Task Force on Research Specific to Pregnant Women and Lactating Women (PRGLAC): *Implementation Plan*

Lisa Kaeser, J.D.

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NIH *Eunice Kennedy Shriver* National Institute of Child Health and Human Development

Talk Outline

- The Problem to be Solved
- PRGLAC Activities 2017 – 2020
- Early Actions
- PRGLAC Working Groups and Implementation Plan
- Key Themes

Underrepresented Groups in Research

VIEWPOINT

Improving Public Health Requires Inclusion of Underrepresented Populations in Research

Catherine Y. Spong, MD
Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, Maryland.

Diana W. Bianchi, MD
Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, Maryland.

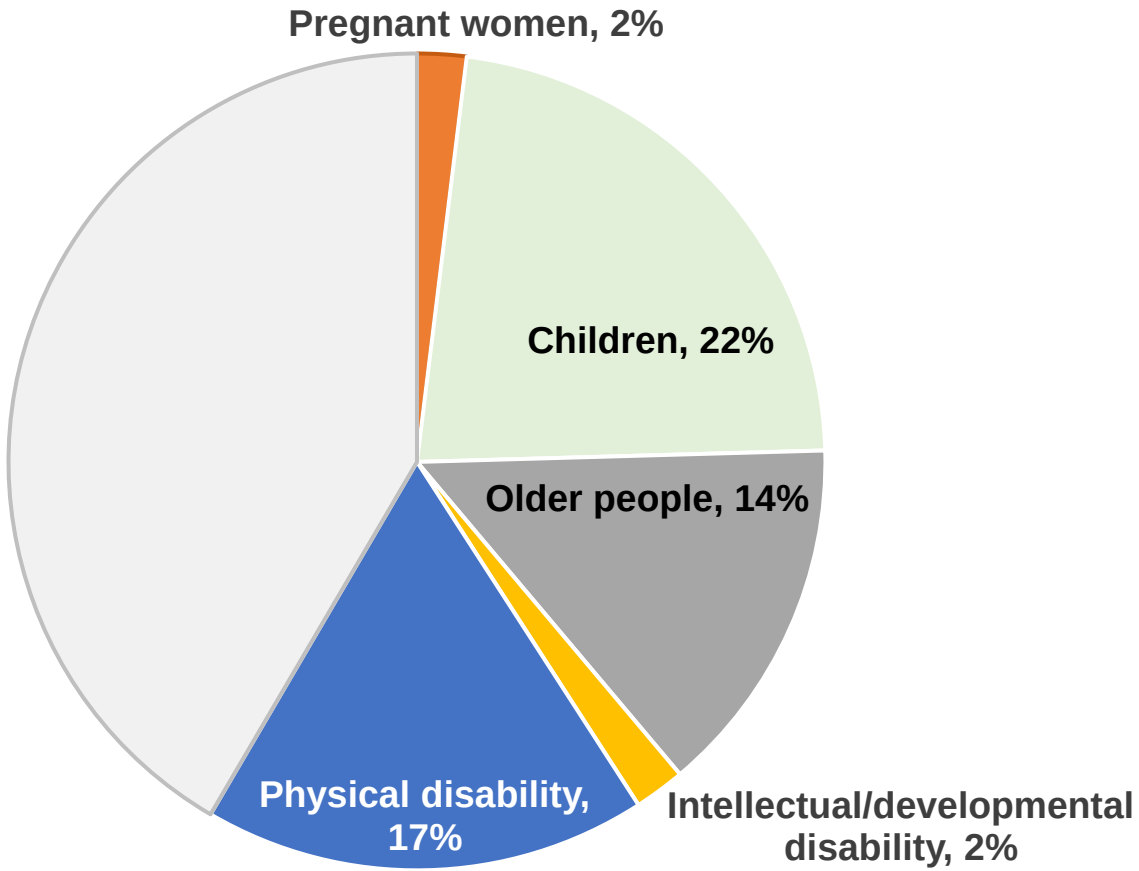
Supplemental content

Advances in genomics have ushered in promising therapies tailored to the individual. Personalized medicine is promoted and has begun to positively influence care. For example, medications such as trastuzumab for the 30% of breast cancers that overexpress *ERBB2* and vemurafenib for patients with late-stage melanoma who carry the V600E variant have been beneficial.[1] Despite these advances, for many sectors of the population—children, older adults, pregnant and lactating women, and individuals with physical and intellectual disabilities—limited evidence-based therapies optimized to their specific medical needs exist. Combined, these groups comprise as much as 58% of the US population (eTable in the Supplement). Research focusing on or at the very least includes members of these groups is critically needed.

