



ALLO HOPE  
— FOUNDATION —

# MATERNAL RED CELL ALLOIMMUNIZATION AND RESULTANT HDFN: Disease and Treatment

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Anti-K Antibodies











# MATERNAL ALLOIMMUNIZATION



ANTIGEN NEGATIVE WOMEN CAN CREATE RED CELL ANTIBODIES WHEN THEY ARE EXPOSED TO ANTIGEN POSITIVE BLOOD

ONCE A WOMAN CREATES RED CELL ANTIBODIES, SHE HAS THEM FOR THE REST OF HER LIFE

MAJORITY OF ALLOIMMUNIZED WOMEN FIND OUT ABOUT THEIR DIAGNOSIS IN FIRST TRIMESTER

EXPOSURE USUALLY HAPPENS THROUGH PREGNANCY OR BLOOD TRANSFUSION

# Antibodies that are known to cause HDFN

- K, k (Kell blood group)

- D, E, C, c (Rh blood group)

- Fya, By3 (Duffy blood group)

- Jka, Jkb, Jk3 (Kidd blood group)

- M, N, S, s, U, Mia (MNSs blood group)

- Mta, Vw, Mur, Hil, Hut (MSSs blood group)

- Lua, Lub (Lutheran blood group)

- D1a, Dib (Diego blood group)

- Xg PP (Tja) Yta, Ytb, Lan, Ena, Ge, Jra, Coa, Co1-b- (Public antigens)

- Batty, Becker, Berrens, Biles, Evans, Good, Gonzales, Heibel, Hunt, Jobbins, Radin, Rm, Ven, Wrighta, Wrightb, Zd (Private antigens)

# ANTIBODY PREVALENCE

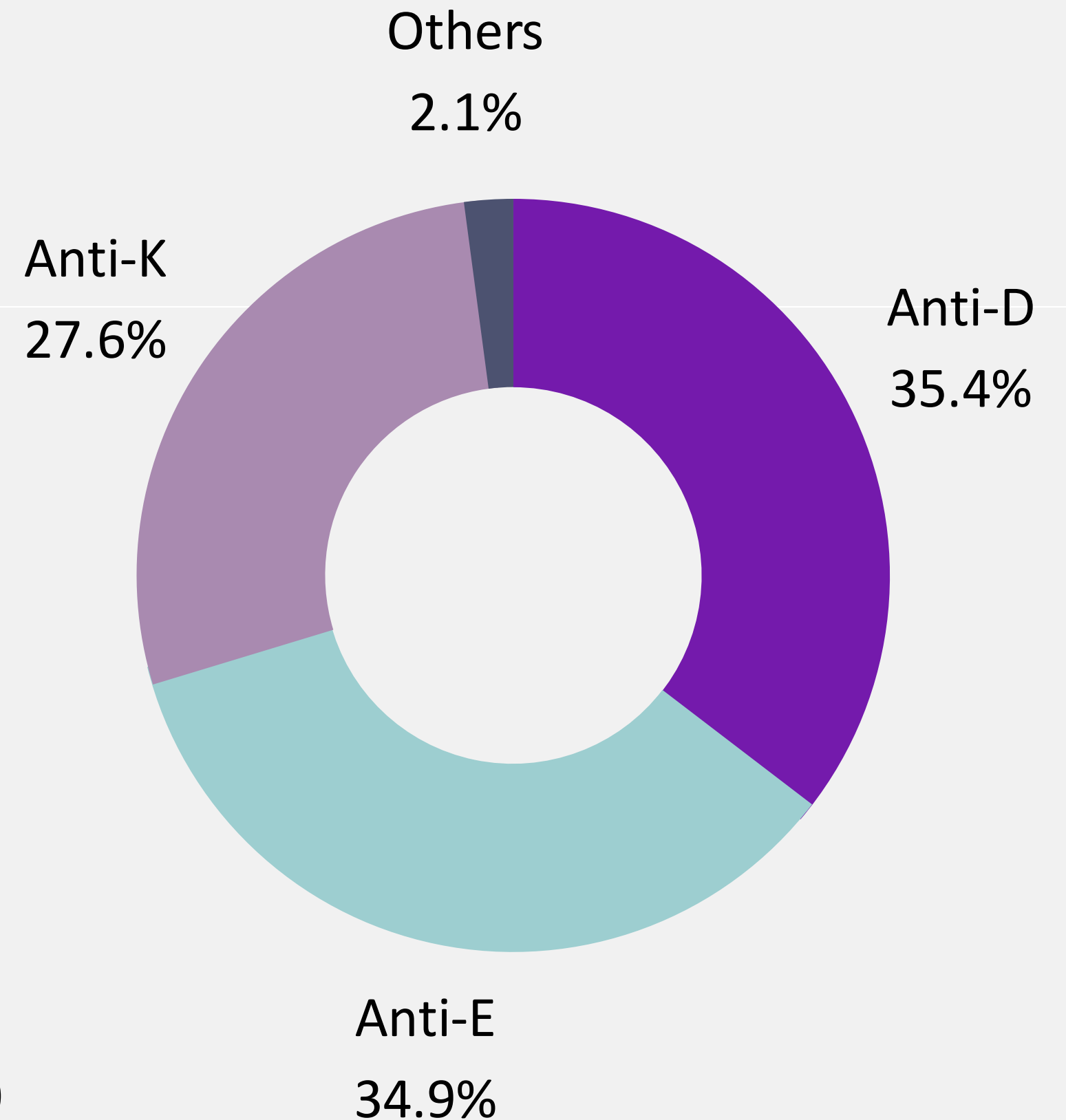
OUT OF 200 PREGNANCIES,  
THESE WERE THE TOP THREE  
ANTIBODIES:

Anti-D 35.4%

Anti-E 34.9%

Anti-Kell 27.6%

**\*DEVELOPMENT OF MULTIPLE ANTIBODIES IS COMMON (43%)**



\*Allo Hope Foundation. 2023. "Anonymous Online Patient Questionnaire Study Examining Disease Diagnosis, Monitoring, Treatment, Progression and Experience in Maternal Alloimmunization Causing Hemolytic Disease of the Fetus and Newborn" (IRB Tracking Number 20224681).





MATERNAL ANTIBODIES CAN GO THROUGH THE PLACENTA DURING PREGNANCY AND DESTROY THE BABY'S RED BLOOD CELLS, CAUSING HDFN

## RISKS OF HDFN

### In Utero

Anemia  
Ascites  
Fetal Hydrops  
Heart Failure  
Death

### After Birth

Hyperbilirubinemia  
Severe Jaundice  
Hearing Loss  
Brain Damage  
Anemia  
Heart Damage  
Death

\*HDFN is temporary and treatable.

