Blood group Antigen Matching Influence on Gestational Outcomes (AMIGO) study

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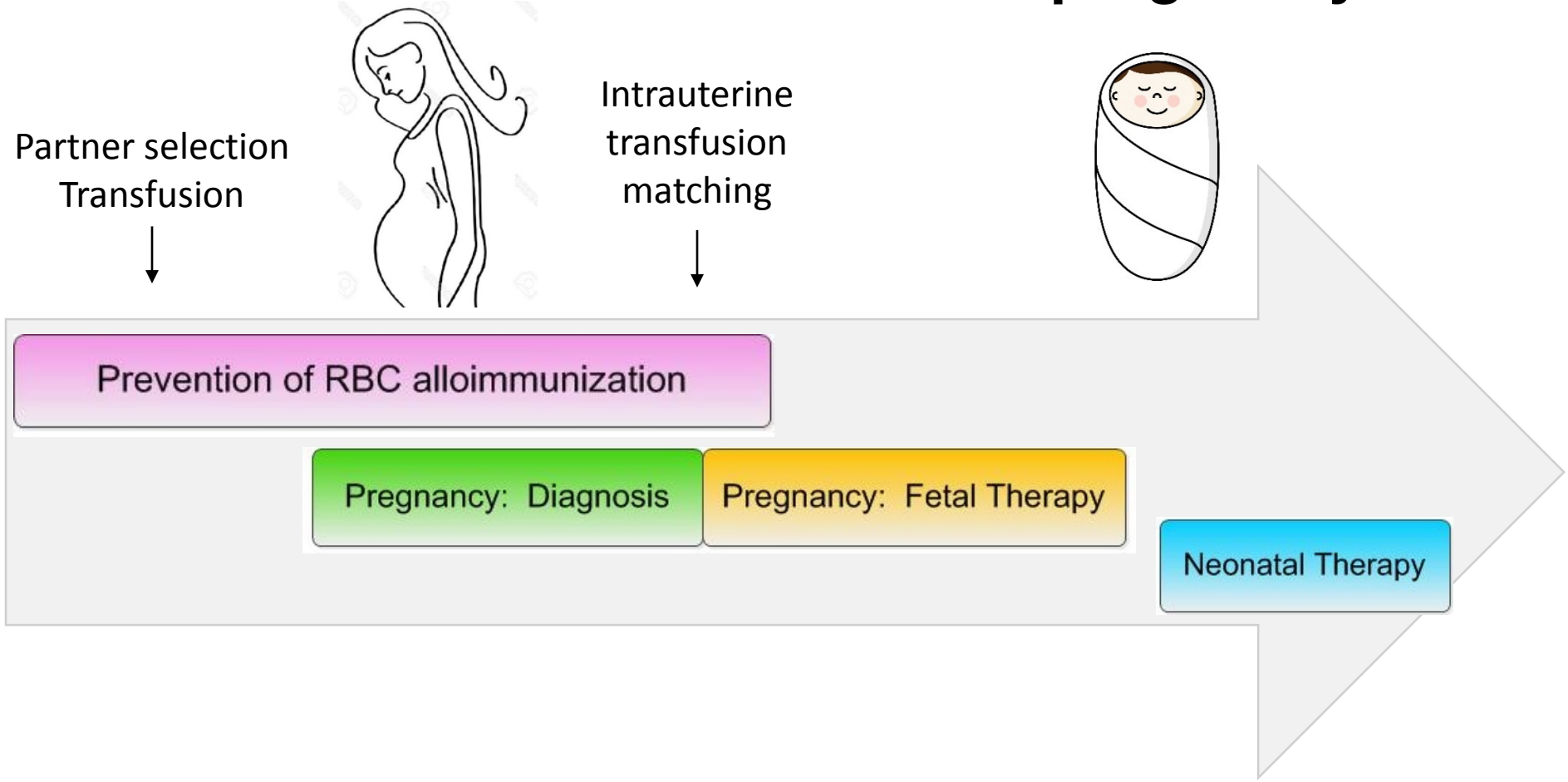
Challenges for the prevention and management of RBC alloimmunisation in pregnancy



Challenges for the prevention and management of RBC alloimmunisation in pregnancy

