

Review of Platelet Transfusion Practices in the NICU and Newborn Nursery

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Disclosures



I have no financial disclosures or conflicts of interest with the presented material in this presentation

Case #1

Baby Boy AZ:

- 31 1/7 week male
- Pregnancy c/b growth restriction, gHTN, GDM
- Urgent C/S for NRFHT → Now in NICU

NICU Course:

- Prematurity/SGA, ?sepsis
- Platelets: downtrend from 73 to 46 → **Transfused 1u platelets**

Case #2

Baby Boy ZA:

- 31 1/7 week male
- Pregnancy c/b growth restriction, gHTN, GDM
- Urgent C/S for NRFHT → Now in NICU

NICU Course:

- Prematurity/SGA, ?sepsis
- Platelets: downtrend from 73 to 46 → **Not Transfused**

Discussion & Objectives

Same Case, Different Transfusion Practice:

- Which choice do you agree with?
- Which choice was correct?

Objectives:

- Define platelet transfusion thresholds
- Unique considerations in preterm neonates
- Application of these data in our institution

Standard Platelet Transfusion Thresholds

When to Transfuse

Active Bleeding:

- Generally < 100K if C
- <100K if C

BIDMC Guidelines for Adult Inpatient Transfusion Practice

The following represent an evidence-based approach to transfusion practice agreed upon by the BIDMC Transfusion Committee. Transfusion therapy should always be individualized for each patient.

Surgical/Pre-surgical:

- Varies by

→ How were these thresholds developed?

Prophylactic transfusion indications

*Platelet count
(x 10³ per μ L)*

, no ≤ 50

active ≤ 100

Prophylactic:

- Generally <10k for uncomplicated/inpatient
- Generally <20k for complicated/outpatient

Transfusion Thresholds

Evidence-Based Transfusion Practices

- Various trials - different patient populations



Applicability:

- Broad vs Narrow?
- Demographic differences?
- Study design?

Recommendation 1: The AABB recommends that platelets should be transfused prophylactically to reduce the risk for spontaneous bleeding in hospitalized adult patients with therapy-induced hypoproliferative thrombocytopenia. The AABB recommends transfusing hospitalized adult patients with a platelet count of 10×10^9 cells/L or less to reduce the risk for spontaneous bleeding. The AABB recommends transfusing up to a single apheresis unit or equivalent. Greater doses are not more effective, and lower doses equal to one half of a standard apheresis unit are equally effective. (Grade: strong recommendation)

→ **Narrow, well-defined populations**

Recommendation 2: The AABB suggests prophylactic platelet transfusion for patients having elective central venous catheter placement with a platelet count less than 20×10^9 cells/L. (Grade: weak recommendation; low-quality evidence).

Recommendation 3: The AABB suggests prophylactic platelet transfusion for patients having elective diagnostic lumbar puncture with a platelet count less than 50×10^9 cells/L. (Grade: weak recommendation; very-low-quality evidence).

Not Without Risk!

	Frequency, Episodes: Unit
Reactions	
Febrile (FNHTR)	• 1–4:100
Allergic	• 1–4:100
Delayed hemolytic	• 1:1000
TRALI	• 1:5000
Acute hemolytic	• 1:12,000
Fatal hemolytic	• 1:100,000
Anaphylactic	• 1:150,000
Infections^a	
Hepatitis B	• 1:220,000
Hepatitis C	• 1:1,800,000
HIV-1, -2	• 1:2,300,000
HTLV-1 and -2	• 1:2,993,000
Malaria	• 1:4,000,000
Other Complications	
RBC allosensitization	• 1:100
HLA allosensitization	• 1:10
Graft-versus-host disease	Rare

