225th Meeting of the
NATIONAL DIABETES and DIGESTIVE and KIDNEY
DISEASES ADVISORY COUNCIL
Hybrid: Virtual | In-person (Building 31C, 6th fl., Rooms F&G)
Division of Diabetes, Endocrinology, and Metabolic Diseases
Sub-committee Meeting – Open Session
May 8, 2024

DDEMD Sub-committee Members: Dr. David D'Alessio, Dr. Debra Haire-Joshu, Ms. Davida Kruger, Ms. Neicey Johnson, Dr. Philipp Scherer, Dr. Elizabeth Seaquist

DDEMD Staff Members: Dr. Beena Akolkar, Dr. Guillermo Arreaza-Rubin, Dr. Raj Basu, Dr. Olivier Blondel, Dr. Miranda Broadney, Dr. Hank Burch, Dr. Art Castle, Dr. William Cefalu, Dr. Maureen Monaghan Center, Dr. Brad Cooke, Dr. Thomas Eggerman, Dr. Minnjuan Floyd, Dr. Rafael Gorospe, Mr. Neal Green, Dr. Jay Gupta, Dr. Carol Haft, Dr. Teresa Jones, Dr. Maren Laughlin, Dr. Jean Lawrence, Dr. Ellen Leschek, Dr. Yan Li, Dr. Hanyu (Maggie) Liang, Dr. Barbara Linder, Dr. Chris Lynch, Dr. Saul Malozowski, Mr. Louis Martey, Ms. Mansi Mehta, Mr. Michael Mensah, Mrs. Heidi Otradovec, Dr. Nishadi Rajapakse, Mr. Daniel Rothwell, Dr. Griffin Rodgers, Dr. Salvatore Sechi, Dr. Corinne Silva, Dr. Lisa Spain, Dr. Pamela Thornton, Dr. Xujing Wang, Dr. Theresa Woo, Dr. Norann Zaghloul

NIDDK/NIH Staff: Dr. Michelle Barnard, Mr. Terry Barnes, Mr. John Bellafiore, Ms. Alison Caro, Dr. John Connaughton, Ms. Dee Doherty, Ms. Nina Hall, Dr. Sophia Jeon, Dr. Jan-Michael Klapproth, Dr. Jia Nie, Mr. Paul Myers, Ms. Odessa Seng, Dr. Jaime Smith, Dr. Tori Stone, Dr. Thomas Tatham, Mr. Phi Truong, Dr. Kenneth Wilkins, Ms. Ginger Webb

Other: Dr. Paul Franks, Dr. Stephen Rick

Welcome and Approval of January 2024 Sub-committee Minutes (Dr. Cefalu)

Dr. Cefalu welcomed everyone to the DEM Sub-committee Open Session meeting and provided an overview of the agenda. Minutes from the 202401 meeting were moved for approval and approved by committee members. He then introduced and welcomed a new DEM program director Dr. Minnjuan Floyd who will have a scientific portfolio on health disparities and health equity. Dr. Cefalu also thanked Dr. Debra Haire-Joshu for her service as a Council member on the DEM subcommittee.

NIDDK Special Allocations (Dr. Cefalu)

Dr. Cefalu gave an update on the NIDDK Special Allocations (Special Diabetes Program and the Diabetes Related Research Allocation).

The Special Diabetes Program (SDP) for type 1 diabetes (T1D) consists of Trans-HHS programs that are administered by NIDDK with funding going to multiple NIH institutes and centers. It is different from regular NIH funding and supplements but does not supplant regular appropriation research. The next planning meeting under the Diabetes Mellitus Interagency Coordinating Committee for the SDP is in Fall 2024 where new initiative concepts and several on-going

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programs will be reviewed. The funding provided by SDP has supported numerous impactful programs such as TrialNet, the Environmental Determinants of Diabetes in the Young (TEDDY), the Human Islet Research Network (HIRN), the Artificial Pancreas Program, the Diabetic Foot Consortium, Closed Loop and Education for Hypoglycemia Awareness Resolution, Cardiovascular Biorepository for T1D, Understanding and Reducing Cardiovascular Disease in T1D, and most recently the Evaluating Neurocognitive Complications of T1D program. This year the SDP funding has increased for the first time since 2004 from $150 million to $160 million.