~~**Partner selection**~~
Transfusion

Intrauterine transfusion matching

Prevention of RBC alloimmunization

Pregnancy: Diagnosis

Pregnancy: Fetal Therapy

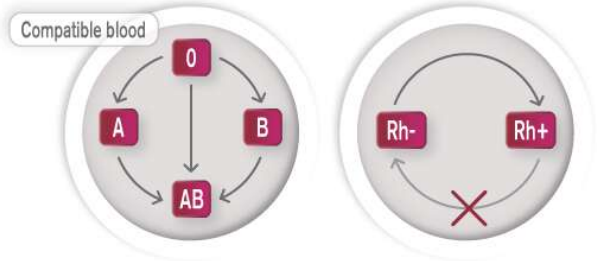
Neonatal Therapy

Prevention of maternal RBC alloimmunisation

Primary

Prevent transfusion sensitisation

- D matching



- Extended RBC matching
  - K, C, E, c

Secondary

- Anti-D
  - Prevent RhD positive fetal RBCs from causing sensitisation in RhD negative mother

Tertiary

- Extended RBC matching for IUT

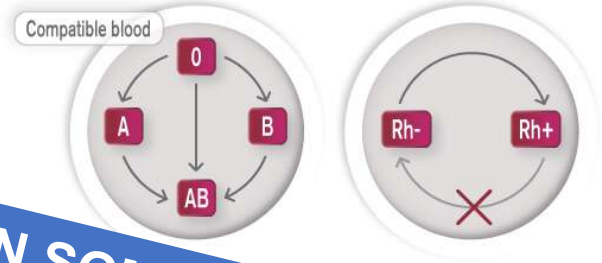
Prevention of RBC alloimmunization

Prevention of maternal RBC alloimmunisation

Primary

Prevent transfusion sensitisation

- D matching



matching

USED IN SOME COUNTRIES AND CENTRES
BSH RECOMMENDS K NEG BLOOD
N.B. MOST FCPs ARE NOT TRANSFUSED

Secondary

- Anti-D
  - Prevent RhD positive fetal RBCs from causing sensitisation in RhD negative mother

Tertiary

- Extended RBC matching for IUT

Prevention of RBC alloimmunization

AMIGO Research Question: ***Is a policy for blood group antigen matching effective in decreasing the risk of non-D alloimmunisation?***

To determine this, the study was designed in 2 stages:

1. What proportion of haemolytic disease of the newborn (HDFN) is due to maternal sensitisation from transfusion?
2. Is the incidence of HDFN lower in centres that routinely match for RBC antigens for females of childbearing potential (FCP) who require transfusion compared with centres that do not?

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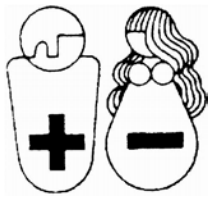
14 centres: North America, Europe, Australia

Woman with clinically significant HDFN

Maternal history check: Cause of sensitization

- Transfusion
- Previous pregnancy
- Unable to determine



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Inclusion criteria:

Mother had either had a pregnancy with a fetus that required intrauterine transfusion (IUT) and/or given birth to an infant that required neonatal exchange transfusion (NEX) between 1/1/00 and 31/12/12

Exclusion criteria:

IUT and/or NEX was required for causes other than RBC alloimmunisation

Mother was receiving extended matched RBC transfusions for any reason e.g. sickle cell disease

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- Approach to data collection:
  - Details about the patients' pregnancies and treatment
  - Classify the aetiology of the causative antibody
    1. Transfusion-related antibody — transfusion preceded HDFN and there was no history of a prior pregnancy
    2. Pregnancy related — transfusion did not precede antibody detection and a there was a history of a previous pregnancy
    3. Unable to discern — neither a documented transfusion nor a previous pregnancy preceded the index case of HDFN or the transfusion was administered in the setting of a postpartum hemorrhage making it difficult to establish the antibody's origin
- The paternal antigen status was collected if available; data on different fathers were not collected
- Data were individually collected at each site, de-identified, and then submitted for analysis using an electronic, secure online case report form system (RedCap)

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- Attribution: "Intention to Match" approach –
  - If medical record review revealed that a transfusion attributed to a MATCH centre's subject was found to have potentially been administered outside of the MATCH centre's catchment area, the transfusion was still attributed to the MATCH centre.
  - This attribution was made because this study is an analysis of the real-world application of matching policies by transfusion services or, stated another way, an "intention-to-match" analysis.
- Transfusion episodes were defined by indication for transfusion or during one hospitalisation
  - e.g., the receipt of 4 RBC units after trauma was considered 1 transfusion episode

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- **Results: Participating centre demographics and matching policies**

TABLE 1. Center demographics and policies (n = 14)