Unique Considerations in Preterm Neonates

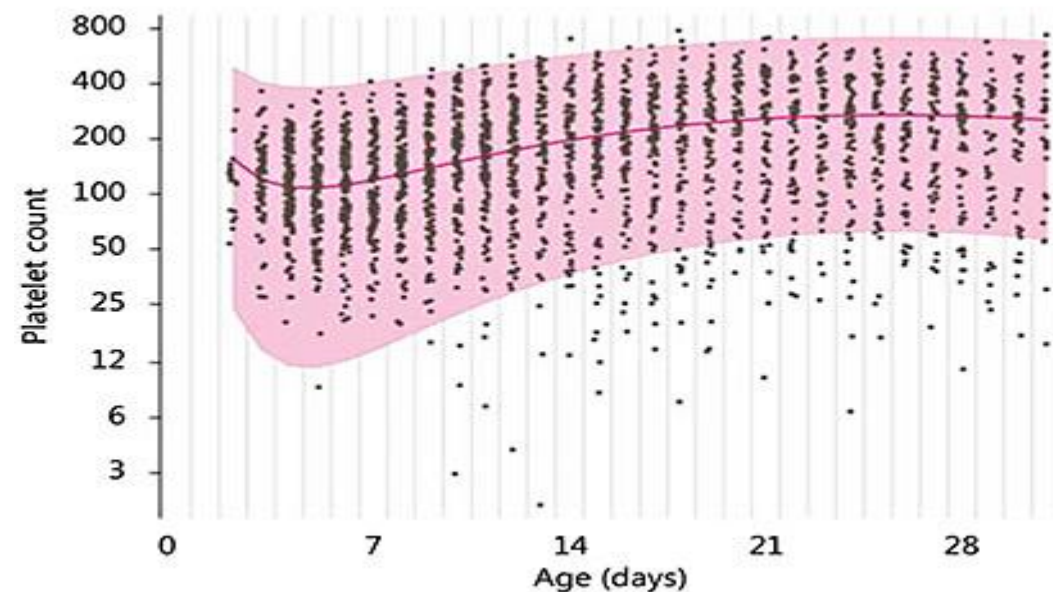
Thrombocytopenia in Neonates

Common Complication in Preterm Neonates

- Incidence inversely proportional to GA
- Predicts poor outcomes

Diverse Etiologies

- Maternal factors
- “Early” vs “Late” onset



	Ill-Appearing, Premature		Well-Appearing, Full Term	
Type	Early Onset (<24 h)	Late Onset (>72 h)	Early Onset (<24 h)	Late Onset (>72 h)
Common	Sepsis TORCH infection Birth asphyxia DIC NEC	Sepsis Thrombosis DIC NEC Drug-induced	Placental insufficiency Autoimmune Alloimmune (NAIT) Occult infection	Occult infection NEC
Rare	Chromosomal disorders <ul style="list-style-type: none"> • Trisomy 13 • Trisomy 18 • Trisomy 21 • Turner syndrome 	Inborn errors of metabolism Fanconi anemia	Inherited syndromes <ul style="list-style-type: none"> • Bernard-Soulier • Wiskott-Aldrich • Thrombocytopenia absent radii • Others Vascular tumors <ul style="list-style-type: none"> • Kasabach-Merritt 	Inborn errors of metabolism Fanconi anemia

Thrombocytopenia in Neonates

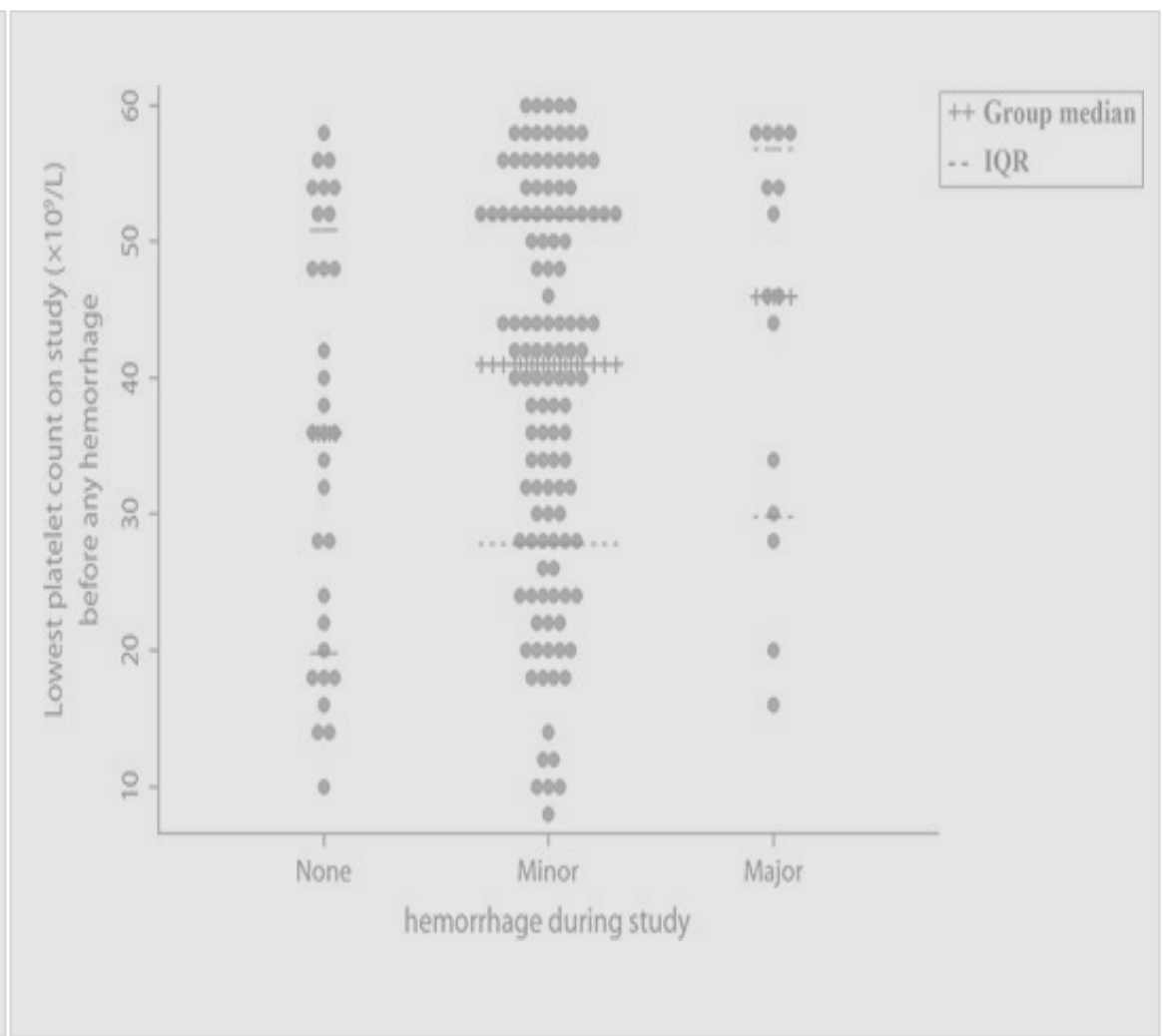
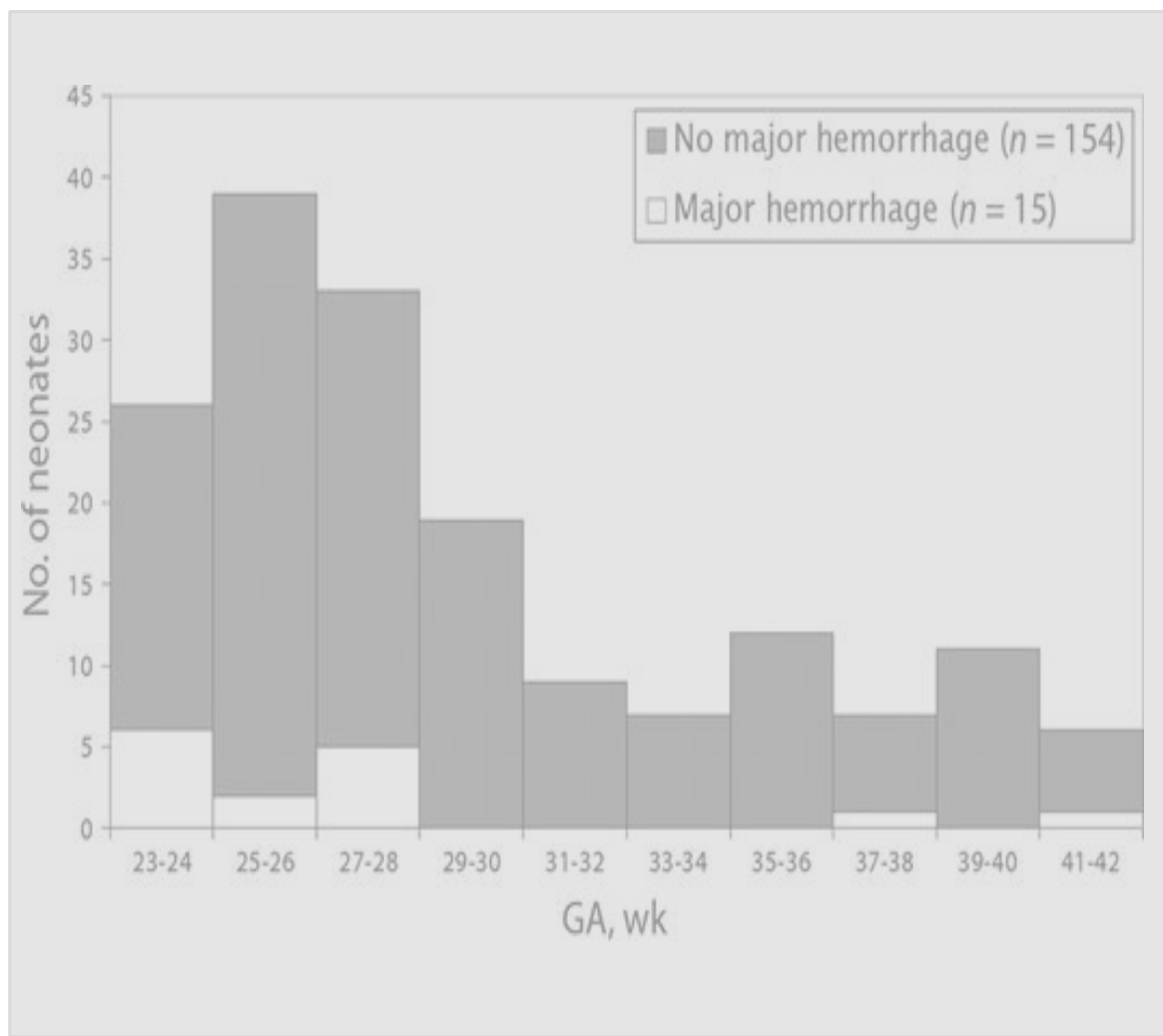
Relationship of Platelet Count to Bleeding Risk:

- IVH vs other
- Benefit vs Harm
- Observational data – Trials?

Table 3 Bleeding conditions in 371 neonates with neonatal thrombocytopenia

Bleeding condition	Number (%)
Intra-/periventricular hemorrhage (I/PVH)	104 (55.3)
IVH I	36 (19.2)
IVH II	15 (8.0)
IVH III	26 (13.8)
PVH	27 (14.3)
Cutaneous bleeding	46 (24.5)
Gastrointestinal bleeding	16 (8.5)
Pulmonary hemorrhage	14 (7.4)
Hematuria	4 (2.1)
Umbilical cord bleeding	3 (1.6)
Adrenal gland hemorrhage	1 (0.6)

PlaNeT-1 Trial



→ Need for high-quality comparative RCT...

PlaNeT-2 Trial

PlaNeT-2 Trial

Multicenter RCT

Goal: Establish optimal platelet transfusion thresholds in preterm neonates

Primary Comparison: Restrictive vs Liberal threshold

- Restrictive: <25k
- Liberal: <50k

PlaNeT-2 Trial

- **Demographic:** Preterm neonates with thrombocytopenia
- **Inclusion Criteria:**
 - GA <34w
 - Platelet count <50k
 - No IVH – Confirmed by cranial US
- **Exclusion Criteria:**
 - H/o serious bleed
 - Terminal comorbidity/malformation
 - Immune thrombocytopenia
 - Did not receive parenteral VitK
- **Primary Outcome:** Death or new major bleed within 28d
 - Many secondary outcomes

