Published in final edited form as:

Int J Palliat Nurs. 2012 September ; 18(9): 441–445. doi:10.12968/ijpn.2012.18.9.441.

Design and Implementation of Electronic Data Collection to Assess Pain in Thalassemia

Felicia L Trachtenberg, PhD¹, Marie Martin, RN², Sage Green, BA², Olivia Oliveros, BS³, Susan Carson, MSN, CPNP⁴, Eric Gerstenberger, MS¹, Racquel Allen, MA¹, Jennifer Eile, MS, PNP⁵, and Dru Haines, MSN, CPNP³ for the Thalassemia Clinical Research Network⁶

¹New England Research Institutes, Watertown, MA

²Children's Hospital of Philadelphia, PA

³Children's Hospital & Research Center Oakland, CA

⁴Children's Hospital Los Angeles, CA

⁵Children's Hospital Boston, MA

Abstract

Aim—To assess the feasibility of collecting electronic pain data in thalassemia patients, based on acceptability and convenience to participants and the study team.

Methods—Participants in the Thalassemia Clinical Research Network Assessment of Pain Study completed the Brief Pain Inventory (BPI) quarterly by paper or phone interview. Participants in a substudy completed the BPI-Short Form daily over three non-consecutive transfusion cycles through an automated telephone system.

Results—The consent rate for the main study was 93%, with 93% retention. The substudy had 75% retention, with more than 75% of scheduled calls completed. Regular monitoring of enrollment, missed calls, data quality, and the performance of the subcontractor for the automated system was crucial to fulfillment of study goals.

Corresponding Author: Felicia Trachtenberg, Senior Research Scientist, New England Research Institutes, 9 Galen Street, Watertown, MA 02472, ftrachtenberg@neriscience.com, Phone: 617-972-3120, Fax: 617-923-4176.

⁶This is publication number 26 of the Thalassemia Clinical Research Network (TCRN). A list of TCRN member institutions and staff appears in Appendix 1

Other Authors

Marie Martin, RN, Research Nurse, Children's Hospital of Philadelphia, Division of Hematology, 34th and Civic Center Blvd., Philadelphia, PA 19104.

Sage Green, BA, Clinical Research Coordinator, Children's Hospital of Philadelphia, Division of Hematology, 34th and Civic Center Blvd., Philadelphia, PA 19104

Olivia Oliveros, BS, Clinical Research Coordinator, Children's Hospital & Research Center at Oakland, Hematology/Oncology Department, 747 52nd Street, Oakland, CA 94609

Susan Carson, MSN, CPNP, Research Nurse, Children's Hospital Los Angeles, Hematology Program, 4650 Sunset Boulevard, MS #54, Los Angeles, CA 90027

Eric Gerstenberger, MS, Research Scientist, New England Research Institutes, 9 Galen Street, Watertown, MA 02472

Racquel Allen, MA, Data Manager, New England Research Institutes, 9 Galen Street, Watertown, MA 02472

Jennifer Eile, MS, PNP, Research Nurse, Children's Hospital Boston, Division of Hematology, Fegan 706, 300 Longwood Ave, Boston, MA 02115

Dru Haines, MSN, CPNP, Research Nurse, Children's Hospital & Research Center at Oakland, Hematology/Oncology Department, 747 52nd Street, Oakland, CA 94609

Conflicts of Interest

The authors report no conflicts of interest.

Conclusions—Use of electronic data collection for patient-reported outcomes was convenient for both patients and study personnel, but required human interactions beyond the automated system to maximize data quantity and optimize quality.

Keywords

pain; thalassemia; electronic data collection; patient-reported outcomes; brief pain inventory

INTRODUCTION

Recently there has been a focus on patient-reported outcomes in many disease populations in order to study the patient perspective and provide an overall assessment of chronic illness (Gershon et al., 2010). Patient-reported outcomes can be collected either inside or outside the clinic by a nurse/coordinator, patient diary, or automated systems. Electronic data collection has become an increasingly useful way to collect outcomes at the convenience of the patient, either by phone or computer (Carr and Worth, 2001). Patient-reported outcomes have been developed to measure many important domains, including quality of life, physical function, fatigue, sleep, and pain (Gershon et al., 2010).

