Significant Publications


The objective of this study was to use quality improvement science methodology to develop a multidisciplinary intervention improving occurrence of best-practice airway clearance therapy (ACT) in inpatient adolescents with cystic fibrosis during routine clinical care. The model for improvement was used to develop and implement interventions. Primary outcomes were quality of ACT (% ACT meeting criteria for best practice) and quantity of ACT (% of hospital days patients received ACT four times/day). Annotated control charts were used to document the
impact of the interventions. Results Quality of ACT significantly improved from 21% best practice ACT at baseline to 73%. Quantity of ACT significantly improved from 41% days with ACT four times/day at baseline to 64%. A multidisciplinary, evidence-based intervention was effective for improving occurrence of best-practice ACT.


While it is well-known which groups of children are more vulnerable to poor health care access, quality, and outcomes, less is known about how and why this occurs. Barriers to care - sociobehavioral processes that interfere with successful interaction with the healthcare system - may be a link between vulnerability and access, experiences, and outcomes. The objective of this study was to examine the reliability, validity and responsiveness to change of the Barriers to Care Questionnaire (BCQ) in a sample of children with persistent asthma recruited from Federally-Qualified Health Centers (FQHCs). To do this, we analyzed data from children (n = 252; ages 2-14 years) with persistent asthma and their parents (93.7% mother, 83.3% Hispanic, 76.9% Spanish-speaking; 72.6% less than a high school diploma), enrolled in a clinical trial. Parents completed the BCQ, questions relating to access to care, the Parent’s Perceptions of Primary Care Measure, and the PedsQL™ 4.0 at baseline and 3-months. The BCQ was internally consistent. Barriers to care were worse for children without health insurance or an identified provider, and who had problems with care or foregone care. Higher barriers correlated with poorer primary care and lower patient health-related quality of life (HRQOL). The BCQ was responsive to change, showing within and between subject differences for subjects with improved Realized Access from baseline to 3 months. We concluded that the BCQ is a reliable, valid and responsive measure of barriers to care for vulnerable children with asthma. Barriers to care were associated with poorer access, lower primary care quality, and worse health-related quality of life.


Maternal cigarette smoking is the major risk factor for Sudden Infant Death Syndrome (SIDS). The underlying mechanism is currently unknown. Infants who succumbed to SIDS have evidence of apoptosis of neurons and glial cells in respiratory control areas of the brainstem which may result in modulation of hypoxic and arousal responses in SIDS victims. Our previous study has showed that prenatal nicotine exposure results in modulation of hypoxic ventilatory depression, a specific component of biphasic hypoxic ventilatory response for which activation of PDGF-β receptor (PDGFR) and downstream anti-apoptotic pathway occur in neurons of the caudal brainstem. In this study, we have demonstrated that prenatal nicotine exposure is associated with modulation of PDGFR phosphorylation and subsequent attenuation of the anti-apoptotic cascade through the Akt/BAD pathway in the caudal brainstem of developing animals. This modulation of anti-apoptotic mechanisms leads to hypoxic vulnerability of neural cells as shown by an increase in the early apoptotic marker. The effect of prenatal nicotine exposure on anti-apoptotic processes in developing animals may be the pathophysiological mechanism underlying the increased risk of SIDS in infants born to smoking mother.


This manuscript demonstrates the usefulness of serum VEGF-D in diagnosing Lymphangioleiomyomatosis (LAM). The investigators found that serum VEGF-D levels are elevated in most women with LAM, but not in women with other lung diseases or healthy individuals. For women with cystic lung disease or Tuberous Sclerosis Complex, this study establishes serum VEGF-D as a biomarker and diagnostic test which can eliminate the need for surgical lung biopsy in many patients with LAM.


Division Highlights

Michael Seid, Ph.D.

Michael Seid, Ph.D. (Psychology, University of Illinois, Urbana-Champaign, 1995) is a Professor of Pediatrics and Director of Health Outcomes and Quality of Care Research in the Division of Pulmonary Medicine and Core Faculty in the Center for Health Care Quality in the Division of Health Policy and Clinical Effectiveness at Cincinnati Children’s Hospital Medical Center (CCHMC). Prior to CCHMC, he was a behavioral/social scientist at the RAND Corporation and before that, Associate Director for Research at the Center for Child Health Outcomes at Children’s Hospital, San Francisco.
Diego.

