



— CELEBRATING A —
QUARTER CENTURY
IN WOMEN'S HEALTH RESEARCH

Office of Research on Women's Health

National Institutes of Health

Advisory Committee on Research on Women's Health

42nd Meeting, September 26, 2016

Meeting Minutes

Call to Order

*Janine A. Clayton, M.D., NIH Associate Director for Women's Health
Director, Office of Research on Women's Health (ORWH), NIH*

Dr. Clayton called the meeting to order at 9:07 a.m., welcoming participants to the 42nd meeting of the NIH Advisory Committee on Research on Women's Health (ACRWH). She noted that the proceedings were open to the public and would be videocast on the NIH network. In addition, she explained that committee members could participate via teleconference with prior approval. Members participating by teleconference were David Page, M.D., Ana María López, M.D., M.P.H., FACP, Angela Kashuba, Pharm.D., and Wei-Jung Chen, Ph.D.

Dr. Clayton reviewed the confidentiality and conflict-of-interest (COI) requirements, noting that the COI recusal list includes universities and organizations in which advisory committee members have financial interests. She reminded participants to sign and return the forms before the meeting ended.

The amended minutes from the last meeting were approved unanimously by voice vote. They will be posted to the NIH website. Upcoming advisory committee meetings are scheduled for April 4 and September 13, 2017. Committee members took turns introducing themselves. The new Deputy Director of ORWH, Elizabeth Spencer, RN, joined the meeting.

Introduction of New Members

Dr. Clayton

Dr. Clayton introduced new members to the committee: Geert de Vries, Ph.D., Dr. Chen, and Dr. López.

Dr. de Vries is a Professor and Director of the Neuroscience Institute at Georgia State University (GSU). Dr. de Vries joined GSU in 2012, leaving a longstanding position at the University of Massachusetts Amherst, where he directed the Center for Neuroendocrine Studies and an NIH-funded training program in neuroendocrinology. He is past president of the Organization for the Study of Sex Differences, as well as past president of the Society for Behavioral Neuroendocrinology. Ever since discovering the sexually dimorphic nature of vasopressin innervation of the brain as a graduate student, Dr. de Vries has studied the development and function of sex differences in the brain. This culminated in proposing the overarching idea that such differences both cause and prevent sex differences in physiology and behavior. Dr. de Vries also demonstrated that differences in vasopressin innervation depend on gonadal hormones as well as on direct sex chromosomal effects. Finally, his lab has traced the origin of vasopressin innervation in the rodent brain.

Dr. Chen is a professor, Associate Dean for Faculty Affairs and Curriculum Management, and Assistant Dean for Student Affairs at Texas A&M University. In addition, he participates in graduate training as a member of the faculty in the Interdisciplinary Program in Neuroscience. Dr. Chen received his Ph.D. in psychobiology/neuroscience from the State University of New York in 1992 and completed post-doctoral training in neuroanatomy at the University of Iowa. His research focuses on the effects of substance abuse (e.g., alcohol, cocaine, nicotine) on the developing brain, polydrug interactions on brain and cognitive developments, fetal alcohol syndrome, and use of three-dimensional stereological cell-counting techniques, immunohistochemistry, radioimmunoassay, high-performance liquid chromatography, gas chromatography, and behavioral assessments in animal models such as rodent, ovine, and zebrafish.

Dr. López is Associate Vice President for Health Equity and Inclusion at the University of Utah Health Sciences, Associate Director for Collaboration and Engagement at the Utah Center for Clinical & Translational Science, Director of Cancer Health Equity at the Huntsman Cancer Institute, and Professor of Medicine at the University of Utah School of Medicine. She is the founding Medical Director of the Arizona Telemedicine Program. Dr. López is a medical oncologist, researcher, and educator who has dedicated her work to the amelioration of health care disparities. She has a longstanding commitment to underserved populations and is dedicated to increasing access to high-quality medical specialty care to all communities. Her academic and clinical interests are focused on cancer prevention, specifically on women's malignancies and in the development of outreach programs.

ORWH Director's Report

Dr. Clayton

New NIH Institute and Center (IC) Directors and NIH Senior Officials

Dr. Clayton announced that four new IC directors have been appointed: Patricia Brennan, Ph.D., RN, as Director of the National Library of Medicine; Diana Bianchi, M.D., as Director of the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD); Joshua Gordon, M.D., Ph.D., as Director of the National Institute of Mental Health (NIMH); and Eliseo Pérez-Stable, M.D., as Director of the National Institute on Minority Health and Health Disparities.

Matthew Gillman, M.D., has been appointed Program Director of the Environmental influences on Child Health Outcomes (ECHO) Program; Maureen Goodenow, Ph.D., is the new Director of the Office of AIDS Research (OAR); P. Kay Lund, Ph.D., is Director of the new Division of Biomedical Research Workforce Programs at the Office of Extramural Research (OER); and Eric Dishman has been appointed Director of the Precision Medicine Initiative® (PMI).

Sex as a Biological Variable (SABV)

Dr. Clayton displayed a quotation from Stephen Covey: “Begin with the end in mind.” This is the goal in applying “design thinking,” which first defines the problem and then implements the solutions that take into consideration the needs of the user demographic. In this way, design thinking suits the mission of the NIH in “turning discovery into health.” Dr. Clayton reviewed the ORWH “Beyond Inclusion” framework on sex/gender influences on health and disease. In order to achieve a goal of healthy women all aspects of research, including preclinical studies, translational research, and clinical trials, must work in concert to address sex differences. Studies must include appropriate analyses of data on sex differences; the information must also be disseminated in order to inform policy and health care.

The [SABV policy](#) became effective January 25, 2016. The policy states, “NIH expects that sex as a biological variable will be factored into research design, analyses, and reporting in vertebrate animal and human studies.” Journals have also set new sex and gender guidelines. The European Association of Science Editors established the Sex and Gender Equity in Research (SAGER) guidelines in May 2016, with principles such as reporting data by sex regardless of the outcome (positive or negative) and providing a justification if sex differences are not reported. The potential implications of sex and gender for a study should also be discussed.

Dr. Clayton noted that policy implementation is a team effort. The first round of review of SABV 2.0 is completed. Town hall meetings are ongoing to disseminate the policy and guidance resources among NIH scientific review officers and program staff. Training materials for NIH scientific staff and peer reviewers are also available, including updated frequently asked

questions (FAQs). A trans-NIH SABV research working group has been established; the updated SABV policy will also include evaluation of the rigor and reproducibility of SABV results.

The SABV policy includes emphasis on rigorous approaches to ensure robust and unbiased results. Briefly, Dr. Clayton reviewed the research strategy approach for both applicants, who must explain how the relevant sex variables are incorporated into their study design, and reviewers, who must assess whether the plans are adequate. The Center for Scientific Review and OER have created a [detailed framework](#) for reviewer guidance. Dr. Clayton also showed an example of an updated FAQ on consideration of sex in use of primary cells and tissue explants; 13 such queries have been [addressed](#).

