Sandy, J. (2019). Making a difference for children born with a cleft in the UK. *Journal of Orthodontics*, *46*(1_suppl), 77-80. https://doi.org/10.1177/1465312519842878

Making a difference for children born with a cleft in the United Kingdom

Journal:	*Journal of Orthodontics*
Manuscript ID	JOO-18-0036
Manuscript Type:	Review
Keywords:	Cleft lip and palate, service centralisation, outcomes
Abstract:	This short review is an opportunity to focus on significant positive changes for those children born with some form of oro-facial clefting and who are treated in a centralised service within the National Health Service (NHS). There has also been an opportunity to provide a focus for research as part of this service model. Orthodontists have played a key role in all aspects of this and will continue to be central to further improvements in caring for cleft children.

Making a difference for children born with a cleft in the United Kingdom

This short review is an opportunity to focus on significant positive changes for those children born with some form of oro-facial clefting and who are treated in a centralised service within the United Kingdom National Health Service (NHS). There has also been an opportunity to provide a focus for research as part of this service model. Orthodontists have played a key role in all aspects of this and will continue to be central to further improvements in caring for cleft children.

Introduction

The birth of a child with an oro-facial cleft is a world-wide common occurrence and occurs somewhere approximately every three minutes. There is variable expression of phenotype from simple notching or pitting of lip tissue to more complex bilateral clefts of the lip and palate. The immediate issues relate to the health of the new-born, parental anxieties and infant feeding. There are also three questions that are commonly asked and usually from the mother.

1) What has caused this?
2) What are the best treatments?
3) What kind of life will my baby have?

These questions are very difficult to answer but we are now able to set the framework for research, which will be of meaning for service delivery and configuration, and will improve the lives of these children.

Why did cleft services centralise?

What happened in the United Kingdom (UK) is a good example to other healthcare systems of how the NHS can conduct meaningful audit, which provides information to change clinical care. This started with work in the late eighties and early nineties by Mike Mars in developing outcome measures for children born with oro-facial clefting, and Bill Shaw in establishing complex multi-centre cleft research studies (Sandy et al., 2012). These two approaches showed that UK outcomes for cleft children were poor and that there was more than cause for concern. In 1996 a Clinical Standards Advisory Group (CSAG) was formed and a Chair appointed (Professor John Murray) who subsequently commissioned a research team. The team collected and analysed data from the 57 existing UK cleft centres in a remarkably short period, which required much hard work and determination. There were some seminal observations as a result of this study (Williams et al., 1999) and the research informed the CSAG report, which was warmly accepted at first offering and the recommendations agreed by the Government. The main thrust was that cleft services needed to be centralised and the

number of cleft centres reduced from 57 down to 11-15. There was also a recommendation that a national registry should be developed and that the service reconfiguration should be re-evaluated at some point (Sandy et al., 1998; Bearn et al., 2001).

Many of these recommendations were easier to articulate than to action but these have now, in the main, been implemented. The national Cleft Registry and Audit NEtwork (known as CRANE) was set up in 2000 by the Department of Health and is funded by the NHS through the Specialist Service Commissioners. The latter have responsibility for the delivery of care to children born oro-facial clefting in England, Wales, and Northern Ireland. An independent body, the Cleft Development Board with patient representative groups, clinicians and commissioners, has the overall responsibility for running the database. The CRANE project team report both annually and through publication (Fitzsimons, 2014). This is a considerable step forward from the days when Mark Hammond (Consultant Orthodontist, Birmingham) used to collect all available data and enter this into his spreadsheet on his own home computer! These days data protection governance requirements would prohibit such actions, but it was a measure of the commitment that this was done outside of work and directly by many of the cleft team carers.

How were cleft services centralised?

The implementation of centralisation was not a matter of flicking a switch, there were many consultations and iterations as to where these cleft centres should be based. Dr June Crown (Consultant in Public Health Medicine) was appointed to lead this process through the Cleft Implementation Group which then morphed into the Cleft Monitoring Group with various representation. This process was not helped by devolution, which meant that Scotland, Wales and Northern Ireland could all choose to develop centres with their own interpretation of the CSAG recommendations. Fortunately, the impact of devolution was relatively low and today it is heartening to witness the sense of common purpose amongst the community of health carers for those born with a cleft. Naturally, existing teams and carers who were no longer to be involved in cleft care took some convincing that this would improve outcomes. To prove these service changes had improved care was always going to involve a repeat of the CSAG study at an appropriate time. Indeed, the CSAG report had recommended that the changes to the service would need to be re-evaluated but it was not clear when, or indeed how.

