

# On The Horizon

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**Professor of Pediatrics and Genetics**

April 24, 2019

# Advisory Committee on Heritable Disorders in Newborns and Children Charter May 2015

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**Objective and Scope:** The Committee provides advice, recommendations, and technical information about aspects of heritable disorders and newborn and childhood screening to the Secretary of HHS for the development of policies and priorities that will enhance the ability of the State and local health agencies to provide for such screening, counseling and health care services for newborns and children having, or at risk for, heritable disorders.

# Advisory Committee on Heritable Disorders in Newborns and Children Charter May 2015

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**Duties:** Provide advice, recommendations and technical information to the Secretary concerning grants and projects awarded or funded pursuant to 42 U.S.C. Sec 300b-8

Make systematic evidence-based and peer-reviewed recommendations...provide technical assistance to individuals and organizations regarding the submission of nominations to the uniform screening panel...

# Advisory Committee on Heritable Disorders in Newborns and Children Charter May 2015

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... develop a model decision-matrix for newborn screening expansion, including an evaluation of the potential public health impact, including the cost of such expansion, and periodically update the recommended uniform screening panel, as appropriate, based on such decision matrix;...

Consider ways to ensure that all States attain the capacity to screen for the conditions [recommended for the RUSP]

Provide such recommendations, advice or information as may be necessary to enhance, expand or improve the ability of the Secretary to reduce the mortality or morbidity from heritable disorders

# Workgroups

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# Education and Training

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- Workgroup Charge
  - Review existing educational and training resources
  - Identify gaps and make recommendations regarding the following five groups
    - health professionals
    - parents
    - screening program staff
    - hospital/birthing facility staff
    - the public



# Follow-Up and Treatment

- Workgroup Charge
  - Identify barriers to post screening implementation and short- and long-term follow-up, including treatment, relevant to newborn screening results;
  - Develop recommendations for overcoming identified barriers in order to improve implementation and short- and long-term follow-up, including treatment, relevant to newborn screening results; and
  - Offers guidance on responsibility for post-screening implementation and short- and long-term follow-up, including treatment, relevant to newborn screening results.



# Laboratory Standards and Procedures

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- Workgroup Charge
  - Define and implement a mechanism for the periodic review and assessment of:
    - The conditions included in the uniform panel
    - Infrastructure and services needed for effective and efficient screening of the conditions included in the uniform panel
    - Laboratory procedures utilized for effective and efficient testing of the conditions included in the uniform panel



# Workgroups

- EDUCATION and TRAINING
- FOLLOW-UP and TREATMENT
- LABORATORY STANDARDS and PROCEDURES
- Ad Hoc workgroups
  - Interpreting NBS results
- Is the current charge and scope meeting Committee needs?
- Are they adequate to address current and future needs?
- Interactions with Committee and each other
- Product development

# Transparency



*Toledo Museum of Art*

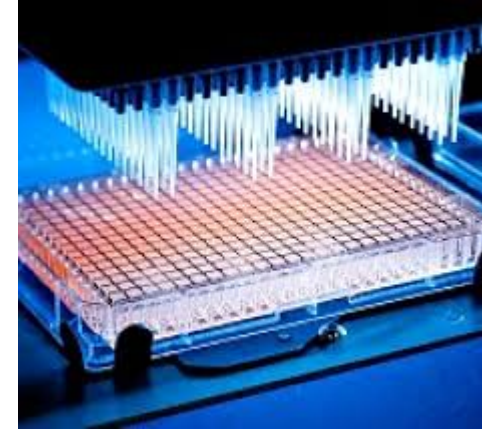


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# Challenges

- Treatments for rare disorders
  - 7000 rare disorders
  - ~5% with treatment
  - More than 450 medicines in development
  - Pre-symptomatic treatment often superior
  - Early diagnosis important
  - Likely accelerated pace of conditions submitted for nomination
  - How to keep up with volume while maintaining thorough evidence-based reviews
  - Will we need to have a high-throughput review process?



