Pediatric Short Bowel Syndrome : Real-World Evidence on Incidence and Hospital Resource Use From a Finnish Data Lake

Puttonen, Minna

John Wiley and Sons Inc.
2023-10

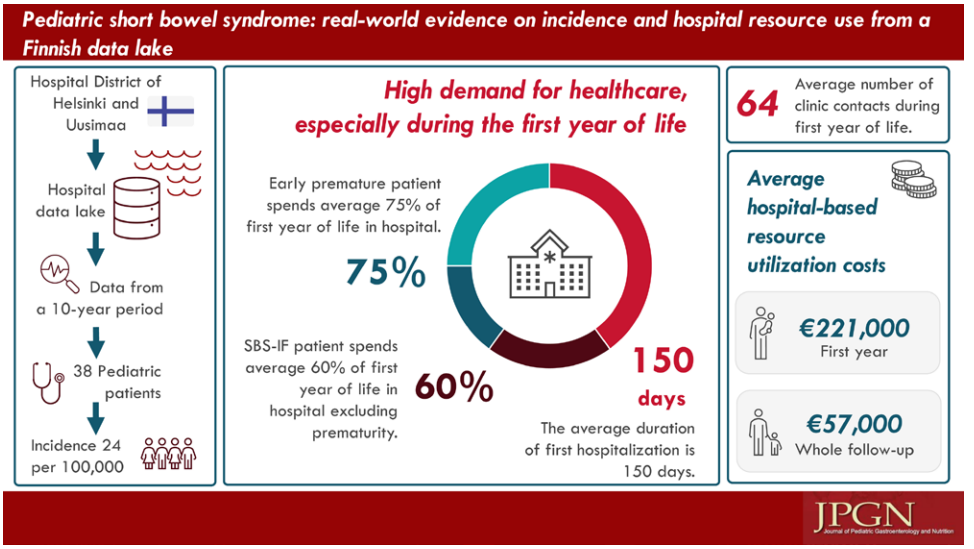
Puttonen, M, Tuominen, S, Ukkola-Vuoti, L, Lassenius, M I, Virtanen, H, Merras-Salmio, L & Pakarinen, M P 2023, 'Pediatric Short Bowel Syndrome : Real-World Evidence on Incidence and Hospital Resource Use From a Finnish Data Lake', Journal of Pediatric Gastroenterology and Nutrition, vol. 77, no. 4, pp. 479-485. https://doi.org/10.1097/MPG.0000000000003894

http://hdl.handle.net/10138/566901
10.1097/MPG.0000000000003894

OPEN

Pediatric Short Bowel Syndrome: Real-World Evidence on Incidence and Hospital Resource Use From a Finnish Data Lake

*†Minna Puttonen, PhL, ‡Samuli Tuominen, MSc, ‡Liisa Ukkola-Vuoti, PhD, ‡Mariann I. Lassenius, PhD, *Heidi Virtanen, PhD, §Laura Merras-Salmio, MD, PhD, and ‖¶Mikko P. Pakarinen, MD, PhD



ABSTRACT

Objectives: Little is known about the epidemiology and healthcare burden of pediatric intestinal failure (IF). We aimed to assess the incidence, prevalence, healthcare resource utilization (HCRU), and related costs of pediatric short bowel syndrome (SBS) using follow-up data from the largest hospital district in Finland.

Methods: This retrospective registry study utilized electronic healthcare data covering all pediatric patients with SBS-IF born between 2010 and 2019 at the Hospital District of Helsinki and Uusimaa in Finland. Patients were followed from birth until the end of 2020 and compared to control patients, all from the same hospital system.

Results: In total, 38 patients with SBS-IF and 1:5 matched controls were included, with median follow-up time of almost 6 years from birth. Over half

Received February 28, 2023; accepted July 11, 2023.

From *Takeda Oy, Helsinki, Finland, the †Division of Pharmaceutical Technology and Chemistry, Industrial Pharmacy, University of Helsinki, Helsinki, Finland, ‡Medaffcon Oy, Espoo, Finland, the §Pediatric Gastroenterology Unit, Helsinki University Hospital, University of Helsinki and Helsinki University Hospital, Helsinki, Finland, the ‖Section of Pediatric Surgery, Pediatric Liver and Gut Research Group, Children's Hospital, University of Helsinki and Helsinki University Hospital, Helsinki, Finland, and the ¶Department of Women's Health, Karolinska Institute, Solna, Sweden.

Address correspondence and reprint requests to Liisa Ukkola-Vuoti, PhD, Medaffcon Oy, Metsänneidonkuja 8, 02130 Espoo, Finland (e-mail: liisa.ukkola-vuoti@medaffcon.fi).

Sources of Funding: This study was funded by Takeda.

Ethics Approval: The study was conducted with permission from the Hospital District of Helsinki and Uusimaa (HUS) (data permit no. HUS/141/2020) by the provision of the Act on the Secondary Use of Health and Social Data (Finland's Ministry of Justice 552/2019), therefore no informed consent from the patients was required.