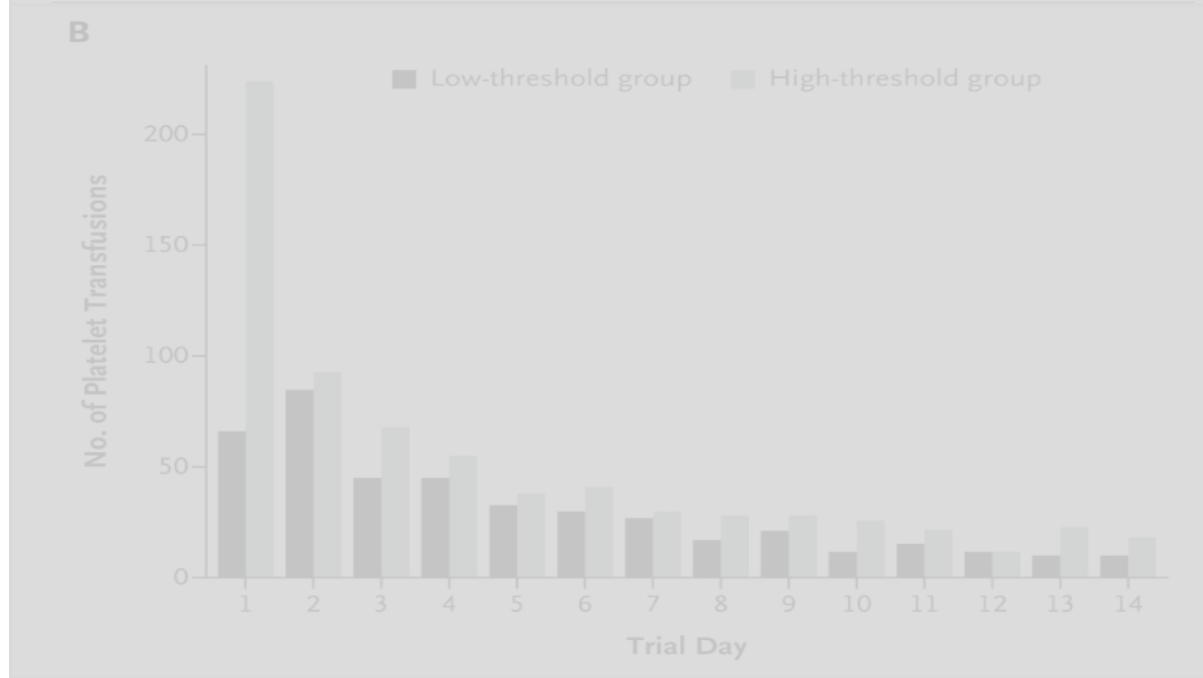
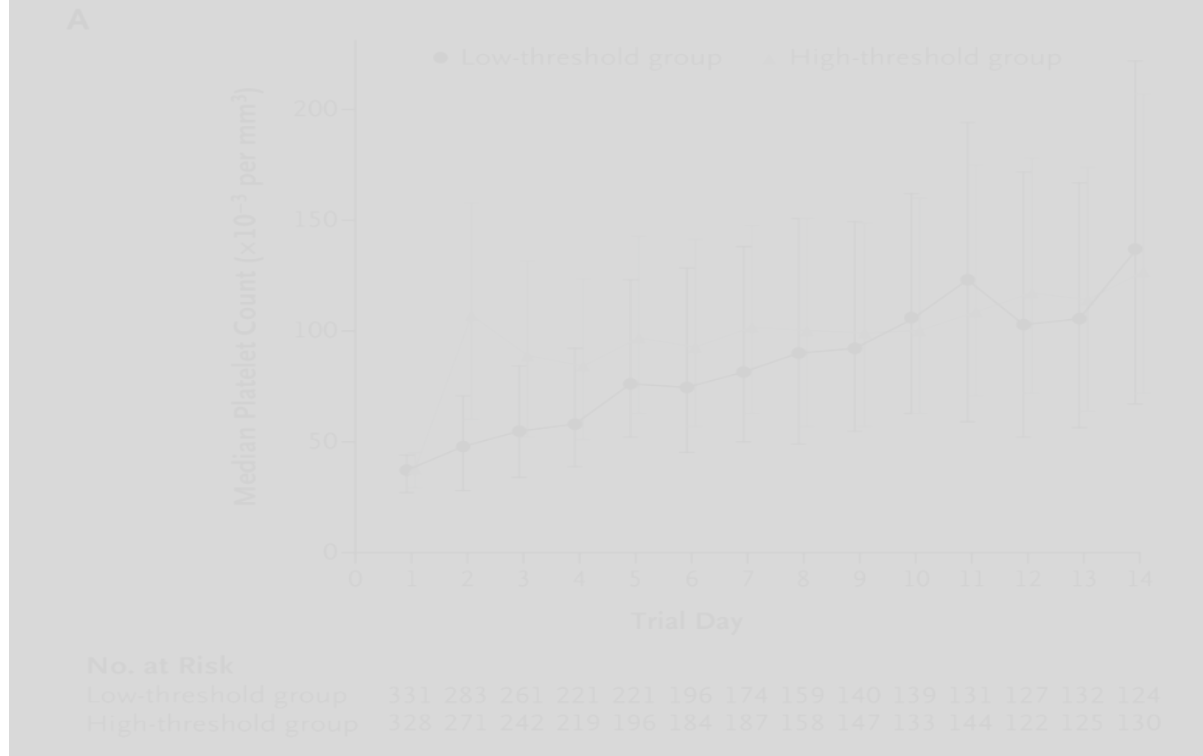
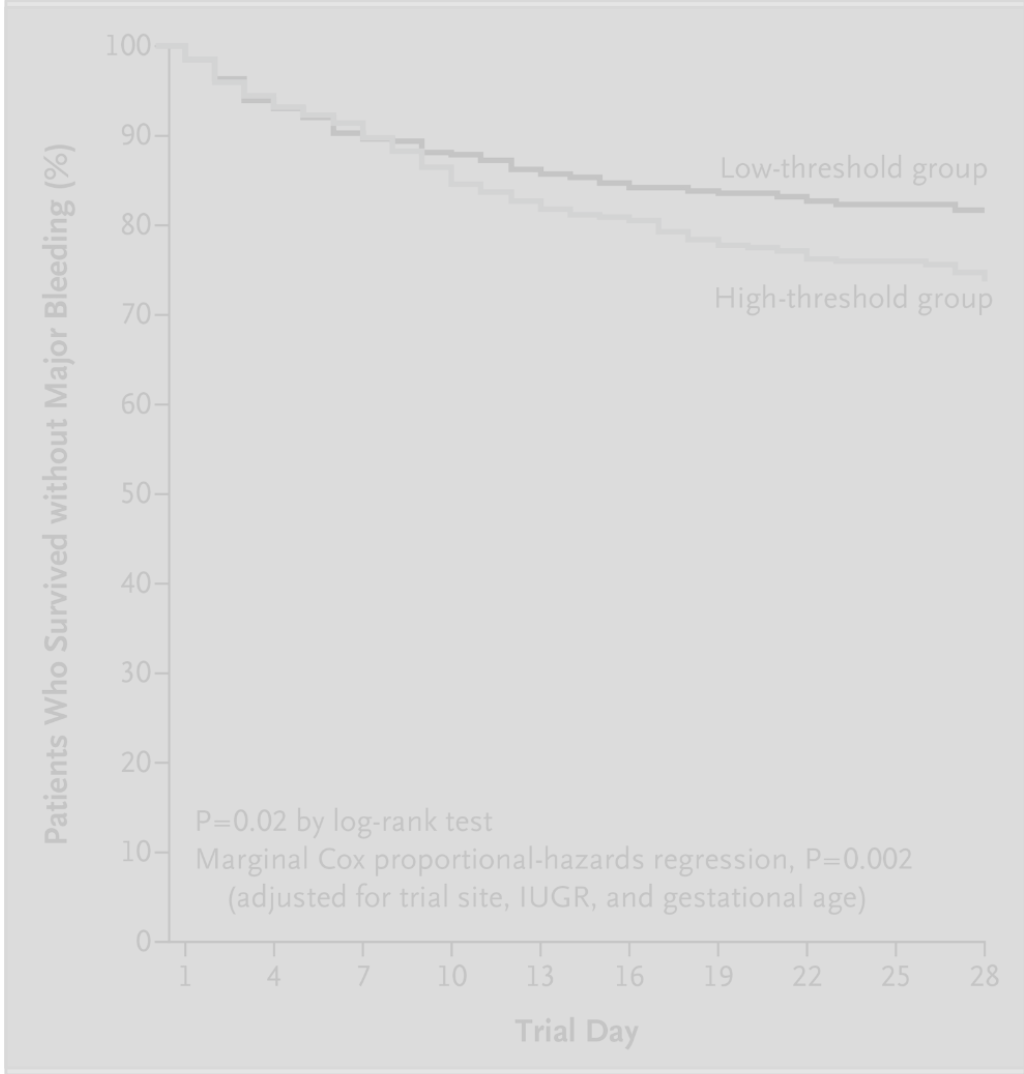
Table 1. Characteristics of the Trial Population.*