# MONITORING AND TREATMENT

In order for the fetus to be at risk for HDFN, these things MUST be present:



- Mother with anti-D antibodies
- Mother with critical antibody titer
- Antigen positive father
- Antigen positive baby

# BLOOD TESTS PERFORMED ON THE MOTHER, FATHER AND FETUS



Antibody screen,  
identification and titer



Antigen phenotype



Cell free fetal DNA  
test, amniocentesis

# MONITORING AND TREATMENT

In order for the fetus to be at risk for HDFN, these things **MUST** be present:



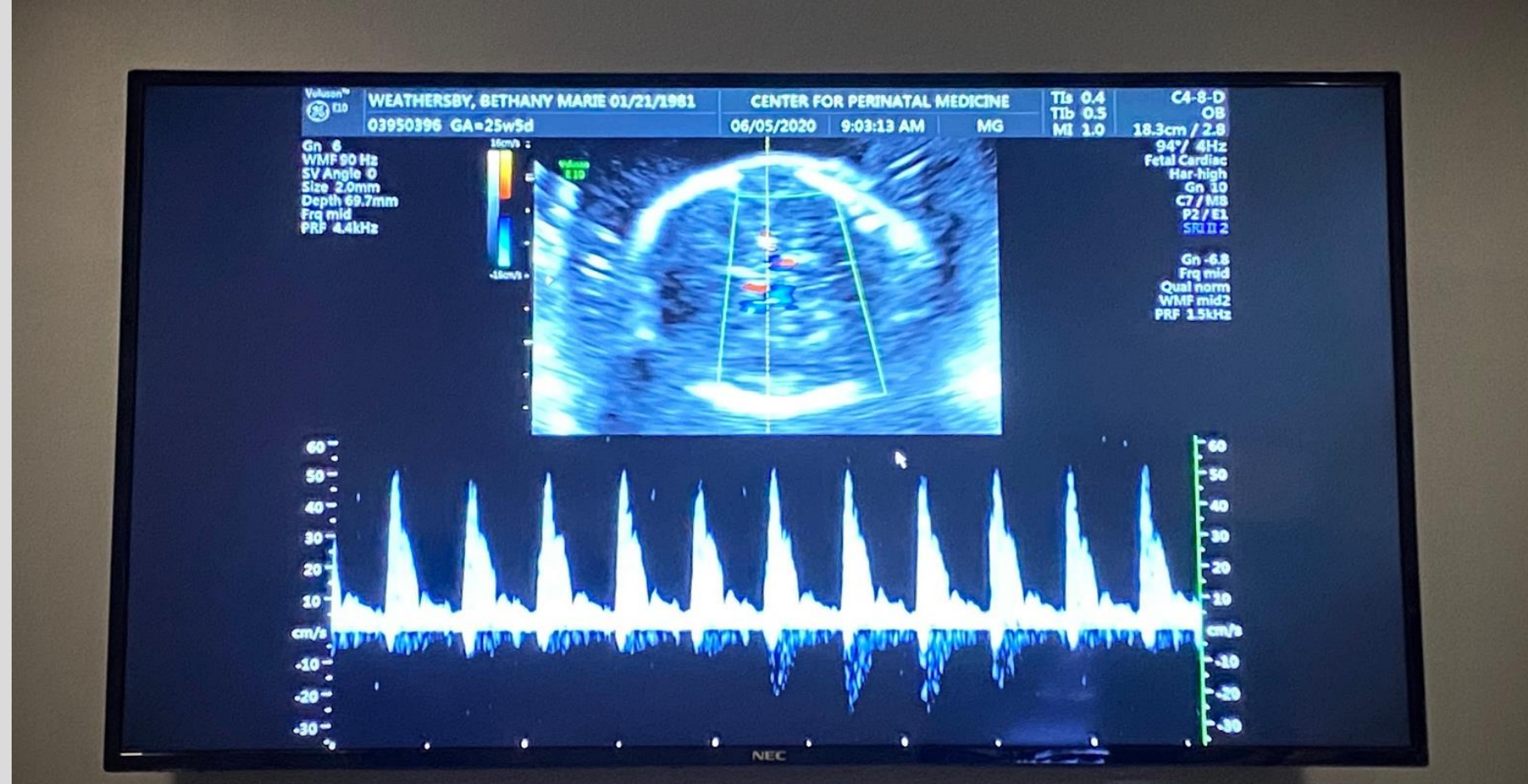
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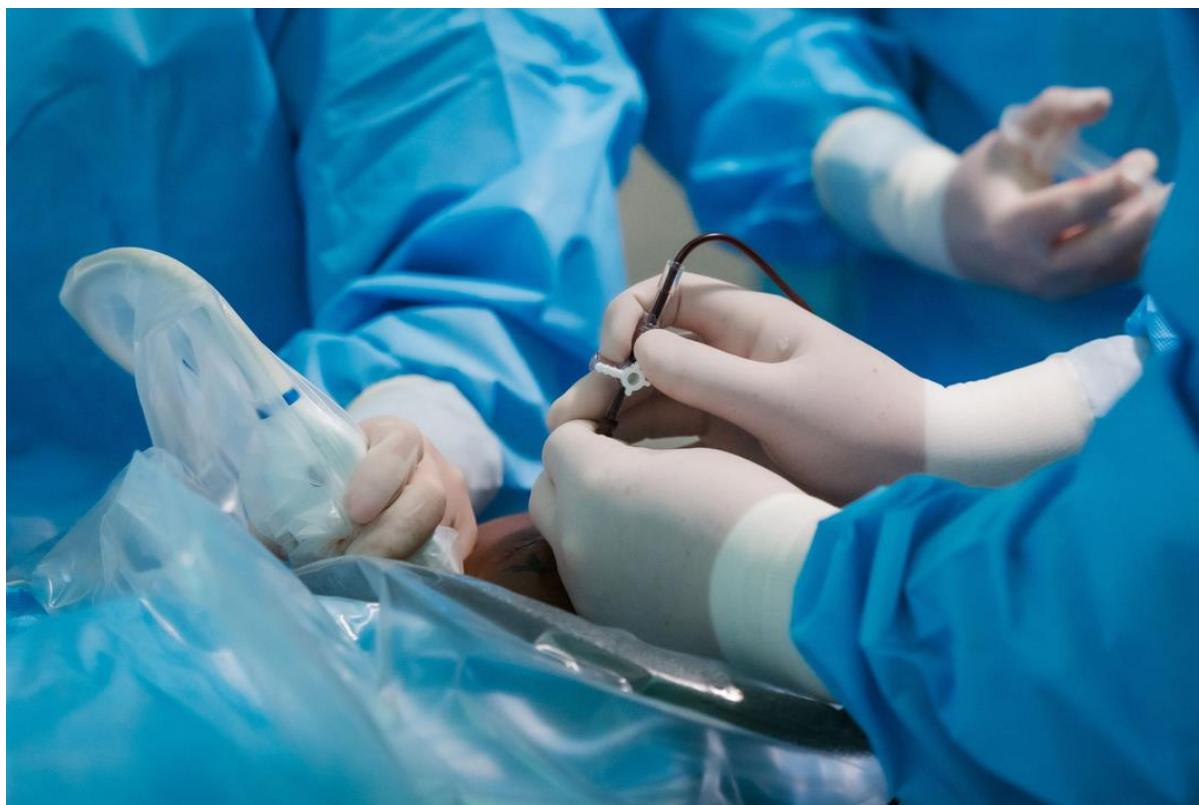
## TITERS

- Critical titer = enough maternal antibodies to possibly cause severe fetal anemia
- Critical titer for D and all antibodies besides Kell = 16
- Any titer is critical for Kell antibodies
- Check antibody titer every 4 weeks until 24 weeks, then every 2 weeks until delivery.