Dr. Seid’s research focuses on using behavioral and social science to improve care and outcomes for children with chronic health conditions. He has been Principal Investigator of numerous federally-funded grants, including grants to measure quality of care for vulnerable children (R01 HS10317), to reduce barriers to care for vulnerable children with asthma (R40 MC 001214/08044), to determine predictors of health-related quality of life for children with juvenile idiopathic arthritis (R01 subcomponent of P60 AR047784-06A2, Glass PI) and to develop and test a cell-phone based adherence intervention for adolescents with asthma (R21HL089524) and Type 1 diabetes (R21DK085483). Dr. Seid is the Research Center Director of CCHMC’s AHRQ-funded Center for Education and Research in Therapeutics (CERT; U18HS016957, Lannon PI) and Co-PI for a Transformative R01 (R01DK085719), “Open Source Science: Transforming Chronic Illness Care.”

He has published widely in such journals as Medical Care, HSR: Health Services Research, Archives of Pediatrics and Adolescent Medicine, Pediatrics, The Journal of Pediatrics, American Journal of Public Health, the Journal of Academic Pediatrics, Health Affairs, and Milbank Quarterly.

William Hardie, M.D.

Pulmonary fibrosis is a major aberrant component of a number of clinically significant disorders. In many of these diseases pulmonary fibrosis is progressive, leading to significant morbidity and mortality. Currently there are no medical treatments approved for pulmonary fibrosis underscoring the need to discover novel targets. The major goal of our lab is to identify signaling pathways mediating pulmonary fibrosis and to determine the effectiveness of pharmacological inhibitors currently in oncology trials which target these pathways. Our laboratory has generated a transgenic model of conditional transforming growth factor-alpha signaling through the epidermal growth factor receptor (EGFR) in the lung epithelium, which causes pulmonary fibrosis with many of the features seen in patients, including progressive collagen deposition, cachexia, lung restriction and secondary pulmonary hypertension. Recent studies from our laboratory have identified critical roles for PI3K/Akt, MAPK/Erk and mTORC1 signaling pathways mediating pulmonary fibrosis downstream of EGFR activation. Moreover, some of these signaling pathways have recently been identified in other models of fibrosis including transforming growth factor-beta and platelet derived growth factor. Therefore, data from our laboratory may modify fibrosis from a number of upstream molecular causes. In addition to testing the efficacy of pathway inhibitors in our pre-clinical models, the laboratory is also testing biomarkers of these pathways in mouse models of fibrosis and in human lung biopsy samples of patients with pulmonary fibrosis.

Raouf Amin, M.D.

**Division Collaboration**

**Collaboration with Pediatric Otolaryngology/Head and Neck Surgery ; Pediatric Surgery; Gastroenterology, Hepatology and Nutrition; Interdisciplinary Feeding Clinic**

Collaborating Faculty: Richard Azizkhan, MD; Robin Cotton, MD; Alessandro de Alarcon, MD; Victor Garcia, MD; Thomas Inge, MD; Ajay Kaul, MD; Charles Myer III, MD; Philip Putnam, MD; Michael Rutter, MD; Sally Shott, MD; J Paul Willging, MD

Aerodigestive and Sleep Center - Treatment of chronically ill children with complex airway, pulmonary, upper digestive tract, sleep and feeding disorders.

**Collaboration with Anesthesia; Cardiology; Endocrinology; Developmental and Behavioral Pediatrics; Gastroenterology, Hepatology and Nutrition; Genetic Counseling; International Health; Neurology; Nutrition Therapy; Orthopaedics; Palliative Care; Pediatric Surgery; Physical Therapy; Rehabilitative Medicine; Social Work**

Collaborating Faculty: Rebecca Brown, MD; Jim Collins, MD; Linda Cripe, MD; Thomas Inge, MD; Viral Jain, MD; Ajay Kaul, MD; Mary McMahon, MD; Mark Meyer, MD; Susan Rose, MD; Meilan Rutter, MD; Irena Rybalsky, MD; David Schonfeld, MD; Robert Spicer, MD; Jeffrey Towbin, MD; Martha Walker, MS; Norbert Weidner, MD; Brenda Wong, MD

Comprehensive Neuromuscular Center. Treatment of children with neuromuscular disorders.

**Collaboration with Allergy and Immunology; General Pediatrics**

Collaborating Faculty: Amal Assa‘ad, MD; Gurjit Hershey, MD; Maria Britto, MD; Thomas DeWitt, MD; Keith Mandel, MD; Mona Mansour, MD; Marc Rothenberg, MD; Jeffrey Simmons, MD

Asthma Center - Treatment of children and adolescents with asthma; development of an asthma repository

**Collaboration with Molecular Immunology; Pulmonary Biology**

Collaborating Faculty: Julio Aliberti, PhD; Christopher Karp, MD; Bruce Trapnell, MD; Jeff Whitsett, MD

Cystic Fibrosis Research
Collaboration with Pulmonary Biology
Collaborating Faculty: Thomas Korfhagen, MD; Jeffrey Whitsett, MD
Pulmonary Fibrosis Research

Collaboration with Pulmonary Biology; Radiology; Orthopaedics; University of Cincinnati
Collaborating Faculty: Alan Brody, MD; Alvin Crawford, MD; Gail Deutsch, MD; Thomas Inge, MD; Bruce Trapnell, MD
Diagnosis and management of children with rare lung diseases, including interstitial lung disease, surfactant mutations, lung development disorders, lymphatic disorders and chronic lung diseases associated with immunodeficiency/immune dysfunction, rheumatologic disorders and other systemic disorders.

