

CCTSI External Advisory Committee Report - 2023

The External Advisory Committee for the Colorado Clinical and Translational Sciences Institute (CCTSI) was held in person and virtually on Thursday & Friday, January 12, 2023 - January 13, 2023. The following Committee members were present to hear presentations and provide feedback to CCTSI leadership. Their formal report is provided below.

Steven M. Dubinett, MD (EAC Chair)

Interim Dean, David Geffen School of Medicine at UCLA
Associate Vice Chancellor for Research, UCLA
Director, UCLA Clinical and Translational Sciences Institute

Dan M. Cooper, MD

Professor of Pediatrics
Chief, Pediatric Pulmonology Division
Founding Director of the Institute for Clinical Translational Science
Program Director of the UC Irvine Clinical Research Center

Peter J. Embi, MD, MS, FACP, FACMI, FAMIA, FIAHSI

Chair, Department of Biomedical Informatics
Senior Vice President for Research and Innovation
Professor of Medicine
Vanderbilt University Medical Center

Alexander H. Krist, MD

Co-Director, Ambulatory Care Outcomes Research Network
Department of Family Medicine and Population Health
Virginia Commonwealth University

Jareen Meinzen-Derr, PhD, MPH

PI Center for Clinical and Translational Science & Training
Professor Dept. of Pediatrics
Co-Director, Faculty Diversity, Equity & Inclusion,
Cincinnati Children's Hospital Medical Center
University of Cincinnati SOM (CTSA MPI)

Cynthia Morris, PHD, MPH

Professor of Medical Informatics and Clinical Epidemiology, School of Medicine
Assistant Dean, Admissions, Office of the Dean, School of Medicine
Biomedical Informatics Graduate Program, School of Medicine
Clinical Research - Human Investigations Program, School of Medicine
M.D./Ph.D. Program Committee, School of Medicine
Oregon Health & Science University

Progress Report of Yr 5 and Summary of Future Directions and Goals

Following exceptional progress since its inception in 2008, the Colorado Clinical and Translational Sciences Institute at the University of Colorado Denver continues to transform the research and training environment that fosters a biomedical enterprise throughout the region. The CCTSI promotes a collaborative environment that facilitates the translation of discoveries and is enabling equitable patient care. Since its inception, the CCTSI has had an increasing impact with membership rising to more than 7,000 members with partnerships among 3 universities and 6 affiliated hospitals and health care organizations. Since the start of the CCTSI, CU Denver total research grant funding has increased from \$400M to over \$700M annually and NIH funding doubled.

The CCTSI infrastructure was in place and facilitated critical resources during the pandemic. The CCTSI facilitated the largest enrollment center, 10% of all enrollees, for the Pfizer/BNT COVID vaccine trial in 5-11-year-old children. The CCTSI initiated numerous adult therapeutic trials, led the Colorado CEAL program, was a Clinical Cohort Site for the RECOVER Long COVID program, and participated as a Real-World Evidence Data Center for N3C.

The CCTSI has formed a Diversity, Equity, Inclusion, Social Justice Committee which has fostered several new programs and training. Both the number of URM medical students and faculty have significantly risen during the past several years. SUMMiT, Summer Undergraduate Minority Mentoring in Translational Science continues as a pathway program. A full slate of professional workforce development programs continues with new programs in Teaming for Early Career Researchers and Communicating Your Science to the Public.

The CTRCs have had robust activity including inpatient and outpatient facilities and mobile teams. Two hundred PIs participate in more than 500 protocols annually with up to 15,000 visits per year. The Trial Innovation Network Hub Liaison Team continues to serve as a resource for project management, contracting, central IRB facilitation, recruitment and navigation. The CCTSI has been participating extensively in national and CTSA consortium initiatives including Dr. Sokol's participation on the national CTSA steering committee as well as CCTSI members participating in CD2H, N3C, I-Corps, CEAL and all Enterprise committees.