Variable	Low-Threshold Group (N = 331)	High-Threshold Group (N = 329)
Intrauterine growth restriction — no./total no. (%)†‡	125/331 (38)	120/328 (37)
Antenatal glucocorticoids — no./total no. (%)	289/329 (88)	292/326 (90)
Full course of glucocorticoids, ≥2 doses — no./total no. (%)	191/281 (68)	194/281 (69)
Clinical evidence of chorioamnionitis — no./total no. (%)	26/330 (8)	28/322 (9)
Cesarean delivery — no./total no. (%)†	201/329 (61)	208/328 (63)
Female sex — no./total no. (%)†	140/331 (42)	123/328 (38)
Median weight at birth (IQR) — g†	743 (605–990)	728 (600–940)
Median gestation at birth (IQR) — wk†	26.7 (24.9–28.7)	26.6 (24.9–28.9)
Median corrected gestational age at randomization (IQR) — wk†	28.9 (26.9–31.6)	29.0 (27.2–31.5)
Median weight at randomization (IQR) — g§	892 (670–1190)	860 (668–1170)
Median postnatal age at randomization (IQR) — days†	7.0 (3.7–18.9)	8.4 (4.0–21.0)
Randomization ≤5 days of age — no./total no. (%)	125/331 (38)	116/328 (35)
Was receiving treatment for necrotizing enterocolitis at randomization — no./total no. (%)†¶	49/331 (15)	58/328 (18)
Was receiving antibiotic treatment for sepsis at randomization — no./total no. (%)†	206/331 (62)	209/328 (64)
Major bleeding before randomization — no./total no. (%)†	62/331 (19)	60/328 (18)
Pulmonary bleeding — no./total no. (%)	31/62 (50)	22/60 (37)
Frank rectal bleeding — no./total no. (%)	8/62 (13)	9/60 (15)
Intraventricular hemorrhage — no./total no. (%)**	40/59 (68)	39/58 (67)
Intracranial hemorrhage — no./total no. (%)	10/62 (16)	7/60 (12)
Other bleeding — no./total no. (%)	7/62 (11)	4/60 (7)
Median platelet count at randomization (IQR) — × 10 ⁻³ per cubic millimeter†	38 (28–44)	38 (29–44)