Briefly, Dr. Clayton reviewed the status of the SABV roadshow talks across NIH, half of which have now been completed; the hope is to complete them all by the end of the calendar year. She also reviewed the feedback ORWH has received about the roadshow, which was generally positive. Common themes have included clarifying issues related to study power, providing guidance on disentangling sex and gender, providing examples, explaining how the policy will be evaluated, and requesting a one-page summary of the policy for ease of use. Currently, OER has available a one-page document on rigor and reproducibility for SABV, but a single document about the policy is being created.

Dr. Clayton reviewed several examples of SABV in action through NIH funding opportunities for fiscal year (FY) 2016 issued by the National Institute of General Medical Sciences (NIGMS), the Office of Behavioral and Social Sciences Research (OBSSR), and ORWH.

Other ORWH Activities

On June 6, 2016, NIH held a [conference](#) to support women in biomedical research careers. The meeting was well attended, with 550 registrants and 364 online views. *Academic Medicine* published a series of articles in a special issue about the role that the government plays in the advancement of women in academic medicine. Social media were also used successfully during this event, using the hashtag [#WomenInScience](#), through which women shared their wisdom with junior female scientists.

ORWH has a new website launched in September 2016. It is mobile friendly and conforms to plain language standards. Dr. Clayton provided an example of the NIH Outreach Toolkit from the new site. She also showed an educational outreach video about sickle cell disease from a participant perspective that addresses why the person chose to participate in clinical research. This video is part of an eight-part series of women in clinical trials.

ORWH is also working with the Food and Drug Administration (FDA) in the [Diverse Women in Clinical Trials Campaign](#) to encourage the participation of women in clinical trials. In addition, the PMI will address sex and gender through its goals to create a national cohort for disease

treatment and prevention. Sex and gender considerations are integral in the study of genetics, lifestyle, and environment, all of which are to be studied in the PMI.

Dr. Clayton showed a graph depicting the chance of women from different countries surviving to age 50; within the last decade, this number has been significantly lower for U.S. women compared to women in other high-income countries. Importantly, it is not clear why this discrepancy exists. The PMI and SABV are critical to understanding the status of women's health in the United States. The [Workshop on Raising the Bar—The Health of Women in America: A National Perspective on Women's Health](#) workshop was held to consider factors influencing differences in women's health outcomes, research on factors influencing differences in morbidity and mortality, and future directions. This workshop's report of gender as a social determinant of health was published in April 2016; ORWH held a working group related to the report in August 2016.

Program Review

Dr. Clayton provided an update on the ORWH portfolio in FY 2016: 28 percent of ORWH research funding is dedicated to the Specialized Centers of Research (SCOR) on Sex Differences program, 12 percent to the Research Scholar Grants (RSG) program, 15 percent to administrative supplements, 25 percent to the Building Interdisciplinary Research Centers in Women's Health (BIRCWH) program, and 20 percent to co-funded programs. ORWH co-funds efforts with almost all NIH ICs, although it works more frequently with some, including NICHD. Twenty million dollars of ORWH funds are invested in administrative supplements for existing grants to add study of sex and gender differences; these funds are distributed across NIH ICs. The majority of these supplements add a new sex to single-sex research studies; others add subjects to existing studies to increase the power to assess sex difference or allow analysis of existing samples or datasets. The majority of these supplements propose preclinical research.

Dr. Clayton also provided a review of R56 funding in FY 2016. ORWH has partnerships with OAR and the Office of Disease Prevention (ODP) to fund 14 applications from 10 ICs, awarding approximately \$4 million for a variety of research projects on topics such as marijuana use and pregnancy, helping behavior in older adults, and phthalates and ovarian toxicity.

There are 11 funded [SCORs](#) that involve interdisciplinary collaborations to bridge basic and clinical research on factors underlying women's health. The program is currently under evaluation. Dr. Clayton provided some examples of recent SCOR-funded projects in the fields of neurocognition, addiction, reproductive organs/female urinary tract, and musculoskeletal studies.

The BIRCWH program has 10 funded awards. A new request for applications was released in the summer of 2016, with a deadline of October 6. For summer 2017, up to 10 awards, with \$5

million direct costs from ORWH and IC co-sponsorship, are planned. Dr. Clayton reviewed the promise of interdisciplinary research and the definition to be used for BIRCWH: “a mode of research that *integrates* information, data, techniques, tools, perspectives, concepts, and/or theories from two or more disciplines or bodies of specialized knowledge to advance fundamental understanding or to solve problems whose solutions are beyond the scope of a single discipline or area of research practice.” Interdisciplinary science teams work to advance fundamental understanding and solve problems that those from a single discipline could not.

ORWH has also invested \$3.4 million over three years in the Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative, which Dr. Clayton noted had adopted the SABV language early in its processes.

Dr. Clayton ended her presentation by thanking the staff at ORWH for hard work forging and enhancing relationships.

Discussion

Carmen Green, M.D., complimented the amount of work accomplished by the relatively small staff at ORWH. She urged empowering deputies to discuss SABV with other organizations.

Inclusion in NIH Clinical Research: An Update

Meredith Temple O'Connor, Ph.D., Senior Scientific Advisor to the NIH Deputy Director for Extramural Research, OER, NIH

Inclusion Data

Dr. O'Connor began her presentation by discussing inclusion data, noting that 2016 was an off year for reporting but that this discussion would be a snapshot for what will be available in spring 2017.

The inclusion re-engineering project began in 2011 with a new data system and functionality that emphasized scientific oversight rather than data entry and counting. It streamlines data entry, reduces staff workload through tools for staff to monitor progress and better integration with award workflow, and enhances data accuracy, ownership, and accountability.

The challenges and caveats of the data analysis include the data system transition, form changes for completing applications and progress reports, simplification of internal procedures, and change management for staff and investigators.

The system distinguishes prospective studies from existing datasets. Dr. O'Connor provided a specific definition of an existing dataset for the purposes of the inclusion policy; in general, studies in the dataset will meet the NIH definition for clinical research with a prospective plan

to analyze existing data and/or derive data from an existing resource, with no ongoing or future contact with participants anticipated.

FY 2015 Inclusion Data

Dr. O'Connor reviewed inclusion data record information from 2011 to 2015 for clinical research and phase III clinical trials; the transition in data tracking took place between 2014 and 2015. These data track the number of individual data records, the number with and without enrollment, and enrollment by sex for studies within the United States. Some of the numbers dropped between 2014 and 2015, but it is not clear that this is due to the transition, and Dr. O'Connor did not see any concerns with the numbers recorded to date. The overall total for clinical research was larger in 2015 than in previous years; the total number went from 28 million in 2014 to more than 99 million in 2015. Existing dataset analysis is available for 2015; more than 77 million were counted, but there is one large dataset for which the sex, gender, and racial/ethnic information of participants is unknown (an insurance review involving information from more than 38 million participants). For the trials with the remaining participants, excluding sex-specific trials, 56.8 percent of enrollees were women and 43.2 percent were men. Dr. O'Connor stressed that these numbers are from an interim report and may be affected by the data system transition.