Demographic	MATCH centers (n = 5)	NoMATCH centers (n = 9)
Center type		
Blood supplier, testing service that supports more than one hospital with obstetrical care	1	0
Blood supplier, testing service that supports one hospital with obstetric care	1	1
Hospital that supports obstetrical care	3	8
Center size: number of deliveries/year		
≤5,000	2	6
5,001-10,000	2	2
10,001-30,000	1	1
Center size: number of RBC transfusions/year		
≤10,000	1	4
10,001-50,000	3	5
50,001-100,000	1	0

Prophylactic RBC Transfusion Matching Policy	
MATCH Centres	Protocol
UK	K, < 50-60 years
Sweden	K, C, <50-60 years
Netherlands	K, c, E, <45 years
Switzerland	K, C, c, E, e, <50 years
Australia	K, <50 years
NoMATCH Centres	
USA (7 centres)	
Canada	

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- **Results: Demographics of included subjects**
- N = 293
- No significant differences between patients in Match and NoMatch centres
- Patients in both groups had 2 – 3 pregnancies on average (range 1 – 11)

TABLE 2. Demographic, obstetric, and transfusion demographics of FCPs by MATCH and NoMATCH centers (n = 293 FCPs)

FCP demographics	MATCH	NoMATCH
FCP, total number (% of total number of FCPs)	179 (61%)	114 (39%)
FCP age (years), mean (range)	33.1 (19-46)	31.1 (20-46)
Ethnicity, number (% of total number of FCPs)		
Black	6 (2%)	18 (6%)
Asian, Polynesian	5 (2%)	0
Caucasian	141 (48%)	71 (24%)
Hispanic, Latina	1 (0%)	7 (2%)
Native American, Inuit	1 (0%)	1 (0%)
Other	25 (9%)	17 (6%)
Number of pregnancies per FCP, median (range)	3 (1-11)	2 (1-11)

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Blood Group Antigen Matching Influence on Gestational Outcomes (AMIGO) Study

- **Results: Information about transfusion**
- N = 293
- There were 50 transfused patients
- 63 transfusion episodes
- Median 1 transfusion episode (range 1-7)

TABLE 2. Demographic, obstetric, and transfusion demographics of FCPs by MATCH and NoMATCH centers (n = 293 FCPs)

FCP demographics	MATCH	NoMATCH
Number of FCPs who received transfusions, FCPs (% of total number of FCPs)	33 (11%)	17 (6%)
Number of FCPs who received transfusions by indication (number of transfusion episodes)*†		
Obstetric hemorrhage	24 (24)	6 (8)
Unknown, other	5 (6)	7 (8)
Trauma	2 (2)	2 (2)
Surgery, non-trauma related	2 (2)	2 (2)
Cancer	1 (1)	0
Nonmalignant hematologic disease	0	1 (7)
Anemia	1 (1)	0 (0)
FCP received platelet transfusion in isolation from RBCs	0	7 (2)
FCP with history of IVDU	2 (1)	10 (3)

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TABLE 3. Outcomes and interventions for each affected pregnancy, fetus, and/or infant due to HDFN

Characteristic	MATCH	NoMATCH
Number of FCPs	179	114
Total number of pregnancies	534	301
Number of pregnancies affected by severe HDFN	272	153
Fate of each pregnancy affected by severe HDFN*		
Term infant (>37 weeks), live born, survived	107	67
Preterm infant (<37 weeks), live born, survived	148	70
Preterm infant (<37 weeks), live born, expired	4	6
Still birth	5	3
Miscarriage	3	1
Unknown	5	6
Clinical findings and interventions		
IUTs, total	169	109
IUT per pregnancy per enrolled mother	2.75	3.15
Hyperbilirubinemia, no treatment needed	5	2
Phototherapy	81	56
Simple RBC transfusion	27	39
Exchange transfusion	57	57
Intravenous immune globulin	0	32
Unknown, other	17	28

*Includes term and preterm infants who survived; does not include fetal interventions such as IUT.

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- **Results: Clinical Outcomes**
- Match: 534 pregnancies/179 patients
- NoMatch: 301 pregnancies/114 patients
- 51% of pregnancies in both groups were associated with HDFN
- > 90% survival following a broad range of interventions