The plans for the CCTSI 4.0 strategy are well articulated in 6 overall goals that cover the full spectrum of clinical and translational science, promoting innovative programs to improve the efficacy and impact of translational investigation. This includes plans to strengthen collaboration and team and data science that address health inequities. They will further operational efficiencies, promote a safe and flexible research environment addressing public health needs. The training programs will continue to educate a diverse workforce of clinical and translational investigators.

Recommendations from the EAC:

The highly impactful and transformative work of the CCTSI continues under the direction of their founding leader, Dr. Ron Sokol. The consistency of this leadership, the organizational structure, and the presence of experienced program leaders enable outstanding continued progress and impact. The EAC views the CCTSI as being among the top tier of CTSA hubs nationwide.

CCTSI Admin Core and Management

The Administrative Core continues to provide the requisite support in management of the entire program and financial matters. Mr. Tim Lockie, CTSA Executive Director, had continued to manage the complex budgetary administrative support that has enabled the CCTSI to meet its missions and continue extraordinary institutional and community impact.

CTS Resources and Services

The Colorado Hub has done an extraordinary job in developing resources and services (R&S) that address the unmet needs of their CTS investigators. The difficulties we all face in the years to come is the continually evolving vision for Hub R&S by NCATS. It is difficult to invest funds, personnel, and organizational energy into

complex activities (such as regulatory knowledge, or the complex and sometimes conflicted statistical consulting service) only to find that NCATS has evolved a different vision for what the Hub is supposed to do to advance translational research and the science of translation. The Colorado CTSI leadership presented to the EAC a very large, comprehensive, and quite admirable set of R&S, all relevant and well-justified. My concern, however, is twofold: 1) the scope of work presented is, realistically, beyond the budgetary limits imposed by the grant, so how does an individual Hub parley its grant resources in a way that allies with and synergies existing campus resources that are also focused on translation (and, of course, at every AHC such institutional activities exist, IRB training, GCP, mock study sections, etc.); 2) how does one ensure that the R&S elements supported by the Hub contribute to the vision for CTS that has been presented over the years by NCATS.

In the presentation of Colorado Hub R&S, for example, the Administration Core, “helps R&S Core Leaders set up billing procedures and manage their accounts.” While this is an admirable and necessary function, one cannot but be concerned that given the overall tenor of NCATS over the past 10 years to reduce the role of the Hub in administration of clinical research, a purely management function such as this might not be seen as adding to the Hub’s ability to advance translational science.

The two R&S laboratories (Exercise/nutrition and cardiac imaging) are much needed components of a robust clinical trial and translational center. However, what was not clear from the presentation was how these two labs were stimulating investigators to tackle themes relevant to the science of translation. Surely, the kernel of translational science can be found in virtually all investigator-initiated human observational or clinical research. It would be useful for the R&S leaders to clearly delineate how the existence of these two particular labs met the NCATS criteria of “disease agnostic” and producing novel approaches that could bridge current gaps in translation that extend beyond the particular the way a particular use-case was involved in either of these exceptional labs.

Community and Stakeholder Engagement & Research and Health Equity

The CCTSI remains a leader in community engagement. Community engagement has achieved its stated Strategic Goals (develop the capacity of investigators, research staff, communities, and stakeholders; establish and maintain trust with communities; and continuously evaluate and improve capacity). The multiple practice-based research networks in Colorado (SNOCAP, High Plains Research Network, CaReNet, Bighorn, COCONet) have an impressive footprint with deep reach across Colorado into a diverse collection of communities. The networks are undergoing some changes as current investigators and staff retire and new investigators and staff are incorporated into the networks. The PACT Council, Community Research Liaisons, Boot Camp Translation, Community Immersion Training, CE Pilot training, Community Clinical Trials Advisory Board, and longitudinal relationships continue to do well by engaging patients and communities as active partners across the full spectrum of CTS. This results in research that addresses the priorities of community members, study designs that are culturally sensitive and participant friendly structure, dissemination of findings into the community, and enhanced public trust and participation in research. Community engagement is clearly integrated across CCTSI activities. An example is the impact community engagement has had on the antibody work with the use of boot camp translation to develop recruitment material, use of the immersion experience with training programs, and input from the community and users to guide informatics designs. The overall focus on diversity, equity, and inclusion is a real strength for community engagement and the CCTSI in general. There are demonstrated successes particularly for Hispanic people and communities.

