



Work Weekend Summary Letter to CHSS and Message from the Directors:

We held the Data Center's Fall Work Weekend November 22-24. A total of 29 people attended including 16 members and 3 guests (see Appendix 1). We welcomed several cardiologists—Rich Lorber, Rene Herlong, and Shubhika Srivastava,—who worked on a draft of a manuscript based on our “expert review” of echocardiograms from our AAOCA cohort. Travis Wilder, our current Kirklin-Ashburn Fellow, was also present with the Data Center staff.

Of our 11 cohorts, we focused on three of these: AAOCA, LVOTO, and tricuspid atresia. We also discussed a potential new cohort, namely, Ebsteins' anomaly proposed by Joe Dearani, Christopher Knott-Craig and Christian Pizzaro. We discussed other topics, such as the CHSS-STS data linkage (Jeff Jacobs), the Biobank registry (Peter Gruber), Technical Performance Score project (Emile Bacha & Chris Caldarone), and grant opportunities, and the future of the Data Center.

The AAOCA registry championed by Julie Brothers (CHOP) continues with open & enthusiastic enrollment. In the past year we have completed a study on the morphology of AAOCA from data extracted from operative reports. The resulting manuscript has been submitted for publication. During the work weekend, we reviewed results of “core lab review” of 147 echocardiograms from the AAOCA cohort. Echos reviewed by our cardiology team, led by Rich Lorber, were compared with the original reports from source institutions with attention to morphologic details (given the diagnosis of AAOCA). Agreement was generally good except for diagnosis of interarterial or intramural course, and an “acute angle” of takeoff of the anomalous coronary. The group worked on a draft of a “best practice” paper based on these results and on the experts' design of a protocol for obtaining echo data from such a patient.

We also obtained operative descriptions of the morphology from operative reports. We will incorporate these data into the echo analysis to assess agreement between reports and surgery vs. core lab review and surgery and recommend a protocol for surgical reporting of operative data.

In addition, Jeff Poynter, Gus Mavroudis led a group that examined “What was found and what was done” at surgery. This analysis is accepted for presentation at the upcoming STS meeting in Orlando

Finally, we proposed two future projects. First, we will examine the association between expert echo and operative findings and clinical presentation. With this, we will look at provocative testing, nature of management decisions, the spectrum of surgical procedures performed, and the details of “medical” management. Second, we will plan to examine psychosocial evaluations and QOL considerations in patients managed both medically and surgically. The long term aim of the registry, of course, is to compare the outcome of those managed medically with those managed surgically. **It is critical to capture patients managed medically at each institution.** *Please implore your data coordinator to collaborate with your cardiologists in capturing these patients into the registry.*

The LVOTO cohort continues with open enrollment. This cohort consists of 675 patients, 82% of which have followed an intended single ventricle pathway. 512 of these babies have the diagnosis of hypoplastic left heart syndrome. The data entry & follow-up of this cohort has become quite labor intensive, thus we sought to develop discreet questions to address what would enable us to better define the breadth of follow-up and use limited resources efficiently. After a lively discussion, we converged on four questions for analysis in the coming 1-2 years. **First**, among neonates with critical aortic stenosis, what factors influence the initial decision to attempt two ventricle repair (valvotomy) versus single ventricle procedure, and what are the outcomes? **Second**, for the entire cohort and various subgroups, what is the time course of ventricular function (by echo) and how does it correlate with survival? **Third**, what factors influence the initial decision to take a “hybrid” approach of some sort? What is the subsequent course and what determines that course? Has this made a difference in clinical outcomes? **Fourth**, what is the “era effect” on the management pathways and outcomes and how do they compare? *If you have suggestions and ideas to add, contact Christo Tchervenkov and Ed Hickey.*

The tricuspid atresia (TA) cohort continues with active enrollment. This cohort consists of babies presenting within 3 months of birth with TA and normally related great vessels only. Our 2005 paper analyzed outcomes for 150 patients. There are now 302 in the registry. The work weekend group suggested the following questions for further analysis: **First**, does the way that pulmonary blood flow is managed prior to the Glenn procedure influence outcomes? **Second**, what is the time course of LV function and AV valve status in TA, and what are the associations with deterioration in these? How does this course compare with that of RV-dominant single ventricles? (Here, the latter group could be taken from our LVOTO cohort.) *If you have additional thoughts, contact Ed Hickey at the Data Center.*