GAO Report Update

Dr. O'Connor reviewed the status of recommendations from a recent Government Accountability Office (GAO) report. Recommendation 3, which ensures that program officers have a means of recording their monitoring of awardees' plans for and progress in conducting analysis of potential sex differences, has been completed. The remaining four recommendations are in progress:

- **Recommendation 1:** Make IC-level enrollment data readily available through public means, such as through its biennial report to Congress on the inclusion of women in research or through its website. Dr. O'Connor noted that the summary data have always been accessible online but that the information is now included on the OER website with other types of reports, with a web page dedicated to inclusion.
- **Recommendation 2:** Examine approaches for aggregating more detailed enrollment data at the disease and condition level, and report on the status of this examination to key stakeholders and through its regular biennial report to Congress on the inclusion of women in research. Dr. O'Connor said that now that data are in the new system they have started to consider the framework needed for this recommendation.
- **Recommendation 4:** On a regular basis, systematically collect and analyze summary data regarding awardees' plans for analysis of potential sex differences, such as the proportion of trials being conducted that intend to analyze differences in outcomes for men and women. Dr. O'Connor discussed recommendations 4 and 5 together, noting

that they have begun to address how information from program officers is addressed. A better understanding of the data is needed to understand the best methods for analysis.

- **Recommendation 5:** Report on this summary data analysis in the regular biennial report to Congress on the inclusion of women in research.

Currently, changes are taking place with respect to the oversight of clinical trials; Dr. O'Connor hoped that the new data system for inclusion could be rolled in with those proposed changes.

Upcoming events for OER include the biennial inclusion report, due in 2017; the continuing implementation of the GAO recommendations; and continued examination of different approaches to analyzing inclusion data.

Discussion

The committee discussed the large study that lacked data on sex, gender, and ethnicity; it was a child health study that used insurance records to obtain data. It was verified as meeting the criteria of clinical research. The investigators stated that they were unable to obtain information on sex. The governance group struggled with how to report this study but decided to include it in the data and adjust analyses accordingly.

Carolyn Mazure, Ph.D., asked whether recommendation 2 was designed to determine where to focus programmatic efforts. She noted that some areas of research, such as some cancers, might affect more men than women or vice versa. Dr. O'Connor noted that under- or over-enrollment of a particular sex would be found at the study level, which should be addressed by investigators. Recommendation 2 was crafted because GAO was concerned that OER lacked clarity on gaps in particular areas. Research, Condition, and Disease categorization data are one way to track that information. Dr. Clayton noted that once the data are available, ICs will be able to better understand their research portfolios and priorities. Ideally, the data will help to address important research questions.

Dr. Mazure asked whether the data on the inclusion of women in clinical trials were misleadingly promising. Dr. O'Connor acknowledged that they struggle with interpretation of aggregated datasets. These data include recruitment but not retention or analysis. NIH also has less influence on the management of industry-sponsored studies. Outcome measures also can affect recruitment. Teresa Woodruff, Ph.D., recommended random sampling of clinical trials to track them to publication. Less than a third of NIH-funded publications have sex-specific results. Also, the law is silent on how to define male and female. Much can depend on how protocols are designed and how information is collected.

Dr. Green said that good-quality science needs to include information about gender, race, and ethnicity and questioned whether the NIH should continue to support studies that cannot collect that information, such as the large insurance study that was detected in the inclusion

data progress report. Dr. O'Connor noted that the study in question complied with policy, but peer review is needed to scrutinize whether the investigators are collecting all of the necessary information.

Summary of ORWH Career Development Activities

Jennifer Plank-Bazinet, Ph.D., Research Program Officer, ORWH, NIH

ORWH conducted a meeting on women's health career development programs in April 2016. The Conference on Evidence-Based Innovations to Support Women in Biomedical Research Careers was held in June 2016 prior to the annual BIRCWH and SCOR meetings to discuss recruitment, retention, and advancement of women in biomedical careers through a variety of programs.

The first session of presentations included a presentation from Reshma Jagsi, M.D., D.Phil., on a longitudinal study of 2010 K08 and K23 recipients with a follow-up in 2014. Key findings from the study were that women were more likely to have patient-focused R23 awards, while men had more science-focused K08 awards; women disproportionately reported lack of access to grants administrators and statisticians; the majority of men and women reported a strong preference for work-life balance, with slightly more women reporting this preference; and men were more likely to considering leaving the K-awarding institution for a better opportunity, while women were more likely to leave for a partner's job. It appears that factors affecting women's careers are often difficult to measure.

The inaugural Ruth L. Kirschstein Memorial Lecture was given by Dr. Shirley Malcom, a friend of Dr. Kirschstein. Dr. Plank-Bazinet, Ph.D., quoted Dr. Malcom: "There will be demographic shifts, with non-Hispanic whites becoming a minority by 2044. What does it mean to have intervention programs for the majority?" The last session of the conference focused on the intersection of gender and race/ethnicity. Emorcia Hill, Ph.D., reported that co-authorship was higher for men and that networking was lowest for minorities. The size of the network affects one's career trajectory. Differences in mentoring were also seen by race or sex/gender, and mentoring programs should be tailored to the individual to ensure success.

The Workshop on Advancing Women in Independent Positions was held in July 2016. This was largely an information-sharing event to provide attendees with information to assist with the advancement of women at their own institutions. The workshop included a career-building session, implicit-bias training, the representation of women in leadership positions, the inclusion of women, and accountability and transparency.

Academic Medicine released a theme issue on gender diversity in academic medicine careers in August 2016. Many of the papers comprising this issue are from the Research Partnership on Women in Biomedical Careers, a group that is supported by ORWH.

Discussion

Judy Regensteiner, Ph.D., requested a list of upcoming events; Dr. Plank-Bazinet stated that she can add Dr. Regensteiner to the Advancements and Insights listserv that provides those types of announcements.

Zika Virus: A Pandemic in Progress

Anthony Fauci, M.D., Director, National Institute of Allergy and Infectious Diseases (NIAID), NIH

Background on the Zika Virus

Dr. Fauci began his presentation by acknowledging that this Zika virus outbreak is unique because it is a pandemic in progress; public health officials are attempting countermeasures while the consequences of the outbreak are unfolding. The circumstances have changed quickly. In January 2016, Dr. Fauci co-authored an article in the *New England Journal of Medicine* noting that Zika is an arbovirus, a family of viruses well known to scientists and the Americas. Other arboviral diseases have been tracked in the Americas, including dengue fever in the 1990s, West Nile virus in 1999, and chikungunya virus in 2013.