Recommendations from the EAC:

1. A potential criticism of the CCTSI is that its footprint and impact is primarily in the Denver and Bolder Colorado regions. A key reason for this is that Colorado’s health systems are primarily located in these two regions. Authentic community partnerships, through the PBRNs and community-based organizations are essential for the CCTSI to have a broad impact. To continue to support this the CCTSI can increase its funding and support of Colorado’s PBRNs to ensure their continued success and hold the PBRNs accountable by creating metrics to demonstrate how the PBRNS are extending the translational research footprint of the CCTSI.

2. Community engagement has been an essential tool to engage diverse and underrepresented communities in translational research. The current community engagement metrics assess numbers, types, and strengths of partnerships, but there is no direct connection on how these partnership activities are extending the reach and impact of translational research for these communities. The CCTSI can create metrics to show the association of the “reach” of translational research supported by the CCTSI with the community engagement efforts, with specific attention to the reach and impact of translational science for diverse and underrepresented people and communities.

CTS Workforce Development

The translational research program is a clear strength of CCTSI and demonstrates the benefits of strong, consistent leadership that is well integrated into the hub. This includes a clinical science graduate program that provides advanced training in translational science to the campus.

Several programs developed by the workforce group are exemplars and have been disseminated to other hubs. The Teaming and Leading program has provided training to individuals and established teams in team science to apply situational leadership and collaboration to build trust. The CO-Mentor program has similarly trained more than 600 mentors and mentees in principles of mentorship, and development of individual mentorship plans. An additional program provides support for grant review to pre-K grant applicants; this seems successful in leading to excellent success rates.

Key program themes include weaving diversity throughout all the programs, providing outreach and a pathway to increase the number of under-represented minority trainees in all aspects of the program. In particular, the workforce programs have seen an increase in diversity overall. The TL1 and KL2 programs are strengths and appear to be the primary way for integrating early trainees into clinical and translational research in the CCTSI. Both programs use best practices for training and mentoring scholars, and indeed have been leaders in implementing training in team science and leadership. While the cohort composition of the TL1 and KL2 programs was not discussed, several scholar presentations provided very clear examples of scholars trained in the program who are now very successful faculty members with funded research.

Clinical research professionals can receive training in Good Clinical Practice, Responsible Conduct of Research, regulatory compliance and diversity and equity. The overall prominence of this program to include professionals at Colorado is not clear but there are opportunities to expand training, including to research professionals at CCTSI partner institutions. The competencies for clinical research professionals could be adopted to expand the scope of this training and provide career progression.

Recommendations from the EAC:

1. The TL1 and KL2 programs are well established and clearly develop the next generation of scholars. To date, these have not integrated KL2 scholars from CCTSI partner institutions such as CSU but have integrated post-Doc TL1 scholars from CSU. While it would create new challenges, including predoctoral and postdoctoral trainees from partner institutions would increase their integration into CCTSI and provide a resource for clinical and translational research training to individuals in domains that may not be present at the University of Colorado.
2. An important component of workforce is continuing education for clinical research professionals. The workforce program has an opportunity to grow as Colorado adapts to a wage equity law. The profile of training may need to grow, adopt clinical research competency goals, and become a key resource for career advancement for CCTSI and partners.
3. The leadership of the workforce program is in contact with many early career trainees at Colorado. Consider discovering barriers and facilitators to developing research at Colorado from the perspective of a new junior faculty member who wants to begin a research pathway. What would help the trainee to become aware of how CCTSI could facilitate their research plans?

