AMIA
INFORMATICS PROFESSIONALS. LEADING THE WAY.

OXFORD

Case Report

Developing a pediatric pain data repository

Carolina Donado (iD) **,[1] Kimberly Lobo,[1] Charles B. Berde,[1,2] and Florence T. Bourgeois[3,4]**

[1]Department of Anesthesiology, Critical Care and Pain Medicine, Boston Children's Hospital, Boston, Massachusetts, USA, [2]Department of Anaesthesia, Harvard Medical School, Boston, Massachusetts, USA, [3]Pediatric Therapeutics and Regulatory Science Initiative, Computational Health Informatics Program, Boston Children's Hospital, Boston, Massachusetts, USA and [4]Department of Pediatrics, Harvard Medical School, Boston, Massachusetts, USA

Corresponding Author: Carolina Donado, MD, Boston Children's Hospital, Pain Treatment Service, 333 Longwood Avenue, Boston, MA 02115, USA; Carolina.DonadoRincon@childrens.harvard.edu

ABSTRACT

The management of pediatric pain typically consists of individualized treatment plans and interventions that have not been systematically evaluated. There is an emerging need to create systems that can support the translation of clinical discoveries, facilitate the assessment of current interventions, and improve the collection of patient-centered data beyond routine clinical information. We present the development of the pediatric pain data repository, a custom-built system developed at Boston Children's Hospital by a multidisciplinary pain treatment service. The Repository employs a web platform to collect standardized patient-reported outcomes and integrates this with electronic medical record data. To date, we have collected information on 2577 patients and anticipate adding approximately 500 new patients per year. Major strengths of the Repository include collection of extensive longitudinal patient-reported outcomes, automated clinical data abstraction, and integration of the system into clinical workflows to support medical decision making.

Key words: data repository, pain conditions, pediatric populations, patient-reported outcomes, electronic health records

INTRODUCTION

The treatment of pediatric pain has undergone a profound transformation over the past few decades. Pain is increasingly recognized as a complex experience with interactions between biological, cognitive, emotional, behavioral, and social factors. This new perspective has required development of novel treatment avenues and interventions.[1] The standard in pain management now consists of individualized treatment plans that have often not been systematically evaluated, especially in pediatric populations. There is, therefore, an emerging need to create systems that can facilitate assessment of current interventions, support evidence-based translation of clinical discoveries, and improve collection of patient-centered data beyond routine demographic and clinical information.

Prospective randomized controlled trials play a crucial role in establishing efficacy for analgesics and other treatments of pain.

However, there are unique ethical and practical challenges in the conduct of pain-related controlled clinical trials in children.[2,3] These include consenting children to studies and exposing them to risk, small sample sizes and patient heterogeneity, and challenges with blood sampling for pharmacokinetics.[4,5] Even with Congressional mandates to study and develop drugs for children, the number of analgesics with pediatric labeling remains very low.[6–8]

The National Academy of Medicine[9] in 2011, in a report on advancing pain research, care, and education, called for the creation of clinical data repositories that collect and curate data for high-quality analyses. The secondary use of rich clinical data contained in the electronic health record (EHR) has become a cost-effective method for performing research on clinical outcomes in a number of fields.[10] These datasets may be particularly advantageous for overcoming many of the barriers encountered with pediatric clinical

trials and may support examination of a wide breadth of clinical interventions.[11]

However, information available through EHRs consists primarily of demographics, clinical diagnoses, and treatments administered to patients. There are limited data on subjective elements guiding decision making, including patient preferences for certain clinical interventions. Furthermore, there is broad recognition in the clinical environment on the importance of monitoring patients outside of clinical encounters and at specific time points after interventions to enable providers to assess progression and side effects, as well as increase patient involvement in their care.

To address this gap, we created a data repository at Boston Children's Hospital for patients with pediatric pain conditions, building a system that combines EHR data with extensive patient-reported outcomes.

