

Developing Health Networks in Rare and Neglected Diseases: contributing to a clinical score for Niemann-Pick Disease, type C



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Abstract

The Center for Rare and Neglected Diseases at the University of Notre Dame created a class titled, "Topics in Developing Health Networks in Rare and Neglected Diseases". This class emerged as a result of meetings with NP-C families, the Ara Parseghian Medical Research Foundation, the National Niemann-Pick Disease Foundation, the Niemann-Pick Disease Group (UK), the Center for Social Concerns, and the Center for Rare and Neglected Diseases at the University of Notre Dame. Our goal was to establish whether Notre Dame students in class could assess medical records, contribute to the development of an NP-C score, and create a medical record summary to assist NP-C families when they consult with specialists. The class began with a discussion of critical concepts about rare and neglected diseases with emphasis on NP-C. Through these experiences we were able to learn about the personal and familial aspects of living with NP-C to becoming knowledgeable advocates for NP-C. Following IRB approval and HIPAA training, the students examined clinical records to assemble progressive disease scores based on symptoms associated with NP-C, as defined by a recent study from the NIH (Yanjanin et al., 2009). We were able to establish that graduate and upper level undergraduate students can be trained to follow clinical records, extract relevant disease indices, and thus combine *in-class* clinical research with service to the community. This will allow us to retrospectively mine clinical records from currently unused sources to expand the data and strengthen the emerging clinical score. The class was an active collaboration between Notre Dame students, faculty, clinicians, and nurse practitioners from the NIH. In addition, a trip to Riley Children's Hospital in Indianapolis, investigated possibilities of interacting with local centers for rare diseases through the Indiana Clinical Translational Science Institute (ICTSI).

Introduction

The Center for Rare and Neglected Diseases at the University of Notre Dame created a class, "Topics in Developing Health Networks in Rare and Neglected Diseases," with the purpose of contributing to an emerging clinical score for Niemann-Pick Disease, type C (NP-C). The ultimate goal was to score medical records of NP-C patients and incorporate these scores into an ongoing study at the NIH. Students also helped in creating a Medical Summary to return to the families when seeing new specialists. This was accomplished through collaboration with the Center for Social Concerns at Notre Dame, the National Institutes of Child Health Development (NICHD) and Riley Children's Hospital.

Creation of Class

We met with NP-C families to gather knowledge of the obstacles families must face with the regards to lack of official treatment, day-to-day modifications, and the ever changing needs of children with NP-C. Phone conferences were set up with the AraParseghian Medical Research Foundation, National Niemann-Pick Disease Foundation, the Center for Social Concerns, and Niemann-Pick Disease Group (UK). We concluded that as an initial approach, students should evaluate and score medical summaries provided by the NIH in order to expand the data and strengthen the emerging clinical score.

Class

Why are we doing this?

Class 1&2. Students were introduced to critical concepts and definitions in rare and neglected diseases. Specific emphasis was made on research funding, lack of drug development, and the stigma on researching rare and neglected diseases.

Class 3. Students presented on five separate NP-C narratives that were available via internet. They were exposed to how different families functioned with NP-C and gained knowledge of the disease itself.

Class 4. HIPAA training to ensure confidentiality of patients.

Introduction to the human clinical score.

Class 5. Read "Linear clinical progression, independent of age of onset in Niemann Pick Disease, type C" Yanjanin et al. This was done to introduce the developing clinical score to the students.

As a class we went through the dissection of the terminology, explained the study, analyzed the results, and reemphasized the overall big picture of why we were conducting the class.

Scoring.

Class 6. Received two medical records from the NIH. One was compiled by parents, the other was compiled by clinicians. Each student was assigned one admission summary from the medical history created by the clinician to score using the score from the manuscript. The students brought back scored data so we could compile a progression chart for this patient (Fig. 1).

Figure 1. Compilation of scores as a class

	11/30/87	5/15/88	11/13/95	11/17/97	10/6/99	5/12/03
Eye Movement	0	0	1	2	2	2
Speech	1	1	1	0	0	1
Fine Motor Skills	0	0	1	1	2	2
Hearing	0	0	0	0	0	0
Seizures	0	0	0	0	0	0
Ambulation	0	0	1	1	1	1
Swallow	2	2	1	0	2	3
Cognition	0	0	1	1	3	3
Memory	0	0	0	0	2	1
Modifiers	0	0	0	1	0	0
Total	3	4	5	6	12	13

Class Score

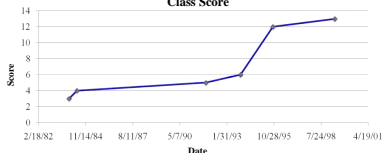


Figure 1. Compilation of the medical admission summaries scored by students on their first assignment. Each student was assigned an individual date.

Class 7. Each student was then assigned to score the whole record (Fig. 2). The students were initially uncomfortable with certain aspects of scoring such as the ambiguity of domains and how to score inconsistently recorded data. After compiling the graphs from each student, we realized all the graphs had the same trends and similar results.

