



Staking Your Claim Through Educational Research

February 15, 2008

Sara K. Vesely, Ph.D., Presbyterian Health Foundation Presidential
Associate Professor

*As a courtesy to our speaker,
please turn all cell phones to silent or vibrate. Thank You!*

**Staking your Claim in
Educational Research**

Sara K. Vesely

Objectives

- **Principles of patient-oriented research**
 - How to make sure your data is analyzable
- **How to involve students in your research**
 - Teaching students to be researchers

Oklahoma TTP-HUS Registry

- **A platform for illustrating the principles of clinical research**
- **A resource for students/trainees**
 - Do you have a resource too?

- **Johnson KK, Terrell DR, Vesely SK, George JN. 'The Oklahoma Thrombotic Thrombocytopenic Purpura – Hemolytic Uremic Syndrome Registry: A Resource for Medical Education' J Okla State Med Assoc, 2007;100:309-314**

Clinician - Biostatistician

- **Clinician: diagnose and treat patients**
- **Clinician-scientist: define and solve clinical problems**
- **Biostatistician: ensure quantitative and reproducible data**
- **Clinician-scientist + biostatistician: create a study design that will answer the clinical question**

Principles

- Patient selection
- Generalizability of data
- Prospective and uniform data collection
- Reproducible definitions
- Complete patient follow-up
- Collaboration across disciplines

Thrombotic Thrombocytopenic Purpura – Hemolytic Uremic Syndrome (TTP-HUS)

- A rare hematological disorder characterized by a low platelet count and microangiopathic hemolytic anemia with no other known cause.
- There is no gold standard for diagnosis.
- The only curative therapy is plasma exchange therapy.

ADAMTS13 Deficiency in TTP and HUS

- **Assay of ADAMTS13**
 - Detailed methodology
- **Patient selection**
 - No methodology

Principle 1

- **Inception cohort of consecutive unselected patients**
- **Uniform inclusion and exclusion criteria**

The Oklahoma TTP-HUS Registry

- **The OBI is the sole provider for plasma exchange (PE) services in our region**
- **Therefore, we identify and enroll all patients for whom PE is requested for a clinical diagnosis of TTP or HUS**

- **All consecutive patients within a defined geographic area are identified at a uniform time early in the course of their illness.**

Problem 1

- **Initial vs recurrent episode**
- **Clinical vs renal biopsy diagnosis**

Solution 1

- **First episode of clinically diagnosed TTP-HUS**

Principle 2

- **Generalizable to community practice while retaining uniform inclusion and exclusion criteria**

Problem 2

- **Variety of patient referrals**
- **Death prior to beginning PE**

Solution 2

- **The defining criterion for inclusion is the order for the OBI to begin PE for TTP and/or HUS**

Principle 3

- **Prospective, uniform data collection**

Problem 3

- **Narrative summaries and patient records**
 - designed for patient care
 - for research data, patient records are typically incomplete
 - therefore retrospective studies are never as reliable as prospective data collection

Solution 3

- **Data collection forms**
 - Developed specifically for the research question
 - May evolve during the course of the project
 - Systematic follow-up
- **Data are entered into Microsoft Access®**

Principle 4

- **Quantitative reproducible definitions for patient clinical features and outcomes**

Problem 4

- **Diverse clinical categories**
- **TTP vs HUS**
- **No standardized definitions for response, exacerbation, and relapse**

Solution 4

- **Establishment of *a priori*, consensus definitions**
- **Consistent application of these definitions to all patients**

Solution 4

- **Clinical categories**
 - **Stem cell transplantation**
 - **Pregnancy/postpartum**
 - **Drug-associated**
 - **Prodrome of bloody diarrhea**
 - **Additional/Alternative disorder**
 - **Idiopathic**

Solution 4

- **Definition of TTP vs HUS**

Acute renal failure:

- [1] an increasing serum creatinine (≥ 0.5 mg/dL per day for 2 consecutive days)
or
- [2] a serum creatinine ≥ 4.0 mg/dL plus dialysis that began within 7 days of diagnosis.

Principle 5

- **Patient follow-up is complete, to ensure identification of rare events.**

Solution 5

- **Patients and their primary care physicians are contacted by phone or mail every 6 months. Follow-up is complete for 99% of patients.**

Principle 6

- **Investigators collaborate across disciplines.**

Solution 6

- The Registry is a joint effort of the Colleges of Medicine and Public Health at the University of Oklahoma Health Sciences Center and the Oklahoma Blood Institute.

Contributions of a Biostatistician

- Refine initial idea
- Develop plan
- Create definitions
- Determine endpoints
- Design data collection form and database
- Ensure adherence to rules
- *Last and least: Analyze data*

Involving students in your research

- **Student learning objectives**
- **Types of student research projects**

Student Learning Objectives

- **Patient evaluation**
 - **interview skills**
 - **systematic data collection**
 - **data entry and summarization using Microsoft Excel® and Access®**
 - **patient confidentiality**

Student Learning Objectives

- **Regulatory issues**
 - **ethical considerations for patient-oriented research**
 - **protocol and consent form development**
 - **Institutional Review Board requirements**

Student Learning Objectives

- **Literature assessment**
 - **search strategies**
 - **systematic review methodology**

Student Learning Objectives

- **Presentations and publication**
 - **abstract and manuscript preparation**
 - **powerpoint and poster presentations**

Student Learning Objectives

- **Career development**
 - **integration of research principles into clinical and research careers**

Students working with the Oklahoma TTP-HUS Registry

- **4 undergraduate students**
- **6 masters level students**
- **2 PhD students**
- **2 PharmD students**
- **5 MD students**
- **3 MD residents**
- **3 MD Heme-Onc Fellows**

Students working with the Oklahoma TTP-HUS Registry

- **17 abstracts (15 first author)
presented at national or international
meetings**
- **24 publications (17 first author)**

Examples Projects

- Platelet loss during apheresis
- Patient support group
- Disseminated malignancy mistaken for TTP-HUS
- TTP and systemic lupus erythematosus (SLE)
- Cognitive studies
- Patient stories

Platelet Loss during Apheresis

- Prospective study looking at the platelet count before and after plasma exchange for several different disorders using different apheresis machines

Patient Support Group

- **Patient meetings occur 3 times a year over more than 10 years**
- **Experience summarized**

Disseminated malignancy mistaken for TTP-HUS

- **Case report of 1 patient (heme-onc fellow)**
- **Article summarizing all 10 patients in the Registry with a systematic review of all patients in the literature (heme-onc fellow and masters student)**

TTP and systemic lupus erythematosus (SLE)

- **Compared our patients who have concurrent lupus with those who had idiopathic TTP**

Cognitive Studies

- **Summer 2006 medical student and fellow administered cognitive test to about 35 patients that have recovered from TTP-HUS**

Patient Stories

<http://w3.ouhsc.edu/platelets/index.html>

Website that contains information for patients about TTP-HUS and ITP

Contains TTP-HUS and ITP patient stories – students interviewed the patients and wrote their stories

Mentoring Students in Research

- You have information to share
- No project is too small
- Good students can give as much to a project as you can give to them