Drs. Dearani, Knott-Craig and Pizarro proposed that the Data Center establish a new cohort of patients with Ebstein’s anomaly. This was first discussed in the April 2013 work weekend. The rarity of the lesion, the continued challenge of neonatal management, and the emergence of yet more surgical procedures make this cohort ripe for analysis. The list of possible questions includes: what predicts the need for neonatal surgical intervention, and which intervention? In infants and children, what are the predictors of management cross-over? What is the success of one surgical strategy compared to another? What is the time course of functional health status of these patients and what variables affect this status? The suggestion was

made to require patients to have been diagnosed with the anomaly within the first six weeks of life. Because of the rarity of the lesion, it was suggested that enrollment should be both retrospective (five years back) and prospective, seeking an enrollment of about 120 patients in the first two years of the registry. We agreed to convene a conference call of 5-6 members to formulate entry and exclusion criteria and to define the dataset needed for this new cohort, and to decide whether to treat the retrospective arm separately or as part of a single cohort. As with the AAOCA cohort, it will be very important to identify a cardiologist to champion this effort on the medical side, as enrollment of non-surgical patients will be a major component of the cohort. The next milestone will be to submit a proposal to the Research Committee. *Please indicate your interest in being part of the working group and send your additional ideas or suggestions to Joe Dearani, Chris Knott-Craig or Christian Pizarro.*

Peter Gruber updated us on the Biobank Registry project. The core of this project is to create a registry of tissue samples from patients with congenital heart disease managed at our CHSS institutions. Importantly no PHI data is to be collected to simplify data collection. CHSS members could then identify when a critical mass of tissue samples are available to collaborate with other researchers to conduct studies of the tissues registered with the Registry. Typical relevant samples would be blood, thymic tissue, skin (from scar excision during redos), and any other normally discarded tissue, including heart tissue. Many genomic and proteomic studies rely on large numbers of samples. Such studies of rare lesions are virtually impossible without the network proposed by Gruber. Of course, this all begins with your commitment to create your own institutional Biobank of CHD tissues. This could simply be “rented” space in an existing institutional Biobank, or you could share with other specialties in starting up a new one. Following this step, your data coordinator can then work with the Data Center to set up your Data Center registry. He/she can do this by looking at www.chssdc.org/biobank and by emailing Maulik Baxi at the Data Center. To date only 7 CHSS centers have indicated an interest. *We encourage you to initiate a CHD Biobank at your institution now and to join the CHSS Biobank Registry.* This project is a great impact opportunity for the CHSS.

We discussed the Technical Performance Score Project (TPS) briefly. We currently have a beta version of the web-based registry of TPS data, which is being tested by a few of our members. Once this is completed, the registry will be available to all members. This project is an opportunity for research impact. A paper from the SVR trial reporting results of a retrospective study on the correlation of TPC and outcomes for single ventricle operations will be presented at the upcoming STS meeting. What are our opportunities for carrying out prospective studies using our TPS registry? We would like our members’ suggestions. ***As soon as we complete the beta testing, we encourage all members to participate in this TPS registry.*** We assure anonymity and privacy as you report your results. Let us know what your additional concerns are. TPS is a value-added benefit for you and your institution that could enhance your institutional financial support

Jeff Jacobs updated the work group on the STS-CHSS data linkage. This linkage has been described in detail previously and has the potential advantage of increasing the discovery and enrollment of many more eligible patients into our registries. It is enrollment, not follow up, that has limited the power of our registries to address key hypotheses. Of concern is that only 70% of CHSS institutions have signed consent for participation in the linkage. *If your institution has not “signed on”, the Data Center would appreciate you facilitating your institution’s participation in this key research tool.* STS will now send bi-annual reports to each CHSS institution reporting the percentage of eligible patients at that institution that have actually been enrolled in the appropriate CHSS study. The goal will be to increase this percentage through your efforts at your institution to improve capture of such patients. In the early analysis of actively-participating CHSS centers, only 30-35% of eligible patients annually are actually enrolled in an appropriate CHSS study. *Please implore your data coordinator(s) to examine your STS database and to work with you and your cardiologists to capture all possible patients for any of our 11 (soon to be 12) cohorts.*

To date we have two publications on the STS-CHSS linkage that have been submitted for publication:

Linking the Congenital Heart Surgery Databases of the Society of Thoracic Surgeons (STS) and the Congenital Heart Surgeons’ Society (CHSS): Part 1 – Rationale and Methodology

Linking the Congenital Heart Surgery Databases of the Society of Thoracic Surgeons (STS) and the Congenital Heart Surgeons’ Society (CHSS): Part 2 – Lessons Learned and Implications

Of course, CHSS follow-up problems are also important. At the work weekend, the group discussed the problem of “lost” patients. At what point do we conserve resources and “give up” on a ‘lost’ patient? Can we prevent follow-up loss? For example, we will soon start a campaign to convert more patients from snail-mail communication to email communication for follow-up. We would like to ask the membership the following question: **How could your local staff help us at the DC with follow-up?** *Please discuss with your data coordinators and cardiologists the importance of maintaining contact with your cohort patients to prevent the “lost to follow-up” problem, and let us know your suggestions. As noted above, this issue is especially important in the medical cohort of AAOCA.*