Dr Ukkola-Vuoti, Dr Lassenius, and Mr Tuominen are employed by Medaffcon Oy. Mrs Puttonen is a former employee of Takeda Oy and current employee of MSD Finland Oy. Dr Virtanen is a former employee of Takeda and current employee of AbbVie Oy. Dr Merras-Salmio has received consulting and lecture fees from Takeda. Dr Pakarinen has received payments from Takeda for lectures, consulting, and for acting as principal investigator of this study.

Mrs Puttonen is now with MSD Finland Oy, Espoo, Finland. Mr Tuominen is now with AbbVie Oy, Helsinki, Finland.

Availability of Data and Material: The original data were obtained from the Hospital District of Helsinki and Uusimaa (HUS). Data can be acquired with data permission by following the guidance and application process of the registry. All authors had access to the pseudonymized aggregate data, whereas pseudonymized single-level registry data were available only to authors who analyzed the data. Only the personnel of the registry had full access to patient data.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text, and links to the digital files are provided in the HTML text of this article on the journal's Web site (*www.jpgn.org*).

DOI: 10.1097/MPG.0000000000003894

of the patients were born early preterm (gestational age ≤30 weeks). The incidence of pediatric SBS-IF was 24 per 100,000 live births. The HCRU was higher compared to controls and most of the inpatient days incurred during the first year of the SBS-IF patients' life. The average hospital-based HCRU costs were €221,000 for the first year and €57,000 for whole follow-up annually. The costs were higher for the early preterm patients and accumulated mainly from inpatient days.

Conclusions: SBS-IF is a rare disease with a relatively low number of patients treated at each hospital district. The burden on the hospital system, as well as the patient's family, is especially high at the onset as the newborns with SBS-IF spend a significant part of their first year of life in the hospital.

Key Words: burden of disease, pediatrics, prevalence, registry study, SBS-IF

(*JPGN* 2023;77: 479–485)

Pediatric short bowel syndrome (SBS) is a rare disease with a reported incidence of 25–46 cases per 100,000 newborns (1,2). SBS is characterized with insufficient bowel length or function for sustaining enteral autonomy (3,4). In pediatric patients, the major cause of SBS is necrotizing enterocolitis (NEC), followed by intestinal atresias, gastroschisis, midgut volvulus, and Hirschsprung disease (5). SBS results in excessive fluid loss, nutrient malabsorption, electrolyte abnormalities, increased susceptibility to infections, parenteral nutrition (PN) associated complications, and affects weight gain and growth (6).

The primary goal of the treatment is to restore enteral autonomy and reduce long-term dependence on parenteral support while avoiding complications, ensuring adequate growth and development. PN is the main treatment for patients with intestinal failure due to short bowel syndrome (SBS-IF) (7–9). Pediatric patients with SBS-IF may need PN from birth, possibly for decades. Although vital for the patient, long-term PN is associated with serious complications (3). Pediatric SBS-IF requires complex and resource-intensive care at the hospital, including long hospitalization periods, multiple surgeries, and intensive post-discharge long-term care by a multi-disciplinary team. However, there is little real-world evidence (RWE) on healthcare resource utilization (HCRU) and related costs in pediatric SBS-IF.

Epidemiology of pediatric SBS-IF has been studied previously (1,10–12), however, epidemiological data about the incidence and prevalence remains sparse. Low patient numbers, limited data, use of home administered PN (HPN) as proxy for prevalence, and variability in SBS-IF definition (12) have been limitations of previous studies. In a large population-based study, the overall incidence of SBS was 22.1 per 1000 neonatal intensive care unit (NICU) admissions and 24.5 per 100,000 live births, with a much greater prevalence in premature infants (1).

The aim of this study was to evaluate the HCRU of pediatric SBS-IF patients treated at the Hospital District of Helsinki and Uusimaa (HUS) in Finland. In addition, incidence, prevalence, and HCRU related costs were assessed. Due to the Finnish national healthcare system, all patients have equal access to care, and the treatment of patients living at the same region is centralized to one hospital. Thus, our study captured all pediatric SBS-IF patients living in the HUS area.

What Is Known

- Short bowel syndrome-associated intestinal failure (SBS-IF) is a life-altering and life-threatening rare disease.
- Pediatric SBS-IF incidence was 24.5 per 100,000 live births in Canada.
- Prevalence was 25 at The Hospital for Sick Children in Toronto in 1999.
- This complex condition requires long hospitalization periods including neonatal intensive care and surgical operations, followed by intensive long-term care by a multi-disciplinary team, the cost of which is extensive.

What Is New

- Based on data obtained from a 10-year period the pediatric SBS-IF incidence was 24 per 100,000 live births.
- Prevalence was 36 in the Hospital District of Helsinki and Uusimaa in Finland in 2019.
- First year hospital-based healthcare resource utilization costs were €221,000 (prematurity excluded), and for the early preterm infants, €279,000.
- An early preterm SBS-IF patient may spend 75% of the first year of life in hospital.

METHODS

Study Design, Population, and Data Source

This was a retrospective registry study, using existing data generated during routine clinical practice at specialized healthcare facilities and stored in the HUS data lake. HUS is the largest hospital district in Finland covering a population of about 1.6 million.

