Evidence-Based Guidelines for Emergency Transfusion in Females of Childbearing Potential: Mitigating the Risks of Hemolytic Disease of the Fetus and Newborn

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Director of Research
Allo Hope Foundation

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HOW WE STARTED

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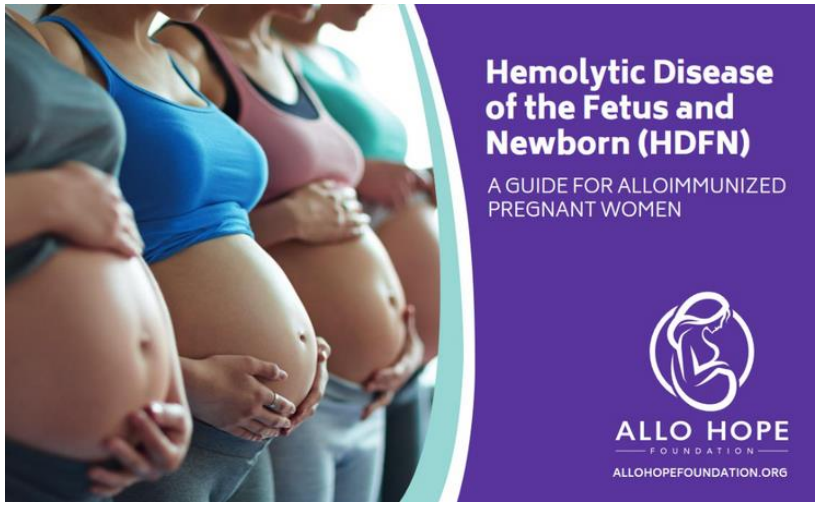
AHF: What We Do

- Provide daily, individualized patient counsel, education, and referrals to skilled practitioners for several thousand alloimmunized women around the world
- Develop evidence-based resources including clinical guidelines, decision trees, and point-of-care materials for patients and providers
- Promote disease awareness and advocacy through speaking engagements, social media, support groups
- Collaboration with global experts for optimal disease management
- Conduct & publication of patient-centered research initiatives



BETHANY WEATHERSBY, MED

EXECUTIVE DIRECTOR

Education (U.S. & International)
Patient advocacy
Management & Vision
Previous role: Educator

KATIE SHANAHAN, MSN, CPNP

DIRECTOR OF DEVELOPMENT

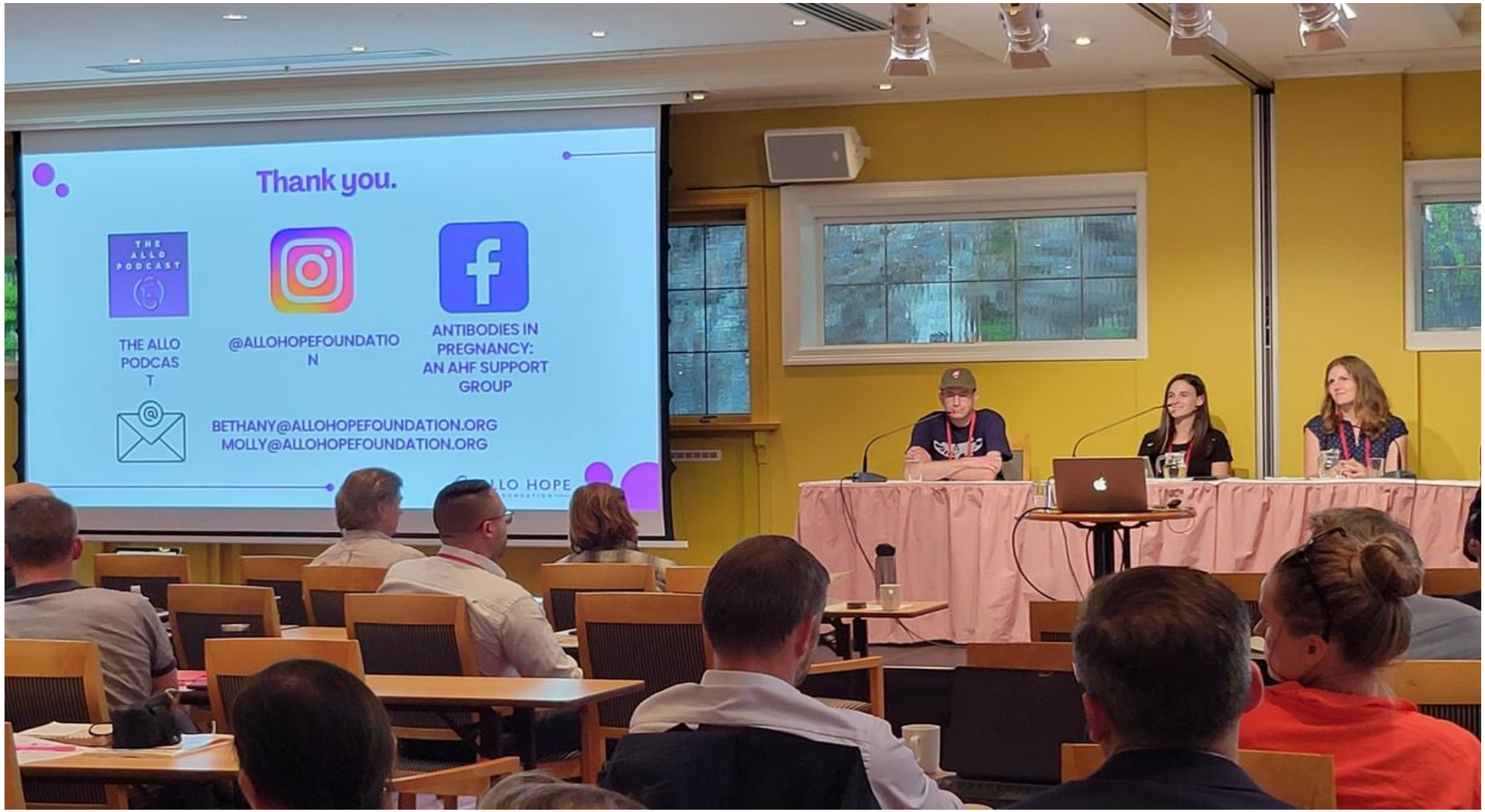
Pediatric clinical care
Clinical trial coordination
Partnerships & fundraising
Previous role: Pediatric nurse practitioner

