



Studies of Pediatric Liver Transplantation

PARTICIPATION IN THE SPLIT REGISTRY

Why Support Pediatric Liver Transplantation Research?

The pediatric liver transplant community faces rapidly evolving treatment with advances in pharmacology and surgical techniques, and their stakeholders are constantly exploring better ways to treat pediatric liver transplant patients to achieve better outcomes. But which care processes and treatments are best? Translational research and clinical trials are critical to understand mechanisms and biology and to define interventions that will simultaneously ensure excellent allograft function and minimize complications of immunosuppressive medications. Yet, alone they do not provide the full picture since they do not address the emerging outcomes and only partially define the biological and social phenotype. The impetus and rationale to conduct such observational research is outlined in a recent report of the NIDDK symposium on long-term outcomes in pediatric liver transplant recipients. Here we propose to address emerging outcomes and define patient phenotype, critical to future mechanistic studies, clinical trials and improvement efforts.

Who we are and what we have done

The Studies of Pediatric Liver Transplant (SPLIT) was established in 1995 by hepatologists and transplant surgeons committed to the success of liver transplant in children. Over time the network expanded to include over 40 transplant centers in the U.S. and Canada and was funded by both Astellas Pharma, Inc. and through a grant from the National Institute of Diabetes and Digestive and Kidney Diseases. The mission of the network is to improve the outcomes in children receiving liver transplantation through research. The research focus of SPLIT has been to characterize patient and graft survival, graft function, and patient morbidity. The knowledge gained to date has helped us understand predictors of pre-transplant risk and post-transplant complications, and has changed practice. The SPLIT registry has served as the foundation for other pediatric liver transplantation research including the Functional Outcomes Grant (FOG), the Medication Adherence study (MALT), and the Immunosuppression Withdrawal study (iWITH). Most importantly SPLIT has generated questions that can only be answered by continued collaborative work.



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Goals Going Forward

Our goal is to restructure the SPLIT research network so that we are better poised to address the gaps in knowledge that remain in the field of pediatric liver transplantation and ultimately improve outcomes in children receiving liver transplants. We believe the best way to meet this goal is by maintaining the SPLIT clinical research network which is composed of transplant centers that have proven that they are capable to conduct clinical research and answer important questions in the field. As part of the restructuring process, we have updated the overall research focus of the Network and expanded the scope of research to be conducted to include quality improvement/comparative effectiveness studies and clinical trials in addition to a core observational study. Observational research conducted through the Network will identify opportunities for quality improvement efforts or alternatively identify gaps in knowledge which serve as a foundation for patient-based research. Quality improvement efforts and/or research projects will be conducted and then applied to the clinical arena through what has been called type 2 translational research which seeks to translate new and existing findings into improvement in clinical practice.

Governance

A steering committee comprised of investigators from all participating centers will bear the final responsibility for the financial, administrative, legal, ownership, and scientific components of the research conducted by the SPLIT registry. The steering committee will define the responsibilities of the DCC and individual centers (regulatory, data quality, etc.) A subgroup of investigators selected by the steering committee will form an operations team and work with the DCC to guide operations. This operations team will report to the steering committee. Roles and responsibilities will be defined and will be logical extensions of the operations manual used to guide the original SPLIT registry

The Core Observational Study

The core component of the SPLIT research network will be an observational study through which we will prospectively collect data elements (baseline and yearly updates) to gain new knowledge about the risk and biology of emerging outcomes and to facilitate the development of targeted clinical studies, whether quality improvement/comparative effectiveness studies or clinical trials.



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Further, we recognize that the efforts to collect and store information require resources and will make efforts to establish robust, reliable and parsimonious data elements.

Quality Improvement/Comparative Effectiveness Studies and Clinical Trials

The SPLIT clinical research network plans to implement quality improvement/comparative effectiveness studies and clinical trials to improve the care delivery process and gain new knowledge.

The Steering Committee will use the data collected through the observational study to identify opportunities for improvement based on center specific analyses of outcomes.

Center level

- Define system leader, day-to-day leader, technical experts and key personnel
- Select high priority aims from those listed by the Steering Committee
- Initial Population of Focus (e.g., “We will start by focusing on standardizing post transplant discharge criteria for all new transplant recipients)
- Initial Changes to be tested (e.g., “We will employ a discharge checklist”)

A learning collaborative will be established which will be charged with development of specific operational definitions for the outcomes and processes required for the QI effort. Models of quality improvement will be used to modify care processes across centers and the impact will be assessed. Learning collaboratives are modeled after the Institute for Healthcare Improvement's Breakthrough Series Model. PCDC provides clinical, technical, and social support to health care organizations in order to help them make dramatic improvements in specific clinical and operational areas. To participate in a learning collaborative, an organization appoints several staff members to a team. Over the course of six to eight months, teams from various organizations that share common goals meet in learning sessions. They learn from expert faculty how to improve their performance and share progress reports. The period between learning sessions is called the "action period"; during this time, teams work intensely to implement what they have learned at the learning sessions, using the Plan-Do-Study-Act cycle. Once a redesign model has been achieved, team members help to disseminate the model throughout the organization.



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Budget and Funding

Core Operational Study

The annual operations budget for the core observational study is \$146,000. Each center is asked to commit \$5,000 per year to support SPLIT operations. We also ask that transplant centers provide staff time for data collection and entry, and regulatory management. We recognize that the cost for staff support at each center might be an additional \$5,000-\$10,000 per year.

Quality Improvement Studies and Clinical Trials

The budget for individual quality improvement/comparative effectiveness studies and clinical trials will depend on the specific study developed. Once the scope of the research effort has been defined, each center that has identified interest in participation will be asked to commit a yearly fee to support operations for the specific trial.

Center Responsibilities

As a member of SPLIT, centers will be expected to

- Provide \$5,000 each year to support SPLIT operations
- Provide support for data entry efforts
- Maintain regulatory compliance
- Meet standards for data quality
- Participate in scientific direction of SPLIT as part of the steering committee. The participation will involve monthly conference calls, assignments not to exceed 3-4 hours each month and review at an annual meeting



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Benefits to the Centers

- Access to web-based center specific analyses and outcome reports
- Ability to develop and participate in QI studies and selected clinical trials
- Benchmarking data reports / Outcome summary reports
- Recognized as an active SPLIT center to be used for local marketing and contracting
- Access to network resources and community – social networking
- Access to study data for center specific analysis