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ARTICLE

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A national registry-based study of surgery and demography comparing internationally adopted and children born in Sweden with cleft lip and/or palate

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ABSTRACT

This national registry-based study compares surgical procedures, demography, and concurrent medical conditions, in internationally adopted and Swedish-born children with cleft lip and/or palate until the age of five years. Data on the cleft type and gender for 331 internationally adopted children and 2064 Swedish-born children born from 2007 to 2018, were extracted from the registry and analyzed. Data on surgical procedures performed in Sweden and concurrent medical conditions and were collected for internationally adopted children and Swedish-born children with unilateral or bilateral cleft, born 2007–2013. A higher prevalence of unilateral and bilateral clefts ($p < 0.0001$), as well as a predominance of male patients with unilateral clefts ($p = 0.0025$), were identified among the internationally adopted children compared with children born in Sweden. Differences in the concurrence of other medical conditions in internationally adopted children versus Swedish-born infants were non-significant. Primary palatal surgeries performed in Sweden were significantly delayed for the adopted group. More secondary palatal surgeries such as speech improving surgery and palatal re-repair were needed for internationally adopted children ($p < 0.0001$) until age five.

Conclusions: The Swedish CLP Registry provided national coverage of the CL/P cohort. Internationally adopted children exhibited a predominance of more severe cleft types, a predominance of males, delayed primary palatal surgery and increased need for secondary surgeries before age five.

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Introduction

Beginning in 2005, there has been a steady global increase in internationally adopted children (IAC) with preexisting congenital disabilities or medical conditions, primarily originating from China [1–4]. In 2009, more than two-thirds of IAC in Sweden were "special needs adoptions," whereof cleft lip and/or palate (CL/P) was the most common diagnosis [3]. Many of these children were adopted at older ages than during previous decades and usually arrived without having undergone palatal surgery [1,2,4–6]. Among IAC cohorts with CL/P, unilateral cleft lip and palate (UCLP) has been found to be the most frequent diagnosis, and differences in gender prevalence have been described, although the results are inconclusive. Some studies have reported a preponderance of young female patients with CL/P among the IAC cohorts [7–9], while other studies report equal female-to-male prevalence ratios [1,10] or a higher prevalence of male patients [4]. Several studies on IAC have also reported on the prevalence of concurrent medical conditions, unknown at the time of adoption [11,12]. However, there is considerable variation in the types of reported concurrent medical conditions and the prevalences thereof [2,13].

Previous investigations of IAC with CL/P cohorts followed a single-center retrospective study design with small sample sizes and notable age variation at the specific time points used for data collection [1,10,14,15]. Furthermore, the majority of studies lack control groups [9,16,17], and there is a need for further, in-depth investigations that address previous shortcomings.

The Swedish CLP Registry was established in 1999 as an agreement between six multidisciplinary university CL/P research centers and has been administered by the Swedish Association of Local Authorities and Regions since 2009 (18). The registry collects data on demography, surgical treatment, speech and dentofacial development from birth until 19 years of age for all children in Sweden with CL/P. As of March 2020, a total of 4382 patients were recorded in the registry. The coverage for children born between 2009 and 2018 is 95.1%, and 92.4% of cleft-related surgeries have been recorded [18]. Therefore, the registry offers a unique opportunity to establish a clear, nation-wide perspective at a level that includes almost the entire population of children with CL/P.

The aim of this study was to, from a national perspective, compare cleft-type, gender and concurrent medical conditions as well as surgical treatment until five years of age, between IAC and children born in Sweden (Swe-born) with CL/P, using the Swedish CLP registry.