Finland has national primarily taxation funded healthcare. All permanent residents in Finland (in 2019 the entire population of Finland was approximately 5.6 million) regardless of their social status or financial situation are entitled to equal public healthcare. Thus, the real-world data (RWD) in the Finnish social and healthcare registries covers all individuals living in Finland. All Finnish citizens registered in the Finnish Population Information System have a unique 11-digit national identification (ID) code. Using the ID code, the modern data lake systems set up in hospitals can combine and harmonize various patient record systems used in clinical practice to one continuously updated data source, which can be utilized for secondary uses, such as scientific studies. In this study, data with personal ID was solely handled by the personnel at the HUS data lake or by the HUS investigators, and pseudonymized at the HUS data lake. Only pseudonymized data was available for the subsequent analyses at the shared data environment of the healthcare register of HUS.

Case and Control Patients

The HUS Children's Hospital has a comprehensive registry of all pediatric SBS-IF patients treated during the last decades (13). All pediatric SBS-IF patients treated and followed-up at HUS and living at the HUS catchment area, between 2010 and 2019 were identified for this study based on the institutional registry. Referred patients who lived at other Finnish hospital catchment area were excluded. The included SBS-IF patients have undergone an >50% small bowel resection and/or had received PN >3 consecutive months. Follow-up of each patient started from birth and ended at December 31, 2020 or at death.

The sex and year of birth matched control patients were included from HUS data lake for the SBS-IF patients (5:1). The controls were required to be alive at the index of the corresponding

TABLE 1. Number of new pediatric short bowel syndrome-associated intestinal failure (SBS-IF) cases per 100,000 live births and 100,000 pediatric patients, prevalence, and incidence during years 2010 and 2019 at Hospital District of Helsinki and Uusimaa (HUS) area in Finland

Year	Patients (N)	Prevalence (N)	Live births at HUS area (N)	Base population at HUS area (age: 0–17)	Incidence per 100,000 live births	Incidence per 100,000 pediatric patients
2010	7	7	18,758	314,716	37.32	2.22
2011	5	11	18,398	315,405	27.18	1.59
2012	<5	15	18,077	316,293	22.13	1.26
2013	<5	18	18,041	318,195	16.63	0.94
2014	<5	22	17,894	320,747	22.35	1.25
2015	<5	25	17,687	323,292	16.96	0.93
2016	<5	27	17,146	326,278	11.66	0.61
2017	5	32	16,532	328,334	30.24	1.52
2018	0	32	16,102	329,436	0.00	0.00
2019	5	36	15,711	330,474	31.82	1.51
Total	38		158,244	4,922,144	24.01	0.77

Small patient groups (<5 patients) have not been reported in detail.

case and have a home address within the HUS area. The controls represent average pediatric patients that had been treated at the same hospital and during the same time period as the corresponding patient cases.

Patient Characteristics, HCRU, and Costs

Demographics and clinical data were retrieved from HUS data lake. The gestational age (GA) for the SBS-IF patients was obtained from the HUS investigators and thus was not available for the controls.

HCRU was assessed based on the recorded inpatient days and hospital outpatient clinic contacts at the HUS specialized healthcare for the patient and control cohorts separately. The number of hospitalization days and outpatient clinic contacts were assessed in 2 time windows: (1) From birth (index) up to 1 year, end of follow-up, or until death (if the patient deceased prior to the 1-year mark), and (2) from index until end of follow-up, death, or end of study (December 31, 2020). The end of follow-up was defined in both time windows as the last in- or out-patient contact.

The contacts were priced according to Mäklin (14) including the average cost of all procedures, treatments, medications, and other inpatient or outpatient visit related costs in each specialty. All costs reported in this paper are in 2020 euros (€). Hospital-based HCRU contacts and total costs were calculated per patient (PP; total divided by the number of patients) and per patient year (PPY; total divided by the total follow-up length). The total, PP, and PPY number of inpatient days and number of hospitalizations were calculated. As the costs for these were the same, only inpatient day costs were shown. Number and cost of inpatient days and outpatient contacts were reported in a table (PPY and PP) and visualized in histograms (PPY). The types and specialties of the outpatient clinic contacts were tabulated and visualized in histograms (PP). The outpatient contact specialty auxiliary visit was defined as an extended visit, which was a contact with a specialist of another department than the department which is responsible for the patient during the visit.

Incidence and Prevalence

Yearly and overall incidence and prevalence of SBS-IF 2010–2019 were calculated. The incidence was calculated against all persons 0–17 of age and the number of newborn children alive at birth at HUS area, which were obtained from Statistics Finland (15). The results were reported per 100,000 patient years.

Statistical Analyses

Statistical analyses were performed using R version 4.0.2 (R Core Team) (16). Only existing data were used, with no imputation of missing values. The proportion of missing values were reported where applicable. The 95% confidence intervals (CIs) for both the costs and the number of contacts were obtained by bootstrapping (with 10,000 bootstrap samples).

RESULTS

Patient Characteristics

Thirty-eight (38) pediatric patients with SBS-IF and 190 control patients were identified from the HUS data lake. Over half of the patients were male (SBS-IF patients 63.2%, n = 24; controls 63.2%, n = 120). The median follow-up time was 5.6 and 5.9 years (range 0.1–10.0 years) and total follow-up 208.2 and 1073.5 patient years for cases and controls, respectively. Of the pediatric SBS-IF patients, 2 died during the study follow-up. SBS-IF patients were mostly premature: 52.6% (n = 20) early preterm (GA ≤ 30 weeks), 39.5% (n = 15) late preterm (GA > 30 weeks), and 7.9% (n = 3) GA missing. Among the SBS-IF patients, 21 presented with NEC of which all were born early or late preterm. SBS-IF onset was during the neonatal period for 63% of the patients, while onset of 95% was during the first 180 days of life.