MOLLY SHERWOOD, BA

DIRECTOR OF RESEARCH

Regulatory/clinical strategy
Scientific writing
Strategic engagements
Previous role: Pharmaceutical research consultant

AHF Leadership Team


Thank you.
THE ALLO PODCAST
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ANTIBODIES IN PREGNANCY: AN AHF SUPPORT GROUP
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THOR 2023

What We Learned from You

- The crux of the WB debate is HDFN risk
- There is inconsistent adoption of WB in centers, and those that do often don't have practices to follow up with FCP receiving incompatible product
- Many of you were trained to believe that an incompatible product = a fetal loss to HDFN
- You care about preventing death from HDFN while offering trauma patients the best chance of survival

Our Missions Overlap

We also help patients losing blood (very tiny ones)
Our shared commitment to improving care can save lives

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Trauma-to-HDFN Event Cascade

- Female of childbearing potential receives Rh+ product during trauma resuscitation
  - Survives
    - Is determined to be Rh negative
      - Becomes sensitized to the D antigen
        - Becomes pregnant
          - Carries an antigen positive fetus
            - Develops significant HDFN requiring treatment
              - Fetal/neonatal death to HDFN

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What we can control

Sharing and improving HDFN realities helps you make informed practice decisions

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Impact of HDFN on the Fetus/Newborn

During pregnancy	After birth	Long-term
• Hemolytic anemia requiring blood transfusion • If untreated, heart failure, fetal hydrops, death (some estimate 50% chance if unmanaged)	• Hemolytic anemia requiring blood transfusion • High bilirubin requiring phototherapy • If untreated, heart failure, kernicterus, death	• Most babies cleared of HDFN ~12 weeks old • Neurological damage from improper management can happen on rare occasion

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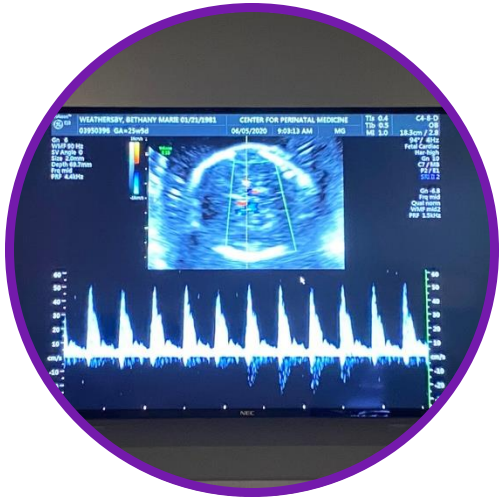
HDFN Monitoring and Treatment



Monitoring

- Titers (monthly; then every two weeks in third trimester)
- Middle Cerebral Artery Doppler ultrasounds (MCAs)

Treatment

- Intrauterine blood transfusion (IUT) (avg 2-3 times in the ~21-23% who need it)
- IVIG w/ or w/o plasmapheresis
- FcRn blocker nipocalimab (investigational)

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An Alloimmunized Pregnancy Can…

- Include management by OB, MFM, neonatologist, pediatrician, hematologist who have never seen HDFN
- Come with an extremely high mental health burden (anxiety in 91%; depression in 68%)
- Involve weekly appointments for monitoring, intrauterine transfusions (21-23%), complications from IUT (3-36%), early delivery, NICU admission, top-up and/or exchange transfusion, fetal/neonatal death due to HDFN (4-5% in U.S.)

What HDFN Looks Like

Lucy

Anti-K titer 1,024
Died 19 weeks GA after lack of monitoring and IUT delay

Max

Anti-D titer 512
Died 3 days old awaiting exchange transfusion

Josie

Anti-D titer 1,024
Died 38 weeks GA with no treatment

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Too Often…

- RhIg is forgotten resulting in preventable sensitization
- An MFM clinic won't see an alloimmunized patient until 22 weeks when fetus has already died
- IVIG isn't available in a severely affected pregnancy because the mother "hasn't lost a baby yet"
- IUTs are attempted in an inexperienced center
- Infrequent monitoring resulting in hydrops, bilirubin-induced hearing loss or brain damage, death
- A mother isn't told she has antibodies until she delivers her stillborn child
- A family is told they will never have a living child

We Should Expect...

- Antibodies to be identified in a trauma patient even before becoming pregnant
- An educated and empowered mother
- Disease management by an attentive and highly specialized MFM and neonatal team
- Potential medication-based treatment in the future
- A living child *even after a previous loss to HDFN*
- A 98% survival rate *even in pregnancies requiring IUT*

What HDFN also Looks Like

Grayson

Anti-E and S titer 4
No intervention needed

Elena

Anti-D, titer 256
1 day phototherapy

Leah

Anti-D and c titer 512
Exchange transfusion, phototherapy

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How do we save the lives of FCP requiring transfusion AND HDFN babies?