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Methods

Sample selection and data collection

The data for 3781 children born between January 1, 2007 and December 31, 2018 with UCLP, BCLP, cleft palate (CP), unilateral cleft lip (UCL), and bilateral cleft lip (BCL) were collected from the Swedish CLP Registry. Immigrated children that were born abroad but not adopted were excluded. After selection, data from 331 IAC and 2064 Swe-born were included and compared regarding cleft type and gender prevalence while the proportion of IAC with a history of pre-adoptive surgery in the country of origin was reported only for UCLP and BCLP. For comparisons of concurrent medical conditions and surgical treatment, the data from 279 IAC and 404 Swe-born with UCLP or BCLP born between 2007 and 2013 were available and analyzed. The surgical data collected from the Swedish CLP Registry was the age at first primary palatal surgery in Sweden, the number of primary surgeries per child performed in Sweden until age five, the number of children receiving secondary palatal surgery in Sweden until five years as well as the number of cleft related anesthetic procedures in Sweden per child until five years of age. Primary palatal surgery included soft palate closure, hard palate closure, or soft *and* hard palate closure together. Data on secondary palatal surgery included fistula closure, palatal re-repair, palato-pharyngeal flap, or orticochea pharyngoplasty.

At all six Swedish university hospitals, it is standard practice to perform the primary lip-nose repair in children aged 3–6 months. At four hospitals, the soft palatal repair is performed at 6 months of age, with or without simultaneous lip-nose repair, followed by hard palate closure performed at 2 years of age. At the remaining two hospitals, one-stage palate repair is performed at 9–14 months of age. Secondary alveolar bone grafting with cancellous bone is performed in mixed dentition at 7–11 years of age. The IAC underwent primary surgery according to modification of the local surgical protocols, after decisions at the respective cleft center.

Statistical analyses

Categorical data are presented as frequencies and percentages, and numerical data are presented as means and standard deviations (mean ± SD). All tests were two-tailed, and p-values <0.05 were considered statistically significant. The chi-squared test was used to compare IAC and Swedish-born patient groups for differences in the prevalence of cleft types. Fisher's exact test was used to analyze gender prevalence and differences in the frequency of concurrent medical conditions between the two groups. Wilcoxon rank sum tests were used for comparison of age at primary palatal surgery, the number of primary palatal surgeries per child, and the number of cleft-related anesthetic procedures per child until the age of five years. For comparison of the number of children who underwent secondary palatal surgery until age five, Fisher's exact test was used. The software SAS v 9.4 (SAS Institute, Cary, NC) was used.

Ethical considerations

The study was approved by the Regional Ethical Review Board in Gothenburg (1020-12, 2013, T 796-18, 2018). Further approval for publication was obtained from the Board of the Swedish National CLP registry and Region Skåne who are responsible for the personal data contained in the Swedish National CLP registry.

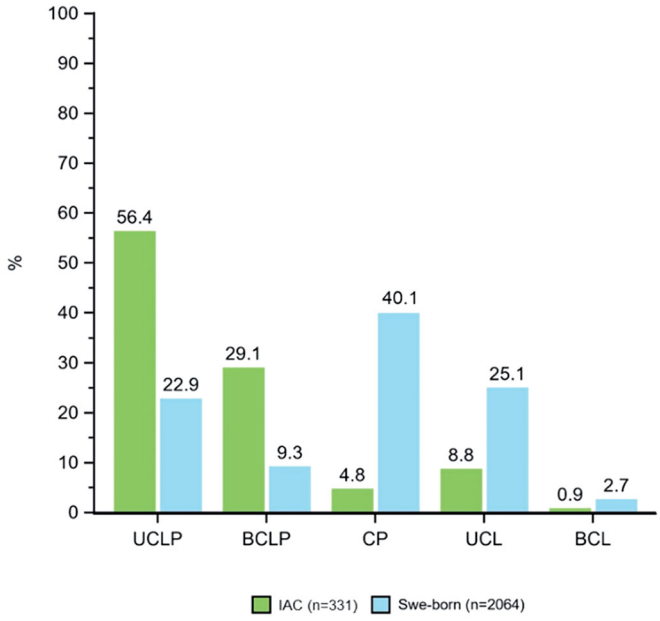

Figure 1. Distributions of cleft-type prevalence for the national cohorts of IAC and Swe-born born with CL/P (2007–2018). These distributions differed significantly between the two groups ($p < 0.0001$). Abbreviations: IAC, internationally adopted children; Swe-born, children born in Sweden; UCLP, unilateral cleft lip and palate; BCLP, bilateral cleft lip and palate; CP, cleft palate; UCL, unilateral cleft lip; BCL, bilateral cleft lip.

