

Hawai'i IDeA Center for Pediatric and Adolescent Clinical Trials

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Abstract

As one of 17 clinical sites of the Environmental influences on Child Health Outcomes (ECHO) IDeA States Pediatric Clinical Trials Network (ISPCTN), the Hawai'i IDeA Center for Pediatric and Adolescent Clinical Trials (HIPACT) was established in 2016 to participate in community-valued and scientifically-valid multi-center pediatric clinical trials to improve health and well-being of diverse multi-ethnic populations of Hawai'i. Hawai'i is home to large populations of diverse rural and underserved populations, including indigenous Hawaiian communities and immigrant populations of Pacific Islanders and Asians. Many of these communities experience significant health disparities, made worse by their geographic isolation and many socio-economic factors. In addition to providing opportunities for children and their families to participate in clinical trials, HIPACT's goal is to provide opportunities for junior faculty of the John A. Burns School of Medicine (JABSOM), University of Hawai'i at Mānoa, to acquire knowledge about and to develop skills in clinical trials. HIPACT's partners include the Hawai'i Pacific Health with Kapi'olani Medical Center for Women and Children, and Waianae Coast Comprehensive Health Center. HIPACT builds on the experiences gained through partnerships with the Mountain West IDeA Clinical and Translational Research-Infrastructure Network, and Research Centers in Minority Institutions Translational Research Network. Apart from participating in ECHO ISPCTN-sponsored studies, HIPACT junior faculty serve as committee members, Working Group leaders, Protocol Study Principal Investigators (PI) and site study PIs with ECHO ISPCTN. Through participation in ECHO ISPCTN, HIPACT has successfully increased the number of pediatric and maternal-fetal medicine faculty involved in the conduct of clinical trials.

Keywords

pediatric clinical trials, network, clinical research

Abbreviations

ACT NOWS = Advancing Clinical Trials in Neonatal Opioid Withdrawal Syndrome
CE = Current Experience
DCOC = Data Coordinating and Operations Center
ECHO = Environmental influences on Child Health Outcomes
ESC = Eat, Sleep, Console
HIPACT = Hawai'i IDeA Center for Pediatric and Adolescent Clinical Trials
HPH = Hawai'i Pacific Health
IDeA = Institutional Development Award
IRB = Institutional Review Board
ISPCTN = IDeA States Pediatric Clinical Trials Network
JABSOM = John A. Burns School of Medicine
NHOPI = Native Hawaiian and other Pacific Islander
NIH = National Institutes of Health
OIF = Opportunities and Infrastructure Fund
UHM = University of Hawai'i at Mānoa
VDORA = Vitamin D Supplementation in Children with Obesity-Related Asthma

Introduction

This special issue of the *Hawai'i Journal of Health and Social Welfare* on Pediatric Health and Research in Hawai'i is sponsored by the Hawai'i Institutional Development Award (IDeA) Center for Pediatric and Adolescent Clinical Trials (HIPACT) program to provide a cross sectional landscape of the research, training, education, treatment, policy and social issues related to maternal-child health in Hawai'i. The National Institutes of Health (NIH) established the IDeA program in 1993 to enhance biomedical research activities in states that have had historically low NIH grant funding success rates.¹ The program currently supports competitive research in 23 states and Puerto Rico through 4 distinct components: Centers of Biomedical Research Excellence, which targets junior faculty research mentoring; IDeA Networks of Biomedical Research Excellence, which targets undergraduate student research development; IDeA Program Infrastructure for Clinical and Translational Research (IDeA-CTR), which supports broad clinical and translational research; and IDeA co-funding, which provides support to NIH R15 or R01 applicants whose proposal received excellent rating through the peer review process but fall short of the NIH Institute or Center pay line.

As the western-most IDeA-eligible state, Hawai'i is home to large populations of diverse rural and underserved multi-ethnic populations including indigenous Hawaiian communities and other immigrant populations of Pacific Islanders and Asians who suffer geographic isolation locally, resulting in significant health inequities. Paradoxically, while 43% of the nation's children come from communities such as these, research in pediatric health disparities is lagging disappointingly behind. This is especially important in communities where the burden of disease is high and often begins in childhood. In Hawai'i, the prevalence of pediatric asthma is among the highest in the nation; nearly 20% of Native Hawaiian children have asthma. Native Hawaiian and Other Pacific Islander (NHOPI) children have high rates of obesity and associated metabolic abnormalities that are likely factors in the high rates of diabetes, cardiovascular disease, and cancer seen in NHOPI adults. While health disparities research has targeted children of African and Latin American descent, few clinical trials have focused on children from these NHOPI populations. NHOPI children are often miscategorized or pooled into the designation of "Asian/Pacific Islander". Even pooling all "Asians" into a single category to study health and disease fails to distinguish the health disparities of large com-

munities of Filipino immigrants in Hawai‘i as compared to the traditional East Asian populations. Pooling of demographic data dilutes the ability to identify health disparities specific to unique populations of young families from the Pacific Rim, and misses opportunities to develop meaningful translational and population health programs that specifically benefit those with the greatest needs. Pacific Island nations, territories, and communities with their geographic isolation and strong community foundation, offer a stable population base that may be ideal for conducting long-term longitudinal studies. Funding for HIPACT, as one of 17 clinical sites of the Environmental influences on Child Health Outcomes (ECHO) IDeA States Pediatric Clinical Trials Network (ISPCTN), enables researchers based at University of Hawai‘i at Mānoa (UHM) John A. Burns School of Medicine (JABSOM) to address these disparities.