Closing the gaps through shared decision making is only possible with engaged, educated clinicians AND patients

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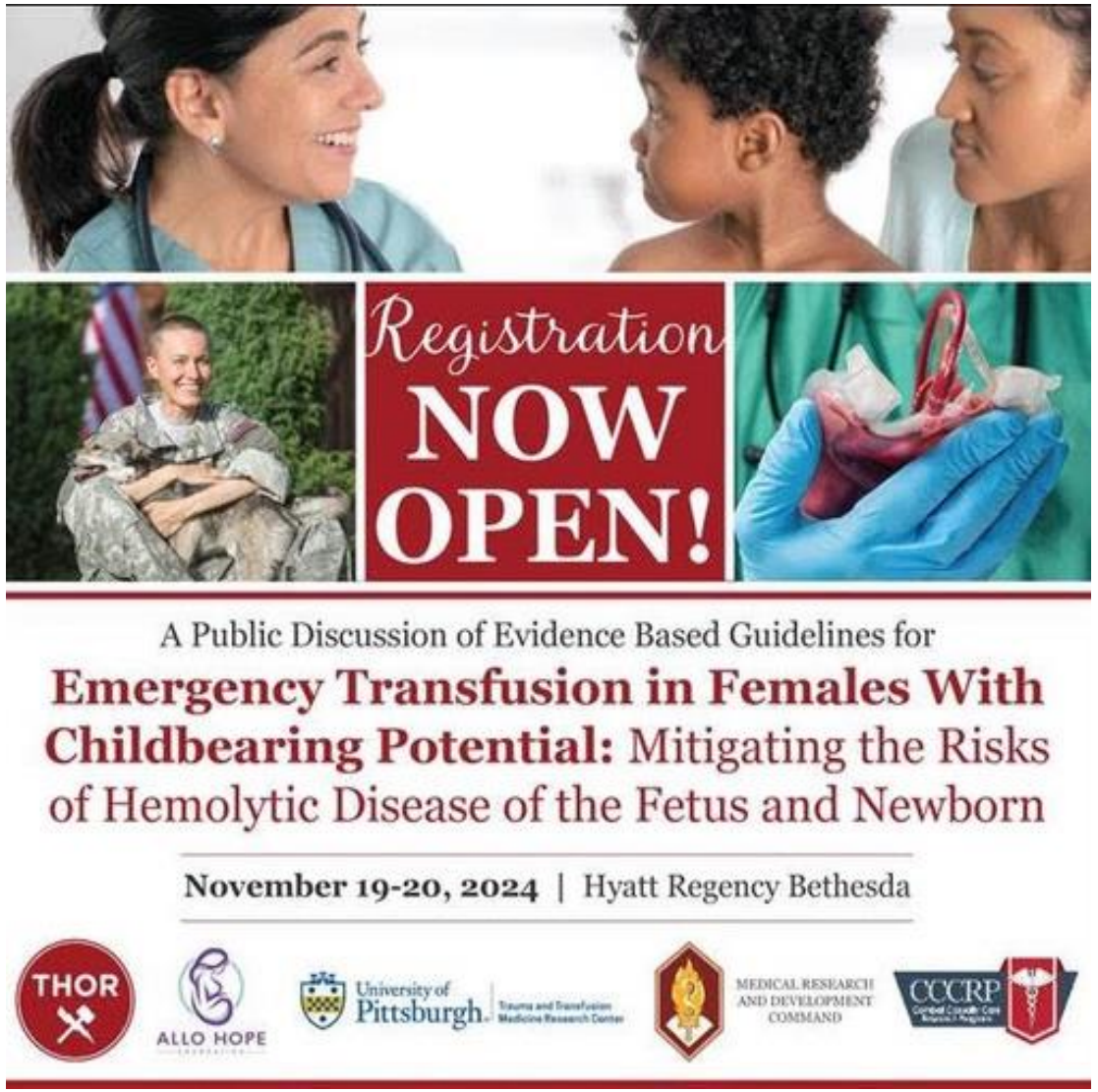
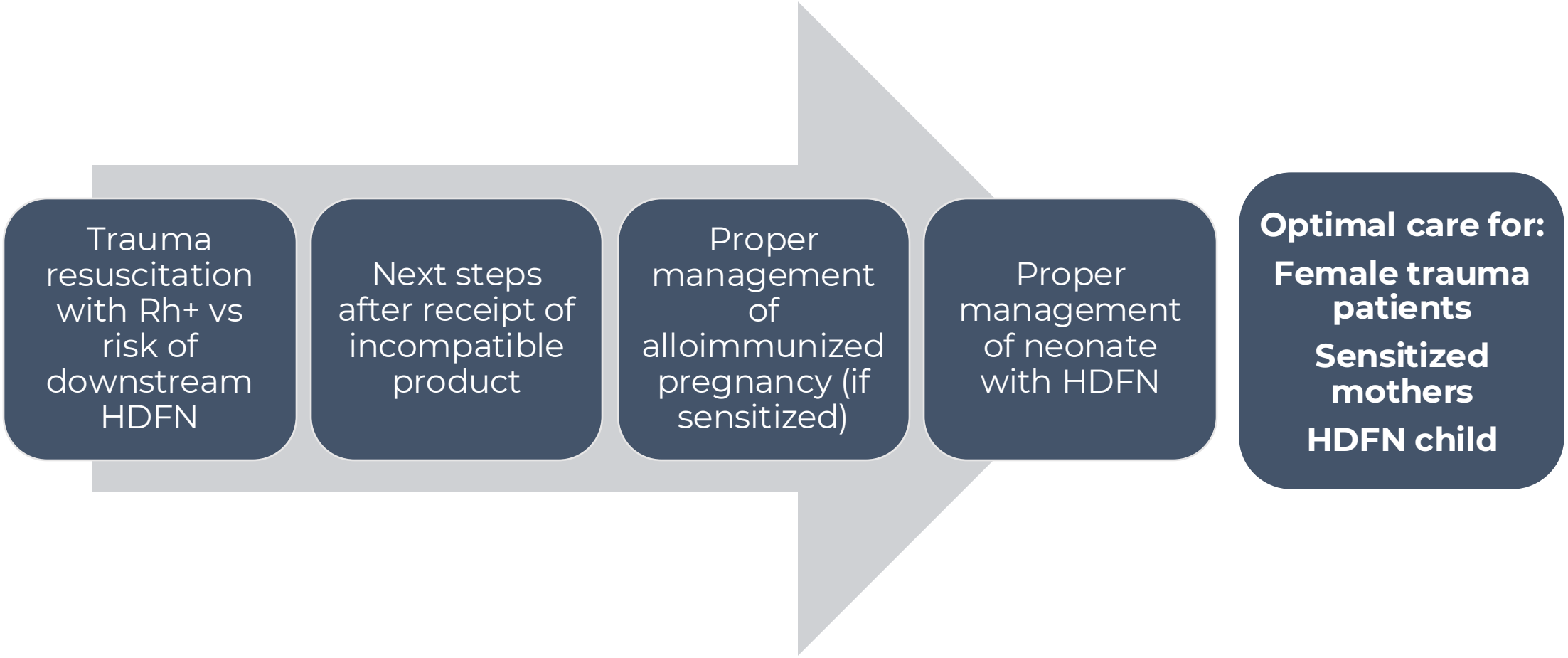
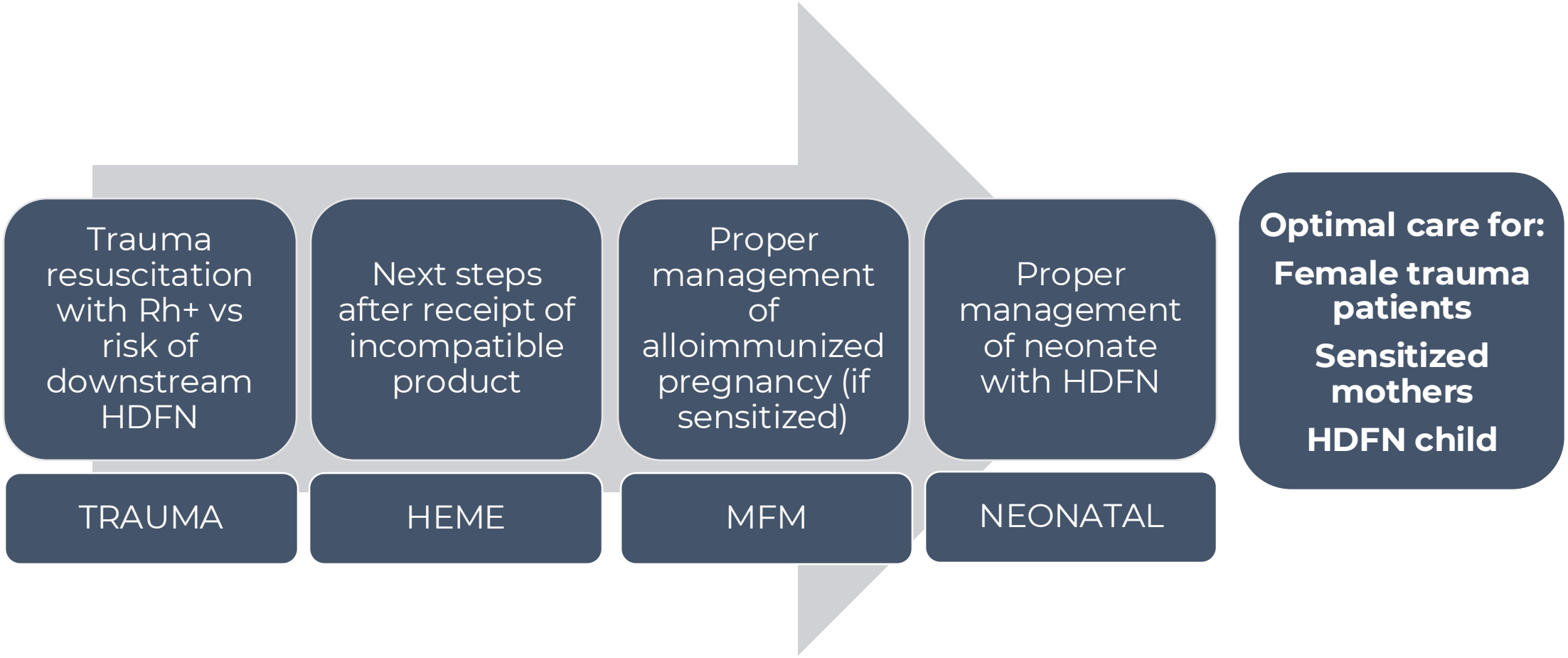