Results

Cleft-type prevalence

There were statistically significant differences in the prevalence of cleft types between IAC patients and Swe-born patients with CL/P born 2007–2018 ($p < 0.0001$). UCLP and BCLP were the most common cleft types among IAC patients, while CP and UCL were the most common cleft types among Swe-born patients (Figure 1).

Gender prevalence

The percentages of male patients in the total group of IAC and children born in Sweden were 72% and 57%, respectively. A significantly higher proportion of male patients was identified for IAC with UCLP when compared with the Swe-born cohort ($p = 0.0025$). No statistically significant difference was found for gender prevalence between IAC and Swe-born for BCLP ($p = 0.52$) (Figure 2). Comparisons of gender differences for CP, UCL, and BCL were not possible because of variations in sample sizes. The gender prevalence for each cleft type is shown in Figure 2.

Pre-adoptive surgery

Among the IAC born between 2007 and 2018, 69.4% of children with UCLP and 65.3% with BCLP had undergone pre-adoptive surgery in their country of origin. The surgery conducted was either lip-nose repair and/or palatal repair.

Concurrent medical conditions

Various syndromes, chromosomal aberrations, malformations, and metabolic disorders were identified as concurrent medical conditions in the study participants from until five years of age. In children born with UCLP, concurrent medical conditions were registered in 9.8% (18/183) of IAC and in 15.3% (42/275) of