IMPLEMENTATION EXPERIENCE

Motivation

The pain treatment service at Boston Children's Hospital, within the Department of Anesthesiology, Critical Care and Pain Medicine, is a multidisciplinary program for pediatric acute and chronic pain management. The patient population consists of multiple subgroups of children and adolescents, including those with chronic musculoskeletal and neuropathic pain conditions, functional abdominal pain, intractable headaches, widespread pain similar to fibromyalgia, and pain associated with severe or life-limiting illnesses. The patient volume consists of approximately 1200 patients with 500 new patients annually, corresponding to 3500 annual outpatient visits. The initial treatment approach typically consists of multidisciplinary outpatient care with medication therapy, physical therapy, cognitive behavioral therapy, and psychoeducation around lifestyle change and re-engagement in school and other activities.[12,13] For a subgroup of patients, we make selective use of nerve block injections, regional anesthetic infusions, and other invasive treatments.[14]

Based in an academic institution, the pain treatment service was engaged in research studies involving prospective clinical trials and retrospective studies, since its inception. The latter required chart reviews of medical records, often complemented by prospective data collection. This created a system where redundancies and duplication of efforts were common across different research groups and datasets. Additionally, there were inconsistencies driven by turnover in project managers that left many databases incomplete or with unclear data structures.

In addition to improving our research infrastructure, there was a need to develop a clinical tool that could aggregate and present patient and family information to clinicians. To address these requirements, in 2013, the division developed a web-based platform called WeCOPE, which collects electronic, standardized patient and family information before first-time visits. The data obtained included information on pain locations and characteristics, previous interventions, and responses to a set of validated questionnaires assessing psychosocial constructs associated with pain and maladaptive coping strategies. Clinicians could log into the provider view of the WeCOPE platform to review information submitted by patients, evaluate the patient's condition and trajectory, anticipate the need for imaging studies or laboratory tests, and plan additional consultations, particularly for patients coming from out of state.

This one-time data feed created a foundation for a registry of patients with pain disorders, but remained disconnected from longitudinal information on the patient's clinical care, disease course, and patient-reported outcomes.

Establishment of the Pediatric Pain Data Repository

Building on the WeCOPE platform, in 2018 we created the Pediatric Pain Data Repository, augmenting the database with clinical information from patients' EHR. The aim was to build a centralized data repository to facilitate data use for clinical purposes and increase research collaboration, quality, and scope. Additionally, as part of the standard of care we expanded data collection through WeCOPE to capture patient-reported outcomes longitudinally (Table 1).

EHR data export into the Repository

EHRs are designed primarily to collect data for clinical care and billing. Information collected in the clinical setting may be incomplete, inaccurate, or have insufficient detail to yield useful information for research purposes.[15] Additionally, EHR data are typically presented in free text format or may present multiple sources of data for a given measure. We developed a series of extract, transform, and load processes that directly query EHR data and automatically populate a database for the Data Repository. Standard information extracted from EHRs includes patient demographics, dates, and types of encounters (ie, pain clinic visit and emergency room visits), diagnoses (ie, ICD10 codes), medications prescribed, and procedures performed by the pain treatment service. For medications, a script was developed to de-duplicate prescriptions, filter by current status (eg, suspended or active), and parse prescription data into components of dose, frequency, total days prescribed, and number of refills allowed. The Data Repository is continuously working with clinicians and investigators to identify data elements of interest and methods to optimize data quality.

In addition, to supplement standard EHR data with additional patient phenotype information, new clinical variables are developed from the clinical notes using a combination of natural language processing and machine learning algorithms. We use regular-expression matching tools[16] to generate labeled datasets in which we train a Support Vector Machine algorithm to identify features of interest for new variables. The Repository also supports statistical learning methodologies such as classification, clustering, and network analysis to analyze patient features, define disease presentation patterns, and identify predictors of disease outcomes. Validated clinical variables can be added to the Repository for use by clinicians and investigators.

Longitudinal patient-reported outcomes in the Data Repository

Patient-reported outcomes describe health-related data provided by patients that facilitate communication and decision making between patients and providers.[17] There are 6 core areas recommended by the International Association for the Study of Pain for the assessment of safety and efficacy of interventions in pain management. These are pain characteristics, physical functioning, emotional functioning, participant ratings of global improvement, symptoms and adverse events, and participant disposition.[18] These outcomes are rarely systematically collected in clinical notes or outside the clinical encounter, but are captured using the previsit questionnaires in WeCOPE.