Thalassemia is a chronic, inherited blood disorder, which, in its most severe form, causes life-threatening anemia. It requires lifelong adherence to a complicated and burdensome medical regimen. Specifically, many patients with thalassemia require frequent blood transfusions, necessitating adherence to a chelation therapy regimen in order to prevent morbidity and mortality as a result of iron-overload. Chronic pain has emerged clinically as a previously unidentified health problem in thalassemia as patients enjoy longer life-spans due to improved treatments (Trachtenberg et al., 2010). Therefore it has become vital to document the extent of the problem, identify causes, and study potential treatments.

The Thalassemia Clinical Research Network (TCRN) is an NIH/NHLBI funded network composed of five core thalassemia centers in North America and their associated satellite sites. As part of its mission to design clinical research studies of thalassemia complications and treatments, the TCRN Nurses and Study Coordinators designed the Assessment of Pain Survey Study to provide a multi-center, prospective, observational assessment of pain in patients with thalassemia. While the primary aim of the study was to assess the prevalence of pain in subjects with transfusion and non-transfusion dependent thalassemia, a secondary aim of this pilot study was to assess the feasibility of collecting pain data in thalassemia patients, based on the acceptability and convenience of electronic data collection to participants and the study team. This paper describes the design and conduct of the study, problems encountered, and solutions implemented. This information may be useful for investigators designing future pain studies in thalassemia or other diseases involving chronic pain.

METHODS

The TCRN Pain study protocol was approved by the TCRN Data and Safety Monitoring Board and by the ethical review boards of all TCRN institutions. Informed consent from participants/parents, and assent in the case of a minor under 18, was obtained. Study

coordinators at sites in Toronto, Oakland, Philadelphia, New York, Los Angeles, Boston, Chicago, Atlanta, Palo Alto, British Columbia, and Houston approached potentially eligible patients at clinic visits from April 2009 to March 2010, and the study was advertised in the newsletter of a large patient advocacy group. Eligibility for the Pain study included patients of all thalassemia syndromes at least 12 years of age. Exclusion criteria included thalassemia trait and thalassemia Hgb S, C or D compound heterozygotes, as well as prior successful bone marrow transplant.

Sample Size

There was no prior information available on general pain in thalassemia on which to base a power calculation for this pilot study. After surveying participating TCRN sites for expected numbers of eligible patients, a target sample size of 200–300 was selected. Stratification by transfusion dependence was desired in order to adequately describe and contrast the different populations. Target enrollment was 200–300 subjects, stratified by transfusion status: 140–200 transfusion dependent, 30–50 intermittently transfused, 30–50 non-transfused. A larger target of transfusion dependent patients was selected as these patients are the majority seen at participating clinics.

Study Instruments

Study participants completed the Brief Pain Inventory (BPI) at four points in time: baseline and quarterly for a nine month period. Baseline survey completion was conducted at a clinic visit where participants completed a paper version of the forms. Follow up pain assessments were conducted via phone interview on a quarterly basis by site study coordinators. Data quality for pain research has been found to be comparable between face-to-face and telephone interviewing (Carr and Worth, 2001).

The BPI was selected to assess pain based on its wide use and demonstrated validity and reliability over multiple cultures and languages (Cleeland, 2008, Dworkin et al., 2005). The primary pain dimensions assessed by the BPI include severity, location and interference with daily life. Participants rate their worst, least, and average pain over the last seven days, as well as their pain right now. Participants also rate the level that pain interferes with activities of daily living on seven aspects of life. Pain is rated on a 0 to 10 scale, with 0=“no pain” or “no interference” and 10=pain “as bad as you can imagine” or “complete interference”. The BPI has been formally validated in individuals 18 and older. Therefore, participants aged 12–17 completed both the BPI and the Adolescent Pediatric Pain Tool (APPT). The APPT has been widely used to assess acute and chronic pain in the pediatric population (Crandall, 2005, Tesler, 1991). The APPT assesses pain on three dimensions: location, severity and quality. Pediatric responses to both measures were compared in order to rely on a validated tool in the pediatric population (APPT) while allowing for comparison with the adult population (BPI).