Dr. Cefalu also provided information about the new Diabetes Related Research Allocation ($10M) to support innovative projects and programs that was recently approved by Congress. Areas of emphasis are now being discussed and an update will be provided in the future. There were no questions from council members on this topic.

NIDDK DEM Council Meeting Update (Dr. Franks and Dr. Rich)

Dr. Cefalu introduced Drs. Paul Franks (Lund University, Sweden) and Stephen Rich (University of Virginia) who are the co-chairs of the Heterogeneity of Diabetes Working Group of Council (WGoC). Dr. Rich first provided a review of the WGoC's charge, rationale, and expected outcomes. He explained that the outcomes include a report that outlines the needs of the field as well as the opportunities available that can be used to stimulate research efforts and develop more discrete definitions of subtypes of T2D. Dr. Rich then went over the structure of the WGoC, breaking down further its groups and subgroups. He also noted the vast global representation in the WGoC members that consists of people from academia, foundations, industry, and other private entities. Next, Dr. Rich introduced the individual Subgroup's charge as well as identifying four cross-cutting themes across subgroups. He provided examples of the health equity and data science cross-cutting themes and explained how they were relevant across all the subgroup topics. Finally, Dr. Rich reviewed the proposed timeline for the WGoC meetings and milestones and noted that the delivery date for the report is late 2024 to early 2025.

Dr. Haire-Joshu expressed her enthusiasm for the WGoC's work and asked if subgroup draft reports will be reviewed by the steering committee along the way or only at the end. Dr. Rich answered that joint meetings amongst subgroups will happen along the way to discuss progress and that the writing of the report will be completed by a professional science writer. Dr. Cefalu added that the report's initial recommendation will be discussed at the Steering Committee meeting to be held at the ADA. At this meeting, subgroup reports will be reviewed, and the discussion will emphasize cross-cutting themes.

Diabetes in America (Dr. Lawrence)

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Dr. Cefalu introduced Dr. Lawrence who talked about the new all-digital edition of Diabetes in America (DIA), which is a descendant of the Diabetes Source Book initially published 1964 and the Diabetes Data Compiled published in 1977. She explained that DIA is a compilation and assessment of epidemiologic, public health, clinical research and clinical trials data including new analyses that highlight publicly available US national data. Thus, it is a valuable resource for researchers, policy makers, clinicians and people impacted by diabetes. DIA is available to the public free of charge and permission is not required to republish data presented including tables and figures created specifically for DIA. She remarked that the 3rd edition was published in print version in 2018 and on the National Library of Medicine's Bookshelf in 2021 which allows chapters to be indexed in PubMed providing greater visibility and access. Dr. Lawrence went over the timeline and review process of how DIA transitioned from a hardcover book to the completely digital version on Bookshelf; in 2023; 6 chapters were published in December 2023 and one more chapter in 2024 with 3 more to be published soon and 9 chapters under development. She presented examples of illustrative tables and figures included in some of the chapters. She also informed about the composition of the Steering Committee, authorship selection and the rigorous peer review process, and about the outreach activities whose current goal is to inform potential readers about the availability and location of the new DIA Chapter content. The outreach is happening through NIDDK's website, Facebook, LinkedIn, X, and Instagram along with reaching out to authors, steering committee members and scientific editors. It is also indexed in PubMed with a link to Bookshelf. The NIDDK website also has a DIA Report which is updated regularly with new content, linking to Bookshelf. The council member Ms. Davida Kruger remarked that this is a great resource, and she is excited to be able to share it and to use it. Dr. Malozowski asked who is involved in the peer review of the book and Dr. Lawrence responded that all five editors (Drs. Herman, Wexler, Lawrence, Cefalu, and Casagrande) plus 2-3 subject matter experts review the content.