Zika virus is a single-stranded, enveloped RNA virus of the family *Flaviviridae*. It is closely related to the dengue, yellow fever, Japanese encephalitis, and West Nile viruses; these are viruses with which public health professionals have experience and against which creation of vaccines has a high degree of success. Zika virus was first isolated from a monkey in the Zika Forest in Uganda in 1947; the first human infection was detected in 1952. It is possible that the Zika virus was present in Africa for much longer but was not detected because of the other diseases present in the area or due to human background immunity to the virus. Zika virus spread across the globe from 2007 to 2014, with documented cases first detected in the Federated States of Micronesia and later in French Polynesia. Zika virus was then detected in Brazil in 2015. Dr. Fauci referred to Zika's presence in Brazil as "a perfect storm," because the country has highly populated areas, virtually none of the people have had previous exposure and thus immunity to the virus, and the mosquitoes that carry Zika are prevalent; while many areas of Brazil lack access to good health care, the health care system is good enough to allow proper detection.

Four of five people infected with Zika exhibit no symptoms; the remainder exhibit flu-like symptoms. Viral incubation occurs for 3 to 12 days, and any symptoms occur for a subsequent 2 to 7 days. Zika virus is unique as a mosquito-borne infection that can be sexually transmitted and can cause congenital malformations during pregnancy. Zika virus is transmitted through mosquito bites, intrauterine and perinatal transmission, sexual transmission, and blood transfusion. Two species of mosquitoes are known to carry the virus: *Aedes aegypti* and *Aedes albopictus*. Both are found in the United States, predominantly in the southern regions; A.

aegypti bites only humans. Intrauterine transmission can result in microcephaly and other developmental abnormalities. Male-to-female, male-to-male, and female-to-male sexual transmission has been documented. Fragments of the virus can be detected in sperm for weeks post-infection; infectious virus is present in sperm up to 24 days post-infection. Twelve countries, including the United States, have reported sexual transmission. Women are more likely to get Zika virus than men of the same age. Dr. Fauci stressed that sexual activity is a significant mode of viral transmission. Lastly, the FDA has determined that all donated blood and blood components will be tested for Zika virus in order to avoid transmission via blood transfusions. Outlier cases of infection include a lab worker and a caregiver who has appeared to contract the virus from their patient; universal precautions are used for all aspects related to Zika treatment.

The Current Outbreak

The current outbreak includes 58 countries and territories, 48 of which are in the Americas and the Caribbean. Travel-related Zika is virtually worldwide but is distinct from Zika in active areas of transmission. Approximately 300 million people in the Americas live in areas environmentally suitable for Zika virus transmission; approximately 5.4 million births occur in these areas per year. Many of these areas do not experience a cold winter, which would slow transmission by interrupting the mosquito lifecycle.

The number of microcephaly cases in Brazil has risen exponentially with the Zika outbreak. Prior to 2015, there were approximately 150 cases per year; in 2015, there were almost 5,000. Association studies have confirmed that Zika infection is the cause of the increase in microcephaly in neonates. Other neonatal manifestations of congenital Zika infection include intracerebral calcifications, hearing loss, vision abnormalities, lissencephaly, pachygyria, ventricular enlargement, arthrogryposis, and muscular atrophy. An association between Zika infection and Guillain-Barré Syndrome has also been found, predominantly in elderly individuals.

In January 2016, there were 18 cases of Zika infection; by September, there were more than 19,000; 1 percent of the population is infected every week. The Department of Health and Human Services (HHS) declared a public health emergency in August 2016 in response to the outbreak. For other areas of the United States there is potential for travel-related infections because approximately 216 million passengers journey to the United States from areas with local Zika virus transmission. In all, 3,358 travel-related cases have been confirmed in the United States, and that number is likely an underestimate. A total of 749 pregnancies in the United States have been affected by Zika; 20 infants were born with birth defects, and five pregnancies were lost. Dr. Fauci stated that more congenital abnormalities in U.S. births as a

result of Zika infection are likely. The number of local cases of Zika infection continues to rise; in September 2016 it had risen to 95.

Strategies for Prevention

Briefly, Dr. Fauci reviewed the methods used to control Zika transmission, which focuses on mosquito control through larvicides and insecticides, removal of standing water, screens and air conditioning, proper clothing, and mosquito repellent with DEET.

NIAID is working on Zika countermeasures via research and development of therapeutics, vector control, vaccines, diagnostics, clinical research, genomics, basic research, and the expansion of research capacity. The current focus has been on diagnostics and vaccines. The Zika in Infancy and Pregnancy (ZIP) Study, co-sponsored by NIH and the Oswaldo Cruz Foundation in Brazil, is a prospective study of 10,000 pregnant women designed to follow the incidence of Zika infection. Infants will be followed through at least one year of age. Basic research on Zika virus includes a drug screening that identified small-molecule inhibitors; two classes of compounds were found to be effective against Zika virus in vitro. Multiple vaccine platforms appear to be effective against Zika; while they require scale-up and manufacture, the creation of a Zika vaccine is not as challenging as the creation of a vaccine for a virus like HIV. A total of five vaccines are in development; two will begin clinical trials this year, and one will have initial results by the end of the year. Continuation of these studies is important because the spread of Zika is a global concern and a perpetual challenge. Zika is now being tracked in Singapore and Malaysia; it is not yet clear that these populations have background immunity.

Discussion

Dr. Mazure asked whether there were any predictions about the spread of Zika virus. Dr. Fauci noted that entry into autumn and winter is an advantage in the United States and that he did not foresee a sustainable, diffuse outbreak. He noted that sexual transmission adds complexity to containment.

Dr. Woodruff asked whether any of the vaccine trials will include pregnant women. Dr. Fauci said that it is preferable to prevent infection prior to pregnancy, so the ideal population for the vaccine is people of childbearing age. The highest-priority populations are in countries with endemic infection.

Briefly, Dr. Fauci reviewed the Zika research funding status. To date, Congress has not authorized any funds. At a recent meeting, congressional leaders assured Dr. Fauci that funding would be included in the next continuing resolution. In the early months, money was taken from tuberculosis and flu funding. Then the remaining balances from Ebola funding were used. In August, the HHS Secretary exercised the 1 percent transfer authority to take funds from other ICs in order to allow Zika research to continue.

Rachel Jones, Ph.D., RN, expressed hope that attention to Zika brings attention to cytomegalovirus (CMV) infections in children and newborns. Dr. Fauci responded that the awareness surrounding microcephaly and Zika infection may lead to more public awareness about the pregnancy outcomes of other infections.

Kimberly Gregory, M.D., M.P.H., asked whether the border between Texas and Mexico is a potential reservoir for Zika infection. Dr. Fauci did not believe that there would be a sustained outbreak in that region, because it lacks the wet areas required for mosquito breeding. Puerto Rico's unwillingness to use pesticides and insecticides has unfortunately contributed to the size of the outbreak.

Chloe Bird, Ph.D., asked whether there are disaggregated data to track the unique attributes of the spread of Zika. Dr. Fauci said that some of the current studies will not provide data for two to three years. Dr. Clayton noted that ORWH recently co-hosted a Zika workshop with NICHD.