## MCA DOPPLER SCANS

- Detects fetal anemia before it becomes life threatening
- Special ultrasound that measures blood flow through middle cerebral artery
- Performed weekly

# INTRAUTERINE BLOOD TRANSFUSION (IUT)



- Long needle inserted through the uterus and into baby to give paralytic medication
- Needle is then inserted into the baby's umbilical vein, peritoneal cavity or intrahepatic vein
- Fetal blood is extracted to test hematocrit
- Fetal hematocrit and estimated fetal weight is used to calculate how much donor blood to give

# INTRAUTERINE BLOOD TRANSFUSION (IUT)



- Antigen negative donor blood is transfused into fetus using ultrasound guidance
- Repeated every 2-3 weeks until delivery



# The success of IUTs greatly depends on several factors:

MFM's level of competence performing IUTs	The baby's gestational age	Severity of anemia	Timing of the procedure
Involves training and how much experience he or she has doing the procedure	Later is safer because the baby is bigger. Once baby reaches viability, delivery is an option	Babies who are already hydropic have a lower survival rate during IUTs	Waiting too long after a high MCA scan lowers survival rate

# Out of 200 alloimmunized pregnancies-

45

required intrauterine blood transfusions

\*Allo Hope Foundation. 2023. "Anonymous Online Patient Questionnaire Study Examining Disease Diagnosis, Monitoring, Treatment, Progression and Experience in Maternal Alloimmunization Causing Hemolytic Disease of the Fetus and Newborn" (IRB Tracking Number 20224681).



# HDFN AFTER BIRTH



- DELIVERY IS RECOMMENDED BETWEEN 37-38 WEEKS
- CLOSE MONITORING FOR HIGH BILIRUBIN AND ANEMIA
- BILIRUBIN IS THE BYPRODUCT OF BROKEN DOWN RED BLOOD CELLS, SO HDFN BABIES ARE AT HIGH RISK FOR HYPERBILIRUBINEMIA
- TREATED WITH PHOTOTHERAPY, IVIG INFUSIONS, EXCHANGE TRANSFUSIONS

- CLOSE MONITORING FOR HEMOYTIC ANEMIA
- TREATED WITH "TOP UP" BLOOD TRANSFUSIONS
- EPOGEN SHOTS
- BABIES IS CLEARED AFTER SEVERAL WEEKS WHEN MATERNAL ANTIBODIES DIE OFF AND BABY STARTS MAKING HER OWN RED BLOOD CELLS AGAIN



# ALLOIMMUNIZED WOMEN SHOULD HAVE ACCESS TO:



- Proactive treatment options
- Proactive monitoring
- Specialists who have ample experience treating HDFN
- Appropriately timed treatments
- Access to educational resources, support and an understanding of how imperative it is that she advocate for the right care

# PLASMAPHERESIS



# INTRAVENOUS IMMUNOGLOBULIN



# NORA

## HDFN COURSE

- Kell Titer 1,024
- Plasmapheresis and IVIG treatments
- 5 IUTs
- Phenobarbital
- Born at 38 weeks
- 2 post birth transfusions



## TODAY

- Healthy seven year old
- Accepted into an International Baccalaureate School for the gifted in first grade
- Loves gymnastics and bossing her brothers around



# CALLUM

## HDFN COURSE

- Kell Titer 1,024
- Plasmapheresis and IVIG treatments
- 3 IUTs
- Born at 34 weeks
- 3 post birth transfusions



## TODAY

- Healthy five year old
- Reading on a 6th grade reading level and starts kindergarten in August
- my gentlest boy

# AUGUST

## HDFN COURSE

- Kell Titer 2,048
- Plasmapheresis and IVIG treatments
- 7 IUTs
- Phenobarbital
- Born at 37 weeks
- 3 post birth transfusions



## TODAY

- Healthy two year old
- Loves trains, cars and taking risks.



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MATERNAL RED CELL  
ALLOIMMUNIZATION AND RESULTANT  
HDFN: PATIENT EXPERIENCE



**Molly Sherwood**

Director of Research, Allo Hope Foundation  
Anti-S and Anti-E antibodies



# What does alloimmunization and HDFN mean to real patients?

- Current state of research
- Disease reality - what portion of disease is 'severe'?
- Patient-reported disease experience
- The impact of quality care
- Rh+ whole blood perspectives in our population and other considerations in transfusion medicine