# Data Resource Needs

- Data and registries



<https://anzact.org/registries/>



# Timing

- There are conditions with onset in newborn period for which newborn screening results come too late



# Prenatal Newborn Screening

- Inborn errors of metabolism may present in the first few days of life prior to NBS results
  - Urea cycle disorders
  - Organic acidemias
  - Fatty acid oxidation disorders
- Disease process too advanced for effective intervention or treatment even with newborn screening
  - Krabbe disease
  - Spinal muscular atrophy
  - In utero stem cell transplant or gene therapy





## Prenatal Treatment Restores Sweating in XLHED

THE NEW ENGLAND JOURNAL OF MEDICINE

### BRIEF REPORT

#### Prenatal Correction of X-Linked Hypohidrotic Ectodermal Dysplasia

Holm Schneider, M.D., Florian Faschingbauer, M.D.,  
Sonia Schuepbach-Mallepell, Ph.D., Iris Körber, Sigrun Wohlfart, Ph.D.,  
Angela Dick, Ph.D., Mandy Wahlbuhl, Ph.D., Christine Kowalczyk-Quintas, Ph.D.,  
Michele Vigolo, M.S., Neil Kirby, Ph.D., Corinna Tannert, R.A., Oliver Rompel, M.D.,  
Wolfgang Rascher, M.D., Matthias W. Beckmann, M.D., and Pascal Schneider, Ph.D.

Citation: Molecular Therapy — Methods & Clinical Development (2016) 5, 16020; doi:10.1038/mtm.2016.20  
Official journal of the American Society of Gene & Cell Therapy All rights reserved 2329-0501/16  
www.nature.com/mtm

### REVIEW

#### In utero stem cell transplantation and gene therapy: rationale, history, and recent advances toward clinical application

Gracia Almeida-Porada<sup>1</sup>, Anthony Atala<sup>1</sup> and Christopher D Porada<sup>1</sup>

Recent advances in high-throughput molecular testing have made it possible to diagnose most genetic disorders relatively early in gestation with minimal risk to the fetus. These advances should soon allow widespread prenatal screening for the majority of human genetic diseases, opening the door to the possibility of treatment/correction prior to birth. In addition to the obvious psychological and financial benefits of curing a disease in utero, and thereby enabling the birth of a healthy infant, there are multiple biological advantages unique to fetal development, which provide compelling rationale for performing potentially curative treatments, such as stem cell transplantation or gene therapy, prior to birth. Herein, we briefly review the fields of in utero transplantation (IUHT) and in utero gene therapy and discuss the biological hurdles that have thus far restricted success of IUHT to patients with immunodeficiencies. We then highlight several recent experimental breakthroughs in immunology, hematopoietic/marrow ontogeny, and in utero cell delivery, which have collectively provided means of overcoming these barriers, thus setting the stage for clinical application of these highly promising therapies in the near future.

Molecular Therapy — Methods & Clinical Development (2016) 5, 16020; doi:10.1038/mtm.2016.20; published online 30 March 2016

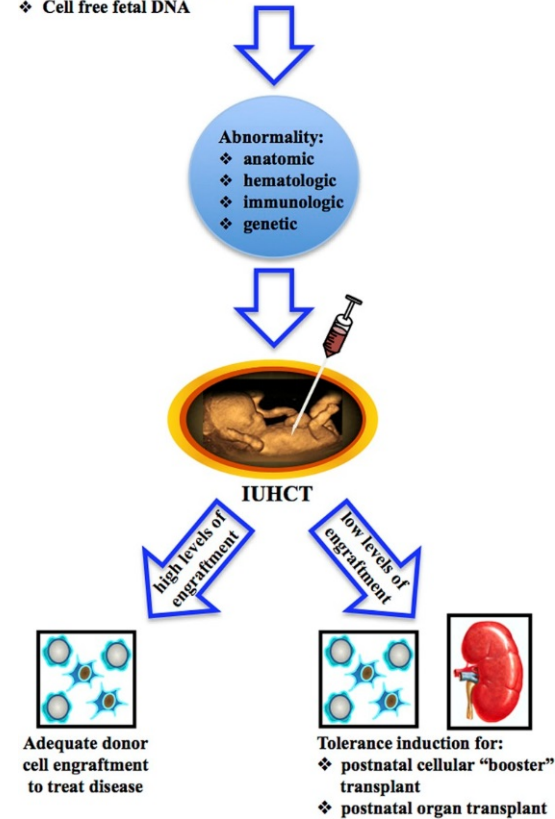
Ex: Hemophilia A, SCID, Alpha-thalassemia. Risks: mother, fetus, fetal germline

### PREGNANCY SCREENING

- ❖ Chorionic Villous Sampling
- ❖ Amniocentesis
- ❖ Maternal serum markers
- ❖ Cell free fetal DNA