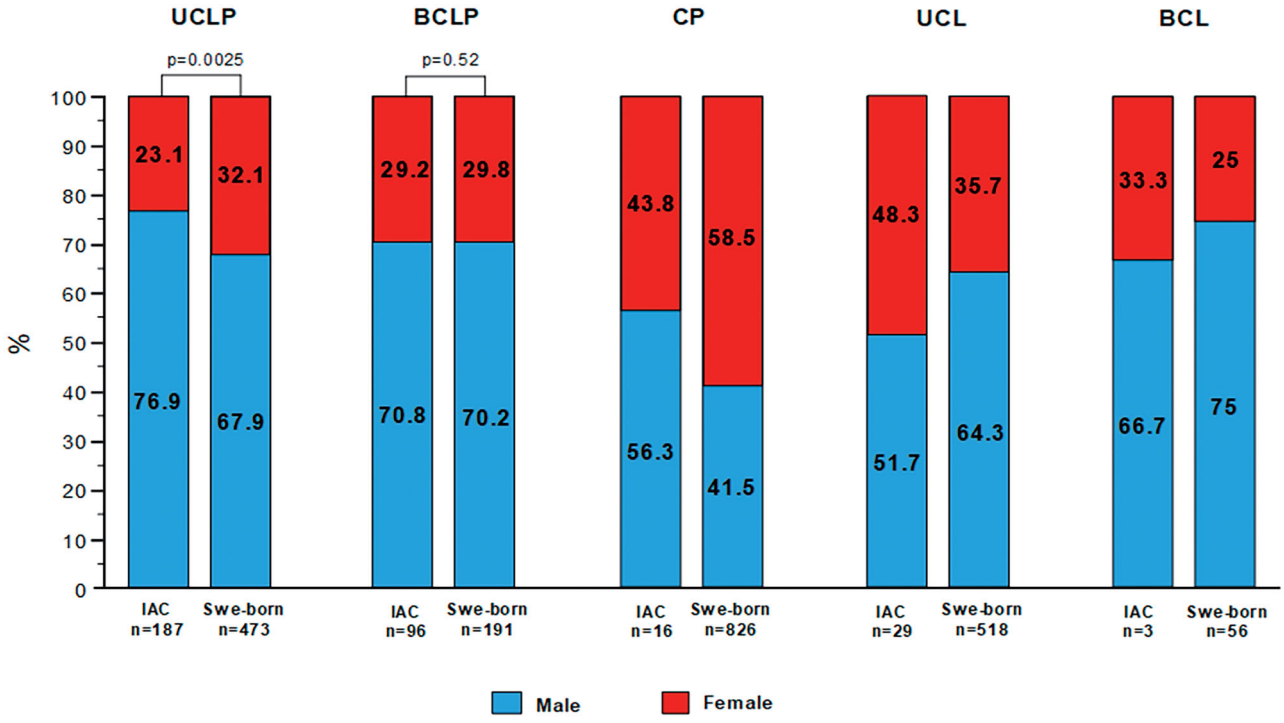

Figure 2. Gender prevalence for the national cohorts of IAC and Swe-born (2007–2018). IAC with UCLP was predominantly male in the IAC group compared with their Swe-born counterparts ($p = 0.0025$). Abbreviations: IAC, internationally adopted children; Swe-born, children born in Sweden; UCLP, unilateral cleft lip and palate; BCLP, bilateral cleft lip and palate; CP, cleft palate; UCL, unilateral cleft lip; BCL, bilateral cleft lip.

Table 1. Surgical treatment in IAC and Swedish born with UCLP and BCLP until age 5 years.

	UCLP			BCLP		
	IAC $n = 138$ Mean ± SD	Swe-born $n = 251$ Mean ± SD	*p*-value	IAC $n = 70$ Mean ± SD	Swe-born $n = 122$ Mean ± SD	*p*-value
Age at first primary palatal surgery (months)*	24.3 ±6.6	10.1 ± 5.0	<0.0001	25.7 ± 7.3	11.2 ± 5.3	<0.0001
Number of primary palatal surgeries per child	1.4 ± 0.8	1.6 ± 0.6	0.0064	1.6 ± 0.8	1.7 ± 0.1	0.9617

	IAC		Swe-born			IAC		Swe-born		
	n	%	*n*	%	*p*-value	*n*	%	*N*	%	*p*-value
Total number of children who underwent secondary surgery	55	39.9	30	12.0	<0.0001	32	45.7	23	18.9	<0.0001
Total number of children who underwent two or more secondary surgeries	14	10.1	6	2.4		10	14.3	5	4.1	

*The results for age at first primary palatal surgery were based on 124 IAC and 243 Swe-born with UCLP as well as 66 IAC and 117 Swedish born with BCLP. Abbreviations: IAC, internationally adopted children; Swe-born, children born in Sweden; UCLP, unilateral cleft lip and palate; BCLP, bilateral cleft lip and palate; SD, standard deviation.

children born in Sweden. In the BCLP Group, concurrent medical conditions were identified in 12.8% (12/96) of IAC and 20.2% (26/129) of Swedish-born patients. However, no statistically significant differences in the prevalence of these conditions were found between IAC and Swedish-born patients with UCLP or BCLP.

In the IAC group with UCLP and BCLP, 12 children were found to have congenital heart malformations such as mitral valve defects or ventricular and atrial septal defects. Genital malformations were recorded in nine IAC. The following medical conditions were registered for one or two children in the IAC group: sagittal synostosis, ear malformation, coloboma, clubfoot, polydactyly, anal atresia, glucose-6-phosphate dehydrogenase deficiency, and thalassemia minor. Only two children with either Van der Woude or Goldenhaar syndrome were registered.

Among children born in Sweden with UCLP and BCLP, congenital heart malformations such as Fallot's triad, mitral valve defects, ventricular and atrial septal defects, and pulmonary atresia were recorded for 21 children. Genital and kidney malformations were registered in six and five children, respectively. Eight children were reported as having dysmelia as well as poly- and syndactyly. Other conditions that were reported in the range of one or two Swe-born children were craniosynostosis, holoprosencephaly, corpus callosum agenesis, coloboma, lymphatic malformation, laryngomalacia, esophageal malformation, choanal atresia, clubfoot, and metabolic disorders. Syndromes and chromosomal aberrations such as Van der Woude syndrome, Wolff-Hirschorns syndrome, Charge syndrome, Shone syndrome, Goldenhaar syndrome, Saethre-Chotzen, 1p22.2 deletion syndrome, 1p36 deletion syndrome, 22q11 deletion syndrome, and trisomy 18 and 21 were registered in 19 Swedish born children.