Initiative Concepts:

<u>Generative Pre-trained Transformers for Diabetes (DiabetesGPT) (Dr. Wang)</u>

Dr. Cefalu introduced Dr. Wang who noted the current challenges for the effective use of the vast amount of data and literature available to better understand heterogeneity of diabetes and deliver precision medicine. Important questions posed by Dr Wang were: How to integrate and extract knowledge from Big Data and literature, and how to use that knowledge to guide studies of diabetes heterogeneity. She then expanded specifically on generative AI and large language models like GPT that have been widely adopted in biomedical research. For instance, GPT-based chatbot or ChatGPT has shown great promise and is beginning to be used in medical education, clinical practice, and patient self-management and as a research assistant. Generative AI is very useful at extracting information from unstructured text and putting it into structured forms for data analysis. Dr. Wang then commented about the foundation AI models and how useful they

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may be for supporting research of a scientist and in solving emerging problems and used to support education, research, and precision medicine. Dr. Wang closed by introducing the proposal of a pilot program called Diabetes GPT which would be utilized to build foundation AI models for diabetes heterogeneity research, by recruiting multi-disciplinary teams to conduct model development, pre-train the models with relevant data sets and validate them to solve scientific problems by fine tuning and developing use cases. These models would then be shared for further validation and application and would complement other research efforts at the basic, translational, and clinical level. There were no comments or questions from council members on this topic.

Advancing Research on the Application of Digital Health Technology to the Management of Type 2 Diabetes (Dr. Burch)

Dr. Cefalu introduced Dr. Burch who provided a summary of Advancing Research on the Application of Digital Health Technology for the Treatment of Type 2 Diabetes. He first gave a brief introduction on how we currently manage people with T2D which is far for being optimal and concluded that there is a critical need to rethink the population health approach to T2D in 2024. Then he commented about the multiple technologies now available including CGMs, remote monitoring, telehealth and embedded in smartphones mHealth and other applications that may assist patients and caregivers with management of the disease. He then proceeded to review the potential role of the virtual diabetes clinics resulting from the application of appealing multi-modality digital approaches, but with important challenges such as limited high quality data demonstrating effectiveness and little motivation by industry to support clinical trials to test them as many are already in the market.

Dr Burch provided a snapshot of the current DHT-T2D portfolio at NIDDK, including type of projects and applicant characteristics for the portfolio, and he reviewed the development of this concept based on previous input of council members. He highlighted input related with barriers to a broader application of DHT including poor uptake by health care organizations, poor interoperability between DHT and EHRs, the digital divide/equity issues, inadequate reimbursement, and limited effectiveness data. Dr. Burch ended with updates on two initiatives for DHT-T2D; the first is a DHT-T2D workshop at NIH on September 5-6, 2024, where leaders in the field will present, and the second is a 2026 initiative proposal. He presented a model of manageable blocks to support research in this field efficiently with the virtual diabetes clinical model that integrates the multimodal approach as the first block, then digital divide mitigation, the EHR integration and finally digital biomarkers heterogeneity/AI and data aggregation.

Dr. Cefalu asked if there were any questions or comments on the direction/approach proposed by Dr. Burch. Dr. Seaquist remarked that it is important to focus on how patients use/wear DHT, whether they like it or not, and how helpful it really is for T2D. Dr. Burch agreed that it is

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uncertain how helpful DHT will ultimately be, and patient engagement and use consistency are very important. He mentioned that there are gaming tactics being used to keep patients engaged as well and more data is needed to elucidate this. Ms. Kruger expressed her praise for the presentation as well and Dr. D'Alessio asked why this is only geared towards T2D and not also T1D. Dr. Burch answered that T1D is of course as important but for this initiative staff decided to focus on T2D and to focus on manageable areas with T2D. The information received will also be translatable to the T1D population. He also mentioned that the use of diabetes technologies in T1D like CGMs antecedes their use in T2D and may inform how they may be adapted to T2D. Dr. Haft asked if any companies or researchers from other countries would be attending/speaking at the DHT-T2D workshop because there might be barriers in other places to using the apps or data. Dr. Burch remarked that it is a challenge that needs to be considered. Dr. Malozowski commented that there will be communities out there that will resist/reject the use of technology for diabetes treatment/management.