Substudy

Based on clinical reports of increased pain prior to transfusion, a substudy was designed to examine a subset of adult transfusion dependent patients who reported at least mild pain in the main study. Transfusion-dependent patients over age 18 consenting to the main study

were approached for consent. Study coordinators targeted patients who had complained of pain at recent clinic visits. Patients who consented to the substudy were found eligible if they then reported at least mild pain in the main study. Target enrollment for the substudy was 25–35 subjects, stratified by age group: 10–15 aged 18–29 years vs. 15–20 aged 30+ years.

Subjects completed the BPI-Short Form daily to assess whether the presence and/or intensity of pain varied over their transfusion cycle. Questionnaires were completed through an automated telephone system during three non-consecutive transfusion cycles, each 3 months apart, and lasting 2–4 weeks, depending on individual transfusion schedules. The TCRN contracted with an independent vendor who had exclusive rights to the BPI in automated telephone response format, to provide the telephone system. This vendor was approved by MD Anderson Cancer Center, creator of the BPI, to provide a valid phone system. Patients were given two options for calls: (1) to make toll-free calls at their convenience, using a username and password, or (2) to schedule the system to call them on their home, cell or work phone at a time of their choice, with password verification. For the second option, the system was set to attempt hourly calls, up to three times, should the subject be unavailable at their scheduled time; the patient was also free to call in at a different time instead.

Electronic Data Collection

The study was designed with two different forms of electronic data collection: (1) telephone interview for the quarterly study, and (2) an automated telephone system for the daily transfusion substudy. The benefit of quarterly phone interviews was interaction with a live coordinator who was reading the questions. For daily calls, however, an automated system was chosen so as not to overly burden the study coordinators. To maintain both quality and quantity of data, efforts at immediate feedback were implemented. The automated system was set to email study coordinators if patients missed their call on a given day, and coordinators were instructed to follow-up with these patients. Coordinators were also given access to data input by patients at their site and instructed to check the data for completeness. Finally, the vendor was asked to provide regular data dumps to the data coordinating center in order to allow for performance of routine quality control checks.

On the other hand, common to both forms of electronic data collection was the challenge of translating a written form to a spoken version. For example, the written form provides respondents with diagrams of the front and back of a human body, with instructions to circle any areas where the respondent has been experiencing pain. In order to translate this information into telephone format, the study team divided the diagram into twelve body parts and asked about each body part as a yes/no question, e.g., “do you feel pain in your head?”. For the automated system, a consistent entry of “1=yes” and “2=no” was established.

The possibility of electronic data collection using a handheld device was considered, as it would have allowed participants to see the questions being asked. However, such a system was not chosen due to cost and the possibility of participants losing the devices. Instead, the study team invested time into developing the script for the automated telephone system, and

then performing beta testing before study participants began data entry. Study coordinators tested the system by calling in as “patients” using a variety of responses.

Monitoring

The study team held biweekly teleconferences to design the study, monitor recruitment and retention, and resolve issues that arose. As the study did not have flexibility in choosing the vendor for the automated telephone system, the study team carefully designed methods of monitoring the contracted vendor. Coordinators were instructed to check the data for consistency daily, and routine quality control checks at the data coordinating center also monitored the data on a regular basis. When quality issues were discovered, study coordinators were asked to immediately follow-up with their patients to maximize data quality. Study coordinators also informally asked their participants for feedback on their experiences in the study.

RESULTS

Enrollment and retention

The consent rate was excellent (93%; Table 1) and almost all consented patients completed their baseline assessment. Retention rates were very high (93%; Table 1), with only a 4% withdrawal rate, including three patients who died during follow-up. The study plan called for enrollment over 14 months. Minimum enrollment in the transfusion dependent arm was met after only 3 months, with maximum enrollment completed after 5 months. Minimum enrollment in the non-transfused arm was met after 10 months, while minimum enrollment in the intermittently transfused arm was never met. After 11 months, a decision was made to end enrollment due to lack of further patients to enroll. The final enrollment was 201 transfusion dependent patients, 14 intermittently transfused patients, and 37 non-transfused patients.