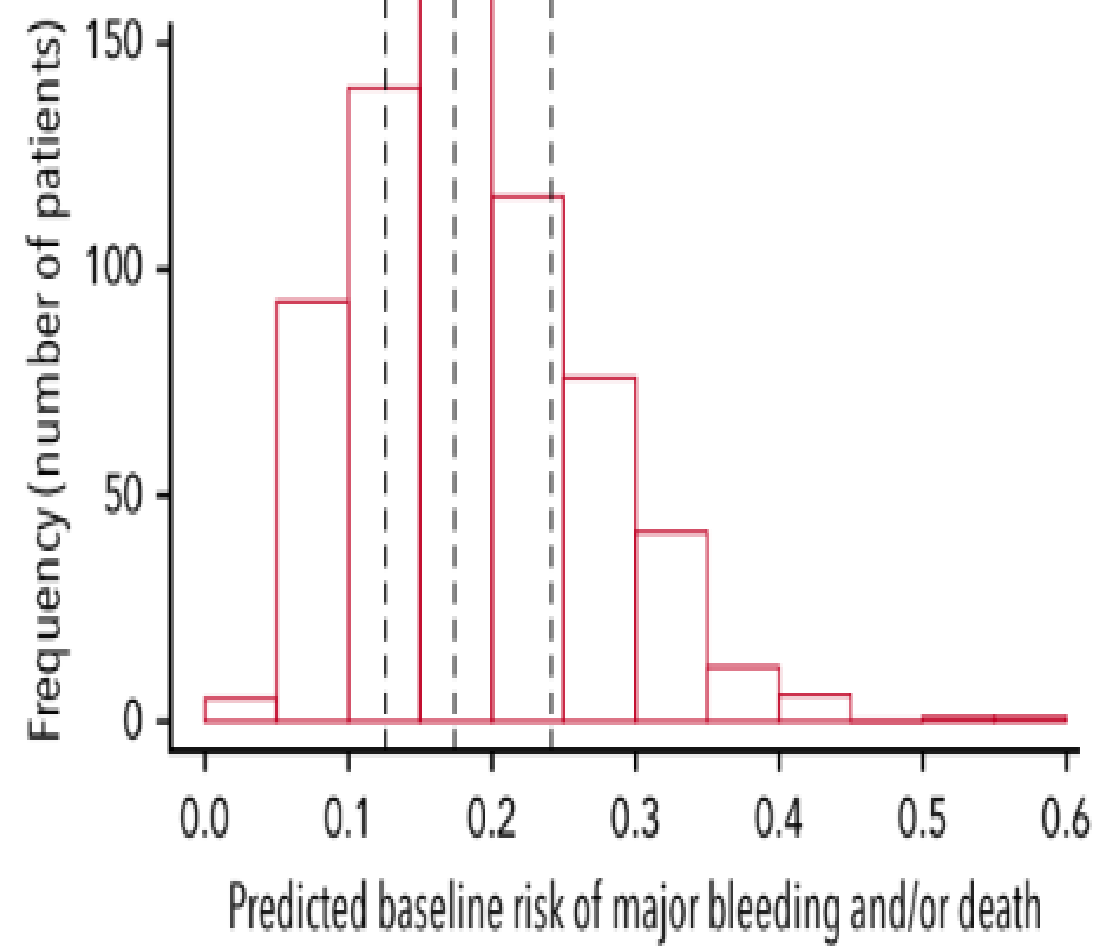
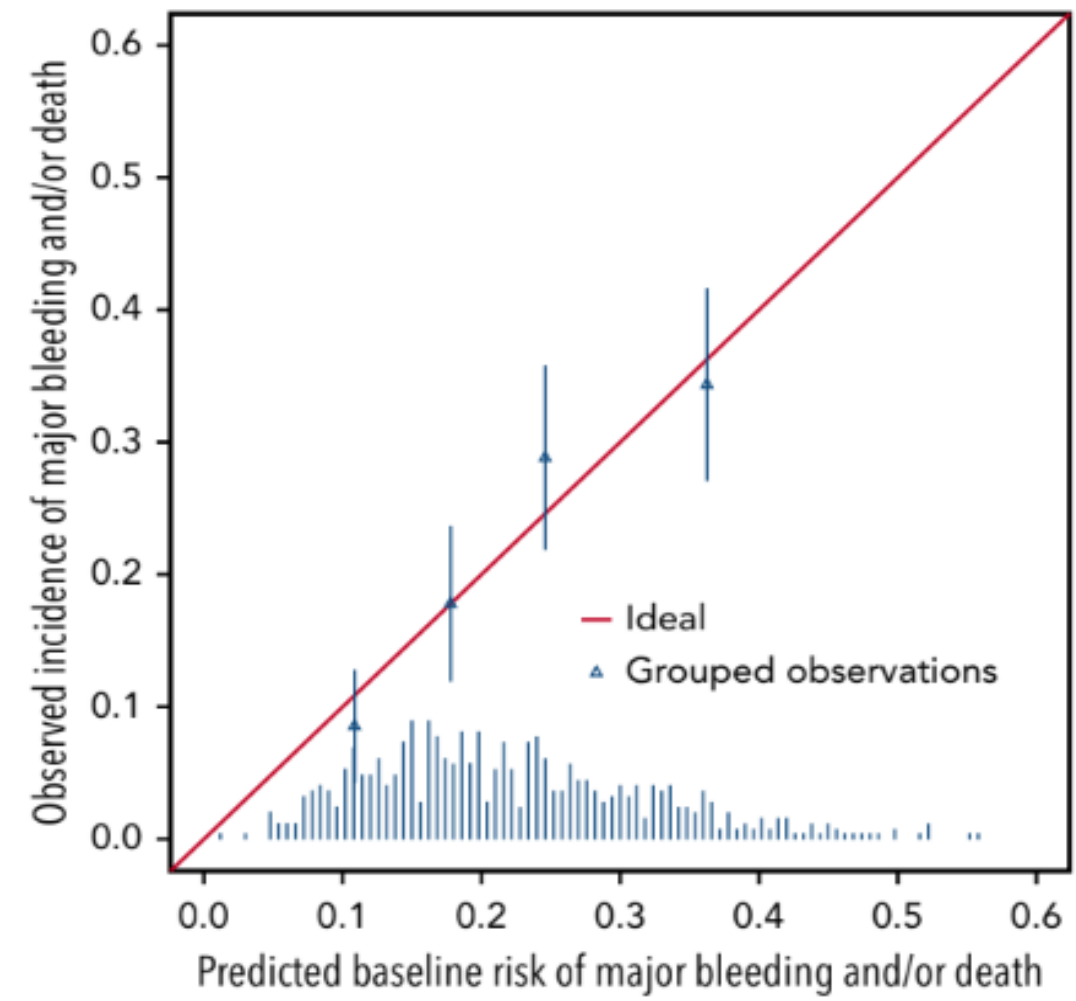
PlaNeT-2 Trial: Data