We are delighted to be selected as one of the sites in this pediatric clinical trials network. Indeed, the ECHO ISPCTN partner institutions cover the nation’s geography from east to west, and from north to south. Moreover, ECHO ISPCTN represents a significant diversity of communities that would be difficult to duplicate in any other concept; with populations representing the spectrum of socioeconomic classes, both urban and rural. Significant numbers of people, from a wide variety of ethnic and cultural groups, including American Indians, Alaska Natives, Native Hawaiians, Asians, Hispanics, Black, and Whites, reside in the ECHO ISPCTN partner states. For many reasons, including historical events and socioeconomic factors, health disparities and inequities exist across the sites, but have been poorly studied, especially among children. As such, this new network now provides the infrastructure for multi-center clinical trials research, comparing health outcomes of geographically distinct communities across the United States, as a means to reduce pediatric health disparities among communities with the greatest needs.

This report summarizes the HIPACT Program with the ECHO ISPCTN activities that HIPACT faculty and personnel participated in during the past three years. The principal objective of HIPACT was to establish and maintain pediatric clinical trials teams in Hawai‘i to participate in large, community-valued, and consequential multi-center research as a partner in ECHO ISPCTN. The overarching goal is to improve the health and well-being of the diverse multi-ethnic populations of Hawai‘i, including those living in rural and underserved communities. This report serves as the foundation and backdrop for the special issue of the *Hawai‘i Journal of Health and Social Welfare* on Pediatric Health and Research in Hawai‘i. Through HIPACT efforts, a call for manuscripts describing the spectrum of research, teaching, service, treatment and policy related to pediatrics and maternal-fetal-medicine was released. While not intended to be all-inclusive, this report and the accompanying articles in this special issue provide a snapshot of the diverse activities related to the health and well-being of infants, children and adolescents in Hawai‘i.

Methods

Along with HIPACT, which is located at the UHM JABSOM in the Department of Pediatrics, the two clinical partners for the program are Kapi‘olani Medical Center for Women and Children of Hawai‘i Pacific Health (HPH) and Waianae Coast Comprehensive Health Center. The principal objectives of HIPACT are: (1) to launch and implement pediatric clinical trials as an ECHO ISPCTN site by providing an experienced, coordinated, and committed team of pediatric-trained personnel; (2) to engage Hawai‘i and other IDeA state communities to provide access to clinical trials including rural and underserved infants, children, and adolescents, many of whom are Asian and; (3) to contribute to the science of ECHO ISPCTN multi-center clinical trials research in disparate underserved and/or rural communities by better understanding and overcoming barriers, with the ultimate goal of improving health outcomes; and (4) to increase the number and to enhance the expertise of pediatric clinical trials faculty and their support teams through professional training and education, ultimately to expand ECHO ISPCTN research capacity.

In order to meet the goals of increasing the faculty research capacity, open invitations were announced to Departments of Pediatric and Obstetrics/Gynecology Maternal-Fetal-Medicine faculty to participate in ECHO ISPCTN activities. The ECHO ISPCTN activities included Professional Development webinars, which were hosted by the ECHO ISPCTN Data Coordinating and Operations Center (DCOC). Additionally, targeted invitation for faculty whose research interested focused on ECHO ISPCTN specific concept/protocol-specific activities and/or ECHO ISPCTN focus areas (upper and lower airway disease, obesity, pre-, peri-, and postnatal outcomes, neurodevelopment, and positive child health outcomes). The current status and accomplishments of the HIPACT Program reflect the clinical trial/research protocols that were launched in Hawai‘i as well as the ECHO ISPCTN activities in which faculty were actively engaged. Clinical research/trial protocols were reviewed and approved by the appropriate Institutional Review Board (IRB) of record (University of Hawai‘i IRB, Western IRB and/or Central IRB at University of Arkansas Medical School).

Results

ECHO ISPCTN Clinical Trials Activities in Hawai‘i

Pharmacokinetics of Understudied Drugs Administered to Children Standard of Care (POPS Study): The POPS Study (NCT01431326) was designed to better characterize the pharmacokinetics of a variety of commonly used drugs in infants and children for which limited information was available in the pediatric population.² HIPACT was one of 15 ECHO ISPCTN clinical sites which joined the POPS Study. The HIPACT Site Study PI, Dr. Venkataraman Balaraman, mentored the junior investigator, Dr. Prashant Purohit, as part of the faculty and

professional development program in HIPACT. The team, including the HIPACT Lead Coordinator (Annette Amiotte, RN), HIPACT Site Coordinator (Moara Palma), and HIPACT Regulatory Affairs Liaison (Andrea Siu), successfully launched and completed the POPS Study in Hawai‘i.