Because study coordinators did not record the number of patients approached for consent before enrollment was met, no consent rate for the substudy is available. Anecdotally, the consent rate was 100% at the two largest sites. Retention rates were adequate (75%; Table 1), with a 25% withdrawal rate, including one patient who died during follow-up and three who cited the study as “too burdensome”. The study plan called for enrollment over 6 months. Minimum enrollment was met after only 2 months in the 18–29 year group and after 3 months in the 30+ group.

On average, participants in the substudy completed over three-quarters of their daily calls (Table 2), typically missing one or two calls per week, with a range of 24–100% of calls completed per cycle. Call rates were consistent over all three cycles; however, participants who no longer wished to complete daily calls may have withdrawn. Completion rates in the younger cohort declined slightly over time, and women had slightly higher completion rates than men. Over time, completion rates in participants with longer cycles (more days of calls to do) seem to have declined.

Data quality

Logically, patients should report pain as least average worst; however, this was not always the case. The data coordinating center found 13 inconsistencies in the main study and 23 in the substudy that were not caught by the study coordinators. As the coordinators worked with the patients to resolve the inconsistencies, there were only two inconsistencies in the final data. The study team chose to recode the data: worst pain was recoded as the maximum response for one subject, and the responses for worst and least pain were reversed for another subject. The study team considered the possible categorization of pain 'right now' < 'least pain' or 'right now' > 'worst pain' as inconsistencies, but decided that the term 'right now' could be interpreted in multiple ways.

The coordinators cited language issues as the main source of inconsistencies. Although the BPI is available in multiple languages, the study team made a decision to use only the English version, based on prior knowledge of this population. Additionally, informed consent was being administered in English, limiting recruitment to English speakers. However, some patients were not native English speakers and, even among the native English speakers, some participants had difficulty understanding the term 'average'. For other participants, the survey may have been cumbersome, leading to quick inconsistent responses. Another possibility was the mode of data entry itself; without a visual reminder of their response to previous questions, participants may have been more likely to respond inconsistently.

Of the 41 children completing both the BPI and APPT reports of pain at baseline, 31 reported experiencing no pain on both forms, 3 reported pain on both forms, and 7 reported pain only on the APPT. This inconsistency was likely due to the difference in the way the question was asked; the APPT asks about any pain in the last week, whereas the BPI asks about any pain other than everyday kinds of pain. Thus one would expect more reports of pain on the APPT. The study team decided to report the BPI data in children in order to compare children to adults; although not a validated instrument in children, as very little pain was reported in children, the primary focus of the BPI results will be pain in adults.

Contracting for the automated telephone system

Multiple difficulties with the independent subcontractor over the course of the study required regular review and resolution. The contractor did not meet their contracted start deadline, thereby causing a delay of three months between the main study and the substudy. During this time, study coordinators kept in contact with consented participants to alert them as to the start date of their calls. During the study period, patients reported problems to the study coordinators, including not receiving scheduled calls, receiving calls at the wrong time, and receiving too many calls. Some of these problems resulted in patient withdrawal from the study. Some of these problems also resulted in protocol deviations if calls needed to be deferred to the next transfusion cycle. The coordinators also noted not receiving missed call alerts via email or receiving duplicate emails. The study team kept in constant contact with the contractor to resolve these problems immediately and maximize the amount of data collected.

DISCUSSION

The TCRN Assessment of Pain Study was able to collect clinically useful information while maximizing convenience to the patients by allowing flexibility in timing and not requiring travel to the clinic. The success of the study was also due in part to a motivated study team who devoted considerable time to closely monitor study progress and immediately resolve arising issues. The study was led by nurses and coordinators who were committed to study success and carved out adequate time in their schedules to devote to it. Study coordinators were expected to monitor substudy patient call compliance on a daily basis, which was crucial to the success of burdensome daily data collection. Lower retention rates were to be expected for a study requiring daily participation compared to quarterly data collection. However, both studies enrolled ahead of schedule. This was likely in part due to the fact that the study was led by nurses and coordinators, who are the ones who consent and enroll patients in practice.