SBS-IF Prevalence and Incidence

Pediatric SBS-IF prevalence was 36 in the HUS in Finland in 2019 (Table 1). The number of new pediatric patients with SBS-IF during 2010–2019 varied between 0 and 7 annually. The overall incidence was 0.8 new SBS-IF cases per 100,000 pediatric patients, and the annual incidence varied between 0 and 2.2. During the overall study period SBS-IF incidence was 24.0 per 100,000 live births.

Number of Hospitalizations, Inpatient Days, and Clinic Contacts

The cases incurred significantly more hospitalizations, inpatient days, and outpatient clinic contacts than the controls during both the first year of life and the whole follow-up (Fig. 1A–C). On average, cases had 10 (95% CI: 8–11) hospitalizations and 217

FIGURE 1. The average number of (A) hospitalizations, (B) inpatient days, and (C) clinic contacts per patient year in cases (all and by gestational age) and controls during the first year since birth (grey bars) and during the whole follow-up (black bars). The whiskers around the bars indicate the 95% confidence intervals. Early preterm = GA ≤ 30 weeks; late preterm = GA > 30 weeks; PPY = per patient year.

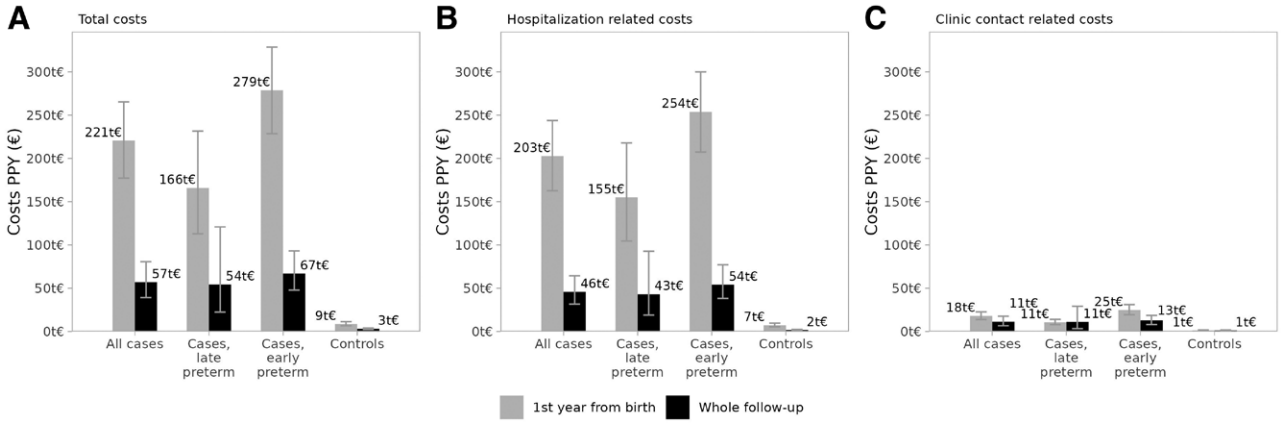


FIGURE 2. The average hospital-based healthcare resource utilization (HCRU) costs in cases (all and according to gestational age) and controls during the first year since birth (grey bars) and during the whole follow-up (black bars). In the figure total costs (A) are broken down into hospitalization related costs (B) and clinic contact related costs (C). The whiskers around the bars indicate the 95% confidence intervals. Early preterm = GA ≤ 30 weeks; late preterm = GA > 30 weeks; PPY = per patient year.

(95% CI: 174–261) inpatient days (controls 3 and 9, respectively) during first year, and annually during whole follow-up 3 (95% CI: 2–5) hospitalizations and 49 (95% CI: 34–69) inpatient days (controls 1 and 2, respectively). The number of clinic contacts was 64 (95% CI: 50–81) during first year and 41 (95% CI: 24–63) whole follow-up (controls 5) PPY. Overall, HCRU was higher for the early preterm cases (GA ≤ 30 weeks). On average, early preterm patients were hospitalized 11 (95% CI: 9–14) times during the first year of life and 4 (95% CI: 3–5) times during the whole follow-up, spent 271 (95% CI: 222–320) days as inpatients during the first year of life and 58 (95% CI: 222–320) days during the whole follow-up, corresponding numbers were 89 (95% CI: 69–112) and 46 (95% CI: 29–67) for outpatient clinic contacts PPY.

Hospital-Based HCRU Costs

An average PPY HCRU cost during the first year from birth was €221,000 for SBS-IF patients and €9000 for controls (Fig. 2A). The costs were higher for the early preterm SBS-IF-patients (GA ≤ 30 weeks; €279,000) compared to late preterm patients (GA > 31 weeks; €166,000). The HCRU costs were high during the first year of life, consisting mainly of inpatient days (Fig. 2A–C). Entire follow-up costs were lower (€57,000) with higher share of clinic contact costs (€11,000) PPY. More than half of the total follow-up HCRU related costs PP were accrued during the first year of life (Table 1, Supplemental Digital Content 1, *http://links.lww.com/MPG/D235*).

