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

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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.

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## **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

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3 number of cleft centres reduced from 57 down to 11-15. There was also a recommendation  
4 that a national registry should be developed and that the service reconfiguration should be re-  
5 evaluated at some point (Sandy et al., 1998; Bearn et al., 2001).  
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9 Many of these recommendations were easier to articulate than to action but these have  
10 now, in the main, been implemented. The national Cleft Registry and Audit NETwork (known  
11 as CRANE) was set up in 2000 by the Department of Health and is funded by the NHS through  
12 the Specialist Service Commissioners. The latter have responsibility for the delivery of care to  
13 children born oro-facial clefting in England, Wales, and Northern Ireland. An independent  
14 body, the Cleft Development Board with patient representative groups, clinicians and  
15 commissioners, has the overall responsibility for running the database. The CRANE project  
16 team report both annually and through publication (Fitzsimons, 2014). This is a considerable  
17 step forward from the days when Mark Hammond (Consultant Orthodontist, Birmingham) used  
18 to collect all available data and enter this into his spreadsheet on his own home computer!  
19 These days data protection governance requirements would prohibit such actions, but it was  
20 a measure of the commitment that this was done outside of work and directly by many of the  
21 cleft team carers.  
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### 31 *How were cleft services centralised?*

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

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57 The challenge of a second "CSAG" some 15 years after the original survey was never going  
58 to be easy. Research permissions and regulatory changes were supposed to have made it  
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3 easier to conduct national studies, but this was very much theoretical. The original CSAG  
4 study was carried out on a shoestring budget but the costs of repeating this had grown by an  
5 order of magnitude. A major National Institute of Health Research (NIHR) programme grant  
6 under the Applied Research scheme (RP-PG-0707-10034) was awarded to Professor Andy  
7 Ness, and a research team was recruited to start this complex and sensitive study. It was  
8 ironic that the original CSAG was recognised as audit (which did not require ethical approval)  
9 but the follow up study, known as Cleft Care UK (CCUK) was deemed research and required  
10 a lengthy and complex approval process to involve all cleft centres across the UK (Sandy et  
11 al., 2011). Centralisation had of course, reduced the number of centres and it was reasoned  
12 that the study should have taken less time and been simpler to prosecute. This was not the  
13 case, but it was reassuring that the two studies recruited very similar numbers over an almost  
14 identical birth period. CCUK recruited only 5-year-old children, all born with complete unilateral  
15 cleft lip and palate (UCLP) since these would have all been cared for within the centralised  
16 service (Persson et al., 2015). There were no 12-year-old children recruited (as in CSAG) and  
17 consequently there was no information on other cleft issues such as alveolar bone grafting.  
18 There were 15 years between the two studies and they were sufficiently similar to evaluate  
19 the impact of moving to a centralised model within a multi-disciplinary team (MDT) framework  
20 for care.  
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32 In CCUK, compared to CSAG, there were far fewer cleft surgeons operating but with  
33 much higher caseloads and there were significantly improved outcomes. In particular, speech  
34 - assessed with the Cleft Audit Protocol for Speech CAPS-A (Britton et al., 2014) and dento-  
35 alveolar relations - measured with the 5-year-olds' index (Atack et al., 1997) were improved to  
36 levels seen in some of the better European centres, but not the best. There were however  
37 some outcomes that did not improve (hearing loss and dental caries) and there is no room for  
38 complacency. Dental caries is considered by most to be wholly preventable and no change in  
39 a very high level of disease in caries susceptible children born with a cleft does need to be  
40 tackled. The cleft centres do not all have uniform support and resource in paediatric dentistry  
41 but there are examples of where intense caries preventative strategies for cleft children have  
42 resulted in considerable improvements within 5 years (Hewson et al., 2001). There are some  
43 other key observations that indicate there is still more work to be done. First, there are better  
44 centres in Europe and the UK should continue to aspire to reach these levels of care and  
45 outcomes. Second, and interestingly, in both CSAG and CCUK there were 20% of children  
46 with poor speech results, despite centralisation. In CCUK there were also 20% of children with  
47 poor dentoalveolar relations and potentially these are possibly intractable groups, which  
48 require more intense care and investigation (Ness et al., 2015; 2018). These may be the cases  
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3 where further information on environment and genes could provide a more tailored level of  
4 care and fall into the realms of “precision medicine”.