Robert  
Anti-D Antibodies  
Titer 32

# State of the literature: Annual scientific production

## Bibliometric analysis: Trauma-related hemorrhagic shock

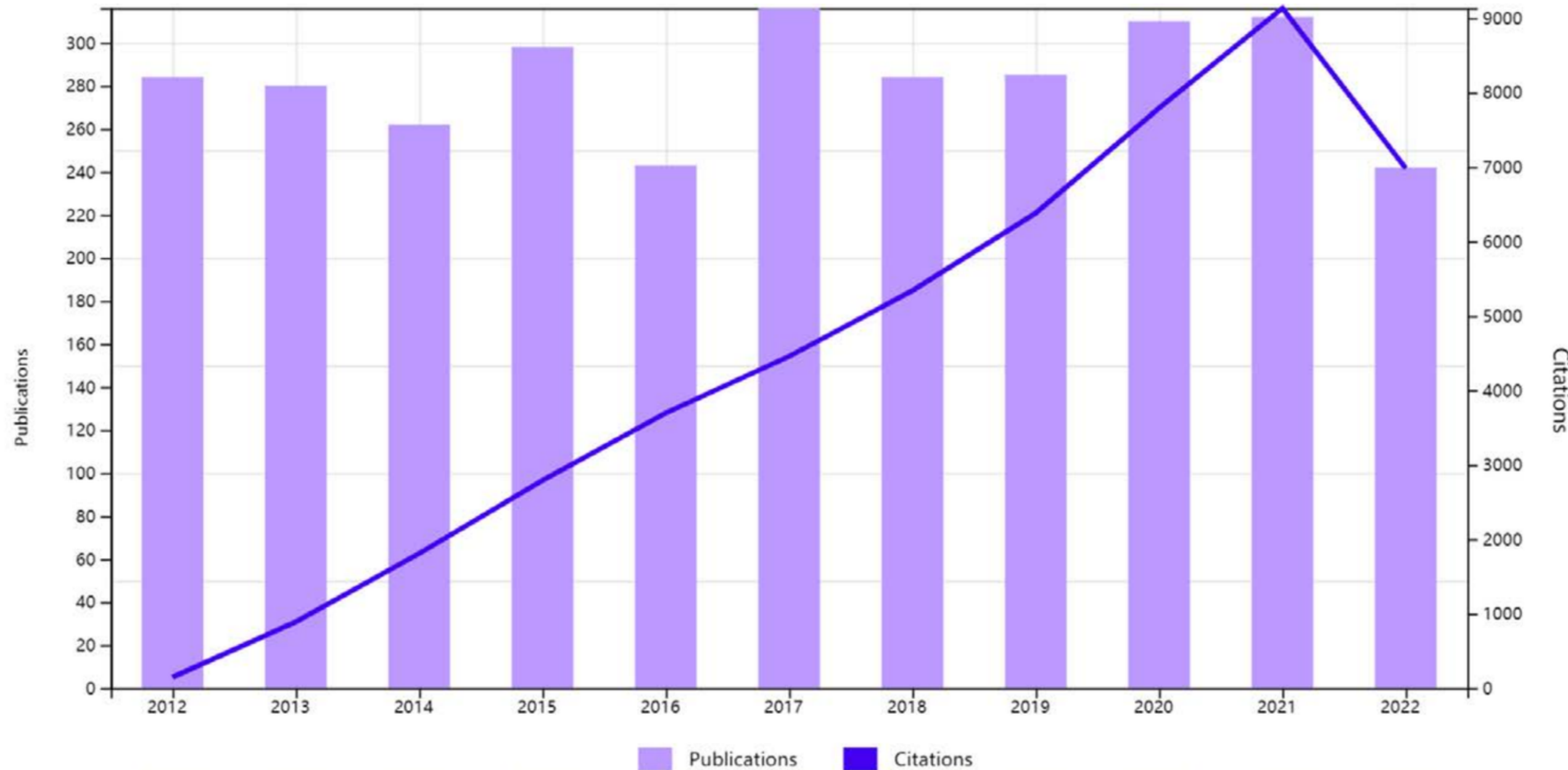
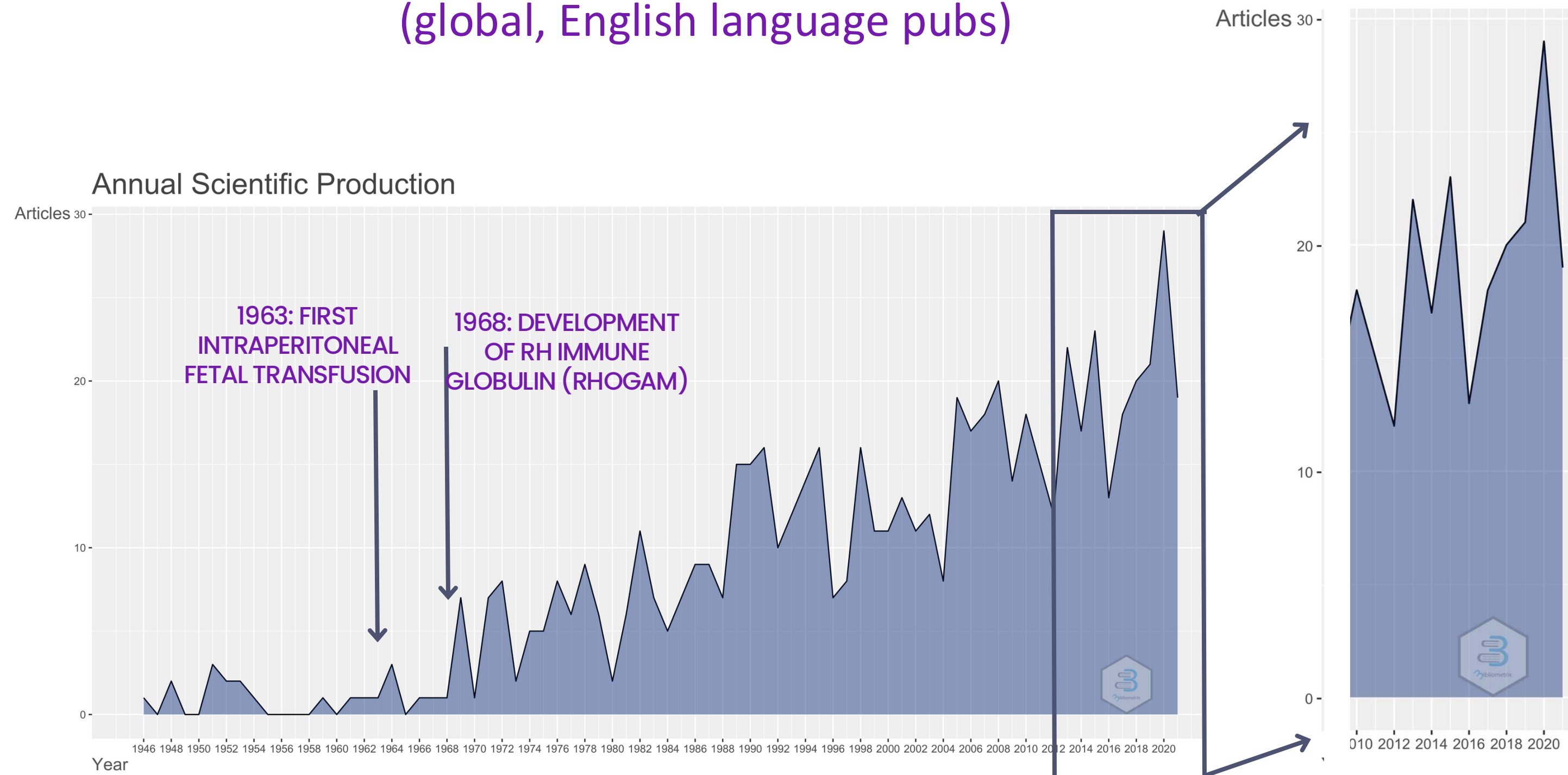


Figure 2. Temporal distribution map of publications and citations.

# State of the literature: Annual scientific production

Bibliometric Analysis: Maternal red cell alloimmunization and HDFN  
(global, English language pubs)



# AHF's patient questionnaire study

## Development

AHF staff and Medical  
Advisory Board  
Piloted by Patient Advisory  
Board  
Topics: disease  
presentation, treatment,  
severity, outcomes, and  
psychosocial impact

## Recruitment

IRB approval Sept 2022  
Recruitment November  
2022-Feb 2023  
AHF online support group  
(1,400 members, 1,000  
U.S.)