To facilitate ongoing data collection, WeCOPE was expanded to collect longitudinal data, focusing on patient-reported outcomes. Patients now receive validated questionnaires assessing pain charac-

Table 1. Information collected in the Pediatric Pain Data Repository

Type of data	Description and examples	Source of information
Demographics	• Sex, age, and ethnicity	EHR WeCOPE initial visit questionnaire
Pain characteristics	• Body map used to assess pain location • Pain scores and factors associated with the pain per location • Healthcare utilization • Medication used, including dose and perceived benefits • Pain at school • Sports and extra-curricular activities participation • Pain interventions	WeCOPE initial visit questionnaire WeCOPE follow-up questionnaire
Family information	• Parental demographic information • Family medical history	WeCOPE initial visit questionnaire
Patient psychological inventories	Standardized questionnaires assessing: depression, anxiety, quality of life, functional disability, fear of pain, pain catastrophizing	WeCOPE initial visit questionnaire WeCOPE follow-up questionnaire
Caregiver psychological inventories	Standardized questionnaires assessing: adult responses to child's symptoms, family relationship, pain catastrophizing and pediatric quality of life	WeCOPE initial visit questionnaire
Medical encounters	• Dates and types of encounters (eg, clinic visit or hospitalization) • Pain and functional scores • Diagnoses (based on ICD9 and ICD10 codes) • Medications prescribed • Interventions performed	EHR

Abbreviations: EHR: Electronic Health Record; ICD: International Classification of Diseases.

Figure 1. WeCOPE data capture. Panel A shows the enrollment rates over the years, and Panel B, the patient survey view including pain locations and functional scores.

teristics, as well as school, sleep, mood, and physical functioning every month and after all interventions (Figure 1). The data elements collected in these surveys were selected to serve clinicians in ongoing patient monitoring and to allow for rapid adjustments in treatment plans, as needed. Clinicians can review patient responses in the WeCOPE platform prior to or during a clinic visit, including trends over time across specific questions and domains. The platform also includes a "summary view" that presents survey data synthesized into a standardized summary text followed by scores across question types and individual surveys.

Repository governance and management

The Repository is governed by a research protocol approved by the Institutional Review Board (IRB) at Boston Children's Hospital. Information collected in the WeCOPE system is part of the clinical standard of care, and a waiver of consent was obtained for use of the data in research studies. While patients and families are strongly encouraged to complete the surveys, it is not obligatory and patients receive all indicated medical treatment irrespective of completion status. A committee was created to oversee management and use of the Data Repository, with representation from clinicians and investigators with a wide range of expertise in pediatric pain management. Processes were established to ensure data quality and standardization to facilitate data extraction and visualization, and guiding documents were created to support investigators in the use of this resource. Members of the Data Repository are also available to offer mentorship in the use of the Repository and in development of research projects.

The committee acts as the "honest broker" for data requests for projects using de-identified data and distributes data to investigators after scientific review and approval of the research protocol. Data requests for studies requiring patient identifiers must be accompanied by an IRB-approved protocol justifying the use of identifiable patient data. In all cases, investigators sign a data use agreement committing to use of the data as outlined in the proposal, and a regulatory guidance document is provided to highlight security and confidentiality provisions.

ASSESSMENT

Since the development of the WeCOPE system, 2577 patients have been added to the Repository, with 1993 (77.3%) providing partial or complete data on previsit patient-reported clinical information and psychological surveys. We are currently enrolling approximately 10 new patients per week. Table 2 provides basic demographic and clinical information on patients currently enrolled in the Repository.

In previous pediatric clinical outcome studies of chronic pain, it has become apparent that there are trade-offs between burden on patients and need for data collection at intervals more frequent than what can be derived from follow-up clinic notes.[14,19,20] Longitudinal patient data collection in our Repository has been designed to occur once per month and 1 week after any procedure performed by the pain treatment service, with the initial roll-out of the follow-up questionnaires occurring in the second quarter of 2019. This component will be assessed as data become available to optimize the frequency and content of the questionnaires.

Since the implementation of the Data Repository in January 2019, seven research projects have been launched using the Repository. Among these, three are associated with an IRB-approved protocol for use of patient identifiable data and four are exempt from IRB review as they require only de-identified data. Examples of the types of studies underway include an assessment of the emergence of overlapping pain conditions in children and adolescents, examination of the association between patient-reported measures of psychological stress, pain, and pain-related impairment in youth with chronic pain, and characterization of suicidal behaviors (eg, self-harm) associated with the use of gabapentin in children with chronic pain. We have also completed requests for data extraction to assist patient cohort selection and sample estimation in planning prospective studies.