Has centralisation worked?

The challenge of a second “CSAG” some 15 years after the original survey was never going to be easy. Research permissions and regulatory changes were supposed to have made it

easier to conduct national studies, but this was very much theoretical. The original CSAG study was carried out on a shoestring budget but the costs of repeating this had grown by an order of magnitude. A major National Institute of Health Research (NIHR) programme grant under the Applied Research scheme (RP-PG-0707-10034) was awarded to Professor Andy Ness, and a research team was recruited to start this complex and sensitive study. It was ironic that the original CSAG was recognised as audit (which did not require ethical approval) but the follow up study, known as Cleft Care UK (CCUK) was deemed research and required a lengthy and complex approval process to involve all cleft centres across the UK (Sandy et al., 2011). Centralisation had of course, reduced the number of centres and it was reasoned that the study should have taken less time and been simpler to prosecute. This was not the case, but it was reassuring that the two studies recruited very similar numbers over an almost identical birth period. CCUK recruited only 5-year-old children, all born with complete unilateral cleft lip and palate (UCLP) since these would have all been cared for within the centralised service (Persson et al., 2015). There were no 12-year-old children recruited (as in CSAG) and consequently there was no information on other cleft issues such as alveolar bone grafting. There were 15 years between the two studies and they were sufficiently similar to evaluate the impact of moving to a centralised model within a multi-disciplinary team (MDT) framework for care.

In CCUK, compared to CSAG, there were far fewer cleft surgeons operating but with much higher caseloads and there were significantly improved outcomes. In particular, speech - assessed with the Cleft Audit Protocol for Speech CAPS-A (Britton et al., 2014) and dento-alveolar relations - measured with the 5-year-olds' index (Atack et al., 1997) were improved to levels seen in some of the better European centres, but not the best. There were however some outcomes that did not improve (hearing loss and dental caries) and there is no room for complacency. Dental caries is considered by most to be wholly preventable and no change in a very high level of disease in caries susceptible children born with a cleft does need to be tackled. The cleft centres do not all have uniform support and resource in paediatric dentistry but there are examples of where intense caries preventative strategies for cleft children have resulted in considerable improvements within 5 years (Hewson et al., 2001). There are some other key observations that indicate there is still more work to be done. First, there are better centres in Europe and the UK should continue to aspire to reach these levels of care and outcomes. Second, and interestingly, in both CSAG and CCUK there were 20% of children with poor speech results, despite centralisation. In CCUK there were also 20% of children with poor dentoalveolar relations and potentially these are possibly intractable groups, which require more intense care and investigation (Ness et al., 2015; 2018). These may be the cases

where further information on environment and genes could provide a more tailored level of care and fall into the realms of “precision medicine”.

Why did centralisation improve outcomes?

The original CSAG study provided compelling evidence for centralisation based on poor outcomes and that the dispersed model of care seemed to be the key. It did not mean that all these small units were providing poor outcomes, but the low case load made it impossible to prove with any certainty what quality of care they were delivering (Bearn et al., 2001). The CCUK with bigger caseloads ascribed to surgeons, who were possibly better trained as well, was at least able to show some hefty improvements in major outcomes. The teams received additional resource after CSAG, but this was not equitable across the UK and is an area constantly probed with cost saving targets. Potentially the move to better integration of teams with MDT working and an audit culture would also have contributed to the overall improvements. It is essential that we continue to monitor the service and outcomes at a number of levels but there is an argument that repeat surveys similar to CSAG and CCUK should be considered every decade or so (Ness et al., 2017). There is no justification for considering a return to a more dispersed model of care. The UK has confirmed that centralisation of cleft services is a positive, other countries such as New Zealand and the Netherlands have identified similar problems of dispersed cleft care and America has shown that funding of health care is also a blocker when centralisation is considered (Russell et al., 2011).

Other benefits of centralised cleft care

A reduction in the number of cleft centres naturally enabled research and national audit to be more manageable. Fewer centres and frameworks for clinical trials, data collection through CRANE and centre audits as well as establishing Clinical Excellence Networks have all heightened opportunities. In addition, the NIHR Cleft and Craniofacial Conditions Clinical Studies Group (CCCCSG) monitors and provides feedback on research proposals where potential portfolio adoption by the NIHR can substantially increase research support through Trust employed research nurses. The CCCCSG also encouraged the development of an early careers research group which has supported existing national research projects as well as enabling cleft clinicians from all disciplines to increase their understanding of research through active participation (Sainsbury et al., 2018).