Surgical treatment

The group of IAC with UCLP and BCLP underwent their first primary palatal surgery at an older age (24.3 and 25.7 months, respectively) when compared with Swedish-born children (10.1 and 11.2 months, respectively; $p < 0.0001$; Table 1). Overall, IAC with UCLP underwent fewer primary palatal surgeries per child in

Table 2. Cleft-related anesthetic procedures per child.

	UCLP			BCLP		
	IAC $n = 138$ Mean ± SD	Swe-born $n = 251$ Mean ± SD	*p*-value	IAC ($n = 70$) Mean ± SD	Swe-born ($n = 122$) Mean ± SD	*p*-value
Number of cleft-related anesthetic procedures in Sweden per child	2.1 ± 1.0	2.5 ± 0.8	<0.0001	2.6 ± 1.1	2.9 ± 1.2	0.1814

Abbreviations: IAC, internationally adopted children; Swe-born, children born in Sweden; UCLP, unilateral cleft lip and palate; BCLP, bilateral cleft lip and palate; SD, standard deviation.

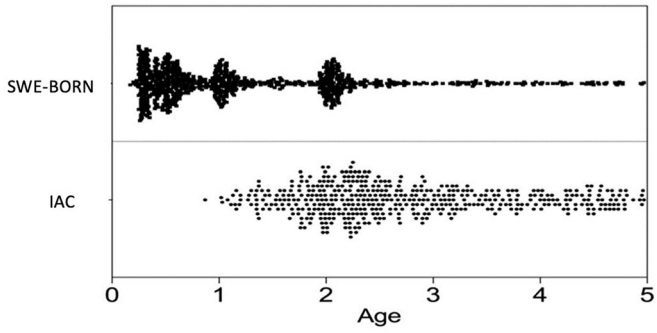

Figure 3. Timing of all cleft-related anesthetic procedures performed in Sweden per child before five years of age for the national cohorts of IAC and Swedish-born children with UCLP and BCLP, born 2007–2013. Age is presented in years and each dot represents one anesthetic procedure; an individual patient may contribute several times. Abbreviations: IAC, internationally adopted children; Swe-born, children born in Sweden.

Sweden than Swedish-born children with the same cleft type ($p = 0.0064$; Table 1). In the BCLP group, no difference was found in the number of primary palatal surgeries. The number of children who underwent secondary palatal surgery was significantly higher for IAC compared to children born in Sweden for both UCLP ($p < 0.0001$) and BCLP ($p < 0.0001$) (Table 1).

The number of cleft-related anesthetic procedures per child performed in Sweden until the age of five was significantly lower among IAC with UCLP than among children born in Sweden ($p < 0.0001$), while no statistically significant differences were found for BCLP ($p = 0.18$; Table 2). The timing of all cleft-related anesthetic procedures performed in Sweden until 5 years of age for UCLP and BCLP, born 2007–2013 are illustrated in Figure 3.

Discussion

The present study aimed at comparing the Swedish population of IAC and children born in Sweden with CL/P for the prevalence of cleft-type, gender, concurrent medical conditions, and surgical treatment until five years of age. Using the Swedish CLP National Registry, we were able to collect and analyze the data from an extensive cohort of IAC with CL/P that was representative of the entire national population. A coverage degree exceeding 90% and regular calibrations ensured a low number of missing individuals, which strengthens the value of our findings [18]. In addition, the registry provided access to the national cohort of Swedish-born patients with CL/P allowing statistical comparison of the two groups. In contrast to earlier studies that followed a retrospective and single-center design [2,5,6,9,14,19], the data collected from the registry were derived from six independent Swedish University hospitals. Finally, the data from registered patients enabled the investigation of a relatively rare condition as i.e. IAC with CL/P [18], and we believe our findings will strengthen the understanding of CL/P dynamics in IAC populations. The main findings from our study showed the predominance of extensive clefts such as BCLP and UCLP among the national cohort of IAC, an increased proportion of males among IAC born with UCLP, and no difference in the prevalence of concurrent medical conditions when comparing the IAC with the Swedish born cohort. The IAC had their first palatal surgery in Sweden around two years of age, which is approximately one year later than children born in Sweden, and an increased portion of IAC underwent secondary palatal surgery in comparison with Swedish-born children until five years of age for both UCLP and BCLP.