Table 2. Demographic and clinical information of Pediatric Pain Data Repository ($n = 2577$)[a]

Outcomes		
Nationality		
United States	2486	96.5%
Massachusetts	1619	65.1%
Out of state	199	8.0%
International	26	1.1%
Mean age, years (SD)	14.7	3.6
Age groups		
0–5 years old	36	1.4%
6–11 years old	503	19.6%
12–17 years old	1693	65.8%
18 years and older	340	13.2%
Gender		
Female	2034	78.9%
Male	527	20.5%
Transgender	14	0.5%
No self defined	2	0.1%
Health utilization during 3-month period prior to first clinical visit		
Number of visits to a physician, mean (SD)	4.8	3.5
Number of visits to the emergency department, mean(SD)	0.9	1.6
Number of hospital admissions, mean (SD)	0.5	1.8
Painful locations		
Number of painful locations, mean (SD)	3.4	4.2
Pain intensity (0–10 scale)[a]	7.4	1.8
Most painful locations		
Multiple/whole body	961	42.4%
Lower extremity	512	22.6%
Back-hip	312	13.8%
Abdomen	206	9.1%
Head	162	7.2%
Upper extremity	112	5.0%
Percentage of school days missed due to pain in 3-month period prior to first clinical visit, mean (SD)	16.6	24.3
School accommodation		
504 plan[b]	562	21.8%
Individualized education program	360	14.0%
Other accommodation	347	13.5%
Home tutoring	199	7.7%
Prior pain interventions		
Exercise	1586	61.5%
Massage	952	36.9%
Physical therapy	864	33.5%
Psychological treatment or counseling	754	29.3%
Transcutaneous electrical nerve stimulation (TENS)	579	22.5%
Acupuncture	520	20.2%
Chiropractic	502	19.5%
Surgery	452	17.5%
Relaxation training	421	16.3%
Homeopathy	288	11.2%
Biofeedback training	150	5.8%
Hypnosis	54	2.1%

[a]Data reported are based on the WeCOPE inital visit questionnaire and EHR data.

[b]504 Plan is a plan developed to ensure that a child who has a disability identified under the law and is attending an elementary/secondary educational institution receives accommodations that will ensure their academic success and access to the learning environment.

DISCUSSION

The Repository is a powerful tool to provide high-quality, longitudinal data on the patient population followed by the pain treatment service at our institution. Key features include the collection of extensive longitudinal patient-reported outcomes, automated data abstraction, dynamic development of new clinical variables, and integration into clinical workflow.

Several enhancements are currently underway. We are examining patient adherence to follow-up data collection and approaches to maintain patient engagement with data collection and research initiatives within the Department. This includes evaluation of the types of platforms (eg, mobile apps) preferred by patients and most amenable to integration with our existing systems. Additionally, we are exploring new avenues to facilitate adherence and accuracy of patient reports through passively collected data, such as functionality and sleep as measured by actigraphy.[21] To support clinical use, we are working to improve the presentation of the patient-reported outcomes data to clinicians and thereby increase integration and use of the Repository in clinical workflows. This will be achieved using visualization tools supporting synthesis of large amounts of data to facilitate rapid interpretation and easy application of the data to clinical questions. Future collaborations across institutions to develop a multicenter data repository would further support the generation of much-needed evidence on interventions for acute and chronic pain management in pediatric populations.

CONCLUSION

The Pediatric Pain Data Repository is a unique resource that integrates longitudinal patient-reported outcomes with clinical data derived from the EHR. The Repository supports clinical care functions and allows investigators to efficiently assess interventions and pain mangement approaches in our population. To date, 2577 patients have contributed information to the Repository, with approximately 500 new patients added annually. In the near term, additional modifications will be made to further enhance data capture and visualization and further build our capacities for research supporting evidence-based pain management in pediatric populations.

AUTHORS CONTRIBUTIONS

All authors participated in the conceptualization and design of the Data Repository. CD and KL lead the implementation efforts of the repository. CD took the lead in writing the manuscript with all authors input. All authors provided critical feedback and approved the final version.

CONFLICT OF INTEREST

None of the authors report conflicts of interest related to this manuscript.