Collaboration with Cardiology; Endocrinology; Neurology; Otolaryngology; Pediatric Surgery; Psychology; Radiology
Collaborating Faculty: Dean Beebe, PhD; Alan Brody, MD; Robin Cotton, MD; Larry Dolan, MD; Lane Donnelly, MD; Chuck Dumoulin, MD; Robert Fleck, MD; Thomas Inge, MD; Thomas Kimball, MD; Timothy Knilans, MD; Sally Shott, MD; Janaka Wasapura, MD; J. Paul Willging, MD
Sleep Research: Cardiovascular morbidity secondary to obstructive sleep apnea in children and the neurocognitive outcome of the disease.

Collaboration with Audiology; Human Genetics; Neursurgery; Otolaryngology; Pediatric Dentistry; Orthodontics; Plastic Surgery; Psychology; Speech Pathology
Collaborating Faculty: David Billmire, MD; Richard Campbell, MD; Kerry Crone, MD; Christopher Gordon, MD; William Greenhill, DMD; Ann Kummer, PhD; Francesco Mangano, DO; Janet Middendorf, MA; Cynthia Prows, MSN; Gayle Riemer, MD; Howard Saal, MD; Iris Sageser, RDH; J Paul Willging, MD
Craniofacial Team
Collaboration with Orthopaedics
Collaborating Faculty: Alvin Crawford, MD; Viral Jain, MD; Gary McPhail, MD; Eric Wall, MD
Spine Center

Faculty Members

Raouf Amin, MD, Professor; Director, Division of Pulmonary Medicine
Research Interests: Cardiovascular morbidity of sleep apnea in children

James Acton, MD, Assistant Professor; Director, Cystic Fibrosis Center
Research Interests: Cystic Fibrosis (CF), quality improvement, clinical outcomes and pulmonary function testing in infants

Thomas Boat, MD, Professor; Executive Associate Dean, University of Cincinnati College of Medicine

R. Paul Boesch, DO, Assistant Professor Clinical; Director, Transitional Care Center

Ronald Bokulic, DO, Associate Professor Clinical

Barbara Chini, MD, Associate Professor Clinical; Director, Pulmonary Fellowship Program
Research Interests: Sleep Disordered Breathing, Outcomes Research, Self-Management of Chronic diseases

William Hardie, MD, Associate Professor Clinical; Director, Pulmonary Function Laboratory
Research Interests: Molecular mechanism of pulmonary fibrosis, pediatric pulmonary function tests, pediatric pneumonia complications

Patricia Joseph, MD, Associate Professor
Research Interests: Cystic fibrosis infections and quality improvement

Carolyn Kercsmar, MD, Professor; Director, Asthma Center; C-Director Pulmonary Medicine
Research Interests: Asthma, inner city asthma, clinical outcomes and clinical trials, airway inflammation

Karen McDowell, MD, Associate Professor
Research Interests: Asthma self management, utilization of technology for chronic disease management, bronchoscopy and wheezing/asthma, health care effectiveness, outcomes.

Gary McPhail, MD, Assistant Professor; Associate Director, Fellowship Training Program
Research Interests: Cystic fibrosis, quality improvement, clinical outcomes, pulmonary vascular disease

Michael Seid, PhD, Professor; Director, Health Care Quality and Outcomes Research
Research Interests: Health outcomes for children with chronic health conditions, interventions to overcome barriers to care and adherence, clinical behavior and effects on self-management, quality improvement research

Abu Shamsuzzaman, MD, Research Assistant Professor
Research Interests: Sleep and Cardiovascular Diseases

Narong Simakajornboon, MD, Associate Professor; Director, Sleep Disorders Center; Program Director, Sleep Medicine Fellowship
Research Interests: Sleep-disordered breathing in children, sleep apnea, restless legs syndrome, periodic limb
Robert Wood, PhD, MD, Professor; Director, Pulmonary Bronchology Program
Research Interests: Airway abnormalities; pulmonary alveolar proteinosis