The average cost of the first hospitalization was €145,000 (€73,510–254,700; average duration 150 days) for all cases, €226,000 (€145,000–303,600; average duration 251 days) for early preterm cases, and €73,000 (€38,000–121,500; average duration 74 days) for late preterm cases PPY.

Outpatient Clinic Contacts

An average number of the most common outpatient contact type auxiliary visits patients had PP was over 10-fold compared to controls during follow-up (62.4 and 4.7 visits, respectively; Fig. 3A). Home visits, phone calls, revisits, and nurse visits were the next common clinic contact types. The most common specialty involved in outpatient contacts was gastroenterology or pediatrics (combined) followed by surgery and pediatric neurology (Fig. 3B). The number of gastroenterology or pediatrics contacts per SBS-IF

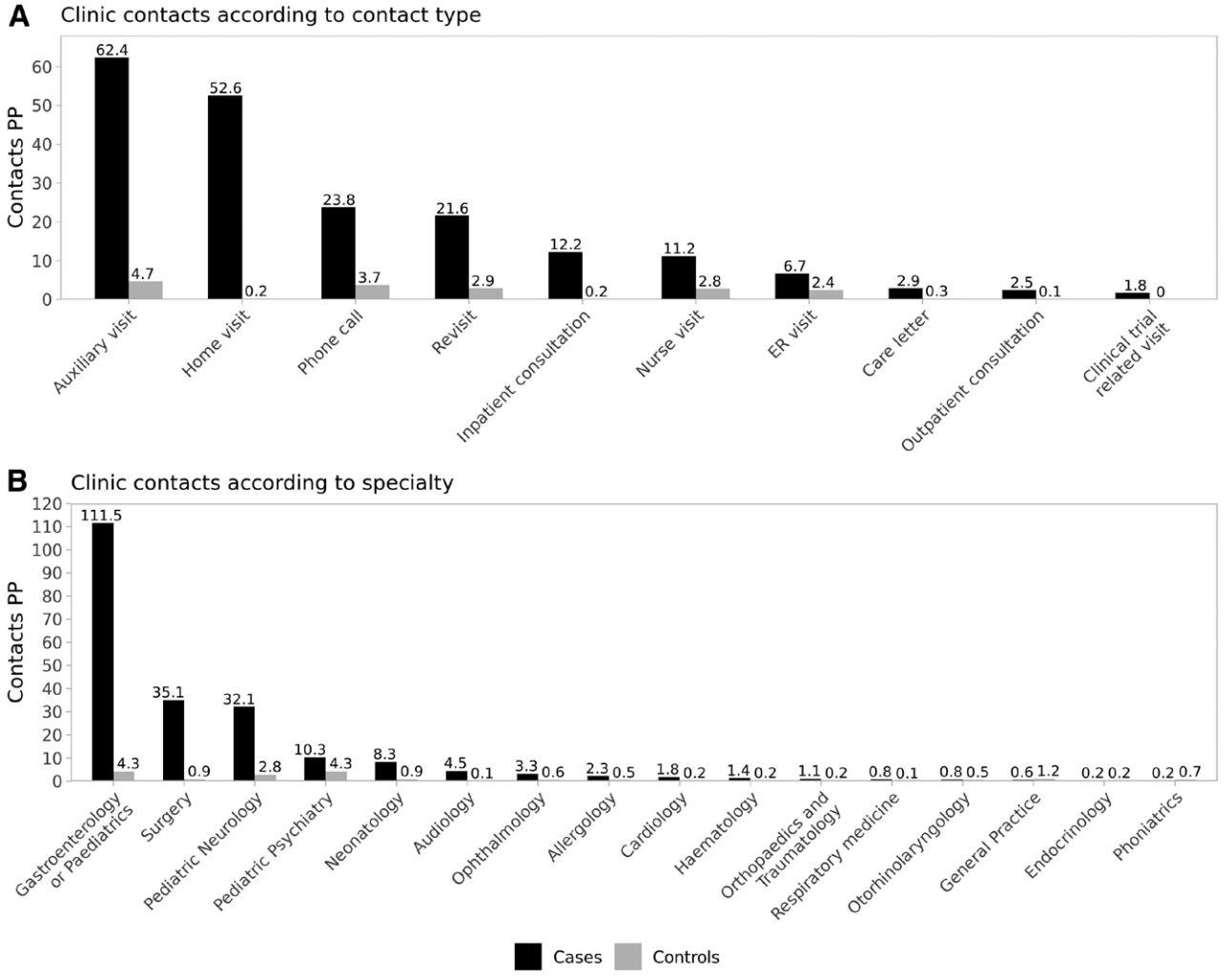


FIGURE 3. The average number of outpatient clinic contacts per patient during whole follow-up according to (A) contact type and (B) specialty in short bowel syndrome-intestinal failure (SBS-IF) cases (black bars) and controls (grey bars). ER = emergency room; PP = per patient.

patient during follow-up was almost 20 times the number of controls, 76.2 and 4.2, respectively.