Another key to the success of the study was the choice of a topic of high salience to thalassemia patients. Pain is a direct concern to many patients with thalassemia as it has a direct impact on daily life. Many patients were happy to participate in this study and hopeful that a study of this topic would benefit them. Although substudy participation required a commitment to daily participation, there were adequate numbers willing to do so. Recruitment of regularly transfused patients was quick, as these patients are seen in clinic on a regular basis. Thalassemia intermedia patients were difficult to enroll because they are seen less regularly than transfusion dependent patients (e.g. annually rather than monthly) and are more likely to receive the majority of their care outside of a thalassemia center. Differing recruitment strategies may be required to enroll adequate numbers of these patients, and future studies should give careful consideration to recruitment plans.

We also advise future studies to investigate and choose subcontractors carefully, when possible, and monitor them closely. The immigrant thalassemia population also requires closer consideration to overcome language barriers in survey administration. It is vital that patients understand the questions being asked in order to maximize data quality. Tracking for inconsistent data and recoding of this data before analysis benefited quality as well. Finally, a pain instrument that is validated in both adults and children would be ideal. However, with little pain reported in children (Trachtenberg et al., 2010), use of an adult instrument is less problematic.

Several of the issues addressed in this report are likely to be generic and applicable in studies of pain in many chronic diseases, particularly those related to language in immigrant populations, feasibility of telephone-based electronic data capture, and contracting issues. We conclude that a study of pain in thalassemia is feasible if the study team is motivated and continually monitors study progress and potential pitfalls. Use of electronic data collection for patient-reported outcomes was convenient for both patients and study personnel, but required human interactions beyond the automated system to maximize data quantity and quality.

Acknowledgments

This work was supported by the following NIH-NHLBI cooperative agreements: U01-HL65232 and NIH/NCRR UL1-RR-024134 to the Children's Hospital of Philadelphia, U01-HL72291 and by Harvard Catalyst CTSC U-01RR025758 to Children's Hospital, Boston, U01-HL65233 to University Health Network Toronto General Hospital, U01-HL65239 to Children's Hospital & Research Center Oakland, U01-HL65244 and CTSC UL1-RR024996 to Weill Medical College of Cornell University, and U01-HL65238 to New England Research Institutes. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the NHLBI.

The authors also wish to acknowledge the contributions of all the individuals with thalassemia who participated in this study, as well as Dr. Tito Mendoza at the MD Anderson Cancer Center for helpful suggestions.

Appendix 1

The following institutions and researchers contributed to the Thalassemia Clinical Research Network Assessment of Pain Study data reported in this paper.

Children's Hospital, Boston: Ellis Neufeld, MD, PhD, Jennifer Eile, MS, PNP, Research Nurse, Latoya Lashley, Study Coordinator; Satellites: Children's Healthcare of Atlanta, Leann Schilling, MPH, Study Coordinator, Principal Investigator; Baylor College of Medicine, Bogden Dino, Study Coordinator. Weill Medical College of Cornell University: Dorothy Kleinert, RN, Research Nurse, Patricia Giardina, MD; The Children's Hospital of Philadelphia: Alan Cohen, MD, Janet Kwiatkowski, MD, Marie Martin, RN, Research Nurse, Principal Investigator, Sage Green, Study Coordinator; Satellite: Children's Memorial Hospital, Chicago, IL: Alexis Thompson, MD, Janice Beatty, RN, Research Nurse, Diane Calamaras, RN, CPNP, Research Nurse, Pauline Hess, Study Coordinator. Children's Hospital at Oakland: Dru Haines, CPNP, Research Nurse, Principal Investigator, Olivia Oliveros, Study Coordinator, Elliott Vichinsky, MD; Satellites: Children's Hospital of Los Angeles, Thomas Coates, MD, Principal Investigator, Susan Carson, RN, Research Nurse, Principal Investigator, Ani Dongelyan, Study Coordinator, Tatiana Hernandez, Study Coordinator; Children's and Women's Health Center of British Columbia, Jennifer Kies, Study Coordinator. Toronto General Hospital, Toronto, Ontario, Canada: Nancy Oliveri, MD, Cecilia Kim, BS, Study Coordinator; Satellite: Hospital for Sick Children: Manuela Merelles-Pulcini, RN, Study Coordinator. NHLBI oversight, Kathryn Hassell, MD. Data Coordinating Center: New England Research Institutes, Sonja McKinlay, PhD, Principal Investigator, Lisa Virzi, RN, MS, MBA, Project Director, Felicia Trachtenberg, PhD, Senior Statistician, Eric Gerstenberger, MS, Statistician.