Registration
NOW
OPEN!
A Public Discussion of Evidence Based Guidelines for
Emergency Transfusion in Females With Childbearing Potential: Mitigating the Risks of Hemolytic Disease of the Fetus and Newborn
November 19-20, 2024 | Hyatt Regency Bethesda
THOR
ALLO HOPE
University of Pittsburgh
MEDICAL RESEARCH AND DEVELOPMENT COMMAND
CCCRP

TODAY

The Missing Pieces



A Multidisciplinary Solution



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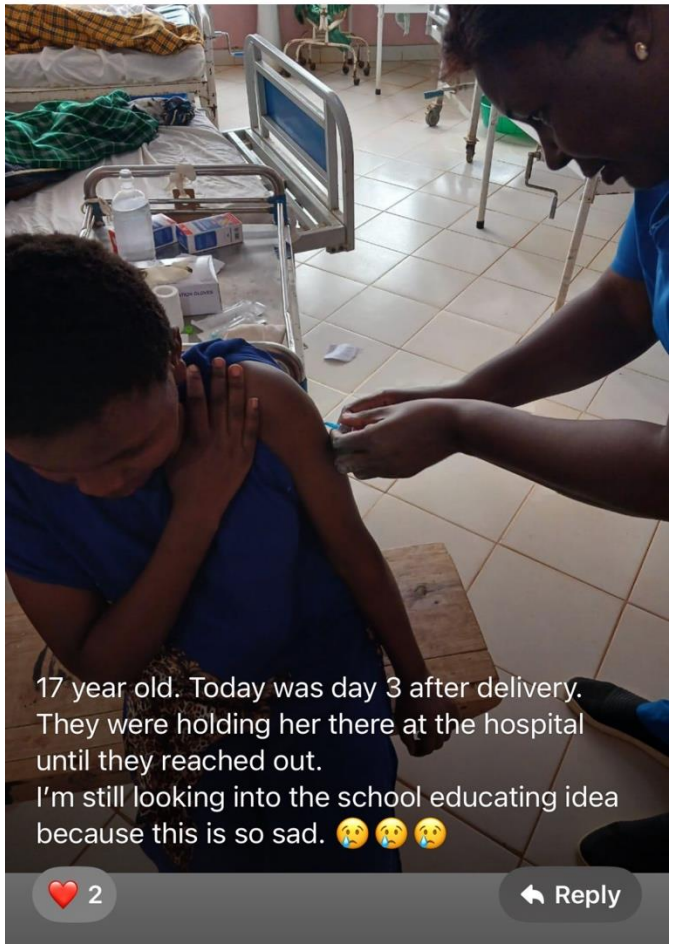
Trauma Subgroup

- Increasing Rh- donation and availability
- Utilizing Rh+ LTOWB in females of childbearing potential when Rh- is unavailable
- Indications for RhIg



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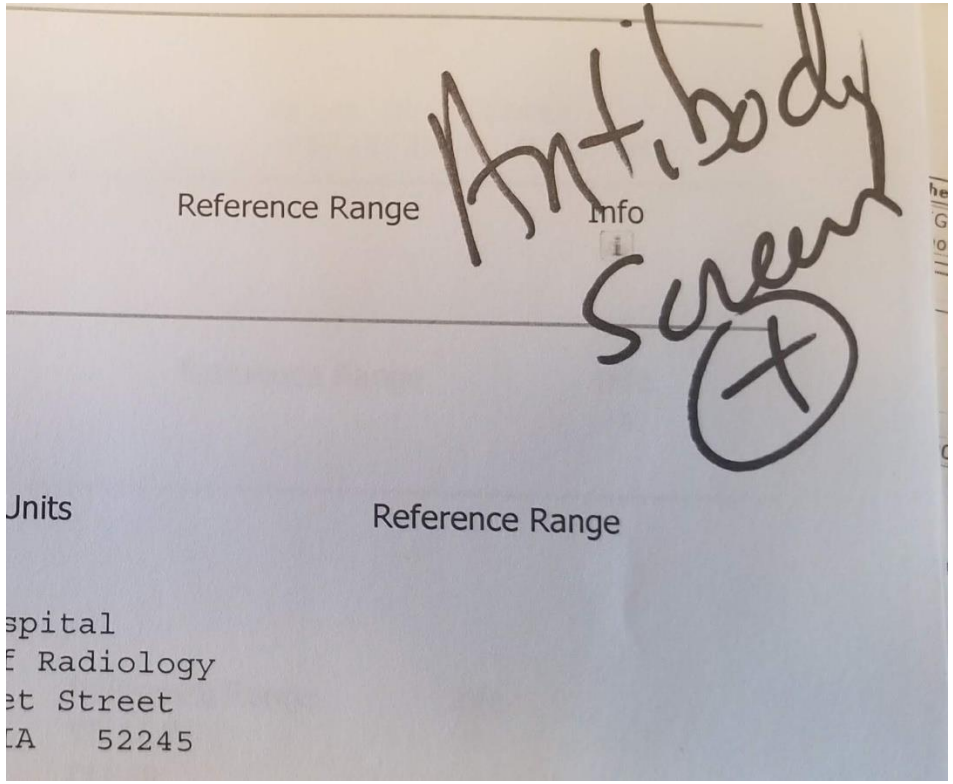
Hematology Subgroup

- Follow-up testing among Rh- females who receive Rh+ product
- When to conduct follow-up testing
- Who orders and manages follow-up testing
- Counseling for alloimmunized women



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Maternal Fetal Medicine Subgroup

- Use of immunomodulation in severe alloimmunization
- Critical titer for Anti-Kell alloimmunized pregnancy
- Cell free fetal DNA to determine fetal antigen status
- Timing of MCA Doppler scans to screen for fetal anemia
- Timing of stopping intrauterine transfusions
- Delivery timing

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Neonatal Subgroup

- Initial laboratory measurements
- Neonatal IVIG to prevent exchange transfusion
- Erythropoietic stimulating agents to reduce number of top-up transfusions
- Transfusion thresholds
- Screening for neurodevelopmental impairment
- Timing of monitoring for delayed onset anemia