One of the other benefits of developing a research active community in the cleft care services has allowed the research questions to be generated by patients, their families and cleft clinicians. The Cleft Lip and Palate Association (CLAPA) have supported families and children born with cleft throughout the centralisation process and are also partners in determining research questions and providing Patient and Public Involvement and

Engagement (PPI/E). A workshop funded by the Craniofacial Society of Great Britain and Ireland (CFSGB&I) held in Bristol in 2005, which included CLAPA representation, created a series of clinical research questions and explored how a "cleft gene bank" would add to a research agenda. Many of these questions remained unanswered and re-iterated in a further exercise to set the priorities for cleft research through the James Lind Alliance in 2011 www.jla.nihr.ac.uk/priority-setting-partnerships/cleft-lip-and-palate. Seeking funding to answer some ambitious questions was a significant challenge but through a series of opportunities the development of a "cleft gene bank" became a reality and is now a resource that some may wish to engage with.

The Cleft Collective Cohort study – why do we need this?

If the "intractable" poor speech outcomes seen in 20% of both the CSAG and CCUK participants born with UCLP are to be understood fully, then genetic and environmental influences have to be determined and longitudinal data collected. We know that there are educational issues for some children born with a cleft (Persson et al., 2011) but are not in a position to understand why. Is educational attainment influenced by speech development, hearing, social exclusion, bullying, absences for clinics, cognitive development? Possibly some genes linked with educational attainment are influenced and cleft related. We also know that some craniofacial features are influenced by genes and with deep phenotyping, such as Three-Dimensional imaging these can be more fully explored (Howe et al., 2018). We can also link records of subjects recruited to the cohort with other data bases such as the National Pupil Database, NHS Digital, CRANE, Hospital Episode Statistics as well as hospital and medical practice records. These considerable data can be linked with data science and the linkage with genetic data has created a significant resource. Furthermore, within the cohort there is the opportunity to conduct nested trials in specific areas such as speech. Currently data is being collected with novel software which records early speech development and maternal interactions with the infant through speech (Wren et al., 2018).

The development of the Cleft Collective was a considerable feat but would not have happened without funding from the Healing Foundation (now the Scar Free Foundation). These funders attended the CFSGB&I workshop in 2005, saw the opportunity and the concept and developed a research strategy with fund raising to answer the clinical and genetic questions. The project launched in 2012 with nearly a year spent in developing a research and operations team as well as obtaining research permissions, portfolio adoption through the NIHR and the commitment from Cleft Teams. The latter also co-created standard operating procedures and collection mechanisms (Stock et al., 2016).

This exciting longitudinal cohort study has sufficient funding to reach a recruitment target of 9,800 individuals (parents, cleft affected child and siblings) with several parallel

cohorts (5-year olds, birth and ante-natal) and a genotyping strategy (with funding) to create an unique resource. We have shown, with this collection, that methylation patterns vary through phenotype which makes it critical that the various cleft types are looked at independently (Sharp et al., 2017). Many of the major genetic studies have tended to consider all clefts together in genome wide association studies and this needs to be re-thought. The continuation of this study will require additional funding (which the British Orthodontic Society might consider partnering) and engagement by clinicians who will continue to ask relevant questions.

Conclusions

- Orthodontists have always been central to cleft care, organisation and research;

- Centralisation of cleft services over the last twenty years appears to have improved outcomes considerably and these outcomes need to be continually monitored with national surveys about every decade. There is still room for improvement and pressures for de-centralisation must be resisted; and

- Research opportunities have been created through centralisation and the Cleft Collective has considerable available genetic and environmental information. This information can be expanded further through linkage to other databases. This resource would build several academic careers for orthodontists who are keen to support the service and research for those children born with a cleft.

References

Atack NE, Hathorn IS, Semb G et al. (1997) A new index for assessing surgical outcome in unilateral cleft lip and palate subjects aged five: reproducibility and validity. *Cleft Palate Craniofacial Journal* 34: 242-246.

Bearn D, Mildinhall S, Murphy T et al. (2001) Cleft lip and palate care in the United Kingdom--the Clinical Standards Advisory Group (CSAG) Study. Part 4: outcome comparisons, training, and conclusions. *Cleft Palate and Craniofacial Journal* 38: 38-43.