## Study Population

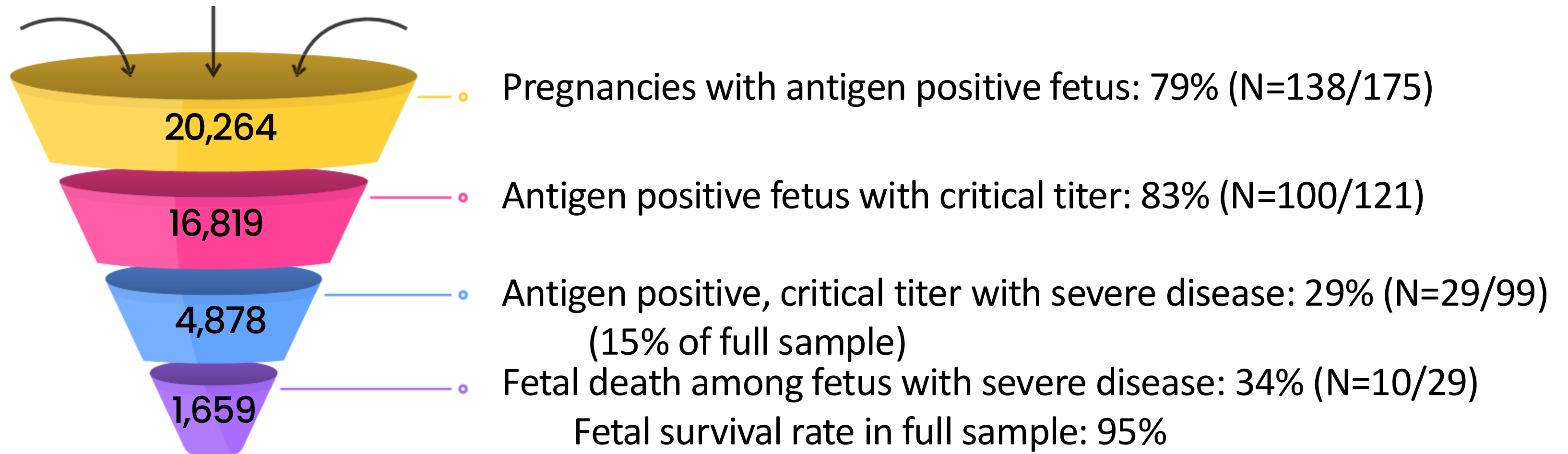
127 U.S. alloimmunized  
women with at least one  
completed alloimmunized  
pregnancy  
200 alloimmunized  
pregnancies



# Outcomes in U.S. alloimmunized pregnancies

Alloimmunization rate to clinically significant antibodies in U.S. pregnancies: 0.7% (N=25,650)

AHF study  
Pregnancies with clinically significant antibodies (N=200)



U.S. BIRTHS: OSTERMAN MJK, HAMILTON BE, MARTIN JA, DRISCOLL AK, VALENZUELA CP. BIRTHS: FINAL DATA FOR 2021. NATIONAL VITAL STATISTICS REPORTS; VOL 72, NO 1. HYATTSVILLE, MD: NATIONAL CENTER FOR HEALTH STATISTICS. 2023. DOI: [HTTPS://DX.DOI.ORG/10.15620/CDC.122047](https://dx.doi.org/10.15620/cdc.122047).

ALLOIMMUNIZATION RATE: MOINUDDIN I, FLETCHER C, MILLWARD P. PREVALENCE AND SPECIFICITY OF CLINICALLY SIGNIFICANT RED CELL ALLOANTIBODIES IN PREGNANT WOMEN-A STUDY FROM A TERTIARY CARE HOSPITAL IN SOUTHEAST MICHIGAN. JOURNAL OF BLOOD MEDICINE. 2019 AUG 20:283-9.

# What's the difference?



Alexis



Max

Anti-D titer 512



Lucas



Lucas

Now two months old

Receiving weekly follow-up at  
hematology

Returns home to meet his dad in  
a few weeks

No long-term effects from HDFN

Rose

AHF's new Ambassador to Kenya

The difference between life and death is not disease severity. It is

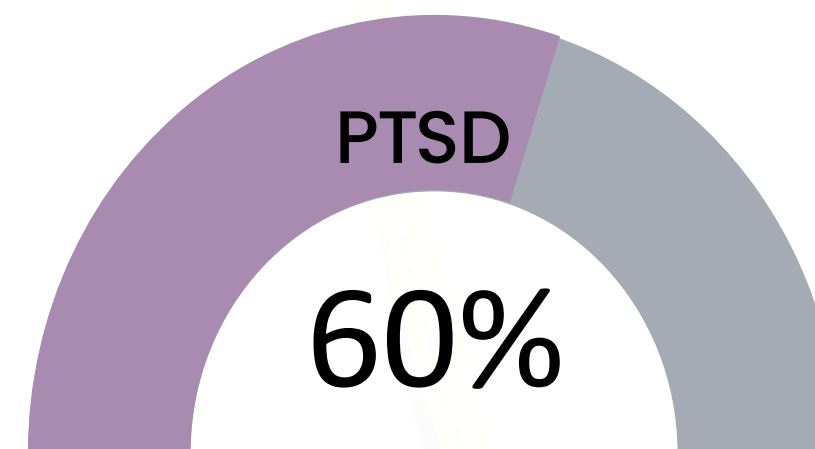
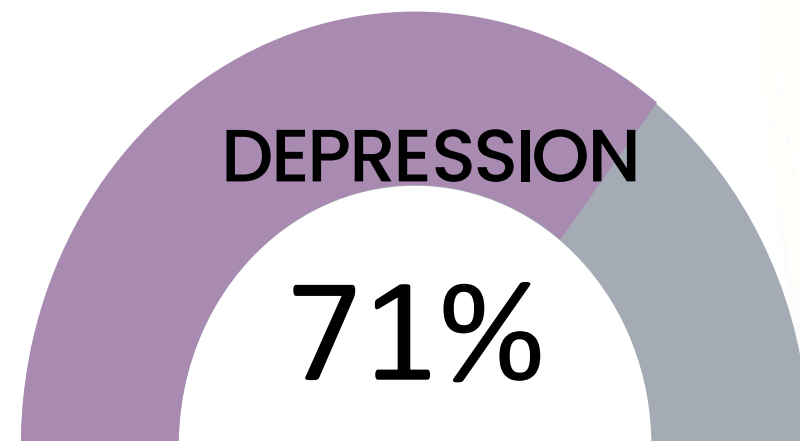
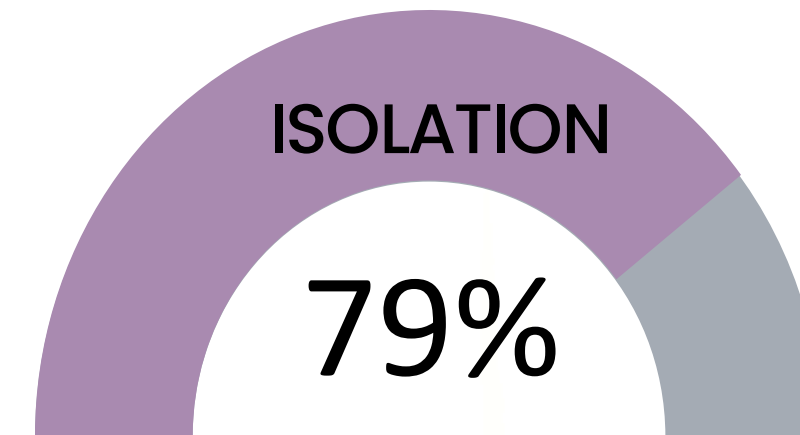
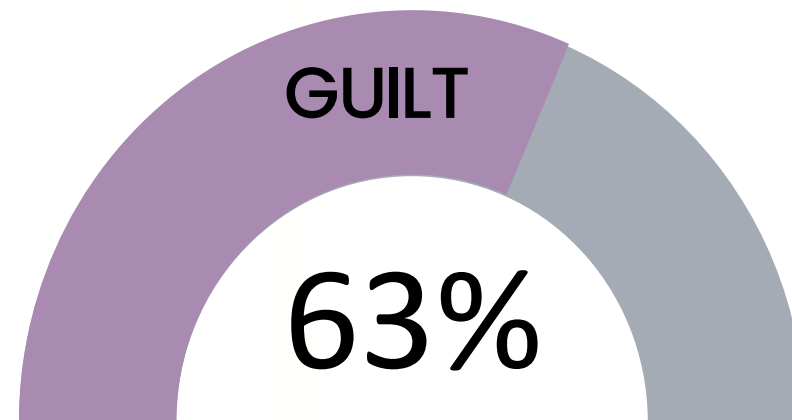
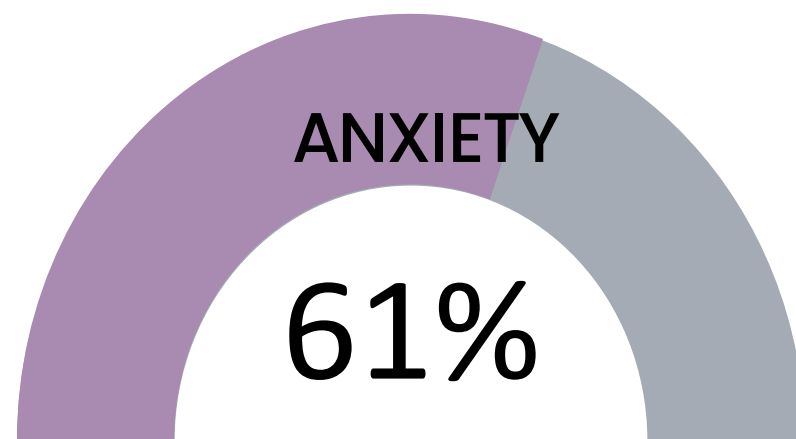
## Quality of Care.