The prevalence of UCLP and BCLP in the national IAC and Swedish-born cohorts was 86% and 32%, respectively (Figure 1). BCLP is considered to require the most complicated surgical procedures; therefore, the higher prevalence in IAC compared with Swe-born (29% and 9%, respectively; Figure 1) is noteworthy. The prevalence of less severe clefts such as UCL and BCL was only 10% in IAC in comparison with 28% among Swedish-born children (Figure 1). Our findings agree with previously published data regarding cleft-type prevalence in IAC cohorts [2,5,16,17,19]. As an interesting comparison, a study including 5,384 infants born with CL/P in southern China between 2015 and 2018, described the prevalence of CL, CP, and CLP to be 2.34/10 000, 2.22/10 000 and 2.98/10 000, respectively. These proportions are reflected in the national Swedish cohort, apart from the higher numbers of CP [18].

The overall male predominance of 72% in the IAC cohort recorded in our study was higher than that reported in earlier studies. Previously, the ratio of male-to-female patients was found to be reversed (i.e. predominantly female) or equal [1,9,17]. Interestingly, a higher prevalence of UCLP in male IAC patients (68%) was also reported in the Netherlands [19]. The most common individual patient in our national IAC cohort was defined as a male with UCLP while in the Swedish-born cohort, the most common individual patient was a female with CP (Figure 2). In the study of the native population from the Guangdong province in southern China, the prevalence of CL/P in male children was only slightly higher than in female children [20]. Therefore, the male predominance of IAC patients with CL/P appears to be a feature unique to populations outside of their country of origin. A comparison regarding gender prevalence for CP, UCL and BCL was not considered possible due to the differences in sample size, why we choose to compare IAC and Swedish-born children solely for the two major cleft types, UCLP and BCLP (Figure 2).

It is well known that the prevalence of concurrent medical conditions varies among different cleft diagnoses [21]. Since the cleft-type distribution varied between IAC and Swedish-born children, a comparison between the total groups was considered unfeasible. A comparison was therefore restricted to UCLP and BCLP, the two most common cleft-type groups in the Swedish CLP registry. Concurrent medical conditions were found in 10% of IAC patients with UCLP, which is lower than that reported in previous studies [2,13,22]. In the Swedish-born group, concurrent

medical conditions were found in approximately every sixth newborn with UCLP or BCLP, which is also in line with previous Swedish and international findings [21,23]. However, one must be cautious when drawing comparisons between studies because of differences in patient age at assessment and the study-specific consideration of different conditions and cleft types. It is important to note that the numbers and types of concurrent medical conditions in children with CL/P are likely to increase as they age. In the Swedish CLP registry, neuropsychiatric diagnoses and developmental delays are also registered. Investigations regarding these diagnoses are complex and might not have yet been undertaken in children before the age of five, especially for late arriving IAC. For these reasons, we chose to exclude these conditions from our analyses. The panorama of diagnoses revealed in the present study indicates a tendency for increased severity of concurrent medical conditions among children born in Sweden (e.g. cerebral malformations or chromosomal aberrations). It is plausible that IACs with severe medical conditions or multiple malformations are less likely to be adopted, which may explain our findings.

A total of 69.4% of IAC with UCLP and 65.3% with BCLP had undergone pre-adoptive cleft-related surgery, i.e. lip- and/or palate repair, before arriving in Sweden. These numbers are in line with, or lower than, previously published results [2,5,16,24]. Since information regarding the type and timing of pre-adoptive surgery is uncertain, we have chosen to only present the frequency of IAC having undergone surgery before arrival in Sweden.

The mean age at first primary palatal surgery in Sweden was 24.3 months for IAC with UCLP compared to 10.1 months for Swedish born, while IAC and Swedish-born patients with BCLP had their first palatal repair surgery at 25.7 and 11.2 months, respectively (Table 1). Hence, IAC received its first primary palatal surgery in Sweden more than one year later than children born in Sweden. Late palate repair is considered unfavorable for speech development, and this study clearly demonstrates a late palatal repair in the IAC cohort at a national level and hence the risk of unfavorable speech outcomes.