Britton L, Albery L, Bowden M et al. (2014) Cross-sectional cohort study of speech in five-year-olds with cleft palate+/- lip to support development of national audit standards: benchmarking speech standards in the United Kingdom. *Cleft Palate Craniofacial Journal* 51: 431–451.

Fitzsimons KJ, Copley LP, Smallridge JA et al. (2014) Hospital admissions for dental treatment among children with cleft lip and/or palate born between 1997 and 2003: an analysis of Hospital Episode Statistics in England. *International Journal of Paediatric Dentistry* 24: 200-208.

Hewson AR, McNamara CM, Foley TF et al. (2001) Dental experience of cleft affected children in the west of Ireland. *International Dental Journal* 51: 73-76.

Howe LJ, Lee MK, Sharp GC et al. (2018) Investigating the shared genetics of non-syndromic cleft lip/palate and facial morphology. *PLoS Genetics* 1;14: e1007501.

Ness AR, Wills AK, Mahmoud O et al. (2017) Centre-level variation in treatment and outcomes and predictors of outcomes in 5-year-old children with non-syndromic unilateral cleft lip treated within a centralized service: the Cleft Care UK study. Part 6: summary and implications. *Orthodontics Craniofacial Research* Suppl 2: 48-51.

Ness AR, Wills AK, Waylen A et al. (2015) Centralization of cleft care in the UK. Part 6: a tale of two studies. *Orthodontics Craniofacial Research* Suppl 2: 56-62.

Ness AR, Wills AR, Waylen A et al. (2018) Closing the Loop on Centralization of Cleft Care in the United Kingdom. *Cleft Palate and Craniofacial Journal* 55: 248-251.

Persson M, Sandy J, Kilpatrick N et al. (2013) Educational achievements in Pierre Robin Sequence. *Journal of Plastic Surgery and Hand Surgery* 47: 36-39.

Persson M, Sandy JR, Waylen A et al. (2015) A cross-sectional survey of 5-year-old children with non-syndromic unilateral cleft lip and palate: the Cleft Care UK study. Part 1: background and methodology. *Orthodontics Craniofacial Research* Suppl 2: 1-13.

Russell K, Long RE Jr, Hathaway R et al. (2011) The Americleft study: an inter-center study of treatment outcomes for patients with unilateral cleft lip and palate part 5. General discussion and conclusions. *Cleft Palate and Craniofacial Journal* 48: 265-70.

Sainsbury DCG, Davies A, Wren Y et al. (2018) The Cleft Multidisciplinary Collaborative: Establishing a Network to Support Cleft Lip and Palate Research in the United

Kingdom. *Cleft Palate and Craniofacial Journal* Epub ahead of print 1 Aug 2018 doi: 10.1177/1055665618790174.

Sandy J, Kilpatrick N, Persson M et al. (2011) Why are multi-centre clinical observational studies still so difficult to run? *British Dental Journal* 211: 59-61.

Sandy J, Rumsey N, Persson M et al. (2012) Using service rationalisation to build a research network: lessons from the centralisation of UK services for children with cleft lip and palate. *British Dental Journal* 212: 553-555.

Sandy J, Williams A, Mildinhall S et al. (1998) The Clinical Standards Advisory Group (CSAG) Cleft Lip and Palate Study. *British Journal of Orthodontics* 25: 21-30.

Sharp GC, Ho K, Davies A et al. (2017) Distinct DNA methylation profiles in subtypes of orofacial cleft. *Clinical Epigenetics* 8 Jun;9:63 doi:10.1186/s13148-017-0362-2. eCollection 2017

Stock NM, Humphries K, Pourcain BS et al. (2016) Opportunities and Challenges in Establishing a Cohort Study: An Example From Cleft Lip/Palate Research in the United Kingdom. *Cleft Palate and Craniofacial Journal* 53: 317-325.

Williams AC, Sandy JR, Thomas S, Sell D, Sterne JA (1999) Influence of surgeon's experience on speech outcome in cleft lip and palate. *Lancet* 13;354(9191):1697-8.

Wren Y, Humphries K, Stock NM et al. (2018) Setting up a cohort study in speech and language therapy: lessons from the UK Cleft Collective Speech and Language (CC-SL) study *International Journal Language Communications Disorders* 53: 421-430.