### FETAL IMAGING

- ❖ High resolution U/S
- ❖ Ultrafast fetal MRI



Peranteau, WH: Front Pharmacol. 2014 Nov 12;5:251



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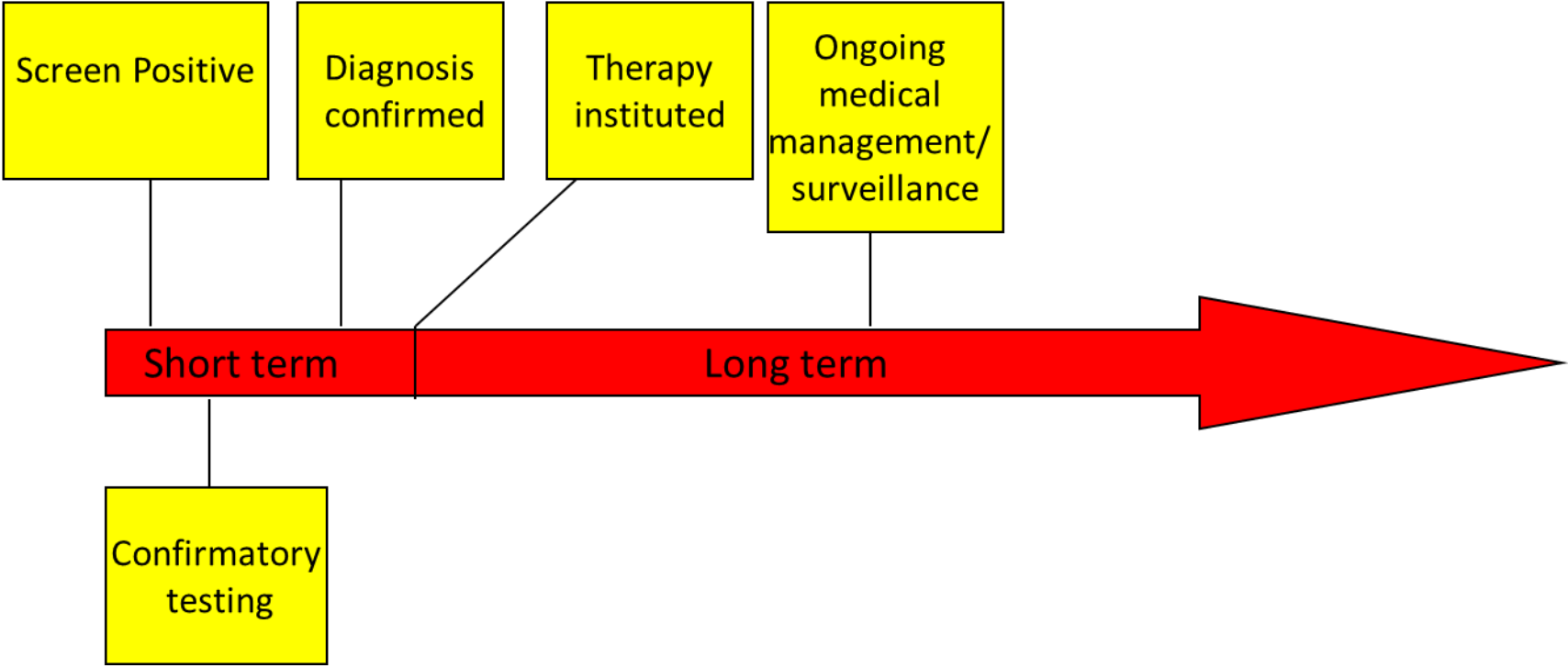


- There are other conditions for which later detection may be sufficient and more appropriate