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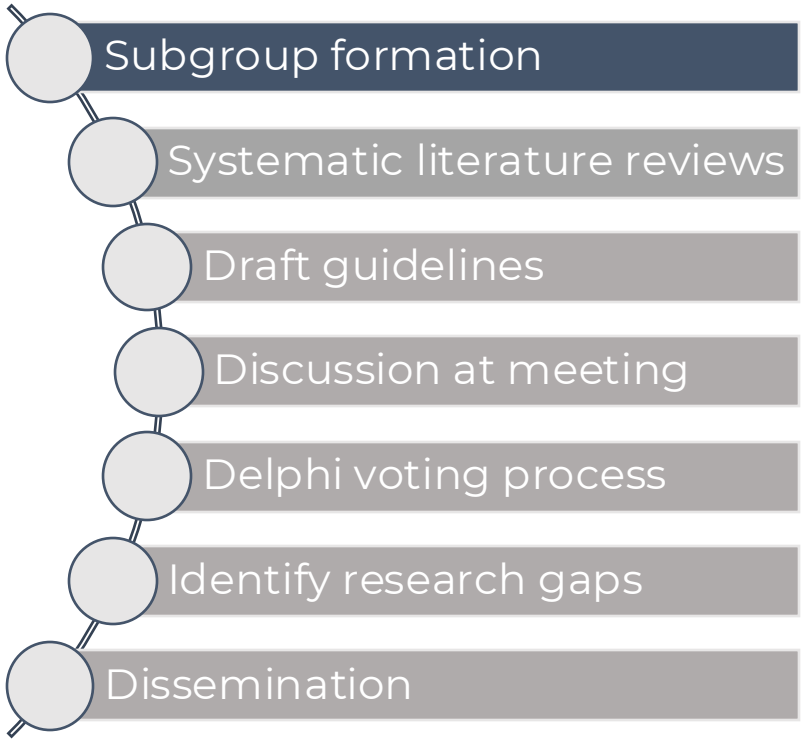
Methodology



Four subgroups with clinical experts invited by subgroup leaders; one patient advocate in each group

Meet periodically to prepare PICO questions for systematic review and draft proposed guidelines

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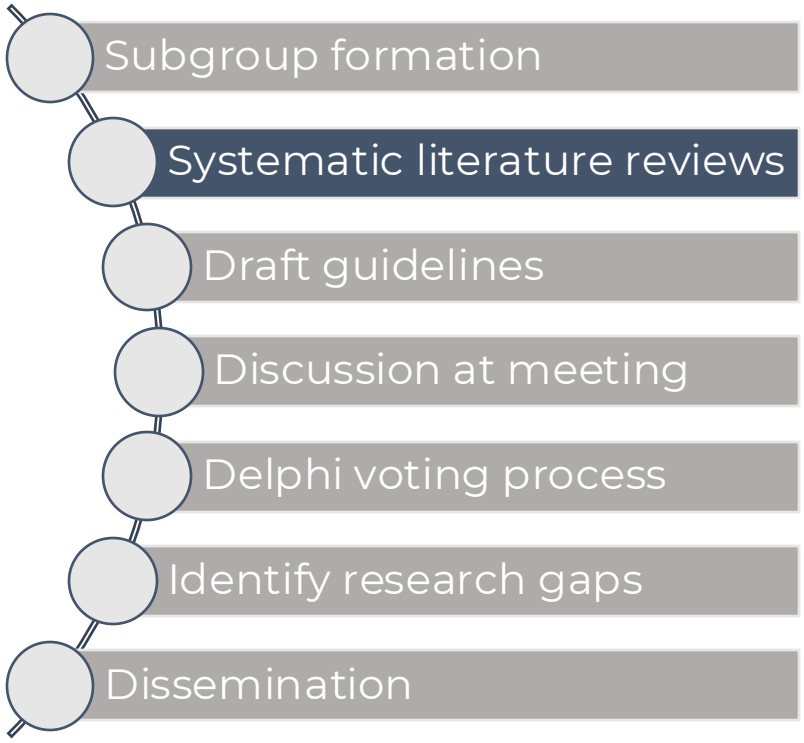
Methodology



Conducted by Johns Hopkins University Evidence Based Practice Center

GRADE system to evaluate certainty of evidence

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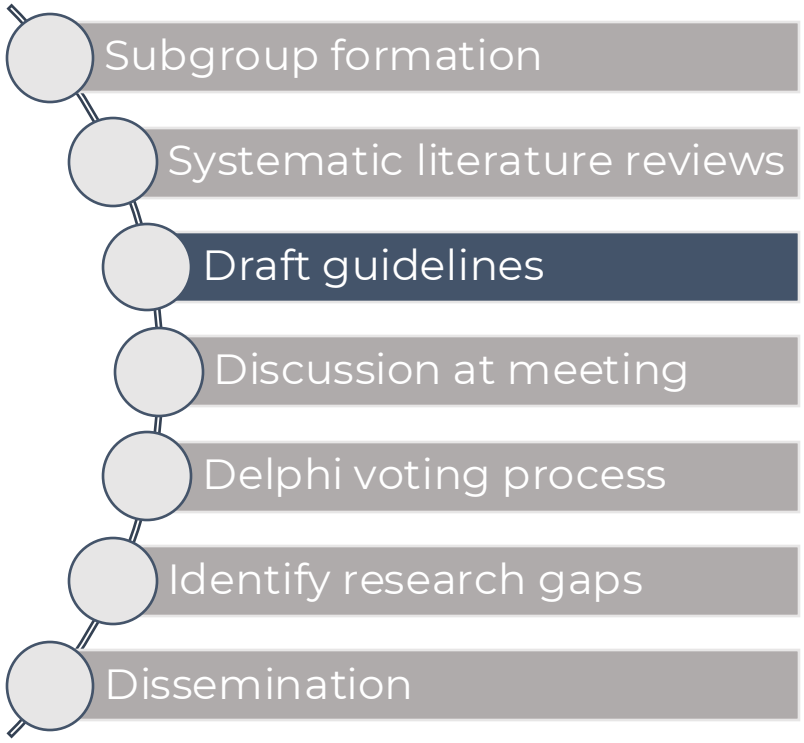

Contributing factors for recommendations:

- Certainty of Evidence (from systematic review)
- Benefits and Harms
- Values and Preferences
- Resource Use and Costs; Equity;
- Feasibility, bioethical and legal implications