A 98% survival rate should be expected in HDFN babies with severe disease who receive high quality care.

(Severe disease accounts for 15% of alloimmunized pregnancies with clinically significant antibodies)

# Patient experience

Most women find out they are alloimmunized while they are already pregnant. They are likely to be sent to the nearest doctor, not the best doctor. Many do not find AHF until after they have lost a child.



**WHAT ABOUT PATIENTS  
WHO RECEIVED BETTER CARE?**

High quality care group (rating 8 or higher out of 10) (N=105)

Median titer: 64

Severe disease: 18% (N=17)

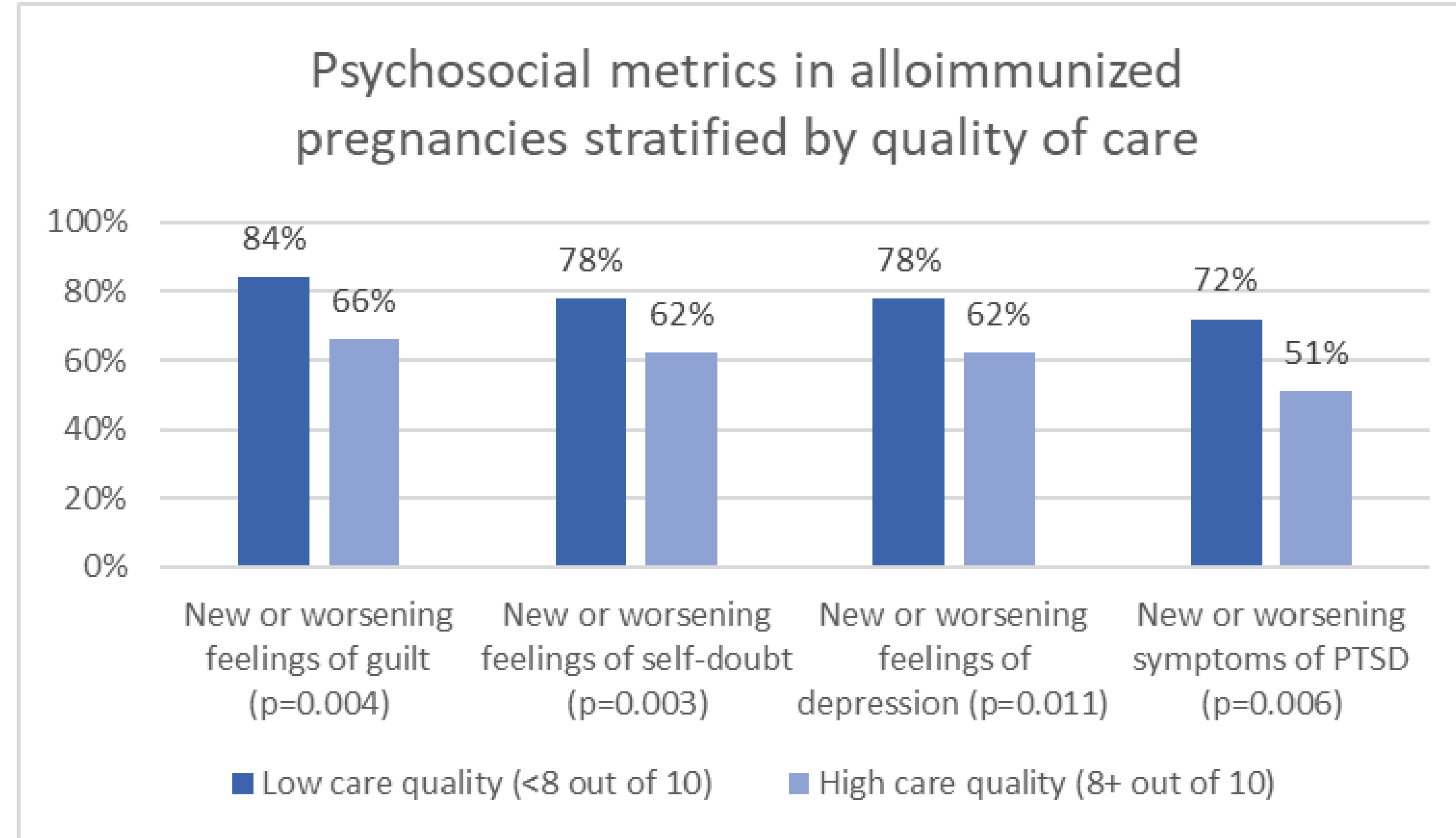
Fetal death due to HDFN: 2% (N=2)