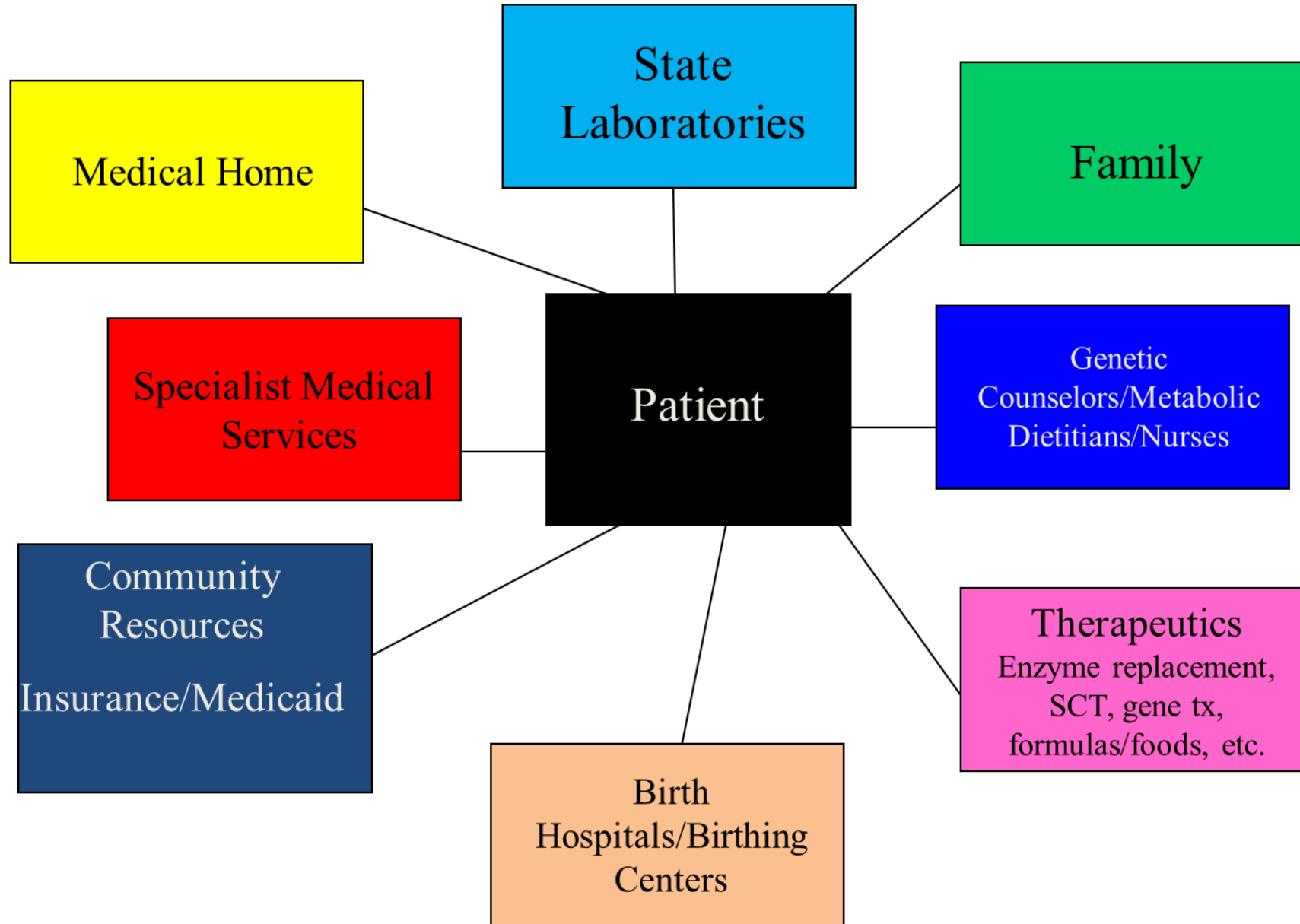


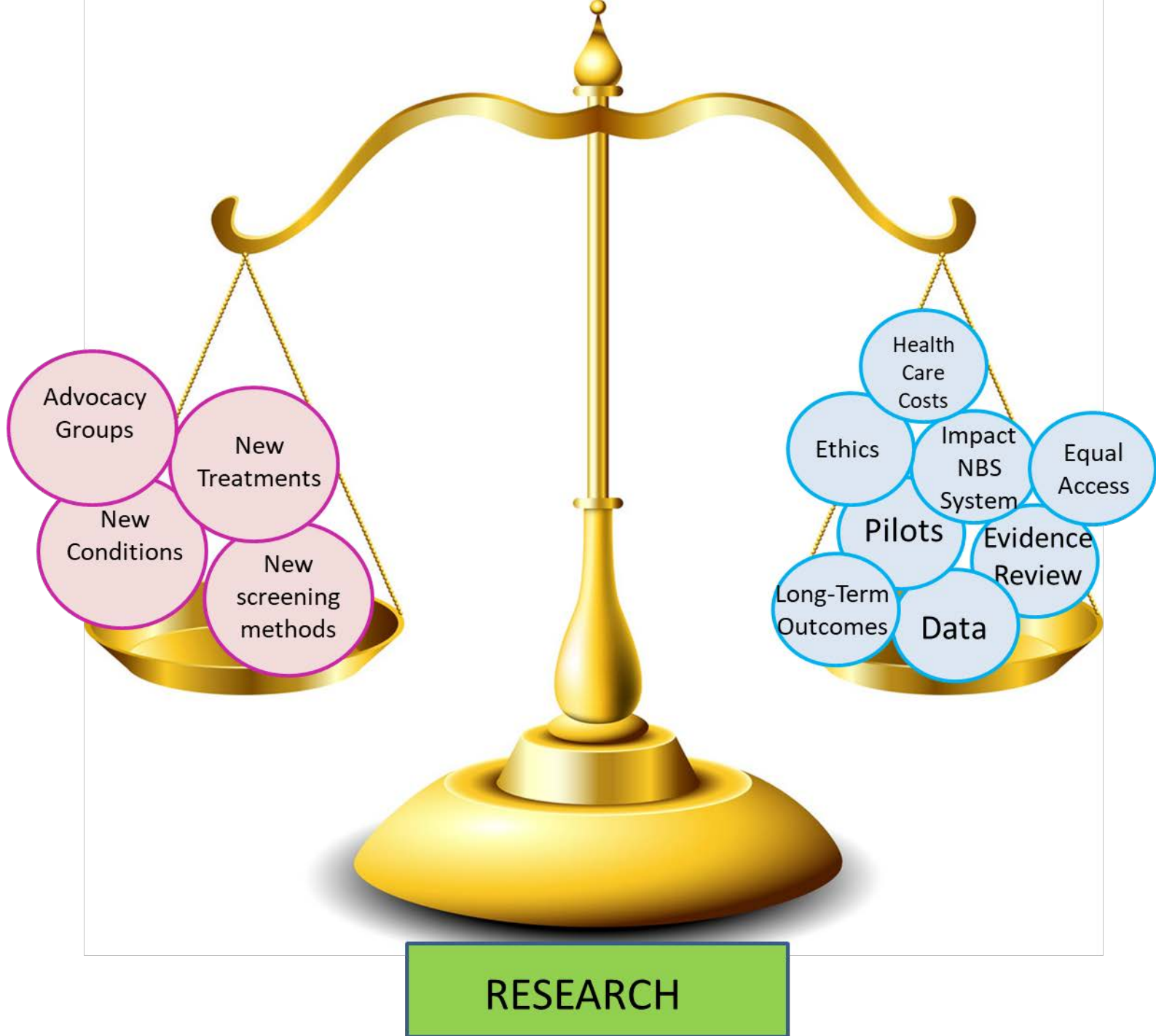


# NEWBORN SCREENING ACROSS THE LIFESPAN



# NEWBORN SCREENING SYSTEM





Advocacy  
Groups

New  
Treatments

New  
Conditions

New  
screening  
methods

Health  
Care  
Costs

Ethics

Impact  
NBS  
System

Equal  
Access