DISCUSSION

This is the first study reporting comprehensive follow-up RWE on pediatric patients with SBS-IF. Data for this study was retrieved from the largest hospital district in Finland, HUS, managing on average of 7 new pediatric SBS-IF patients each year, including referred patients (13). During 2010–2019, a total of 38 pediatric SBS-IF-patients originating from the HUS primary catchment area was treated and followed-up by our unit. To our knowledge, this is the first time that pediatric SBS-IF-patient incidence has been estimated based on registry data obtained from a 10-year period. Previous studies in Europe have estimated the overall number of chronic SBS-IF-patients between 5 and 80 cases per 1 million (17). In our study, the pediatric SBS-IF incidence was 0.8 new cases per 100,000 patients or 24 per 100,000 live births, which was similar to a previously published one institute 2-year incidence from Canada (1).

Our study demonstrated a high demand for healthcare for the pediatric patients with SBS-IF, especially during the first year of life. An early preterm SBS-IF patient may spend 75% of the first year of life in hospital (average 271 days; including time in NICU) and an SBS-IF patient excluding prematurity 60% (average 217 days). The average duration of the first hospitalization was 150 days, which is at comparable level with the 174-day median duration of initial hospital admission observed in the Netherlands (18). A Canadian study by Kosar et al (19) reported the mean length of primary hospitalization as 98 days (SD 36.5). Furthermore, a previous study from United States reported median length of hospital stay 8 days [The interquartile range (IQR) 15 days], which was significantly higher for the SBS-IF patients compared to controls ($P < 0.001$) (20). However, the latter numbers are not fully comparable with our study, due to the fact that hospitalization did not cover intensive care treatment period which is included in our study. The intensive care was previously reported to cover almost half of the pediatric SBS-IF patients initial hospital days (18). In comparison, previous studies have reported for preterm patients without SBS-IF; the average length of stay of the birth hospitalizations was 9 days (21), the median length of hospitalizations during the first year of life from 29 to 69 days (22,23), the average number of hospital admissions during the first year of life from 2 to 3 (22), and the median number of outpatient contacts during first year of life was 25 (23). While the impact on the healthcare system is obvious, the burden on the family cannot be neglected and it is an important area for further investigation to understand the overall burden of SBS-IF.

Considering all pediatric SBS-IF-patients, the total average cost of hospital-based HCRU was €221,000 for the first year and €57,000 annually. The annual cost corresponded surprisingly well with the previously observed in the United Kingdom (£52,800) (24). The costs were even higher for the early preterm patients with SBS-IF. To compare our result with the costs assessed previously for management of preterm infants without SBS-IF, estimated at the level of A$182,300 during the first year of life and A$9900 for the following years (22), which are much lower than in the SBS-IF patients but higher than in our control cohort. Further, the first year of life was particularly expensive covering over half of the total costs accumulated during whole follow-up. The cost estimates presented in our study are underestimations of the actual costs because only mean prices of contacts were utilized for calculations. Treatment of a pediatric SBS-IF patient is markedly more expensive than treatment of an average pediatric patient, as an example the cost of 1 day at NICU is about €2700 (in 2020 euros) (14,25), and a very preterm newborn may spend weeks at NICU. However, a much lower average cost of €936 per a pediatric hospitalization day was considered in our study because it was not possible to specify NICU days from our data. Importantly, the reported cost estimations are based on hospital-based HCRU only, and do not cover all expenses, for example indirect costs related to caregiver absenteeism and HPN. HCRU costs have been estimated to increase during HPN, depending on individual PN fluid requirements (6). According to our own (unpublished) estimates, the HPN costs vary from patients with low PN requirement €16,000 to patients with high PN demand (every night) €46,000 PPY. These HPN costs include medical devices, medicines, and PN fluids, but not home visits or other treatments. The specialty care hospital-based HCRU and home visits are included in costs reported in the present study, even if HPN related costs are not. Previously, cumulative cost of hospital-based HCRU and HPN at the age of 3 years was estimated to be at magnitude of €330,000 (in 2006 euros) (26), which is at comparable level with our estimate. However, the yearly cost is dependent on, for example, patients' GA, PN demand, and the initial hospitalization is much more expensive compared to later management. In Canada, the total costs for the first year after primary discharge were $320,000 (in 2014 Canadian dollars) (19), which is higher than the annual whole follow-up cost we reported. Though, the cost included expenses that are not included in our calculations, as examples HPN, parents' accommodation during hospitalization, and medication.

In our study, hospital-based healthcare costs during first year of life accumulated mainly from inpatient days (92%), similar to previous study (82%), in which hospital days accumulated from prolonged requirements for intensive care resources, multiple surgical procedures, and multiple readmissions during the first year of diagnosis (27). Intriguingly, an earlier Dutch study reported exactly the same share of HCRU expenses for hospital admissions (82%), followed by nutrition (12%), surgical interventions (5%), and outpatient visits (1%) (26). In our study, the number of outpatient contacts increased after the first year. Thus, the share of hospitalization related costs was lower when accounting for the whole follow-up (80%). The reasons for hospitalizations were not in the focus of our study. Previous studies reported infections or sepses a common cause for rehospitalizations (26,27).