Low quality care group (rating 7 or lower out of 10) (N=95)

Median titer: 32

Severe disease: 14% (N=15)

Fetal death due to HDFN: 8% (N=8)



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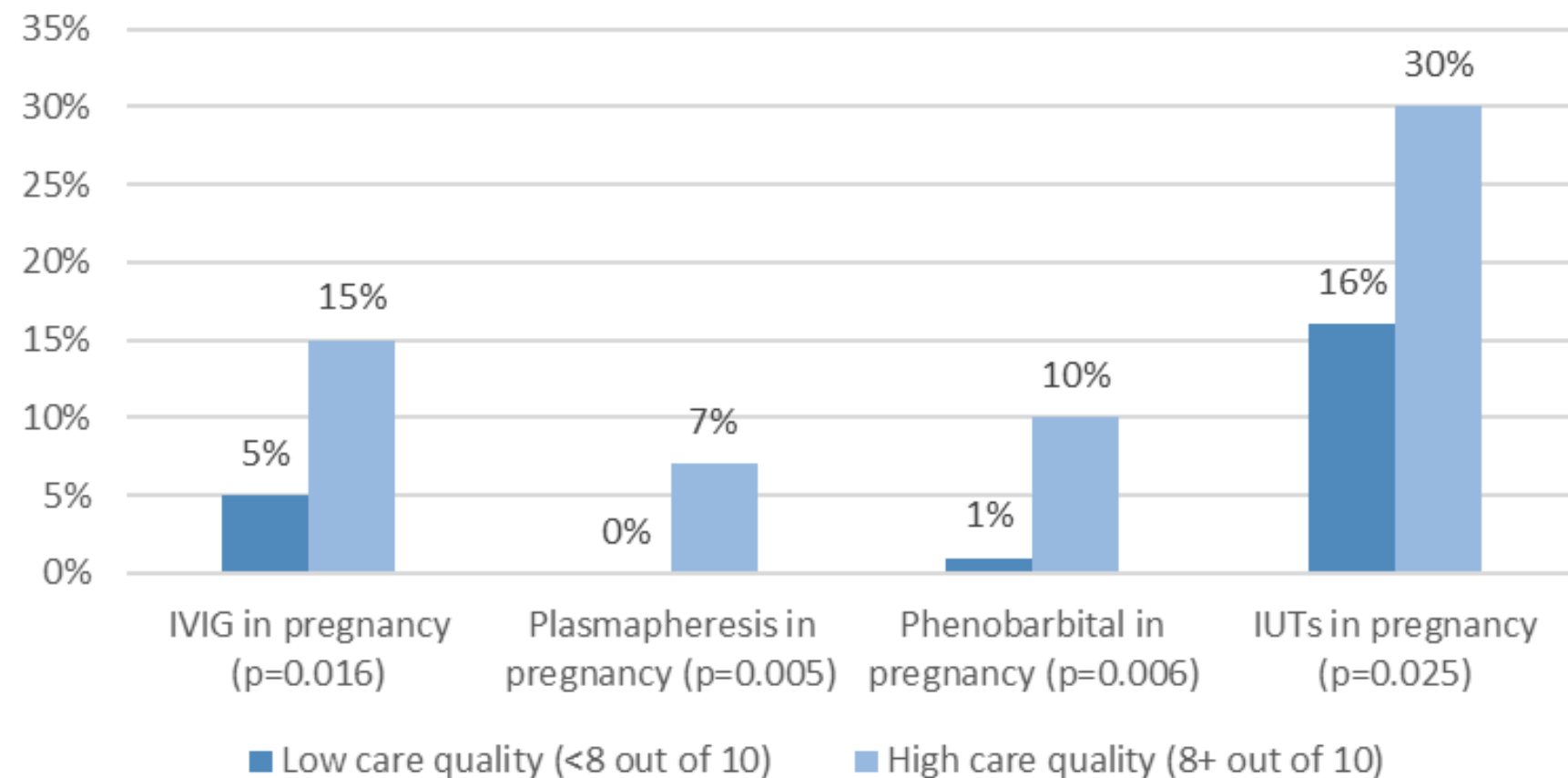
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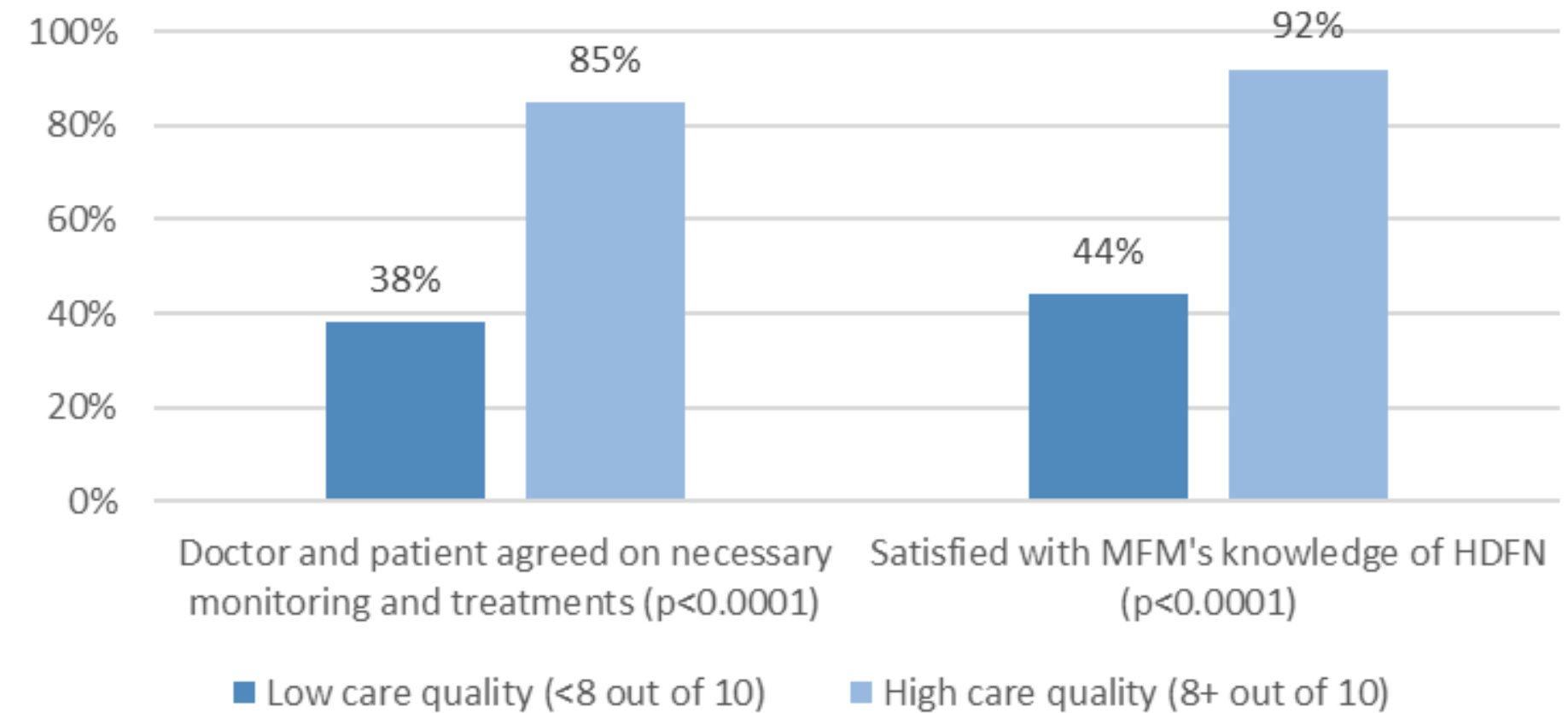
Severe disease: 14% (N=15)