CTS Research Program – Pragmatic EHR Embedded Trials (PEET)

The tools being created in the Pragmatic Embedded Trials (PEET) efforts are essential for pragmatic research to thrive, an essential element of CTS. The CCTSI is developing tools and workflows to integrate research into routine care, extend research participation broadly, and promote standardization and adaptation to the enrollment, design, data collection, and outcomes assessment of pragmatic trials. It is particularly forward thinking that PEET will include both high-intensity participation (e.g., participating clinicians are engaged in research) and low-intensity participation (e.g., no impact on workflow and no needed efforts from participating clinicians). PEET seems to have both top-down and bottom-up support which will also be essential for success.

Recommendations from the EAC:

1. To ensure the success of the project, the CCTSI should continue to develop workflows for more intensive projects where clinicians are “engaged in research” and some where it is minimally or non-intrusive and clinicians are not engaged in research.
2. Given that this process is in its early stages, if the CCTSI should approach this project as a learning opportunity with the expectation that the design and functions will evolve from projects and lessons learned. This should be shared broadly across the CTSA hubs nationally.

The Colorado Program for Integrated Research in Child-Maternal Health

This program highlighted a much-needed approach to build a data-driven mechanism that links a range of health conditions from across the lifespan. The presented goal of the program is to stimulate, “cross-disciplinary and cross-institutional research in children, pregnant women, and mother/child pairs, which will improve child and maternal health and prevent diseases that begin in early life.” One concern regarding this program was its ambitious goals, the question that the Hub must address is what component or part of the broad idea of antenatal or pediatric origins of health and disease across the lifespan can be effectively addressed given the realities of the NCATS or even other NIH budgets. The presentation described a very broad and inclusive data set, and this is surely a meritorious goal. Other projects, however, such as NIH All-of-Us which is about to begin recruitment in pediatrics, might be better funded to achieve the goals presented in the Colorado Integrated Research in Maternal and Child Health Program. We would urge the Hub to define a more feasible focus for this approach, identify a few use-cases that could demonstrate the value of the Colorado approach, and embed mechanisms to identify the “science of translation” kernel that can then be used to enhance the lifespan approach in additional health conditions.

Colorado State University Partnership (including CU-CSU Summit)

CSU Fort Collins is a land-grant institution that provides specific advantages as a partner, particularly with the School of Veterinary Medicine. CCTSI has invested in the One Health program as a particular focus of the partnership. The Natural Animal Models Core at Colorado provides an outstanding and unusual resource for collaboration between researchers in human medicine with naturally occurring disease in animal models that may mimic human disease. They have developed a “veterinary IRB” to facilitate research. Other potential advantages could include including the county extension program into the community outreach efforts throughout the state.

CSU has invested in this partnership through contributing strong institutional support for infrastructure including biostatistical support, as well as a matching grant support provided through CCTSI (\$30K from CSU, \$30K from CCTSI). This demonstrates the commitment of CSU to this partnership. The CCTSI/CSU Summit is an annual day for cross-pollination between universities to consider common interests and develop a program in subsequent grant funding.

CCTSI partners are broader than CSU Fort Collins and include CU Boulder as well as hospital partners however this was the only partnership discussed in detail.

Recommendations from the EAC:

1. The relationship between CSU Fort Collins and CCTSI has strong benefits. Consider expanding the reach and depth of the partnership with CSU to include the full breadth of the program, across all modules of the CCTSI.
2. Are other partners of the CCTSI as well developed as CSU? It would appear that other hospital and health system partnerships are fully integrated but beyond numeric measures, the breadth of these partnerships was not clear.