Survival rates of SBS patients have increased significantly over the years and are currently over 90% (1,18,20,28–30). This is due to the advances in medical and surgical treatment options of SBS-IF (31,32). During our study follow-up the survival rate of SBS-IF patients was 95%.

Prevention and treatment of complications to restore enteral autonomy and reduce long-term dependence on PN, has been the focus of management on SBS-IF. The high demand for healthcare shown in this study indicates a potential unmet need for novel treatments that could cure the disease and thus improve patient care and minimize HCRU burden. The results represent a good overview of pediatric SBS-IF treatment from a time period proceeding new treatment option (end of follow-up 2020) glucagon-like peptide-2 analogue teduglutide, providing a valuable baseline and an interesting comparison for future research.

Study Strengths and Limitations

One strength of RWD setting is the access to diagnoses, procedures, and visits from the same data source. Health record data availability via data lake technology enables extraction and analysis of large data sets including multiple disease-related characteristics and resources, which was also utilized in this study. A further strength of our study is that we captured all pediatric SBS-IF patients living at in the HUS area in 2010–2019.

Limitations of a data lake setup are typically related to secondary nature of data which was originally recorded for primary treatment use. Thus, some information may not have been consistently recorded for all patients, potentially affecting the study population and other outcomes. Another limitation of this study is that all-cause HCRU was reported, not SBS-IF specific. However, SBS-IF is not a single disease and SBS-IF patients typically have several concomitant disorders. Hence, reporting all-cause and not disease-specific HCRU is justified and compared to controls to assess the additional burden posed by the condition. Information on PN was not comprehensively reported at HUS data lake because it is mostly HPN. Thus, we were not able to describe PN related costs, which would be an important topic for the further studies. A further limitation of this study is that GA could not be taken into account when matching the pediatric SBS-IF patients with controls. Because we required the included patients to have received PN over 3 consecutive months we have not captured the children who received PN for a shorter period before weaning off and still need close monitoring and follow-up.

CONCLUSIONS

SBS-IF is a rare disease with a relatively low number of patients treated at each hospital district. Our study provided RWE on high HCRU in the children with SBS-IF. The burden on the hospital system, as well as the patient's family, is especially high at the onset as newborns with SBS-IF spend a significant part of the first year of life in the hospital.

Acknowledgments: The authors wish to thank Heikki Mäkisalo, Sampsa Pikkarainen, Anne Pohju, and Ville Sallinen for their input in the design and execution of this study. We also thank Tanja Nieminen and Tatu Sainio for assisting in evaluating HPN costs.

REFERENCES

1. Wales PW, de Silva N, Kim J, Lecce L, To T, Moore A. Neonatal short bowel syndrome: population-based estimates of incidence and mortality rates. *J Pediatr Surg* 2004;39:690–5. doi:10.1016/j.jpedsurg.2004.01.036.
2. Kurvinen A, Nissinen MJ, Andersson S, et al. Parenteral plant sterols and intestinal failure-associated liver disease in neonates. *J Pediatr Gastroenterol Nutr* 2012;54:803–11. doi:10.1097/MPG.0b013e3182474118.
3. Batra A, Beattie RM. Management of short bowel syndrome in infancy. *Early Hum Dev* 2013;89:899–904. doi:10.1016/j.earlhumdev.2013.09.001.
4. Guarino A, De Marco G; Italian National Network for Pediatric Intestinal Failure. Natural history of intestinal failure, investigated through a national network-based approach. *J Pediatr Gastroenterol Nutr* 2003;37:136–41. doi:10.1097/00005176-200308000-00010.