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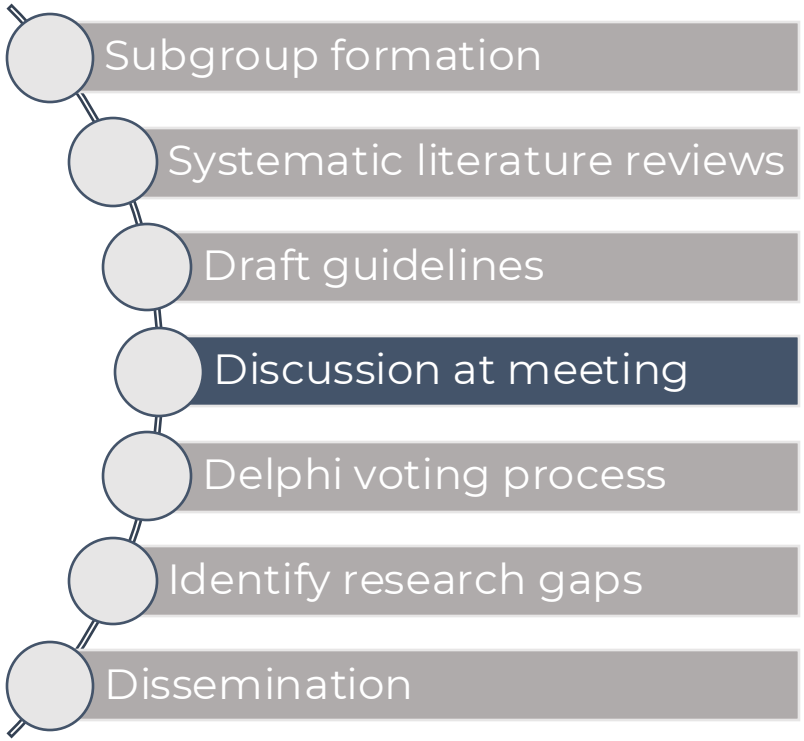

- Open to the public
  - Real-world calls to action
  - Implications for changing practice
  - Current evidence in LTOWB, HDFN practice
  - One-hour sessions for each of the four subgroups
  - Ethics and equity
  - Clinician and patient panel discussions

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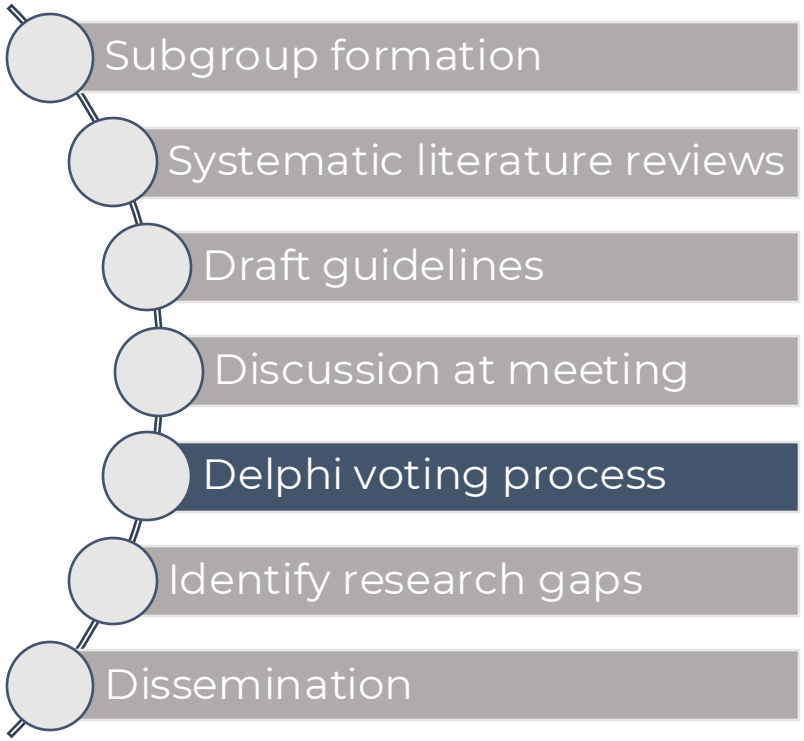

- Open only to voting members
- Subgroup leaders modify recommendations as-needed based on Day 1 activities
- Proposed recommendations are presented to 40-person committee for vote (4-point scale)
- 75% agreement passes the recommendation
- Additional rounds as necessary until agreement is reached

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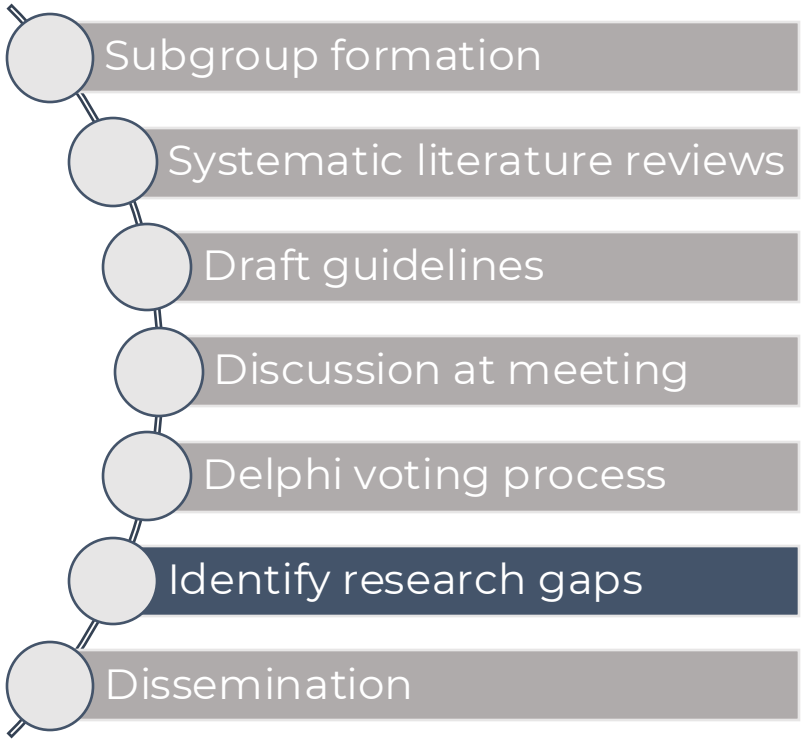

