Making an Impact

As clinicians, we ask, "How can we make a positive impact?" We take pride in having generated and published new outcomes data answering important questions about new therapies in routine care in areas such as **hematology, immunology, neurology, and oncology**. The following is one among a considerable number of examples:

Primary Immune Deficiency Diseases (PIDD)

Affecting approximately 1 in 300-500 people, PIDDs are typically genetic disorders impacting the immune system. Over a five-year period, Churchill designed and implemented a series of patient, caregiver, and provider initiatives focusing on best practices for treatment of PIDD, with immune globulin replacement therapies.

From Bench...

- Publication of pharmacokinetic data, pivotal trial results, and subset analyses
- Initiatives to educate providers about dose conversion for new formulations

to Bedside...

- Training programs for self-administration of subcutaneous therapy
- Case report series on the management of challenging patients

to Better Outcomes

- Retrospective chart reviews and surveys to evaluate therapeutic preferences, clinical outcomes, and best practices
- Identification of dosing and administration factors that impact treatment costs and quality of life

This is just one of a good number of rare diseases where Churchill has demonstrated expertise.

Churchill
COMMUNICATIONS
OUTCOMES RESEARCH

Rare Disease Programs
From Bench...
to Bedside...
to Better Outcomes[SM]

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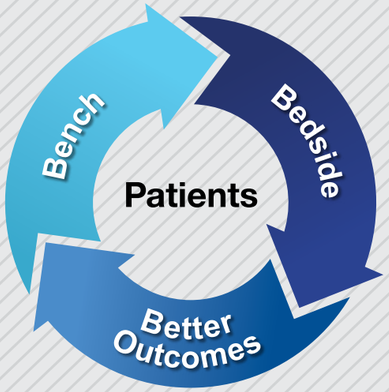


Churchill and Rare Diseases

Challenges of Rare Diseases

Management of chronic, lifelong rare diseases is often fragmented, expensive, and stressful. Patients and caregivers find themselves with a host of unmet medical needs. To address those needs, new therapies for rare diseases must continually evolve:

- Often misdiagnosed
- High rates of comorbidities
- Complex pathology and costly treatments
- Underpowered clinical trials requiring long-term surveillance
- Passionate, highly-specialized, and team-oriented providers
- Diverse stakeholders with very specific information needs
- Influential advocacy groups

From Bench to Bedside to Better Outcomes

As patients with rare diseases face a lifetime of adapting to challenges, new therapeutic interventions should be appropriately attuned to patient needs. Churchill's lifecycle approach – ***from bench to bedside to better outcomes*** – includes comprehensive, multidisciplinary programs designed to translate bench science into bedside clinical practice, while aligning therapeutic advances with patient needs to improve long-term outcomes.

Churchill and Rare Diseases

Churchill was founded in 1989 by practicing clinicians needing information about the impact of new therapies on patients often excluded from randomized controlled trials. Churchill designs comprehensive communications, education, advocacy, and outcomes programs incorporating the perspectives of providers, patients, and caregivers. Our multidisciplinary account teams apply a clinical practice model that includes physicians, pharmacists, PAs, nurses, and other healthcare professionals with experience managing patients with rare diseases.

From Bench…

Publications

The complicated pathology, chronicity, comprehensive care, and stakeholder diversity associated with rare diseases adds layers of complexity to a publications plan. Churchill combines more than 20 years of publications experience with the analytical skills and hands-on clinical practice experience necessary to assure that clinical information needs are met across a diverse audience of providers, patients and caregivers:

Planning

- Global, local, and population-specific publication planning
- Therapeutic gap analyses and publication assessments
- Coordination of publication team activities

Content

- Abstracts, posters, manuscripts, and lecture material development
- Investigator briefs, clinical study reports, presentations, and product monographs
- Patient and caregiver educational materials

Compliance

- Expertise with corporate integrity agreements (CIAs) and their impact on sponsored medical publications
- Certified Medical Publication Professionals (CMPP)
- Preparation of good publication practice (GPP) policies

…to Bedside…

Education

Rare disease stakeholders are a diverse group, each having very specific educational needs. Churchill's clinician-educators possess expertise in translating bench science into practical, useful information effective in improving patient outcomes. Every program is evidence-based, measurable, and designed to answer questions about rare diseases and the role of new therapies:

- Structured feedback advisory boards
- Continuing education programs
- Clinical symposia
- Patient-oriented therapeutic administration training programs
- Print and web-based training programs

Advocacy

Rare disease advocacy groups are vibrant, influential communities of providers, patients, and caregivers. Offering information, support, and a shared voice, these groups can facilitate access to difficult-to-reach patient populations. Churchill partners with advocacy groups to enhance patient recruitment, collaborate on educational initiatives, and develop best practice guidelines.

- Disease management programs
- Web-based patient communities
- Patient recruitment
- Best practice surveys and guidelines
- Patient registries
- Collaborative educational initiatives
- Scholarship programs

…to Better Outcomes

Outcomes Research

Randomized controlled trials (RCTs) for rare diseases are often underpowered and brief in duration, leaving many important clinical questions unanswered. Churchill's real-world outcomes research protocols are designed to complement RCTs and improve patient outcomes. Our protocols strategically assess quality of life, validate best practice guidelines, and evaluate the routine use of newer therapeutic interventions over longer timeframes in larger populations of patients with rare diseases.