NIH Legislative Update

Juliana Blome, Ph.D., M.P.H., Associate Director for Science Policy, Planning, and Analysis, ORWH, NIH

Dr. Blome explained that the current climate is focused on the upcoming presidential election and that people are awaiting the continuing resolution to determine the budget for the upcoming fiscal year. A vote was scheduled for September 26 for funding through December 9, 2016. Another bill of interest is the Federal Funding Accountability for Sexual Harassers Act, in which federal agencies must be notified when a principal investigator discriminates based on sex; a brief description of the bill is posted on the [website of Congresswoman Jackie Speier](#) of California. This bill will have to be reintroduced next session. Dr. Blome did not anticipate that the 21st Century Cures bill would pass prior to the election, but it could be included in an omnibus during the lame-duck session.

Discussion

In response to questioning, Dr. Blome said that 21st Century Cures was delayed mainly because of the inclusion of mandatory funding for NIH; it must be determined who will pay the funding and how.

The Sexual and Gender Minority Research Office: Overview and Sexual and Gender Minority (SGM) Research Activities at NIH

Karen Parker, Ph.D., M.S.W., Director, SGM Research Office, NIH

SGM Research at NIH: Terminology and Context

The position of Director of SGM Research is new, and Dr. Parker began her appointment in June 2016. The office was established as the result of an NIH-commissioned Institute of Medicine (IOM) report. *Sexual and gender minority* is an umbrella term that encompasses lesbian, gay, bisexual, and transgender (LGBT) populations as well as those whose sexual orientations, gender identities and expressions, or reproductive developments vary from traditional, societal, cultural, or physiological norms. Sex and gender are differentiated by constructs in a way that is still being defined at the NIH. Constructs to consider include sexual orientation, sexual attraction, sexual behavior, gender identity, gender expression, and household relationships.

Disorders or differences in sex development (DSD) refers to individuals with atypical reproductive development, which results in chromosomal, gonadal, and/or anatomic sex that varies from typical development and that commonly presents at birth. While considered under the umbrella of SGMs, there is controversy among the DSD community regarding whether to be included in LGBTQ considerations.

The Health of SGM Populations

Dr. Parker reviewed the health of SGM populations, which experience higher levels of violence and high-risk behaviors. Of the homeless youth population, 20 percent to 40 percent are SGMs. SGMs living in states that ban same-sex marriage have high rates of mood disorders, generalized anxiety disorder, alcohol abuse, and psychiatric comorbidity. SGM students also routinely experience more victimization in schools. SGMs attempt suicide at more than twice the rate of their heterosexual peers. There are higher rates of HIV/AIDS among men who have sex with men, and African-American and Latino men are disproportionately affected. Lesbians also have significantly higher 5-year and lifetime risks for developing breast cancer compared to heterosexual women.

Dr. Parker noted that health disparities, including those involving sexual orientation and gender identity, are rooted in historical constructs and that heterosexual and cisgender people, institutions, and systems often function in a way that stigmatizes SGMs, which affects the ability to meet their health needs.

Institute of Medicine (IOM) Report on SGMs and NIH Response

In 2009, NIH commissioned an IOM report titled *The Health of Lesbian, Gay, Bisexual, and Transgender (LGBT) People: Building a Foundation for Better Understanding*. This report

includes an extensive literature review of existing research on LGBT health. The report recommended that HHS collect sexual orientation and gender identity data in federally funded surveys and in electronic health records (EHRs). It also recommended that NIH implement a research agenda on this topic, develop standardized gender identity measures, support methodological research related to LGBT health, create a comprehensive research training approach to strengthen LGBT health, and encourage grant applicants to explicitly address the inclusion or exclusion of SGMs in their studies. In 2011, IOM recommended a research agenda led by the NIH that includes demographic research, social influences on the lives of LGBT people, inequities in health care, intervention research, and transgender-specific health needs.

The NIH has responded to the IOM report through a series of actions. In 2011, the NIH formed the LGBT Research Coordinating Committee (RCC) to address the report recommendations. In 2013, the LGBTI RCC was established as a standing forum for facilitating, developing, and coordinating activities related to LGBTI health research across NIH and with other federal agencies. In 2012 and 2014 the NIH performed portfolio analyses of NIH-funded SGM health research. In 2015 the name of the RCC was changed to “the Sexual and Gender Minority Research Coordinating Committee.” The SGM RCC “provides a trans-NIH forum for discussing the diverse health research issues of SGM communities and serves as a catalyst for developing additional research and research training initiatives in this area.”

FY 2015 NIH SGM Portfolio Analysis

Dr. Parker reported the findings of the FY 2015 portfolio analysis. NIAID has the most funding invested in SGM activities, with more than \$60 million of a total of approximately \$161 million. The National Institute on Drug Abuse (NIDA), NIMH, and NICHD also invest more than \$10 million in SGM-related research. 73 percent of the funds are allocated to HIV/AIDS research; Dr. Parker acknowledged that there are many other SGM-related health issues to explore. NIMH leads other ICs in the number of projects related to SGM with a total of 77; other Institutes with more than 20 projects include NIDA, NIAID, and NICHD. After HIV/AIDS, the most funded issues are mental health and substance abuse. Dr. Parker noted that smoking, suicide, and depression all require more emphasis. She would also prefer to see a more equal distribution of SGM activity across the NIH because three ICs account for 71 percent of the SGM funding.

Development of the NIH SGM Strategic Plan

The SGM RRC is working to develop an SGM Strategic Plan for the NIH. After input from various stakeholders through community listening sessions, a plan was developed that was finalized in September 2015 and released for public comment the following month. The plan identified four goal areas and 11 objectives to serve as a blueprint for the SGM Research Office. The goals are as follows:

- Goal 1: Expand the knowledge base of SGM health and well-being through NIH-supported research.
- Goal 2: Remove barriers to planning, conducting, and reporting NIH-supported research about SGM health and well-being.
- Goal 3: Strengthen the community of researchers and scholars who conduct research relevant to SGM health and well-being. This goal is to be addressed by the NIH Council of Councils this month.
- Goal 4: Evaluate progress on advancing SGM research. Dr. Parker noted that this goal should consider broad concepts beyond research.

Dr. Parker provided the membership list of the SGM Research Working Group.

Development of the SGM Research Office

The SGM Research Office is housed under the Office of the Director at the NIH. The SGM Research Office was established in late 2015 in order to coordinate SGM health research across the NIH, represent the NIH at conferences and events on trans-NIH activities focused on SGM research, coordinate and convene conferences and workshops to inform priority setting and research activities, collaborate with NIH ICs on development of SGM health research reports, manage information dissemination related to SGM research, and work to leverage resources and/or develop initiatives to support SGM health research.

Next steps for the SGM Research Office include examining new opportunities for research/other collaborations, implementing the goals of the NIH SGM Strategic Plan, tracking Strategic Plan progress, exploring opportunities for harmonizing research efforts across the Department, and working with the NIH Clinical Center on SGM-friendly policies.

Discussion

Dr. Jones noted that, when collecting gathering HIV data, her research team now collects data on the transgender population, but the number of transgender individuals in their studies is too small for a separate analysis. She asked whether there is any effort to allow researchers to aggregate data on these populations to allow in-depth analysis. Dr. Parker acknowledged that there has been discussion of how to manage research on small populations. The NIH is working on a document to standardize measures through multiple constructs that would allow data to be coalesced and analyzed. More research is required, but some survey questions have been identified as source material for dissemination. OBSSR is also considering a Request for Application (RFA) on this topic.