The number of primary palatal surgeries per child performed in Sweden until the age of five was slightly lower among IAC with UCLP than Swedish-born peers (Table 1). We have considered two possible explanations [1]: several Swedish university hospitals use a two-stage surgical protocol for palatal repair, which may have been abandoned for late-arrival IAC with an immediate need for palatal surgery, hence receiving one-stage palatal closure, and [2] the proportion of IAC having undergone primary surgery in their country of origin might have influenced the final surgery count.

In the present study, an increased number of IAC required secondary palatal surgery before the age of five when compared with their Swedish-born counterparts. These surgeries included fistula closure, palatal re-repair, palato-pharyngeal flap, or orticochea palatoplasty (Table 1). The increased need for secondary palatal surgery among IAC when compared with native CL/P patients has been frequently described [1,2,5,6,16]. However, in several studies, the consideration of patient age when assessing the type and occurrence of surgical procedures was not defined. Our study addresses this shortcoming by analyzing data collected within a specified time frame (i.e. until the age of five). Hence, our findings provide clear evidence of the increased need for secondary palatal surgery among IAC patients already before the age of five. Velopharyngeal investigations preceding eventual speech-improving surgery (e.g. video fluoroscopy) may be challenging for preschool children; hence, surgery is more often performed after the age of five years. Therefore, it is plausible that the number of secondary palatal surgery will increase as the patient's ages. The pattern of all cleft-related surgical interventions performed in Sweden until five years of age for IAC and Swedish-born children is visualized in Figure 3. Separate aggregations of surgeries were recorded for Swedish-born patients at approximately 3–6 months, and in 1- and 2-year-old patients, which reflect the differences in surgical protocols among the hospitals in Sweden. The first aggregation of surgeries represents results from the national standard of performing lip repair and soft palate repair at three and six months. The second and third aggregation, at one and two years, reflects the one-stage palate repair and hard palate repair approaches, respectively. For the IAC cohort, a more widespread pattern is shown accordingly, with an aggregation of surgical procedures in patients over the age of 2 years.

When discussing "burden of care" regarding surgery for IAC in comparison with Swedish-born children, it is important to bear in mind the additional surgical experience two-thirds of the IAC group have from the country of origin. The addition of the pre-adoptive surgery to the schematic figure would have made the illustration more complete, but due to the uncertainty of the number and nature of the pre-adoptive surgery, we chose to include only surgical procedures performed in Sweden.

Limitations

As with all registry-based studies, it is important to be aware of limitations regarding variations in the accuracy of registered data because of multiple recorders, inadequate calibration, and missing information. The reporting centers that contribute to the Swedish CLP registry have undergone calibration processes to optimize the agreeability of all variables included in the present study [18]. For IAC, information about the patient's country of origin is not recorded in the Swedish CLP Registry. This may be a limitation for future studies because ethnicity may be of interest when evaluating craniofacial growth patterns. Another limitation is the lack of information on the colonization of multi-resistant bacteria which may be of interest while investigating postoperative complications. The study was also limited by the uncertain information about pre-adoptive surgical procedures in the country of origin for IAC patients. For that reason, we have focused our investigations on surgeries performed after their arrival in Sweden.

Conclusions

This study presents a national perspective on internationally adopted children and children born in Sweden with CL/P in terms of surgical treatment and demographics and until five years of age. In conclusion, the national cohort of IAC displayed an increased proportion of UCLP and BCLP when compared with the Swedish-born cohort. In addition, IAC with UCLP comprised a higher number of males in comparison with Swedish-born children. The adopted group had their first palatal surgery in Sweden around one year later than children born in Sweden and a higher number of IAC had secondary palatal surgery before the age of five years. Overall, a national registry is a valuable instrument for strengthening our knowledge and broadening our understanding of population-specific information regarding CL/P.

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Disclosure statement

The authors declare no conflict of interests.

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