#### 6 7 *Why did centralisation improve outcomes?*

8 The original CSAG study provided compelling evidence for centralisation based on poor  
9 outcomes and that the dispersed model of care seemed to be the key. It did not mean that all  
10 these small units were providing poor outcomes, but the low case load made it impossible to  
11 prove with any certainty what quality of care they were delivering (Bearn et al., 2001). The  
12 CCUK with bigger caseloads ascribed to surgeons, who were possibly better trained as well,  
13 was at least able to show some hefty improvements in major outcomes. The teams received  
14 additional resource after CSAG, but this was not equitable across the UK and is an area  
15 constantly probed with cost saving targets. Potentially the move to better integration of teams  
16 with MDT working and an audit culture would also have contributed to the overall  
17 improvements. It is essential that we continue to monitor the service and outcomes at a  
18 number of levels but there is an argument that repeat surveys similar to CSAG and CCUK  
19 should be considered every decade or so (Ness et al., 2017). There is no justification for  
20 considering a return to a more dispersed model of care. The UK has confirmed that  
21 centralisation of cleft services is a positive, other countries such as New Zealand and the  
22 Netherlands have identified similar problems of dispersed cleft care and America has shown  
23 that funding of health care is also a blocker when centralisation is considered (Russell et al.,  
24 2011).

#### 25 26 27 28 29 30 31 32 33 34 35 36 *Other benefits of centralised cleft care*

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

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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

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3 Engagement (PPI/E). A workshop funded by the Craniofacial Society of Great Britain and  
4 Ireland (CFSGB&I) held in Bristol in 2005, which included CLAPA representation, created a  
5 series of clinical research questions and explored how a “cleft gene bank” would add to a  
6 research agenda. Many of these questions remained unanswered and re-iterated in a further  
7 exercise to set the priorities for cleft research through the James Lind Alliance in 2011  
8 [www.jla.nihr.ac.uk/priority-setting-partnerships/cleft-lip-and-palate](http://www.jla.nihr.ac.uk/priority-setting-partnerships/cleft-lip-and-palate). Seeking funding to answer  
9 some ambitious questions was a significant challenge but through a series of opportunities  
10 the development of a “cleft gene bank” became a reality and is now a resource that some may  
11 wish to engage with.  
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### 19 *The Cleft Collective Cohort study – why do we need this?*

20 If the “intractable” poor speech outcomes seen in 20% of both the CSAG and CCUK  
21 participants born with UCLP are to be understood fully, then genetic and environmental  
22 influences have to be determined and longitudinal data collected. We know that there are  
23 educational issues for some children born with a cleft (Persson et al., 2011) but are not in a  
24 position to understand why. Is educational attainment influenced by speech development,  
25 hearing, social exclusion, bullying, absences for clinics, cognitive development? Possibly  
26 some genes linked with educational attainment are influenced and cleft related. We also know  
27 that some craniofacial features are influenced by genes and with deep phenotyping, such as  
28 Three-Dimensional imaging these can be more fully explored (Howe et al., 2018). We can  
29 also link records of subjects recruited to the cohort with other data bases such as the National  
30 Pupil Database, NHS Digital, CRANE, Hospital Episode Statistics as well as hospital and  
31 medical practice records. These considerable data can be linked with data science and the  
32 linkage with genetic data has created a significant resource. Furthermore, within the cohort  
33 there is the opportunity to conduct nested trials in specific areas such as speech. Currently  
34 data is being collected with novel software which records early speech development and  
35 maternal interactions with the infant through speech (Wren et al., 2018).  
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46 The development of the Cleft Collective was a considerable feat but would not have  
47 happened without funding from the Healing Foundation (now the Scar Free Foundation).  
48 These funders attended the CFSGB&I workshop in 2005, saw the opportunity and the concept  
49 and developed a research strategy with fund raising to answer the clinical and genetic  
50 questions. The project launched in 2012 with nearly a year spent in developing a research and  
51 operations team as well as obtaining research permissions, portfolio adoption through the  
52 NIHR and the commitment from Cleft Teams. The latter also co-created standard operating  
53 procedures and collection mechanisms (Stock et al., 2016).  
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58 This exciting longitudinal cohort study has sufficient funding to reach a recruitment  
59 target of 9,800 individuals (parents, cleft affected child and siblings) with several parallel  
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3 cohorts (5-year olds, birth and ante-natal) and a genotyping strategy (with funding) to create  
4 an unique resource. We have shown, with this collection, that methylation patterns vary  
5 through phenotype which makes it critical that the various cleft types are looked at  
6 independently (Sharp et al., 2017). Many of the major genetic studies have tended to consider  
7 all clefts together in genome wide association studies and this needs to be re-thought. The  
8 continuation of this study will require additional funding (which the British Orthodontic Society  
9 might consider partnering) and engagement by clinicians who will continue to ask relevant  
10 questions.  
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## 17 **Conclusions**

- 19 • Orthodontists have always been central to cleft care, organisation and research;
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22 • Centralisation of cleft services over the last twenty years appears to have improved  
23 outcomes considerably and these outcomes need to be continually monitored with  
24 national surveys about every decade. There is still room for improvement and  
25 pressures for de-centralisation must be resisted; and  
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- 30 • Research opportunities have been created through centralisation and the Cleft  
31 Collective has considerable available genetic and environmental information. This  
32 information can be expanded further through linkage to other databases. This  
33 resource would build several academic careers for orthodontists who are keen to  
34 support the service and research for those children born with a cleft.  
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