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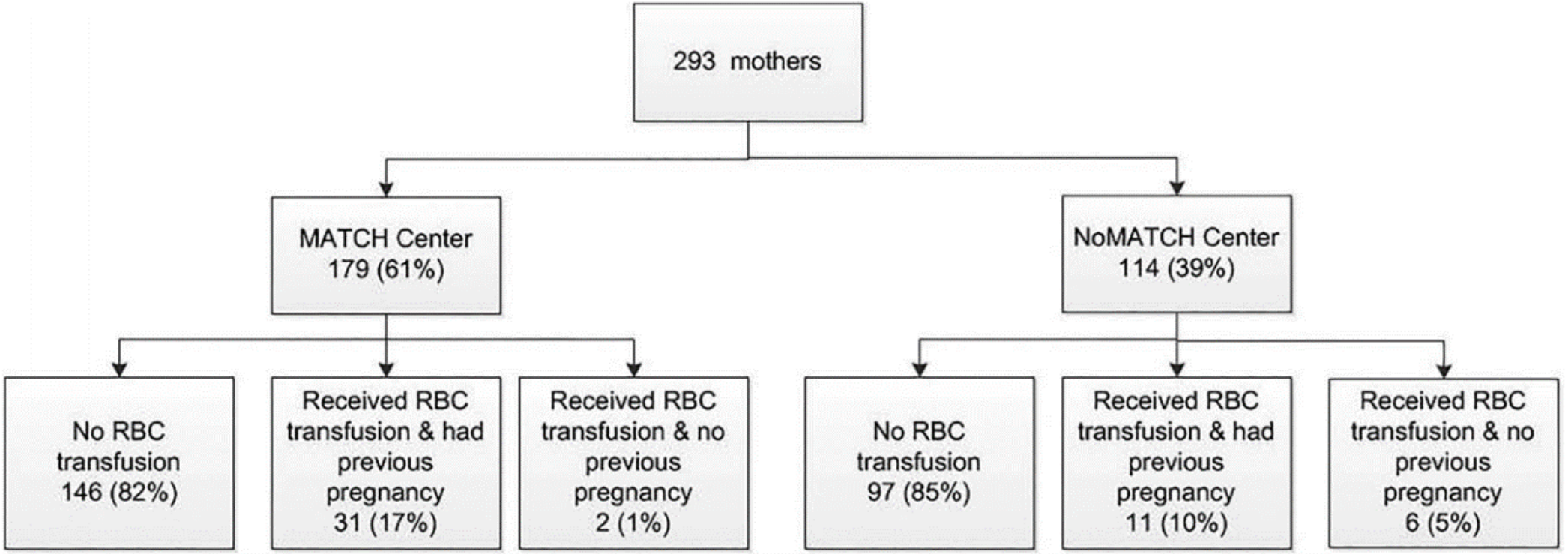

243: Pregnancy related — transfusion did not precede antibody detection and a there was a history of a previous pregnancy

8: Transfusion-related antibody — transfusion preceded HDFN and there was no history of a prior pregnancy

42: Unable to discern — neither a documented transfusion nor a previous pregnancy preceded the index case of

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TABLE 4. Case histories for the eight women with HDFN likely to have been caused by RBC transfusion

Case	RBC antibody(-ies)	Number of transfusion episodes	RBC transfusion indication	Center type	NEX and/or IUT	Pregnancy outcome
1	K, c, E	2	Other	NoMATCH	NEX	Term baby, survived
2	K	1	Unknown	MATCH	NEX, IUT	Term baby, survived
3	c	1	Obstetrical hemorrhage	MATCH	NEX, IUT	Preterm baby, survived
4	E, G	1	Obstetrical hemorrhage	NoMATCH	NEX, IUT	Preterm baby, survived
5	K, C	1	Trauma, MVA	NoMATCH	IUT	Stillbirth
6	D, Wr^a	1	Unknown	NoMATCH	IUT	Term baby, survived
7	C, Jk^b	1	Unknown	NoMATCH	IUT	Term baby, survived
8	D, C, G	1	Trauma, MVA	NoMATCH	NEX, IUT	Preterm baby, survived

MVA = motor vehicle accident.

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TABLE 6. Comparison of MATCH and NoMATCH centers' RBC sensitization rates and antibody specificities in the FCPs who received transfusions (n = 50) and who had pregnancies affected by HDFN*

RBC antibody specificity	FCP sensitized?		MATCH	NoMATCH	OR (95% CI)
K	Yes	17	13	4	2.11 (0.56-7.91)
	No	33	20	13	
C	Yes	8	4	4	3.2 (0.67-15.19)
	No	42	10	32	
c	Yes	19	9	10	1.89 (0.58-6.11)
	No	31	10	21	
E	Yes	13	5	8	1.03 (0.28-3.77)
	No	37	14	23	

*This table lists only antigens that are matched for at the MATCH centers. There were 33 FCPs who were alloimmunized to at least one RBC antigen at the MATCH centers and 17 at the NoMATCH centers.