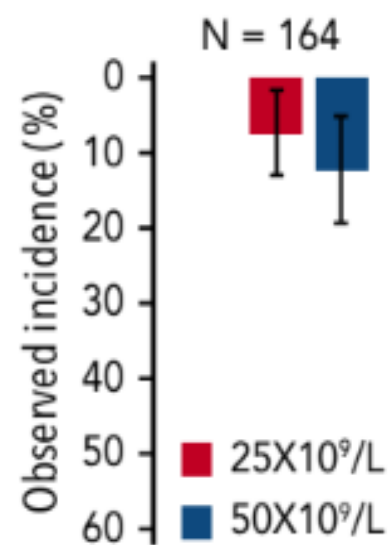
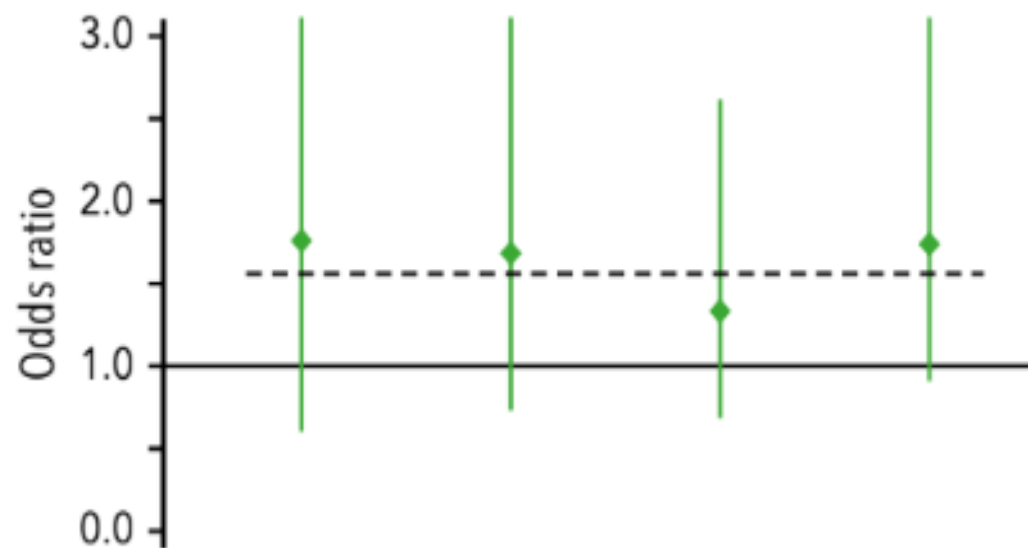
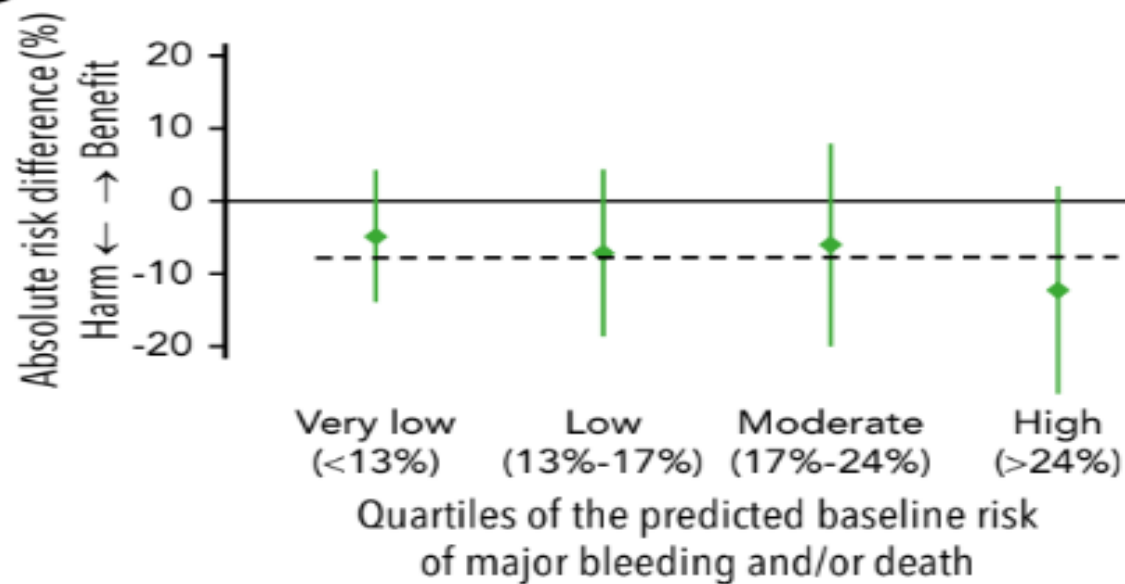
Table 2. Primary and Secondary Outcomes, According to Treatment Group.

Outcome	Low-Threshold Group (N=331)	High-Threshold Group (N=329)	Odds Ratio or Hazard Ratio (95% CI)*
Primary outcome			
Death or major bleeding episode through trial day 28 — no./total no. (%)	61/329 (19)	85/324 (26)	OR, 1.57 (1.06–2.32)†
Secondary outcomes‡			
Death through trial day 28 — no./total no. (%)	33/330 (10)	48/326 (15)	OR, 1.56 (0.95–2.55)
At least one major bleeding episode through trial day 28 — no./total no. (%)	35/330 (11)	45/328 (14)	HR, 1.32 (1.00–1.74)
Survival with bronchopulmonary dysplasia at 36 wk — no./total no. (%)§	153/281 (54)	169/269 (63)	OR, 1.54 (1.03–2.30)
Post hoc outcome of death or bronchopulmonary dysplasia at 36 wk — no./total no. (%)	200/329 (61)	224/324 (69)	OR, 1.56 (1.07–2.27)
Discharge by 38 wk of corrected gestational age — no./total no. (%)	41/328 (12)	29/326 (9)	HR, 0.68 (0.46–1.00)
Survival with unilateral or bilateral retinopathy of prematurity of stage ≥2 at 38 wk of corrected gestational age — no./total no. (%)¶	71/297 (24)	82/279 (29)	OR, 1.37 (0.91–2.08)
Unilateral or bilateral retinopathy of prematurity of stage ≥2 treated with laser or bevacizumab therapy — no./total no. (%)	29/295 (10)	36/278 (13)	OR, 1.38 (0.79–2.42)
New sepsis event after randomization — no./total no. (%)	175/326 (54)	181/324 (56)	HR, 1.10 (0.92–1.33)
New necrotizing enterocolitis event after randomization — no./total no. (%)**	54/326 (17)	42/324 (13)	HR, 0.72 (0.37–1.41)
>1 Major bleeding episode through trial day 28 — no./total no. (%)	14/330 (4)	11/328 (3)	HR, 0.80 (0.40–1.60)
At least one minor or worse bleeding episode through trial day 14 — no./total no. (%)	232/328 (71)	225/324 (69)	HR, 0.96 (0.84–1.09)
At least one moderate or worse bleeding episode up to trial day 14 — no./total no. (%)	114/328 (35)	111/324 (34)	HR, 1.01 (0.86–1.18)
At least one platelet transfusion — no./total no. (%)	177/331 (53)	296/328 (90)	HR, 2.75 (2.36–3.21)
No. of platelet transfusions administered in infants who received at least one transfusion — median (IQR)	2 (1–3)	2 (1–3)	