Dr. Bird noted that the hormone profiles of transgender individuals differ from those of cisgender individuals. She also expressed concern at the lack of studies of cardiovascular disease in the transgender population. Dr. Parker agreed, noting that the ICs must be educated

on this point to emphasize research on SGMs. She also noted it is important to understand the patient–provider relationship with SGMs.

C. Noel Bairey Merz, M.D., noted that a recent protocol was triaged in a proposal study section because they had not tracked menstrual status in transgender individuals with intact testicles. Education is needed for study sections to understand how to evaluate studies that involve transgender individuals.

Dr. Gregory asked whether the mandates to include SGM are funded within the existing budget. Dr. Parker explained that she was the sole staff member in the SGM Research Office, which is housed with the NIH Deputy Director’s office; one part-time contract position supports her. Dr. Gregory has researched how women identify themselves; the questions can be sensitive to different populations. Dr. Parker noted that research indicates a low non-response rate and that participants are more likely to skip a question about income. She acknowledged that adding a gender identity question to EHR data can cause anxiety in staff and said that the NIH is exploring training opportunities.

Mary Palmer, Ph.D., RN, noted that SGM populations will eventually intersect with the long-term care community. Dr. Parker stated that HHS has implemented a rule that federal funding is tied to collection of these data as a first step and that the current administration has moved quickly on SGM-related issues.

Unequal Burdens and Unheard Voices: The Role of Sociodemographic Characteristics on the Pain Care Experience

Carmen Green, M.D., Professor of Anesthesiology, Obstetrics and Gynecology, and Health Management and Policy, School of Medicine and School of Public Health, University of Michigan; Faculty Associate, Institute for Social Research and Institute for Health Policy and Innovation, University of Michigan

Health Disparities and Race and Sex

Dr. Green began by reviewing her disclosures and showing some of her black-and-white photography, noting that the shades of gray provide parallels to the narrative for pain and disparities in pain care.

Dr. Green showed a graph depicting the mortality rates in the United States by age and race/ethnicity. Across all ages, African Americans have a higher rate of mortality, followed by American Indians, whites, Latinos, and Asians. Although the mortality among Asians of all ages appeared consistent, Dr. Green noted that heterogeneity among Asians was not adequately represented in this graph. Population growth by race indicates that the percentage of whites in the U.S. population is falling; by 2050, whites will no longer be the majority. Currently, fewer

white babies are being born in the United States than non-white babies. Dr. Green reviewed a graph that considered gender and aging, noting that aging is predominantly a women's issue, particularly among people 85 years of age or older.

Race and sex affect physician treatment recommendations. For example, some studies have found that race and sex affect whether patients undergo cardiac catheterization when admitted to a hospital. African Americans in particular are more likely to miss work due to pain. More problems arise with age, in part due to obesity and other comorbid conditions.

Health Disparities Related to Pain Management

IOM has reported on health disparities but has only recently addressed the challenge of pain management in the context of health disparities. Dr. Green showed a quotation from Ingham and Foley, 1998: "Among the committee's more disturbing findings is the frequency with which patients experience pain. Sadly, many patients fail to receive state-of-the-art pain relief." Factors involved in this failure include access to coordinated and high-quality care, cultural and attitudinal differences, bias, lack of language proficiency, and knowledge gaps or variability in decision-making. The cost of health inequities is approximately \$1.24 trillion; \$229.4 billion could be saved by eliminating these disparities. If no attempt is made to eliminate disparities, the cost will continue to increase.

The IOM report *Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research* found that more than 100 million Americans suffer chronic pain, which is associated with sleep deprivation, anxiety, and hopelessness. The cost of chronic pain exceeds costs for cardiovascular disease, diabetes, or cancer. The consequences of chronic pain are physical, psychological, social, and economic. People who serve as caregivers to affected family members experience additional stress.

Discussions about pain do not tend to focus on differences by race/ethnicity or gender. Women have a higher prevalence of chronic pain conditions and are more likely to report pain. There is variability in how pain is perceived, and stigma associated with having pain and the pain complaints of women are handled less adequately than in men. The prevalence of pain increases with aging, and accelerated aging is noted in racial and ethnic minorities. Older patients are less likely to receive adequate analgesic treatment, resulting in pain that diminishes quality of life in older adults. There is also a high correlation between pain and depression.

Gender-based surgical disparities were detected in patients with high body mass index (BMI) who were undergoing total knee replacement, leading to a national call to action. These disparities resulted in poorer outcomes and greater risk of complication. Those affected tended to suffer from diabetes, hypertension, or depression and were more likely to be female.

Racial/ethnic minorities have less access to pain management and are less likely to have their pain recorded. They receive less pain medication compared to whites and are at risk for undertreatment. Overall, minority patients suffering from pain have decreased health. African Americans are three to five times less likely to undergo needed total knee replacement therapy compared to whites. In this way, there is an unequal burden of pain in minority groups. Immigrants tend to have better health than their native-born counterparts, but as their length of residence in the United States increases, their health declines. The pain disability index is higher at baseline for African Americans than for whites in almost every activity of life, including family, self-care, and occupation.

Dr. Green noted that in patients with equal access to pain care, more African-American patients had difficulty paying for health care related to pain compared to whites. Dr. Green showed a quotation from a patient: “I see my primary care physician every three months and each time I was there he’d ask me why I am walking with a cane, and I’d tell him it’s because of the pain in my back, that the arthritis pain kept getting worse and acetaminophen and physical therapy didn’t help me. I’d talk to other patients with arthritis who were taking opioids, but all I could get was Tylenol, and I knew there had to be something better.” Dr. Green noted that the patient was subsequently diagnosed with cancer, which was the only reason that pain management strategy changed.

In a study analyzing physician responses to cancer vignettes, males received better-quality recommendations for treatment, including referral to a pain specialist. Consistent pain associated with cancer is higher in non-whites. This is also true for breakthrough pain, which is associated with increased mortality.

In response to the question, “Did the pain scare you?” one patient answered “I don’t fear dying or anything like that because I know that when it happens, I won’t know anything about it anyway. You’re gone... I can’t worry about it. I can’t fear something like that. What I fear would be anticipating that kind of pain, knowing that it was coming, and you couldn’t do anything about it. I don’t know if that would be fear. That would be very uncomfortable if you knew that this kind of pain was coming and you couldn’t do anything about it. You look up at the clock. ‘Now get ready, son. It is 10 minutes to 2:00 p.m. At 2:00 p.m., Thor is going to come out and is going to try to chop his way out of your chest.’ That would be scary. But as long as you know there’s a way to relieve the pain, it’s okay.”

Dr. Green noted that safe prescribing of pain medication is not easy, but much can be done to supplement medication, including physical therapy and counseling. There are no data to suggest more misuse of opioid medications among minorities. Undertreating pain creates a vicious cycle: Concerns about addiction often lead to inadequate analgesia, which leads to communication barriers, diminished trust, and worse health.