Dissemination & Implementation Core

The Dissemination & Implementation (D&I) effort is and has been an essential component of the CCTSI (also described in Element B in the renewal application). It includes the aims 1) Develop a learning community for local dissemination of educational resources; 2) Catalyze and centrally support the research community in D&I to achieve efficiency and economy of scale; 3) Catalyze and centrally support bi-directional D&I with the CTSA consortium and network. The renewal application aims to expand the current service and integrate D&I systems, methods, and principles across all CCTSI components and support and build capacity for use of D&I science methods for all CCTSI members and Partners. The D&I core is guided by a process framework appropriately grounding CTS in 4 phases (conceptualization, design, dissemination, impact).

The CCTSI D&I core continues to make great progress regarding their national presence and has developed a nice array of resources around D&I science that is impressive, which includes the cadre of D&I interactive tools (great addition). The pragmatic research navigation service is a strength and will serve the CCTSI community well with the renewal. The advances made in D&I continue to highlight CCTSI national leadership in this space has positioned the CCTSI in a favorable and solid footing for their competitive renewal. The renewal expands upon the educational offerings for translational science by focusing on topics that address dissemination and implementation. There are plans to identify strategic opportunities for integration of D&I across all Hub activities. One solid example of the success of the D&I core integration is noted in the real-world evidence COVID mAb project. Overall, the CCTSI D&I core remains engaged in excellent work to advance D&I efforts, sharing best practices nationally across the CTSA consortium. It was fun to see the palpable enthusiasm for this work and for the people who will be impacted by this work.

Recommendations from the EAC:

1. Given the successes and strengths of the Core, continue to find synergies across other CCTSI groups and cores that enhance the overall impact of the dissemination activities.
2. The dissemination activities of the CCTSI are impressive. Consider moving a little more into the implementation space of D&I. Scientists/researchers are not always great at broad dissemination of their work, and they are often worse at implementation of their science into practice. Few places are implementation power-houses and the CCTSI is well-poised to get us all going in that direction.
3. The Core does a pretty good job with some evaluation aspects. Consider strengthening the relationship with the CQI and Evaluation Core (coincides with #1 above) so that the CCTSI can fully define and measure success. This could also help in knowing that the dissemination efforts are hitting the right audiences with the right impact.

Continuous QI (CQI) and Evaluation

The CCTSI Evaluation Core, housed at the CU Denver School of Education and Human Development, continues to have a robust and comprehensive evaluation approach efforts related to tracking, evaluation, and impact of the CCTSI. The evaluation metrics seek to:

1. Ensure continued alignment of evaluation and tracking with current and anticipated Common Metrics.
2. Demonstrate the quality and effectiveness of innovative programs and approaches through rigorous program evaluation.
3. Support dissemination of CCTSI's model programs and implementation throughout the CTSA network.

The Core collects data via progress reports, an annual search of secondary databases, online surveys, focus groups, and individual check-ins to formulate a broad picture of the impact of CCTSI programs. Within the renewal application (CCTSI 4.0), evaluation is interwoven throughout, maintaining the vigorous approach that

the CCTSI has established over the years. The Evaluation core and CQI program will focus on identifying and overcoming roadblocks to efficiency, measure metrics of impact for each module and implement solutions. Among continued improvements to the core include understanding how underrepresented minorities in science (trainees and faculty) have benefited from the CCTSI as well as incorporating the Translational Science Benefits Model (TSBM) into the evaluation to provide a more holistic view of CCTSI impact (a particularly useful approach to evaluation).

Recommendations from the EAC

1. A major strength lies with how the core is considering integrating the TSBM into the evaluation process. Continue with this integration throughout the various modules and related projects. Additionally, helping investigators really consider the TSBM for their own research would strengthen the great work that is already occurring.
2. The overall work of the CQI and Evaluation continues to grow and is central to the CCTSI's ability to provide evidence of the impact the CCTSI has had on science. Consider the involvement and synergies of the other cores/modules/CCTSI resources in the evaluation process (such as BERD and Informatics).
3. The team has done an excellent job with providing summative metrics. Consider how informative evaluations could lead to identifying areas for improvement and how the CCTSI has leaned into making shifts towards improvement (examples of how informative evaluations have improved processes that have led to improved outcomes).