Until the initial passage of the Best Pharmaceuticals for Children Act in 2002, pediatric drug doses were based on extrapolation from adults. Importantly, body composition and metabolic processes change as children develop, resulting in different safety and efficacy profiles.[2] Similarly, medication needs change with age cations are often prescribed with minimal evidence to support their use, especially psychotropic drugs with significant adverse effects.

Recently, discussions have arisen about the need for inclusion in research and elimination these gaps. In 2017, the National Institutes of Health (NIH) held a workshop, "Inclusion Across the Lifespan," that highlighted current federal regulations that include protections for "vulnerable populations" (pregnant women, fetuses, neonates, prisoners, and children). Although these regulations were originally designed to protect these individuals, many investigators have called for reconsideration, opting to protect them *through* research, rather than *from* research. Inclusion will likely yield data that will benefit more people.

Many underrepresented populations encounter barriers to participation in research. In a review of 338 phase 3 and 4 NIH-funded actively recruiting studies in Clinicaltrials.gov, explicit exclusion was found in 68% for pregnant women, 47.3% for lactating women, 75.7% for children, 27.8% for older people, 12.4% for those with



Up to 59% of the U.S. population comprises people who typically are not included in research studies (pregnant women, children, older people, and those with intellectual and physical disabilities).

These numbers are approximate to provide a general impact, the numbers do not account for overlap between categories.

Spong CY, Bianchi DW. Improving Public Health Requires Inclusion of Underrepresented Populations in Research. JAMA. 2018;319(4):337–338. doi:10.1001/jama.2017.19138

Pregnancy and Lactation

- 6.3M women become pregnant
  - >90% take at least one medication and 70% use at least one prescription medication
  - 500,000 women have difficulty producing milk
- Concerns re: liability
- Complexity of pregnancy
  - Fetus and placenta change over gestation, timing of exposure
  - Physiologic changes of pregnancy
  - Impact of external factors: obesity, environment
  - Co-existing chronic or acute conditions
- Lactation
  - Benefits of breastfeeding vs. medications in woman
  - Limited assays for assessment of medications in breastmilk

COVID-19: Increasing Urgency for More Research

NIH Strategic Plan for COVID-19 Research:

Objective 5.2 – Understand and address COVID-19 maternal health and pregnancy outcomes

21st Century Cures Act
(Signed December 13, 2016)

SEC. 2041. TASK FORCE ON RESEARCH SPECIFIC TO PREGNANT WOMEN AND LACTATING WOMEN.