REFERENCES

1. Coakley R, Wihak T. Evidence-based psychological interventions for the management of pediatric chronic pain: new directions in research and clinical practice. *Children (Basel)* 2017; 4: 9.
2. Berde CB, Walco GA, Krane EJ, *et al*. Pediatric analgesic clinical trial designs, measures, and extrapolation: report of an FDA scientific workshop. *Pediatrics* 2012; 129 (2): 354–64.
3. Kossowsky J, Donado C, Berde CB. Immediate rescue designs in pediatric analgesic trials: a systematic review and meta-analysis. *Anesthesiology* 2015; 122 (1): 150–71.
4. Joseph PD, Craig JC, Caldwell PH. Clinical trials in children. *Br J Clin Pharmacol* 2015; 79 (3): 357–69.
5. Denhoff ER, Milliren CE, de Ferranti SD, *et al*. Factors associated with clinical research recruitment in a pediatric academic medical center—a web-based survey. *PLoS One* 2015; 10 (10): e0140768.
6. Avant D, Wharton GT, Murphy D. Characteristics and changes of pediatric therapeutic trials under the Best Pharmaceuticals for Children Act. *J Pediatr* 2018; 192: 8–12.
7. Bourgeois FT, Hwang TJ. The pediatric research equity act moves into adolescence. *JAMA* 2017; 317 (3): 259–60.
8. Bourgeois FT, Hwang TJ. Improving the study of new medicines for children with rare diseases. *JAMA Pediatr* 2018; 172 (1): 7–9.
9. Institute of Medicine (US) Committee on Advancing Pain Research, Care, and Education. *Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research*. Washington (DC): National Academies Press (US); 2011. 5, Research Challenges. Available from: https://www.ncbi.nlm.nih.gov/books/NBK92512/
10. Safran C, Bloomrosen M, Hammond WE, *et al*. Toward a national framework for the secondary use of health data: an American Medical Informatics Association White Paper. *J Am Med Inform Assoc* 2007; 14 (1): 1–9.
11. Lopez MH, Holve E, Sarkar IN, *et al*. Building the informatics infrastructure for comparative effectiveness research (CER): a review of the literature. *Med Care* 2012; 50 (Suppl): S38–48.
12. Logan DE, Carpino EA, Chiang G, *et al*. A day-hospital approach to treatment of pediatric complex. *Clin J Pain* 2012; 28 (9): 766–74.
13. Simons LE, Sieberg CB, Pielech M, *et al*. What does it take? Comparing intensive rehabilitation to outpatient treatment for children with significant pain-related disability. *J Pediatr Psychol* 2013; 38 (2): 213–23.
14. Donado C, Lobo K, Velarde-Alvarez MF, *et al*. Continuous regional anesthesia and inpatient rehabilitation for pediatric complex regional pain syndrome. *Reg Anesth Pain Med*. 2017; 42 (4): 527–34.
15. Hersh WR, Weiner MG, Embi PJ, *et al*. Caveats for the use of operational electronic health record data in comparative effectiveness research. *Med Care* 2013; 51: S30–37.
16. Document Review Tools. http://www.documentreviewtools.com/ Accessed January 23rd, 2019.
17. Howie L, Hirsch B, Locklear T, *et al*. Assessing the value of patient-generated data to comparative effectiveness research. *Health Aff* 2014; 33 (7): 1220–8.

18. Turk DC, Dworkin RH, Allen RR, *et al*. Core outcome domains for chronic pain clinical trials: IMMPACT recommendations. *Pain* 2003; 106 (3): 337–45.

19. Kurgansky KE, Rodriguez ST, Kralj MS, *et al*. Epidural steroid injections for radiculopathy and/or back pain in children and adolescents: a retrospective cohort study with a prospective follow-up. *Reg Anesth Pain Med* 2016; 41 (1): 86–92.

20. Simons LE, Sieberg CB, Conroy C, *et al*. Children with chronic pain: response trajectories following intensive pain rehabilitation treatment. *J Pain* 2018; 19 (2): 207–18.

21. Meltzer LJ, Montgomery-Downs HE, Insana SP, *et al*. Use of actigraphy for assessment in pediatric sleep research. *Sleep Med Rev* 2012; 16 (5): 463–75.