Shared Decision Making and Diabetes Care (Dr. Monaghan Center)

Dr. Cefalu introduced Dr. Monaghan Center who presented on behalf of the working group on Shared Decision Making and Diabetes Care. She first defined "shared decision making" along with some gaps in evidence to support the process of shared decision making, best practices, and implementation. She then presented on measurable steps to the decision-making process: fostering choice awareness, provide information about pros/cons, discuss options-based preference and making a collaborative final decision, and research identifying a positive impact of shared decision making on patient reported outcomes (knowledge, engagement, less decisional conflict, better communication, satisfaction, reduced diabetes distress, better uptake of treatment and weight loss). She also stated information demonstrating a less evident impact on diabetes self-management, A1c and quality of life. Dr. Monaghan Center expressed the need to build the evidence base to link shared decision making and health outcomes and the importance of advancing strategies to enhance sustainability in routine care and identification of barriers and facilitators among underserved people. This concept is an area of great importance and offers an opportunity to understand how the shared decision-making processes can be implemented to improve clinical care. The area of shared decision making aligns with NIDDK priorities, as it may reduce health disparities and promote stratified medicine/personalized care for diabetes patients. Dissemination and implementation of shared decision making in care is needed and there is need of additional evidence demonstrating benefit in terms of outcomes to support wider implementation. The process needs community partnership and engagement.
The key aspects of the concept are:
1. Evaluate shared decision-making models, tools, and strategies.
2. Advance precision measurement of shared decision-making engagement.
3. Better assess impact on health outcomes.
4. Provide data on cost/cost effectiveness.

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Dr.-Seaquist expressed her enthusiasm for this concept and remarked that there is a strong need for tools that could be shared as this is a difficult process. Dr. Monaghan Center agreed that there should be an emphasis on tools, sustainability, general visibility, and understanding what can be helpful. Dr. D'Alessio commented that the VA requires the physician to mark that they discussed the glycemic target with the patient in their notes. It helps focus their efforts on the key element of why the patients are being treated and what are the goals of treatment. Ms. Kruger commented that this is not clearly implemented in her practice and health care system, and it is somewhat complicated to incorporate it among other priorities, but it is definitely important. Dr. Seaquist expressed that she liked the emphasis on all sorts of populations given the diverse perspectives that impact the caregiver and patient relationship.

DEM Workshops (Dr. Cefalu)

Dr. Cefalu introduced and presented on future workshops for DEM:

Understanding the Biological Mechanisms Underlying the Health Consequences of Racism Marginalization and Discrimination
April 17-18, 2024
Hybrid: Washington Dulles Airport Marriott/Virtual

Targeted Mass Spectrometric Assays in Diabetes and Obesity Research (TaMADOR) Annual Meeting/Workshop
May 6, 2024
Hybrid: University of Washington/Virtual

DMICC "Artificial Intelligence in Diabetes Precision Medicine: Real World Data, Real World Opportunities and Challenges"
May 30, 2024
Virtual

2024 Endocrine Society Meeting, Boston, MA
2024 ENDO NIDDK Early Investigator Symposium: Emerging Inter-Organ Communication Pathway in Diabetes and Obesity
June 2, 2024

2024 American Diabetes Association Meeting, Orlando FL
NIDDK Early Career Investigator Symposium—Leveraging Social Support to Improve Diabetes Self-Management and Health Outcomes—Innovative Methods and Interventions
June 22, 2024

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The Application of Digital Health Technology to the Management of Type 2 Diabetes
September 5-6, 2024
Hybrid: Building 31, NIH, Bethesda, MD/Virtual

2024 Annual Mid-Atlantic Diabetes and Obesity Research Symposium
September 17, 2024
Hybrid: Natcher Auditorium, NIH, Bethesda, MD/Virtual

Implementation Science and Health Equity: An NIDDK Workshop
October 10-11, 2024
Hybrid: NIH, Bethesda, MD/ Virtual

AI in Precision Medicine for Diabetes and Other Chronic Diseases: Challenges and
Opportunities in Developing Predictive Models and Biomarkers for Disease Initiation,
Progression, Prevention, and Subtypes
October 30-31, 2024
6001 Executive Blvd, Bethesda, MD

Diabetes Mellitus Interagency Coordinating Committee Meeting on Research Supported by the
Special Statutory Funding Program for Type 1 Diabetes Research
November 12, 2024
Natcher Auditorium, NIH, Bethesda, MD

Concluding Remarks (Dr. Cefalu)

Dr. Cefalu thanked the Sub-committee members and DEM staff for their presentations and
comments and asked if there were any other initiatives council members would like discussed
moving forward. Council members remarked that the initiatives presented are very cutting edge
and will provide data needed to answer some important questions.