Acronyms

TCRN	Thalassemia Clinical Research Network
NIH	National Institutes of Health
NHLBI	National Heart, Lung, and Blood Institute
BPI	Brief Pain Inventory
APPT	Adolescent Pediatric Pain Tool

References

- CARR E, WORTH A. The use of the telephone interview for research. *Journal of research in Nursing*. 2001; 6:511–524.
- CLEELAND, C. The Brief Pain Inventory User Guide. 2008.
- CRANDALL M, SAVEDRA M. Multi-dimensional assessment testing using the APPT: a case report. *J. Spec Pediatr Nurs*. 2005; 10(3):115–23.
- DWORKIN RH, TURK DC, FARRAR JT, HAYTHORNTHTWAITE JA, JENSEN MP, KATZ NP, KERNS RD, STUCKI G, ALLEN RR, BELLAMY N, CARR DB, CHANDLER J, COWAN P, DIONNE R, GALER BS, HERTZ S, JADAD AR, KRAMER LD, MANNING DC, MARTIN S, MCCORMICK CG, MCDERMOTT MP, MCGRATH P, QUESSY S, RAPPAPORT BA, ROBBINS W, ROBINSON JP, ROTHMAN M, ROYAL MA, SIMON L, STAUFFER JW, STEIN W, TOLLETT J, WERNICKE J, WITTER J. Core outcome measures for chronic pain clinical trials: IMMPACT recommendations. *Pain*. 2005; 113:9–19. [PubMed: 15621359]
- GERSHON RC, ROTHROCK N, HANRAHAN R, BASS M, CELLA D. The use of PROMIS and assessment center to deliver patient-reported outcome measures in clinical research. *J Appl Meas*. 2010; 11:304–14. [PubMed: 20847477]
- TESLER M, SAVEDRA MT. The word graphic rating scale as a measure of children's and adolescent's pain intensity. *Resch in Nursing and Health*. 1991; 14(5):361–371.
- TRACHTENBERG F, FOOTE D, MARTIN M, CARSON S, COATES T, BEAMS O, VEGA O, MERELLES-PULCINI M, GIARDINA PJ, KLEINERT DA, KWIATKOWSKI J, THOMPSON AA, NEUFELD EJ, SCHILLING L, THAYALASUTHAN V, PAKBAZ Z, YAMASHITA R. Pain as an emergent issue in thalassemia. *Am J Hematol*. 2010; 85:367–70. [PubMed: 20232403]

Enrollment and Retention for the Thalassemia Clinical Research Network (TCRN) Assessment of Pain Study and Substudy.

Table 1

	Enrollment				Retention			
	Target	Consent Rate ^a	Eligibility Rate	Enrollment Rate ^b	Follow-up #1	Follow-up #2	Follow-up #3	Withdrawals ^c
Main Study	200–300	255/274 (93%)	254/255 (>99%)	252/254 (99%)	244/252 (97%)	234/252 (93%)	237/252 (94%)	11/252 (4%)
Telephone Substudy	25–35	NA ^a	39/53 (74%)	32/39 (82%)	27/32 (84%)	24/32 (75%)	NA	8/32 (25%)

^a Number consented out of those contacted. As the numbers approached for consent to the substudy were not recorded, no consent rate is available.

^b Number who completed the baseline visit out of those consented and found eligible.

^c includes 3 deaths on the main study and 1 death on the substudy.

Table 2
Call Completion Rates for the Thalassemia Clinical Research Network (TCRN) Assessment of Pain Substudy.

	Cycle 1		Cycle 2		Cycle 3	
	N	% days completed	N	% days completed	N	% days completed
All participants	32	78%	27	77%	24	76%
Age						
18-29	15	79%	14	75%	11	69%
30+	17	78%	13	80%	13	82%
Sex						
Male	14	74%	11	76%	10	70%
Female	18	81%	16	78%	14	80%
Length of cycle						
2 weeks	4	61%	3	88%	3	93%
>2 – 3 weeks	8	85%	8	92%	9	85%
>3 – 4 weeks	14	78%	7	73%	5	58%
>4 weeks	6	81%	9	64%	7	70%