Jamie Wooldridge, MD, Assistant Professor
Research Interests: Metabolic and nutritional outcomes in patients with Cystic Fibrosis

Lisa Young, MD, Assistant Professor; Director, Pediatric Rare Lung Diseases Clinical Program
Research Interests: Interstitial lung diseases, rare lung diseases, lymphangioleiomyomatosis

Joint Appointment Faculty Members

Julio Aliberti, PhD, Assistant Professor
Molecular Immunology

Kelly Byars, PsyD, Assistant Professor
Psychology
Current research focuses on improving the assessment and treatment of pediatric insomnia and pediatric obstructive sleep apnea

Daniel Grossoehme, DMin, BCC, Research Assistant Professor
Pastoral Care
Religion/spirituality, adherence, coping, cystic fibrosis

Christopher Karp, MD, Professor
Molecular Immunology
Molecular mechanisms, underlying regulation and dysregulation of inflammatory responses in infectious, allergic, autoimmune, metabolic and genetic diseases

Bruce Trapnell, MD, Professor
Neonatology and Pulmonary Biology

Rhonda VanDyke, PhD, Assistant Professor
Biostatistics & Epidemiology
Current areas of interest are Mixture Models and Functional Data Analysis with focus on Bayesian statistics, primarily using Markov Chain Monte Carlo. Content-specific areas include integration of fMRI and MEG modalities; developing statistical models to assess impact of OSA; CF outcomes research

Clinical Staff Members

- Denetra Bamonte,
- Sallie Bauer,
- Diana Betancur,
- Walter Blower,
- Johnny Bryant,
- Rachelle Chitkara,
- Amanda Coffey,
- Amy Cole,
- Janet Cox,
- Melodie Dixon,
- Julie Feldstein,
- Connie Guyor,
- Joann Harmeyer,
- Marion Johnson,
- Robin Johnson,
- Beth Koch,
- Margaret Landers,
- Alison Lowry,
- Susan McCarthy,
- Rachel McGill,
- Karen Montag-Leifling,
Significant Accomplishments

Improving outcomes for asthmatic children

With the goal of becoming the premier center to diagnose and treat asthma, we have combined asthma treatment and research to form a center that includes Pulmonary Medicine, Allergy/Immunology, Adolescent Medicine and General Pediatrics.

Our inpatient asthma consult service increased consults to admitted patients by 25 percent this year. We led the evidence-based clinical practice guidelines for managing acute asthma exacerbations and the task force that revised inpatient care to identify and mitigate risk factors for poor asthma control and future exacerbations.

Our work has included developing an institutional data repository to identify and characterize patients with asthma, facilitate outcomes and other clinical research and promote improvement. We also developed institution-wide outcome measures to track variability, share innovations in care delivery and facilitate research.

Pediatric Bronchoscopy Program

Recognized as the leading pediatric bronchoscopy program in the US, our Airway Center performed more than 1,200 flexible bronchoscopies this year. It is the largest training center for pediatric flexible bronchoscopy, conducting an annual international postgraduate course attended over the years by more than 500 physicians from more than 40 countries.

This year, we will expand the course to include a training site in Spain. The Airway Center supports clinical and basic research and attracts referrals from around the world. There is close integration with ENT, with an emphasis on providing multidisciplinary diagnostic and management services to patients with complex airway problems.

Cystic Fibrosis Center

The Cystic Fibrosis Center was featured in a *US News and World Report* article outlining what Cincinnati Children's has done to improve care for cystic fibrosis (CF) patients. The story focused on how including patients and families in the management of their care has helped improve outcomes. These and other quality improvement efforts have led Cincinnati Children's to become one of the leading CF centers in the country, as measured by the Cystic Fibrosis Foundation through a combination of key metrics. In addition, Cincinnati Children's improved its *US News and World Report* ranking in pediatric pulmonology to number two in the country.

Division Publications
## Grants, Contracts, and Industry Agreements

### Grant and Contract Awards

<table>
<thead>
<tr>
<th>Name</th>
<th>Description</th>
<th>Institution</th>
<th>Grant ID</th>
<th>Start Date - End Date</th>
<th>Direct Costs</th>
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<td>Acton, J</td>
<td>Clinical Trial: ISIS 002</td>
<td>University of North Carolina at Chapel Hill (Cystic Fibrosis Foundation Therapeutics, Inc)</td>
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<td>Randomized Control Study of Adenotonsillectomy for Childhood Sleep Apnea</td>
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<td>Inspiratory Muscle Strength Training in Patients with Upper Airway Obstruction</td>
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### Multidisciplinary Clinical Research Center - Project 4
### Industry Contracts

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Total Current Year Direct: $3,074,633
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