Subgroups each propose five actionable research priorities to be integrated into publication and future funding efforts

Public encouraged to suggest priorities during panel discussions

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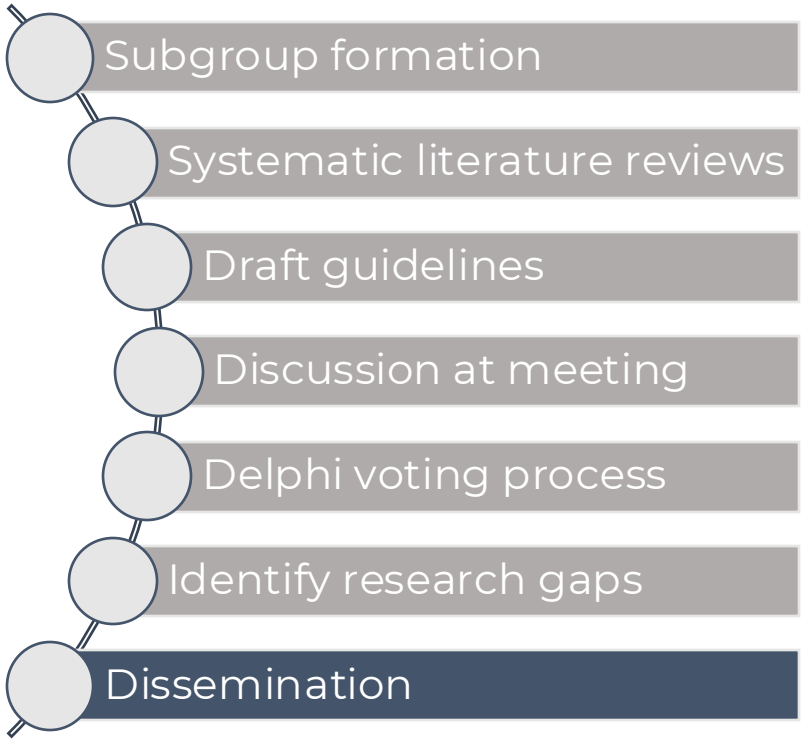

Implementation strategies will be discussed Day 1 for patients and clinicians

Representatives from professional societies will participate to improve likelihood of endorsement

One publication per subgroup; one broader publication summarizing high-level recommendations across all subgroups

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Do No Harm

"Do no harm" in medical terms refers to **the fundamental ethical principle that healthcare professionals should always strive to avoid causing any unnecessary harm to their patients, prioritizing their well-being above all else**, essentially meaning they should minimize risks and potential negative consequences during treatment or diagnosis; it's often associated with the Hippocratic Oath.

Key points about "do no harm":

- Central principle: It is considered the most basic tenet of medical practice.
- Beyond physical harm: This principle extends beyond physical injury to include respecting patient dignity, autonomy, and providing full information about treatments and potential risks.
- Ethical concept: "Do no harm" is not a strict rule but rather a guiding ethical principle that healthcare providers should always strive to uphold.

Do No Harm

"Just as 'health' is not the absence of illness, preventing patient harm is not simply avoiding interventions. To 'first do no harm' health services need to actively improve their focus on health and the entire patient experience."

Luxford K. 'First, do no harm': shifting the paradigm towards a culture of health. Patient Experience Journal. 2016;3(2):5-8.

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We Can Do Something

- Most HDFN deaths are entirely preventable with quality care
- We must work together to ensure the best HDFN outcomes

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We Can Do Something

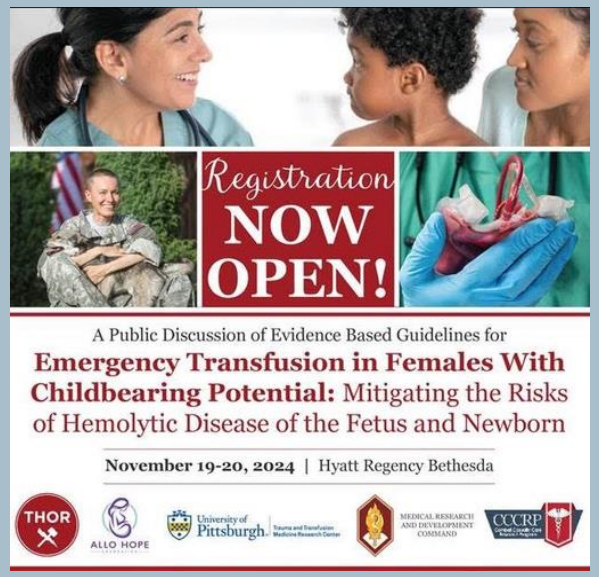
- Follow-up antibody screen after Rh+ exposure in Rh- FCP
- Patient education materials after incompatible transfusion and after positive antibody screen *(get these today)*
- Early referral to MFM when patient is ready (antigen testing for father, selecting an MFM with experience in IUTs, arranging for IVIG)
- Notifying blood donors of their antibody status and its implications
- Support the development of safer guidelines for prevention and management of HDFN

Remember: every transfusion is an incompatible transfusion even if cross-matched for RhD

AHF 2024 INITIATIVES

Subsaharan Africa

Consensus Guideline Development



Awareness, Education & Support

THANK YOU

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THE ALLO PODCAST

Methodology

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