Studies

- Disease and product registries
- Quality of life assessments
- Patient reported outcomes
- Clinical practice surveys
- Electronic medical records reviews
- Claims and epidemiology database studies
- Meta-analyses and systematic literature reviews

Statistics

- Sample size determination
- Data validation
- SAS and SPSS programming
- Interim and final analyses

Support

- Investigator initiated study project management
- Survey design and validation
- IRB documentation and submission
- Site evaluation, training, and monitoring
- Database development and management
- Data collection and data entry
- Posting on www.clinicaltrials.gov

How Do Churchill's Outcomes Research and Publication Programs Improve the Lives of Patients?

Here is one example:

Primary Immune Deficiency Disease

Introduction:

Churchill's challenge was to determine patient preference for subcutaneous immune globulin (SCIG) push vs. administration by pump for primary immune deficiency disease (PIDD), a rare disease that impacts only 1 of every 1,200 Americans.

Methods:

Churchill employed a retrospective chart review of 174 patients, with a total of 1,140 office visits, to evaluate therapeutic preferences, clinical outcomes, and best practices. We identified specific dosing and administration factors that impacted compliance and quality of life.

Results:

In addition to identifying patient preference for SCIG push in the general PIDD population, Churchill identified two other previously unpublished results: dosing strategies for patients with BMIs greater than 30, and the lifecycle administration of SCIG in pediatric patients from infancy through adolescence.

Discussion:

For the first time, clinicians had some real-world evidence for dosing obese patients who often had difficulty administering immune globulin intravenously. Equally important was identifying the lifecycle of immune globulin therapy in younger patients; from SCIG push in infancy, to pump administration as toddlers and grade schoolers, back to push as adolescents. These important findings helped clinicians and patients to tailor strategies specific to these populations.

Shapiro RS. Subcutaneous immunoglobulin therapy given by subcutaneous rapid push vs infusion pump: a retrospective analysis. *Ann Allergy Asthma Immunol.* 2013;111(1):51-5.

Shaprio RS. Subcutaneous Immunoglobulin: rapid push vs. infusion pump in pediatrics. *Pediatr Allergy Immunol.* 2013;24(1):49-53.

Shapiro R. Subcutaneous immunoglobulin (16 or 20%) therapy in obese patients with primary immunodeficiency: a retrospective analysis of administration by infusion pump or subcutaneous rapid push. *Clin Exp Immunol.* 2013;173(2):365-71.

How Do Churchill's Outcomes Research and Publication Programs Improve the Lives of Patients?

Here is one example:

Ventilator Associated Pneumonia

Introduction:

Churchill's challenge was to identify factors impacting the outcomes of ICU patients diagnosed with ventilator associated pneumonia (VAP). While the American Thoracic Society and the Infectious Disease Society of America (ATS-IDSA) established clear guidelines for VAP, many suspected that the guidelines were not being implemented, resulting in higher morbidity and mortality among these seriously ill patients.

Methods:

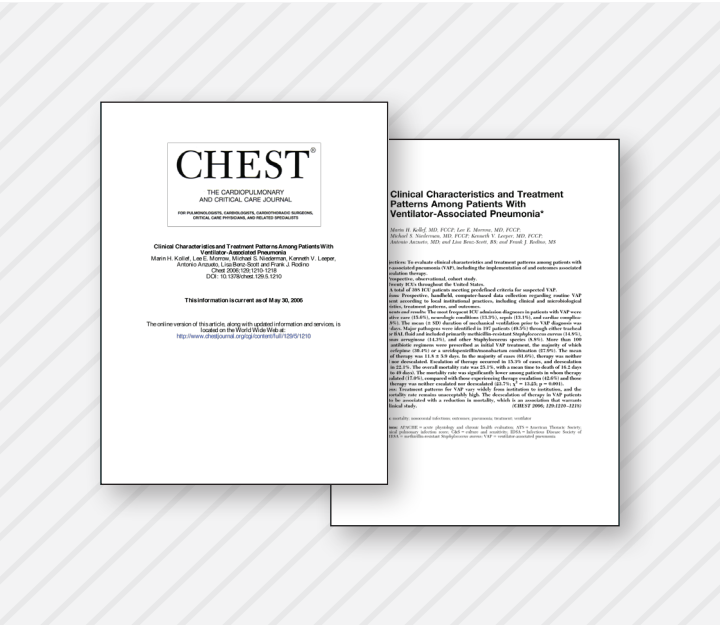
To address this challenge, Churchill designed and implemented an observational, non-interventional study entitled Assessment of Local Antimicrobial Resistance Measures (ALARM). Employing personal digital assistants, real time data was collected on 398 VAP patients in 19 hospitals across the US. Custom software was developed to allow critical care specialists to rapidly record information needed to calculate vital signs, APACHE 2 critical illness scores, and clinical pulmonary infection scores (CPIS). These scores, as well as sputum culture and sensitivities were recorded upon admission and after 72 hours.

Results:

The ALARM study proved the hypothesis that guidelines were not being followed as frequently as hoped. But two other unexpected predictors of outcomes were uncovered. Decreases in CPIS oxygenation levels over 72 hours, and choice of narrow vs. broad-spectrum antimicrobial agents upon admission had a significant impact on patient mortality.

Discussion:

This study established the importance of following ATS-IDSA guidelines for VAP. In addition, the study identified both decreasing oxygenation levels, and antimicrobial escalation as predictors of morbidity and mortality in VAP. The primary manuscript, published in *CHEST,* has been cited more than 125 times in 4 languages and the results have become part of a revised set of guidelines for the treatment of VAP.



Kollef MH, Morrow LE, Niederman MS, Leeper KV, Anzueto A, Benz-Scott L, Rodino FJ. Clinical characteristics and treatment patterns among patients with ventilator-associated pneumonia. *Chest.* 2006;129(5):1210-8.