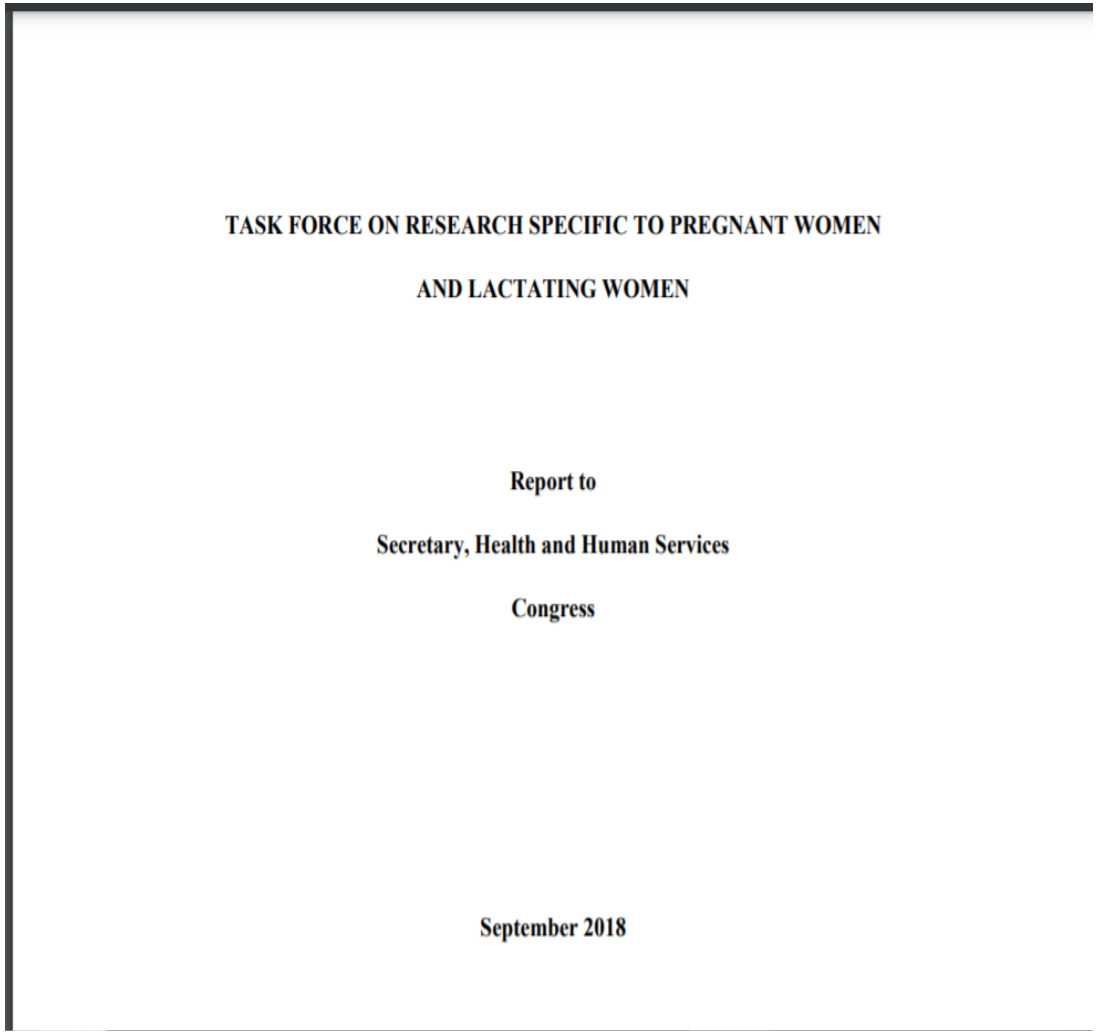
ESTABLISHMENT.—Not later than 90 days after the date of enactment of this Act, the Secretary of Health and Human Services (referred to in this section as the "Secretary") shall establish a task force, in accordance with the Federal Advisory Committee Act…

(2) DUTIES.—The Task Force shall provide advice and guidance to the Secretary regarding Federal activities related to identifying and addressing gaps in knowledge and research regarding safe and effective therapies for pregnant women and lactating women, including the development of such therapies and the collaboration on and coordination of such activities.

PRGLAC Report Submitted to HHS Secretary September 2018

15 Recommendations

https://www.nichd.nih.gov/about/advisory/PRGLAC



TASK FORCE ON RESEARCH SPECIFIC TO PREGNANT WOMEN

AND LACTATING WOMEN

Report to

Secretary, Health and Human Services

Congress

September 2018

PRGLAC: Early Impact

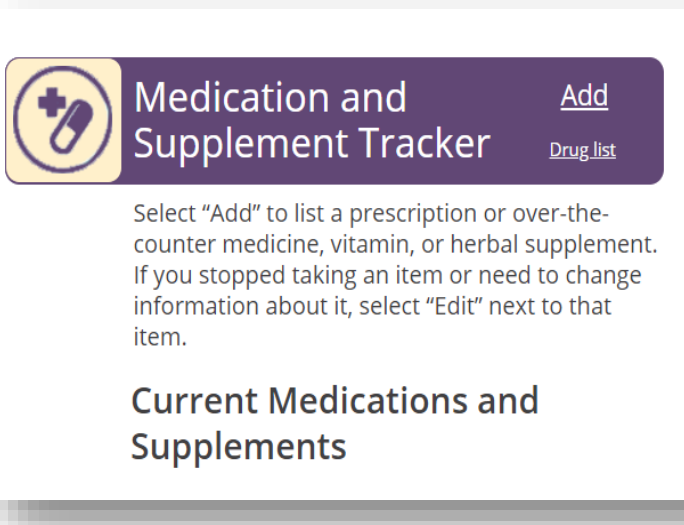
New NIH Reporting Categories

- Pregnancy
- Maternal Health
- Breastfeeding, Lactation, and Breast Milk
- Maternal Morbidity and Mortality

(coming in FY 2020)

https://report.nih.gov/categorical_spending.aspx

PregSource® Medications Tracker



Developing the PRGLAC Implementation Plan

- Charter extended by HHS Secretary until March 2021 (fulfilling Recommendation 14)
- All full PRGLAC meetings open to the public for input
- Established four working groups – *ad hoc* members added to augment expertise
- Expert consultations:

OHRP	BPCA
All of Us	CTSAs

Working Group 1: Research/Training

- *Recommendations*:
  - 2. Increase the quantity, quality, and timeliness of research on safety and efficacy of therapeutic products used by pregnant women and lactating women.
  - 3. Expand the workforce of clinicians and research investigators with expertise in obstetric and lactation pharmacology and therapeutics.
  - 8. Develop separate programs to study therapeutic products used off-patent in pregnant women and lactating women using the NIH BPCA as a model.
  - 11. Leverage established and support new infrastructures/collaborations to perform research in pregnant women and lactating women.