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- 17/35 (49%) of MATCH centre subjects who received transfusions occurred in a region not covered by the MATCH centre's transfusion policy (e.g., transfusion before the FCP moved to a hospital where the MATCH centre provided care)

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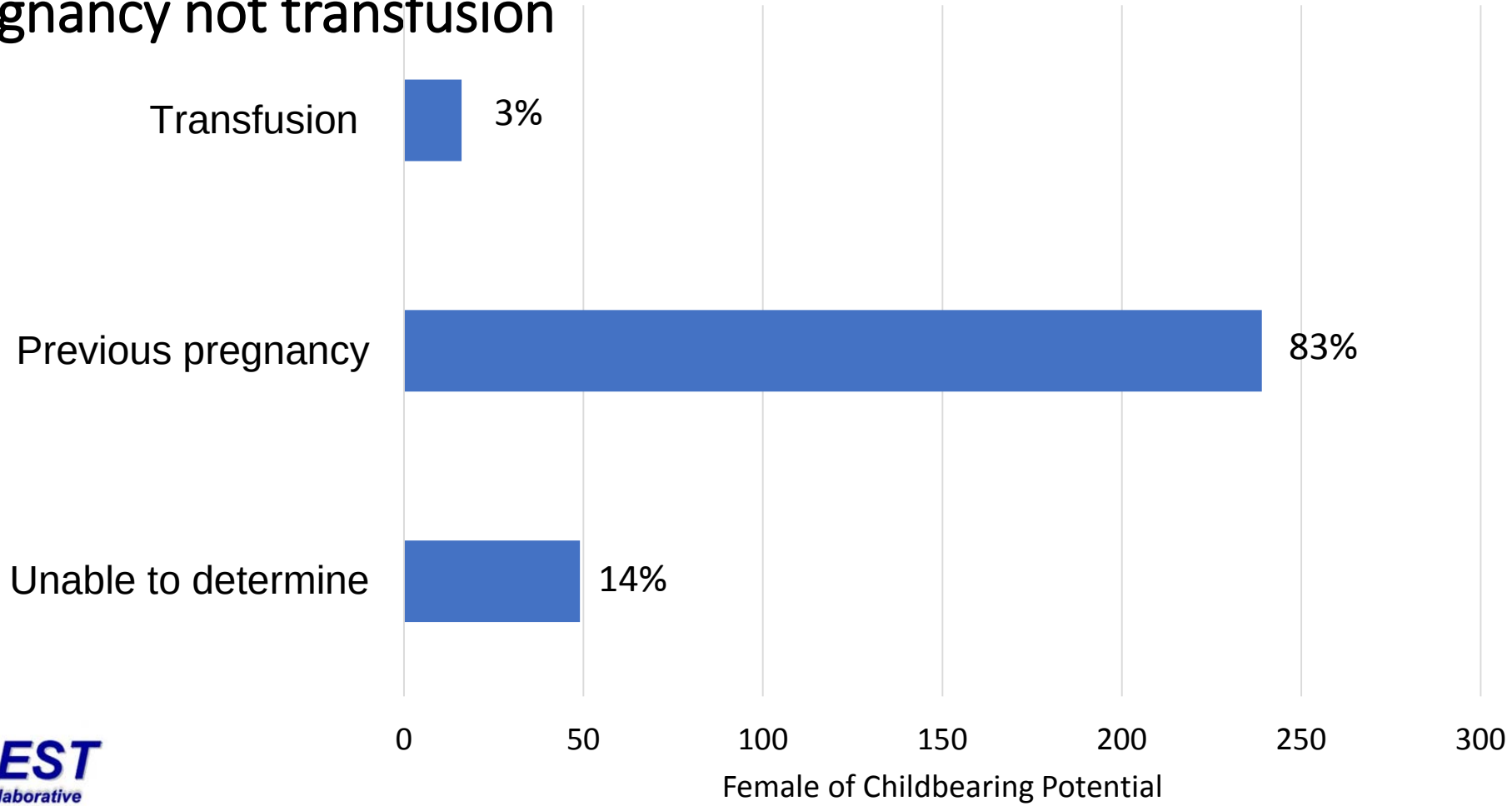
Main conclusion: Source of maternal RBC sensitisation causing severe HDFN is pregnancy not transfusion



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AMIGO -- Conclusions

- In a broad sampling of women with severe HDFN in 7 nations
  - Most HDFN is due to previous pregnancy 83%
  - Proportion of women with HDFN due to transfusion is 3%
- Did not find a protective effect of MATCH centre policies
  - Few transfused subjects
- Future energy around broad based antigen matching transfusion policies throughout the world may improve results, but the use of antigen matching in a metro or regional areas alone e.g. in the United States may not provide an impact
- Limitation: Small number of included subjects

Thank you

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