Dr. Green quoted another patient: “So however long it takes, I know one thing—it ain’t fast enough. When you put your nurse button on to tell her you are having some pain and she shows up an hour or so later and offers you Vicodin, you say, ‘that hydrocodone was for the 12:00 pain (when I first asked for the pain medicine) and it’s now 1:00. Morphine is for the 1:00 pain. I don’t know how long hydrocodone takes, but it’s too long.’ Now when you have that kind of pain, it wears you out. You’re tired.” Dr. Green displayed a picture of numerous medications being taken by a patient near the end of their life and asked whether the drugs were really improving quality of life.

Dr. Green stressed that communication is key; information is not revealed unless the proper questions are asked. Conscious and unconscious bias can come into play and affect treatment decisions.

Environment and Care

Patients live in a variety of environments with varying levels of risk; these environments influence perceptions and ultimately patient care. Some incarcerated people have better access to health care than some people outside the criminal justice system have. Some people in Detroit cannot fill prescriptions because the drugs are not available at the local pharmacy. Many pharmacists in Washington, D.C., are reluctant to carry controlled drugs because of concerns that they will be robbed. As a result, access to some pain medications is better in ZIP codes populated primarily by whites. In Michigan, 90 percent of ZIP codes primarily populated by whites have access to pain medication; for minorities, the access drops to 50 percent. High-income minorities had worse access than low-income whites.

Solving Disparities in Pain Management

Dr. Green summarized the remaining causal problems. There is poor collaboration between disciplines, and the ability to access, assess (including in terms of psychosocial aspects), and treat pain across the lifespan and in all care settings needs to be improved. Clinicians and public health professionals must address the persistent variability in pain management decision-making based on social determinants. Further funding and research to advance knowledge and translate findings into optimal care are needed, with policy designed to support health and palliative care.

Chronic pain outcome measures to use in pain assessment include reduced pain, reduced consumption of analgesics, enhanced activities of daily living, return to work, and other functional outcomes.

The social determinants of pain must be acknowledged. Dr. Green showed a quote from Hubert Humphrey: “The moral test of government is how it treats those who are in the dawn of life, the children; those who are in the twilight of life, the aged; and those who are in the shadows

of life, the sick, the needy, and the handicapped.” Pediatric patients and veterans wounded in combat also deal with pain. Dr. Green noted that health equity and diversity are more than a good idea; they are the law. Provisions from the National Pain Care Policy Act within the Affordable Care Act were enacted in 2010. The U.S. Senate Committee on Health, Education, Labor, and Pensions held a hearing on pain in America, and the HHS Secretary’s Interagency Pain Research Coordinating Committee created a National Pain Strategy Working Group. Centers of Excellence in Pain Education have been created, as has a National Pain Strategy.

The underlying principles of relieving pain in America are as follows:

- Pain management as a moral imperative
- Chronic pain as a disease in itself
- The value of comprehensive treatment
- The need for interdisciplinary approaches
- The importance of prevention
- Wider use of existing knowledge
- Recognition of the conundrum of opioids
- Collaborative roles for patients and clinicians
- The value of a public health and community-based approach

The National Pain Strategy includes education and training, prevention and care, service delivery and reimbursement, population research, professional education and training, and public education and communication. Dr. Green stressed the need to foster cultural transformation. We must find ways to enhance access and address cultural differences in pain. The coordination of care for the patient must be considered, including sensitivity training to avoid bias. Other solutions include use of interpreters to improve communication, increased awareness, encouragement of behavioral changes, increased cultural competency, and creation of effective policies to optimize care and outcomes. Dr. Green ended her presentation with a slide about the Michigan Center for Urban African American Aging Research, which promotes high quality, scholarly research, and community-based interventions focusing on health and health promotion among older racial and ethnic minorities. Millions of people are in the emergency room every day, and their pain is dismissed. This is important to address in order to improve quality of life.

Discussion

Jill Becker, Ph.D., asked whether disparities in access to medication relate to addiction and opioid use. Dr. Green replied that there are no data to suggest that minorities are more at risk than whites. It is not clear whether there is appropriate utilization or overuse in one group versus another. Dr. Becker believed that some data suggest that abuse is less of a risk in African Americans. Dr. Green noted that utilization failure can be driven by lack of access or failure to treat.

The American Pain Society had a campaign promoting pain as the fifth vital sign, but Dr. Becker noted that this switched the problem from managing pain to managing addiction to pain medications. She believed that new, less addictive pain drugs are needed. Dr. Green did not disagree that new pain medications would be helpful but noted that some addiction is due to acute pain problems, whereas abuse is not always found in the population of people with chronic pain. Cross-disciplinary action is needed to consider new treatment modalities for pain.

Dr. Gregory noted that there are patient-centered cultural difference in the treatment of pain and that some people refuse to take their medications. She suggested asking, “How are you coping with your pain?” Dr. Green noted that patient outcome scores and behavior should help dictate pain management.

Dr. Jones said that some people are trying complementary modalities, such as acupuncture, but these modalities are not often covered by health insurance. Dr. Green expressed the belief that any pain management strategies should be tested and proven effective. Dr. Clayton said that future strategies to address pain should be evidence-based and that the National Center for Complementary and Integrative Health is evaluating alternative therapies. More women than men tend to use complementary medicine, which makes it a women’s health issue.

Report from the ACRWH Working Group: Raising the Bar

Amy Mistretta, M.P.H., Epidemiologist, ORWH, NIH

Ms. Mistretta provided an update on the ACRWH Raising the Bar Working Group, which was formed as a result of a recent workshop on the same topic. The goals of the workshop were to delve into the findings the report *U.S. Health in International Perspective: Shorter Lives, Poorer Health*, which documented the relative and growing disadvantage of U.S. women compared with women in other countries, and to discuss important determinants, consequences, effects, and issues attending the relative disadvantage of women in the United States.

As Dr. Clayton mentioned, U.S. women are significantly less likely to live to age 50 than are women in other high-income countries. The Raising the Bar Working Group held its first meeting in August 2016 to provide a platform for ACRWH to consider the health of U.S. women and to identify opportunities for ORWH to inform future activities and initiatives. Ms. Mistretta reviewed the World Health Organization’s conceptual framework for social determinants of health, which include gender. This framework is relevant because it is useful to think about the inequity of the health of US women in terms of their environment. In addition, two institutional factors that influence differences in women’s health outcomes are access to health care and bias in medical care delivery. Socioeconomic and behavioral factors that can influence morbidity and mortality include geography, education, employment, and mental health.

Education has a significant impact on health. Ms. Mistretta showed a graph depicting women's death rates in different regions of the country by level of education; mortality differs more by education than by region. Although the increases in education of women are important, this trend does not seem to result in the same increase in income and assets (or control in the workplace) and other important resources that it does for men. Although regional mortality rates appear similar, mortality rates differ significantly among the states. For example, someone born in Minnesota has a high life expectancy, on par with someone born in the United Kingdom, but someone born in Mississippi has the same life expectancy as someone born in Syria.