Yet another challenge is the cost of our studies. As mentioned by Chris Caldarone at the most recent CHSS Annual Meeting, the cost of our Center will exceed our revenues within the next two years. Thus, we need to both increase revenues through grants and contributions, and decrease costs. The cost of follow-up among our approximately 3400 patients is about \$22/patient/year. The cost of enrollment

is less. The major costs incurred by the Center, however, are in data extraction, not collection. It was suggested that we look at each cohort and avoid extraction of data unless and until those data are targeted for a study. We have been successful in obtaining grants from the Children's Heart Foundation but not from the NIH/NHLBI. The funding patterns of the NIH are a moving target, however, and our opportunities will be a result of our members' careful vigilance of these evolving opportunities. As always, we seek the CHSS members to champion grant applications that use one or more of our cohorts to address hypothesis-driven (and even prospective randomized) proposals that have impact. *If you have some ideas on how to strengthen the funding of the Data Center, please let us know, and/or contact Dave Overman (Chairman of the CHSS Development Committee) directly.*

In addressing the future of the Data Center, several good suggestions were made as to how we might broaden the type and scope of our research. We recognized, for example, that our LVOTO cohort contains 548 patients known to have undergone some sort of single ventricle stage 1 procedure as their initial procedure (among them, 231 Norwood, 219 Sano variant, 115 "hybrid" stage 1). Chris Caldarone suggested that we might look at prospective, randomized clinical trials, using our registries as starting points. Such an approach has been suggested by Lauer and D'Agostino in the NEJM (Sept 2013) and has been described as "the next disruptive technology in clinical research". **To this end we proposed to employ our LVOTO registry to construct an RCT to compare the outcomes of the conventional stage 1 palliation with those of the "hybrid" approach.** A subset (yet to be defined) of patients normally entered into the LVOTO cohort would be randomized to receive either a conventional Norwood or a "hybrid" procedure as their initial palliation. We would then compare successful transition to CPC between the two groups, and to compare, between the two groups, neurological injury sustained during the neonatal period and its relation to later clinical neurodevelopment. **We sent a survey to CHSS members designed to estimate the potential enrollment of an appropriate subgroup. We received 26 responses.** Of these, 11 indicated enthusiasm for randomizing their conventional and hybrid stage 1 procedures over a two year period, for a total of 115 patients per year (assuming 100% enrollment). We will proceed with a power analysis based on 67% enrollment, then construct a study design and grant application over the next year. *More generally, let us know if you have an interest in championing design and funding for a prospective study or RCT based on any of our registries.*

The staff of the Data Center, led by Maulik Baxi, deserve much credit for organizing yet another productive Work Weekend. We encourage members to consider participation in our next work weekend scheduled for **April 4-6, 2014**, either in person or by Webinar. In the meantime, consider participating from your home institution by addressing the points made in this letter in italics. Your input is critical to the success of our enterprise.

Sincerely,

Bill Williams
Bill DeCampi

Appendix: WW Attendees

Christian Pizarro	Nemours Cardiac Center, Wilmington, DE
Christo Tchervenkov	Montreal Children's Hospital
David Drullinsky	Montreal Children's Hospital
Erle Austin	Kosair Children's Hospital, University of Louisville
Eugene Blackstone	Cleveland Clinic, Ohio
Gerhard Ziemer	University of Chicago
Igor Bondarenko	Children's Hospital for Michigan
J. Rene Herlong	Levine Children's Hospital
Jeff Jacobs	Congenital Heart Institute of Florida
Kathryn Stackhouse	Cleveland Clinic, Ohio
Kimberly Holst	Mayo Clinic, Rochester
Marshall Jacobs	Johns Hopkins University
Paul Chai	Columbia University, New York
Paul Kirshbom	Yale School of Medicine
Peter Gruber	Primary Children's Hospital, Salt Lake City
Rich Lorber	Cleveland Clinic, Ohio
Shubhika Srivastava	Mt Sinai School of Medicine
Steven Langley	Oregon Health and Sciences University, Portland, OR
Umar Boston	Washington University School of Medicine

And by GoToMeeting teleconference:

Joe Dearani
Julie Brothers
Tara Karamlou
Dave Overman

Data Center Staff:

Bill Decampli Managing Director
Bill Williams Executive Director
Christopher Caldarone- Staff Surgeon
Edward Hickey- Staff Surgeon
Brian McCrindle – Cardiologist
Statistical Consultant
Travis Wilder- Kirklin-Ashburn Fellow
Maulik Baxi – Data Center Manager

Sally Cai- Database Manager
Veena Sivarajan- CRNC
Susan McIntyre- CRNC
Annette Flynn- Clinical Research
Project Coordinator
Christina Faber- Clinical Research
Project Assistant