Advancing Clinical Trials in Neonatal Opioid Withdrawal Syndrome: Current Experience (ACT NOWS CE): The ACT NOWS CE study was part of a group of NIH-sponsored studies to inform the clinical care of infants who are prenatally exposed to opioids in collaboration with the Eunice Kennedy Shriver National Institute for Child Health and Human Development Neonatal Research Network and ECHO ISPCTN forming the ACTNOW collaborative (Advancing Clinical Trials in Neonatal Opioid Withdrawal). The HIPACT Site Study PI, Dr. Charles Neal, Jr., mentored the junior investigator, Dr. Akshatha, along with the HIPACT site study team, comprising the HIPACT Lead Coordinator and HIPACT Regulatory Affairs Liaison.³ A follow-up network intervention study, ACT NOWS Eat, Sleep, Console (ESC) Study is scheduled to be launched in early 2020, and HIPACT will be an active participant.

Vitamin D Supplementation in Children with Obesity-Related Asthma (VDORA Study): The VDORA Study is an ECHO ISPCTN clinical trial, which was vetted through the ECHO ISPCTN proposal review process. The study was designed to identify the optimal Vitamin D dose for children/adolescents with high body mass index and asthma to inform an interventional trial in the future. The HIPACT Site Study PI, Dr. Brian H. Wu, and HIPACT team with Research Pharmacist, Jan Vita, Regulatory-Data Coordinator, Andrea Siu, and Research Coordinator, Annette Amiotte, RN, activated the ongoing study in 2019.

ECHO ISPCTN/HIPACT Faculty Professional Development Activities

As part of the clinical trials infrastructure building for HIPACT faculty and personnel, ECHO ISPCTN Writing Committees, Working Groups and Professional Development Webinars and the ECHO Opportunities and Infrastructure Fund (OIF) Award were established to provide HIPACT faculty opportunities to improve their professional development skills.

Discussion

Through the ECHO ISPCTN, HIPACT faculty and personnel have contributed to the vision and mission of ECHO ISPCTN as a productive clinical site partner. The opportunities provided through HIPACT for faculty and personnel increased research capacity in the Departments of Pediatrics and Obstetrics/Gynecology Maternal-Fetal Medicine. It was through the ECHO ISPCTN activities that HIPACT successfully engaged junior faculty as study site PIs, ECHO ISPCTN committee members and as ECHO ISPCTN writing group members.

ISPCTN is a well-conceived network of IDeA state centers which focuses on ECHO priority areas of upper and lower airway, pre-peri-postnatal, neuro-development, obesity, and positive health. As one of the IDeA states, Hawai‘i’s underserved and rural populations benefit through the ECHO ISPCTN focus and mission which is to improve the health of underserved and rural populations of children through focused research projects. As a contributing center within the other ECHO ISPCTN clinical sites, HIPACT continues to contribute in a meaningful and proportionate effort. Building research capacity at UH JABSOM is paramount, greatly accelerated by ECHO ISPCTN’s efforts to provide professional development opportunities for junior faculty including for HIPACT faculty in the Department of Pediatrics and Obstetrics and Gynecology at JABSOM.

The ECHO ISPCTN, in three years, has evolved into a functional, productive, and scholarly network. Investigators and coordinators communicate commonly on a first name basis. Real-time teleconferences, despite time differences between network partners, are cordial and collegial. Leadership has emerged from the ranks of the partner institutions, and policies and procedures have evolved. ECHO ISPCTN has embraced not only the network partner PIs and CoPIs, but research nurse coordinators, data analysts, study site PIs, and junior investigators. Several proposals are currently ongoing or in the queue, manuscripts are being written, and some have been already published or are in press. Dozens of network partner-authored research concepts have been vetted for further consideration and two have advanced to the last stages — one of them originating from a HIPACT junior investigator. One of the proposals submitted by a HIPACT investigator in response to the ECHO OIF funding announcement was selected as the only proposal from the network moving forward for final consideration. Finally, we have been informed recently by NIH that the ECHO ISPCTN will be renewed for another five-year cycle, which we are presently actively pursuing.

The concept of the special issue was envisaged to provide opportunities for junior investigators in Hawai‘i from both academia and the community to showcase professional work focusing on pediatrics and maternal-fetal medicine in Hawai‘i. All of the manuscripts were vetted and underwent peer review by the special Editorial Board that was convened for this special edition.

Conflict of Interest

None of the authors identified any conflicts of interest.

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References

1. Introducing the Institutional Development Award (IDeA) Program. 2012; <https://loop.nigms.nih.gov/2012/05/introducing-the-institutional-development-award-idea-program-2/>.
2. Tremoulet A, Le J, Poindexter B, et al. Characterization of the population pharmacokinetics of ampicillin in neonates using an opportunistic study design. *Antimicrobial agents and chemotherapy*. Jun 2014;58(6):3013-3020.
3. Snowden JN, Akshatha A, Annett RD, et al. The ACT NOW Clinical Practice Survey: Gaps in the Care of Infants With Neonatal Opioid Withdrawal Syndrome. *Hospital pediatrics*. Aug 2019;9(8):585-592.