5. Merras-Salmio L, Pakarinen MP. Infection prevention and management in pediatric short bowel syndrome. *Front Pediatr* 2022;10:864397. doi:10.3389/fped.2022.864397.
6. Chandra R, Kesavan A. Current treatment paradigms in pediatric short bowel syndrome. *Clin J Gastroenterol* 2018;11:103–12. doi:10.1007/s12328-017-0811-7.
7. Duggan CP, Jaksic T. Pediatric intestinal failure. *N Engl J Med* 2017;377:666–75. doi:10.1056/NEJMra1602650.
8. D'Antiga L, Goulet O. Intestinal failure in children: the European view. *J Pediatr Gastroenterol Nutr* 2013;56:118–26. doi:10.1097/MPG.0b013e318268a9e3.
9. Bielawska B, Allard J. Parenteral nutrition and intestinal failure. *Nutrients* 2017;9:466. doi:10.3390/nu9050466.
10. Cole CR, Hansen NI, Higgins RD, Ziegler TR, Stoll BJ; Eunice Kennedy Shriver NICHD Neonatal Research Network. Very low birth weight preterm infants with surgical short bowel syndrome: incidence, morbidity and mortality, and growth outcomes at 18 to 22 months. *Pediatrics* 2008;122:e573–82. doi:10.1542/peds.2007-3449.
11. Salvia G, Guarino A, Terrin G, et al. Neonatal onset intestinal failure: an Italian Multicenter Study. *J Pediatr* 2008;153:674–6, 676.e1. doi:10.1016/j.jpeds.2008.05.017.
12. Wales PW, Christison-Lagay ER. Short bowel syndrome: epidemiology and etiology. *Semin Pediatr Surg* 2010;19:3–9. doi:10.1053/j.sempedsurg.2009.11.001.
13. Merras-Salmio L, Mutanen A, Ylinen E, Rintala R, Koivusalo A, Pakarinen MP. Pediatric intestinal failure: the key outcomes for the first 100 patients treated in a national tertiary referral center during 1984–2017. *J Parenter Enteral Nutr* 2018;42:1304–13. doi:10.1002/jpen.1164.
14. Mäklin S. *Terveyden- ja sosiaalihuollon yksikkökustannukset Suomessa vuonna 2017*. Helsinki: THL; 2017:55
15. Anon. Official Statistics Finland: Live births according to sex and mothers age by region, 1990–2021. https://statfin.stat.fi/PxWeb/pxweb/fi/StatFin/StatFin__synt/statfin_synt_pxt_12dq.px/. Accessed November 25, 2022.
16. R Core Team. *R: A Language and Environment for Statistical Computing*; 2018.
17. Pironi L, Corcos O, Forbes A, et al. Intestinal failure in adults: recommendations from the ESPEN expert groups. *Clin Nutr* 2018;37:1798–809. doi:10.1016/j.clnu.2018.07.036.
18. Olieman JF, Tibboel D, Penning C. Growth and nutritional aspects of infantile short bowel syndrome for the past 2 decades. *J Pediatr Surg* 2008;43:2061–9. doi:10.1016/j.jpedsurg.2008.04.017.
19. Kosar C, Steinberg K, de Silva N, Avitzur Y, Wales PW. Cost of ambulatory care for the pediatric intestinal failure patient: one-year follow-up after primary discharge. *J Pediatr Surg* 2016;51:798–803. doi:10.1016/j.jpedsurg.2016.02.026.
20. Pant C, Sferra TJ, Fischer RT, Olyaee M, Gilroy R. Epidemiology and healthcare resource utilization associated with children with short bowel syndrome in the United States. *JPEN J Parenter Enteral Nutr* 2017;41:878–83. doi:10.1177/0148607115616079.
21. McLaurin KK, Hall CB, Jackson EA, Owens OV, Mahadevia PJ. Persistence of morbidity and cost differences between late-preterm and term infants during the first year of life. *Pediatrics* 2009;123:653–9. doi:10.1542/peds.2008-1439.
22. Callander EJ, Atwell K. The healthcare needs of preterm and extremely premature babies in Australia—assessing the long-term health service use and costs with a data linkage cohort study. *Eur J Pediatr* 2021;180:2229–36. doi:10.1007/s00431-021-04009-y.
23. Jackson K, Schollin J, Bodin L, Ternestedt B-M. Utilization of healthcare by very-low-birthweight infants during their first year of life. *Acta Paediatr* 2007;90:213–7. doi:10.1111/j.1651-2227.2001.tb00286.x.
24. Jones BC, O'Sullivan B, Amin SP, Hill S, Eaton S, De Coppi P. Patient-level costing analysis of paediatric short bowel syndrome care in a specialist tertiary centre. *Pediatr Surg Int* 2022;38:533–9. doi:10.1007/s00383-022-05074-6.
25. Sharma D, Murki S. Making neonatal intensive care: cost effective. *J Matern Fetal Neonatal Med* 2021;34:2375–83. doi:10.1080/14767058.2019.1660767.
26. Olieman JF, Poley MJ, Gischler SJ, et al. Interdisciplinary management of infantile short bowel syndrome: resource consumption, growth, and nutrition. *J Pediatr Surg* 2010;45:490–8. doi:10.1016/j.jpedsurg.2009.08.009.
27. Spencer AU, Kovacevich D, McKinney-Barnett M, et al. Pediatric short-bowel syndrome: the cost of comprehensive care. *Am J Clin Nutr* 2008;88:1552–9. doi:10.3945/ajcn.2008.26007.
28. Kaufman SS, Loseke CA, Lupo JV, et al. Influence of bacterial overgrowth and intestinal inflammation on duration of parenteral nutrition in children with short bowel syndrome. *J Pediatr* 1997;131:356–61. doi:10.1016/S0022-3476(97)80058-3.
29. Goulet O, Baglin-Gobet S, Talbotec C, et al. Outcome and long-term growth after extensive small bowel resection in the neonatal period: a survey of 87 children. *Eur J Pediatr Surg* 2005;15:95–101. doi:10.1055/s-2004-821214.
30. Quirós-Tejeira RE, Ament ME, Reyen L, et al. Long-term parenteral nutritional support and intestinal adaptation in children with short bowel syndrome: a 25-year experience. *J Pediatr* 2004;145:157–63. doi:10.1016/j.jpeds.2004.02.030.
31. Gutierrez IM, Kang KH, Jaksic T. Neonatal short bowel syndrome. *Semin Fetal Neonatal Med* 2011;16:157–63. doi:10.1016/j.siny.2011.02.001.
32. Modi BP, Langer M, Ching YA, et al. Improved survival in a multidisciplinary short bowel syndrome program. *J Pediatr Surg* 2008;43:20–4. doi:10.1016/j.jpedsurg.2007.09.014.