Figure 2. Individual Student's Plot

Dannv	11/30/87	5/15/88	11/13/95	11/17/97	10/6/99	5/12/03
Eye Movement	1	1	1	2	1	3
Speech					1	2
Fine Motor Skills			1	1	2	2
Hearing						
Seizures			1	1	2	3
Ambulation			1	1	2	3
Swallow	1	1	2	1	3	3
Cognition				1	3	3
Memory					2	1
Modifiers						
Total	2	3	6	4	13	17

Danny's Clinical Assessment

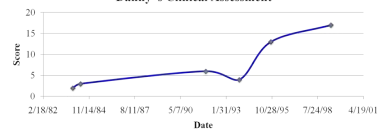


Figure 2. An example of a plot compiled by a student in this class. The student scored all admission dates and compiled a plot with all points.

Class 8. Dr. Forbes Denny Porter from the NIH visited class and spoke about the human clinical score he created. Students shared their plots with Dr. Porter. Discussed and resolved issues that came up with students when scoring. Students also shared results and concluded that it was a robust scoring process. Dr. Porter explained the principle of "carry-over" through clinical visits. Students were assigned to revise the score taking into account the advice provided by Dr. Porter (Fig. 3).

Figure 3. Revised Individual Student's plot

	11/30/87	5/15/88	11/13/95	11/17/97	10/6/99	5/12/03	8/14/06
Eye Movement			1	2	2	3	4
Speech	1	1	1	0	0	1	2
Fine Motor Skills			1	1	2	2	4
Hearing			1				3
Seizures				1	2	3	4
Ambulation			1	1	2	3	5
Swallow	1	1	2	2	2	3	4
Cognition				1	3	3	4
Memory					2	2	2
Modifiers							7
Total	2	3	6	7	14	17	35

Danny's Final Graph

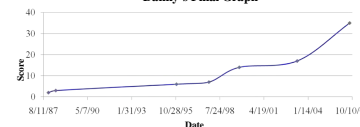


Figure 3. An example of a student's graph that has been modified according to Dr. Porter's suggestions.

Class 9. Nicole Yanjanin, BSN, who works with Dr. Porter scoring NPC children at the NIH, visited. Students shared their scores and medical summaries with Nicole. Students scored a separate set of records of a patient with Nicole to confirm our consistency with scoring. Nicole also offered advice for the class and provided the students with the "NPC Patient Information Sheet and Problem List," which can be used as a cover page for the medical summaries. Students were assigned to complete the cover page, create a medical summary, and make any final revisions to plots.

Class 10. Students presented to class their individual medical summary, cover page, and final plots.

Class 11. Class went to Riley Children's Hospital, IN. Students met with a hepatologist, endocrinologist, and geneticists that have diagnosed children with NP-C. Discussed the process that patients have to go through to reach the final diagnosis of NP-C. Students were given tour of the hospital, and lastly, students met with physician in charge of pediatric research at Riley.

Results

Figure 4. Compilation of All Students' Plots



Figure 4. Compilation of students' final graphs. All the students plot show the same trend.

Figure 5. Linear Regression Points scored by Class

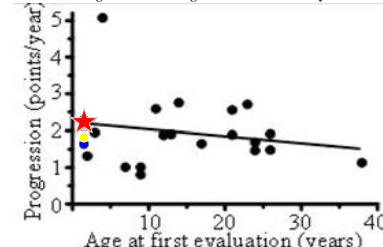


Figure 5. Linear regression points of each student's plots (colored points) and the class mean (colored study face) overlaid on linear regression presented as Fig. 1D by Yanjanin et al., 2009 (black).

Figure 6. Severity Progression Plot of Patient Scored by Class

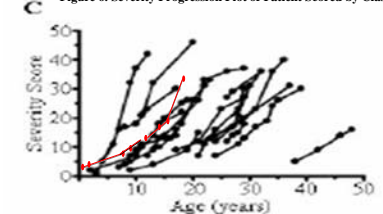


Figure 6. The severity progression plot of the patient record the student's score (red) overlaid on linear regression presented as Fig. 1C by Yanjanin et al., 2009 (black).

Discussion

The students were able to review and assess clinical records once they learned the requisite medical terminology. One of the issues students ran into while creating these plots were the limited data and medical history that was provided. The students were initially uncomfortable with certain aspects of scoring such as the ambiguity of domains and how to score inconsistently recorded data.

After students independently graphed the plots, they realized that there was little ambiguity of domains and concluded that the scoring was robust. Furthermore, for the inconsistently recorded data, advice from Dr. Porter and Nicole helped refine the plots to make all data points consistent. It was also a learning experience to realize the reality of the difficulty scoring patients with limited data that was provided.

The students' plots fell consistently with the original figures from Dr. Porter's manuscript. In figure 5, all the linear regression points of the students fall between 1.8 and 2.3, well within the predicted area of Dr. Porter's progression graph. The class mean was a 2.1. When the patient's score was plotted on the progression chart, Figure 6, the points all fall consistently with the same trend as the rest of the other patients Dr. Porter included on the graph.

Future

This pilot course was very successful in all that it hoped to achieve for this semester. We hope to continue this course next year with a larger number of students as well as receiving more medical records to score.

Acknowledgements

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