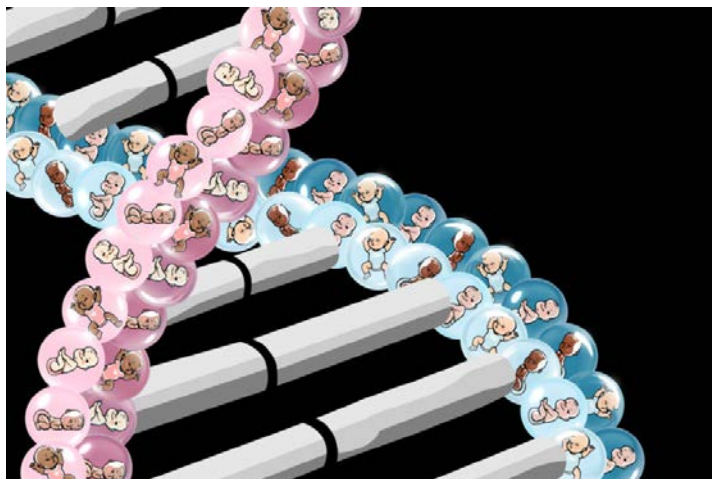
Pilots

Evidence  
Review

Long-Term  
Outcomes

Data

RESEARCH



New conditions identified  
New treatments developed  
New screening methods  
Direct-to-Consumer



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# On The Horizon



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NIH