Fetal death due to HDFN: 8% (N=8)

Clinical management of alloimmunized pregnancies stratified by quality of care



Patient-provider relationship in alloimmunized pregnancies stratified by quality of care



# Alloimmunization and quality care: Key takeaways

Pregnancies receiving higher quality care...

Display more clinician/patient collaboration

Include significantly more interventions but less death

Result in less prevalent negative psychosocial effects

Independent of disease severity

What can you do?

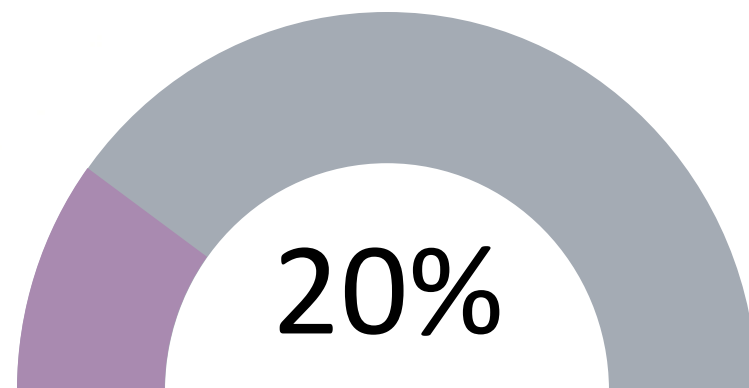
You may meet an alloimmunized female before she becomes an alloimmunized mother.



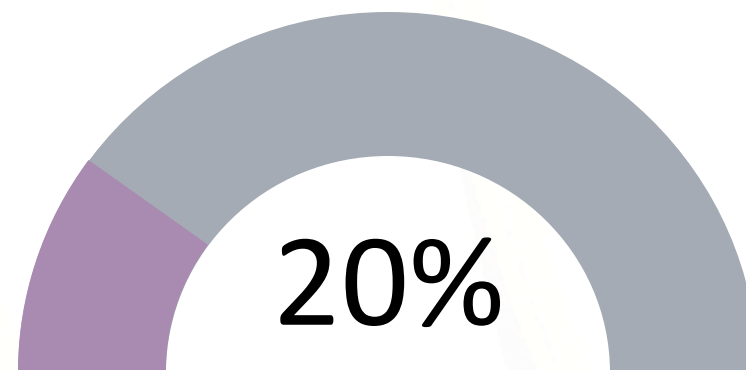
# Rh+ whole blood transfusion: perspective from alloimmunized mothers

"Consider a situation where a child is experiencing a massive bleed due to a traumatic event. Would you accept Rh positive whole blood for an Rh negative female child if it reduced her chance of dying from 24% to \_\_\_\_%:" (median response)

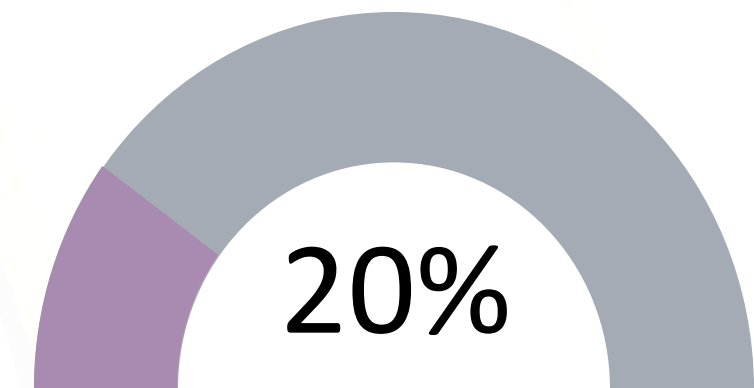
FULL SAMPLE (N=97)



MOTHERS WITHOUT HISTORY OF SEVERE DISEASE (N=74)



MOTHERS WITH HISTORY OF SEVERE DISEASE (N=23)



# Considerations in transfusion

Preliminary data indicates that alloimmunized mothers would accept Rh+ whole blood for an Rh- child if mortality risk was reduced from 24% to 20%.

Alloimmunization to a variety of antigens is common within the alloimmunized community. Any female patient receiving a transfusion, even cross-matched for RhD status, is at risk of becoming sensitized.

Treatment is available for alloimmunization and HDFN. Accessibility is contingent on a country's resources.

If a life-saving treatment results in sensitization, a unique opportunity to educate and support a patient before pregnancy presents itself.

Empowering a patient to seek and advocate for the right care WILL save lives.

# The Allo Hope Foundation

Individualized patient counsel, education, and referrals to skilled practitioners all over the world

Evidence-based resources including clinical guidelines, decision trees, and point-of-care materials

Online rare disease community for alloimmunized patients: friendships, and mental health support

Global reach through our online presence, support group, speaking engagements, and The Allo Podcast

Fundraisers funneling directly back into patient care for underserved populations

Thank you.



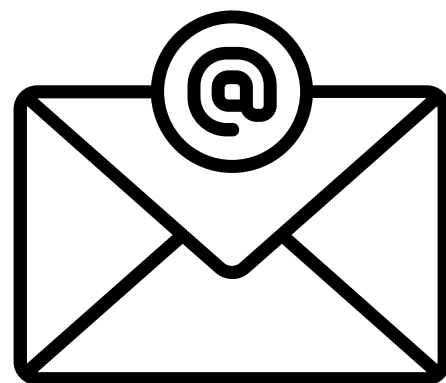
THE ALLO  
PODCAST



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ANTIBODIES IN  
PREGNANCY:  
AN AHF SUPPORT  
GROUP



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MOLLY@ALLOHOPEFOUNDATION.ORG

# What HDFN looks like



Grayson

Anti-E and S titer 4  
No intervention needed



Leah

Anti-D and c titer 512  
Exchange transfusion,  
phototherapy



Amos

Anti-D, titer 256  
5 IUTs, multiple post  
birth transfusions, IVIG,  
phototherapy, EPO