Working Group 2: Regulatory

- *Recommendations*:
  - 1. Include and integrate pregnant women and lactating women in the clinical research agenda.
  - 4. Remove regulatory barriers to research in pregnant women.
  - 7. Reduce liability to facilitate an evidence base for new therapeutic products that may be used by women who are, or may become, pregnant and by lactating women.

Working Group 3: Communication

- *Recommendations*:
  - 5. Create a public awareness campaign to engage the public and health care providers in research on pregnant women and lactating women.
  - 6. Develop and implement evidence-based communication strategies with health care providers on information relevant to research on pregnant women and lactating women.
  - 13. Optimize registries for pregnancy and lactation

Working Group 4: Discovery

- *Recommendations*:
  - 9. Develop programs to drive discovery and development of therapeutics and new therapeutic products for conditions specific to pregnant women and lactating women.
  - 10. Implement a proactive approach to protocol development and study design to include pregnant women and lactating women in clinical research.
  - 12. Utilize and improve existing resources for data to inform the evidence and provide a foundation for research on pregnant women and lactating women.

Overarching Themes Emerged

- Leverage or expand existing federal programs or networks
- Develop new research tools and strategies
- Consider alternative trial designs
- Fully utilize registries and usable data sources
- Establish a prioritization process for studying therapeutics used during pregnancy and lactation
- Address ethical considerations, liability concerns, and potential research incentives to pursue research
- Foster education and awareness among health care providers and pregnant and lactating women
- Create partnerships to accomplish the steps

A Deeper Dive Research/Training Steps

Recommendation 2:

Expand the availability of preclinical models

Recommendation 3:

Expand types of training opportunities

Recommendation 8:

Establish infrastructure to carry out testing of drugs used by pregnant women and lactating women

Recommendation 11:

Facilitate comparative effectiveness and pragmatic trials, case-control studies

Regulatory Steps

- Recommendation 1:

  Develop additional HHS guidance to signal that inclusion of pregnant women and lactating women in research is expected

- Recommendation 4:

  Convene experts to determine what constitutes "minimal risk" for pregnant woman and her offspring

- Recommendation 7:

  Develop formal framework for addressing liability issues when conducting research with pregnant women and lactating women

Communications Steps

- Recommendation 5:

  Using a logic model, develop public awareness campaign to encourage inclusion

- Recommendation 6:

  Explore incentives for healthcare providers to discuss clinical trials with their patients (e.g. obtaining research results)

- Recommendation 13:

  Develop a public-private partnership to host a pregnancy/lactation registry listing website

Discovery Steps

- Recommendation 9:

  Establish a federal program to foster drug discovery and the clinical development of therapeutics for pregnant women and lactating women

- Recommendation 10:

  Authorize the FDA to require drug developers to provide a "PRGLAC Study Plan" and "PRGLAC Assessment" during drug development

- Recommendation 12:

  HHS should lead effort to harmonize definitions used for CDEs in pregnancy and lactation clinical features

Next Steps: Submission to the Secretary and Implementation

Task Force on Research Specific to Pregnant Women and Lactating Women (PRGLAC)

The 21st Century Cures Act established PRGLAC to advise the Secretary of Health and Human Services (HHS) regarding gaps in knowledge and research on safe and effective therapies for pregnant women and lactating women. PRGLAC was tasked with identifying these gaps and reporting its findings back to the Secretary.

Federal members include the directors of NIH, NICHD, the Centers for Disease Control and Prevention, the HHS Office on Women's Health, and the Commissioner of Food and Drugs. Non-federal members include representatives from relevant medical societies, non-profit organizations, and industry.

Advisory Groups

Board of Scientific Counselors (BSC)

National Advisory Child Health and Human Development (NACHHD) Council

National Advisory Board on Medical Rehabilitation Research (NABMRR)

Task Force on Research Specific to Pregnant Women and Lactating Women (PRGLAC)

Learn More

Many Thanks!

To the members of PRGLAC

and

NICHD staff

Questions?