Women's participation in the labor force has also changed dramatically in the last 60 years. Working conditions affect mental health, create environmental exposures, and introduce work/family conflict. Work/family conflict is associated with overall physical health, and job stress has been associated with cardiovascular disease and other illnesses. Women are more likely to be employed in jobs with higher levels of stress.

There is a link between mental health disorders and substance abuse. Women tend to have a higher rate of both mental health and substance abuse problems than men, increasing the complexity of treating women's substance abuse. Trauma is a critical issue among women in substance abuse disorders. Women may not seek help because of stigma or a fear of consequences related to substance abuse.

Gender roles and stress cross all levels of socioeconomic status, with variables such as exposure to toxic environments, caregiving, violence and harassment, work roles, effects on health, and perceived and real stress. Working-age women are particularly at risk.

Given the importance of the many variables at play in women's health, Ms. Mistretta asked the committee for opinions on how to prioritize ORWH's work in the future.

General Discussion

ACRWH Members and Guests

Raising the Bar: Topic Prioritization

Research Approaches

Dr. Woodruff stressed the importance of the participation of women in research with sufficient power to address relevant health concerns. Illinois has a women's health registry of more than 7,000 women, with the goal of including women from every county, to study health of women in the state. Dr. Woodruff stressed participant engagement, communication, and outreach.

Dr. López recommended considering a model for women's health to help prioritize research efforts. One approach might be to pair clinicians with researchers. Another might be to engage women in the community in team science to better understand their needs. Dr. Green recommended a small working group be formed to help prioritize topics for women's health to be addressed by ORWH.

Other areas to broaden reach include forging new public/private partnerships and other agencies to co-fund specific areas of research.

Topics of Research

Dr. Bairey Merz recommended research to better understand the associations between women's health, education, and work status.

Dr. Green recommended considering emerging threats to women's health, such as Zika virus infection. Other topics to consider include addiction, substance abuse, and trauma.

Dr. de Vries suggested that SABV be explored between states.

Dr. Mazure suggested exploration of health in urban versus rural populations.

Dr. Jones noted that there may be health outcomes related to political posturing related to reproductive care. It is important to consider SABV, work environment, and the clinical setting's influence on women's health.

Mortality of Women and Mothers

Dr. Gregory recommended additional study to understand the differences in women's health by state. Issues that could be affecting health include environmental or social stressors and rising maternal mortality. Dr. Clayton noted that maternal mortality may be related to older first-time mothers with chronic diseases. Care may differ by state. Dr. Bird recommended gleaning more information about female mortality, including cause of death, age, race/ethnicity, and education. Dr. Bairey Merz recommended including ICs already investing in this area. Family planning may also be a data point for consideration.

Dr. Woodruff noted that the 2013 IOM report on maternal mortality was very detailed, and she urged everyone on the committee to read it. A follow-up report is expected in 2018; more data related to the Patient Protection and Affordable Care Act will be available at that time. Dr. Palmer added that there also may be information about the impact of the 2008 recession on women's health.

Dr. Bird recommended finding the starkest contrasts in women's health and communicating and engaging their stories.

Questions Raised by Dr. Clayton

Dr. Clayton asked the committee members to respond to the following points:

1. Are there any important issues you would like to highlight?
2. Do you have any questions about the topics from today's meeting?

Some of the issues addressed at this meeting were forging partnerships, engaging in the appropriate level of scientific skepticism, addressing existing datasets, issues related to sex and gender, implementation science, and translating discovery into clinical application.

Dr. Bairey Merz requested clarification on whether cell lines would be included in the SABV policy; Dr. Clayton said that they are included. Dr. Bairey Merz suggested that a flow diagram would be useful for aspects of the SABV policy. She also noted that the Human Genome Project lacked data on the X and Y chromosomes; Dr. Page agreed. He noted that the PMI may need to take special consideration for the inclusion of SABV.

Dr. Bairey Merz stated that one challenge to research is the unwillingness to fund epidemiologic research that requires the use of EHRs. Locally, her institution has added a mandatory field for reproductive history that could be a solid data source within a few years. The ability to analyze these data is critical because it can translate into improved patient care. Funding for observational cohort data is important.

Dr. Becker made three points. First, staff for the Center for Scientific Review should be provided with materials to disseminate to grant reviewers to educate them about the SABV policy. ORWH could also provide the names of potential reviewers to add to study sections. Second, NIH should consider ways to archive data for research use in order to power studies of specific groups; a similar archive is available for mouse data. Third, the NIH web page should include a direct link to the ORWH web page.

Dr. Bird urged continued research on Zika infection and the impact on mothers and babies. She expressed enthusiasm for the efforts related to SGMs. Lastly, she noted that different types of medical care can be siloed. For example, obstetric and gynecologic care may be housed separately from the general medical record. Better integration will allow better monitoring of all aspects of a woman's health.

Dr. Green thanked the committee for the opportunity to speak and acknowledged the work and dedication of the ORWH staff. She suggested engaging with other organizations about the importance of SABV. She also recommended advertising the work of ORWH more publicly. Dissemination of information is important; ORWH could more broadly advertise the results of the IOM report, for example. Dr. Green expressed concern that Dr. Parker was the sole full-time

staff member dedicated to SGMs. She also questioned whether ORWH should modify studies based on updates related to SGMs and an emphasis on race/ethnicity.

Dr. Gregory stressed the need for registries or use of EHR data to understand sex differences in clinical care.

Dr. Palmer complimented the resilience and commitment of ORWH staff. She agreed with other committee members about the importance of EHR data, noting that if scientists cannot access it, registries might enable more data access. Comorbidities are now detected earlier in women. Lastly, Dr. Palmer encouraged ORWH's networking and fostering partnerships.

Dr. López said that she was struck by the graph depicting how women in the United States are not as likely to live to age 50 compared to women in other high-income countries. She stressed the need to understand what it means and work with communities to address significant disparities.

Dr. Kashuba stressed that while aggregate understanding is important, patients are treated one at a time. She also encouraged emphasis on providing best practices for including women and minorities in clinical trials to pharmaceutical companies.

Dr. Page expressed interest in ongoing research to increase uptake of SABV. He also noted the importance of the methods employed by ORWH to leverage activities through ICs. He believed that it is important to stress SABV and inclusion of women in research in the PMI. More thought may be required about genomic analysis for sex given that the necessary research tools to study sex may be lacking. Tools to enable this analysis may require prioritization. Dr. Clayton added that use of design thinking framework would be helpful in this context. It is important to be able to make clinical decisions based on evidence.

Adjournment

Dr. Clayton

Dr. Clayton thanked the participants for their ideas and comments throughout the advisory committee meeting. She also thanked the day's speakers and the ORWH staff. She adjourned the meeting at 3:51 p.m.

Certification:

I hereby certify that the foregoing minutes are accurate and complete.

_____/s/_____/

Janine Austin Clayton, M.D., Chair

_____/s/_____/

Elizabeth Spencer, RN, Executive Secretary