect of clinical care that fits with the general integration of genetic testing in to mainstream healthcare. This focus group-based study of 18 UK-based NHS paediatric dentists has highlighted areas for clarification and development. Some of the changes required can be easily addressed, but others require more fundamental shifts in how dentists are trained and supported as this area of healthcare develops.

References

1. Davies, S.C. "Annual Report of the Chief Medical Officer 2016, Generation Genome London: Department of Health (2017).
2. Newman WG, Black GC. Delivery of a Clinical Genomics Service. *Genes* 2014; **5**:1001-1017.
3. Gene Dossier #331 Amelogenesis Imperfecta 21 Gene Panel (2016). Available from: <https://ukgtn.nhs.uk/> (accessed November 2017)
4. Crawford PJ, Aldred M, Bloch-Zupan A. Amelogenesis imperfecta. *Orphanet J Rare Dis* 2007; **2**:17.
5. Coffield K, Phillips C, Brady M, Roberts M, Strauss R, Wright J. The psychosocial impact of developmental dental defects in people with hereditary amelogenesis imperfecta. *J Am Dent Assoc* 2005; **136**(5):620-630.
6. Parekh S, Almeheateb M, Cunningham SJ. How do children with amelogenesis imperfecta feel about their teeth? *Int J Paediatr Dent* 2014; **24**(5):326-35.
7. Dashash M, Yeung CA, Jamous I, Blinkhorn A. Interventions for the restorative care of amelogenesis imperfecta in children and adolescents. *Cochrane Database of Systematic Reviews* 2013; **6**.
8. Witkop, C. J., Jr. Amelogenesis imperfecta, dentinogenesis imperfecta and dentin dysplasia revisited: problems in classification. *Journal of oral pathology* **17**, 547-553 (1988).
9. Ratbi I, Falkenberg K, Sommen M, Al-Sheqaih N, Guaoua S, Vandeweyer G, *et al.* Heimler Syndrome Is Caused by Hypomorphic Mutations in the Peroxisome-Biogenesis Genes PEX1 and PEX6. *Am. J. Hum. Genet* 2015; **97**(4):535-545.
10. Jaureguiberry G. , De la Dure-Molla M, Parry D, Quentric M, Himmerkus N, Koike T, *et al.* Nephrocalcinosis (enamel renal syndrome) caused by autosomal recessive FAM20A mutations. *Nephron Physiol* 2012;**122**(1-2):1-6.
11. de la Dure-Molla M, Quentric M, Yamaguti P, Acevedo A, Mighell A, Vikkula M *et al.* Pathognomonic oral profile of Enamel Renal Syndrome (ERS) caused by recessive FAM20A mutations. *Orphanet J Rare Dis* 2014; **9**(1):84.
12. Aldred MJ, Savariryan R, Crawford PJ. Amelogenesis imperfecta: a classification and catalogue for the 21st century. *Oral Dis* 2003; **9**(1):19-23.
13. Pietkiewicz I, Smith JA. A practical guide to using Interpretative Phenomenological Analysis in qualitative research . *Czasopismo Psychologiczne* 2012; **18**(2):361- 369.
14. Tong A, Sainsbury P, Craig J, Consolidated criteria for reporting qualitative research (COREQ): a 31- item checklist for interviews and focus groups. *Int J Qual Health Care* 2007; **19**(6):349-357.
15. Smith CEL, Poulter JA, Antanaviciute A, *et al.* Amelogenesis Imperfecta; Genes, Proteins, and Pathways. *Front Physiol* 2017; **8**:435.