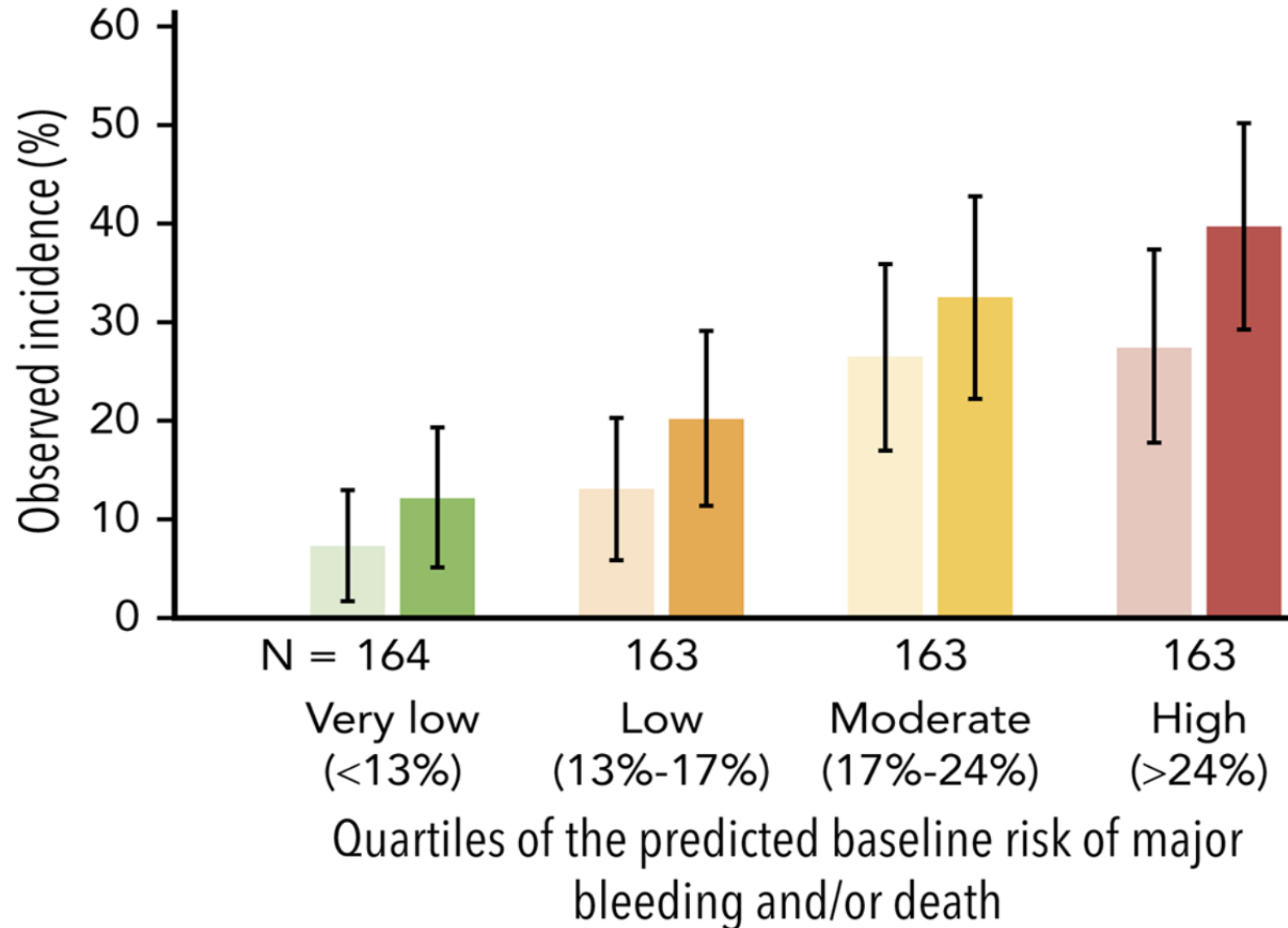


PlaNeT-2 Trial: Post-Hoc Analysis



A**B****C**

Preterm neonates benefit from a $25 \times 10^9/L$ prophylactic platelet count threshold, irrespective of predicted baseline outcome risk



PlaNeT-2 Trial: Final Results

PlaNeT-2 Trial Results:

- “Among **preterm infants** with severe thrombocytopenia, the use of a **platelet-count threshold of 50,000** per cubic millimeter for prophylactic platelet transfusion resulted in a **higher rate of death or major bleeding** than a **restrictive threshold of 25,000** per cubic millimeter within 28 days after randomization.”
- “...a $25 \times 10^9/L$ prophylactic platelet count threshold can be adopted in all preterm neonates, **irrespective of predicted baseline outcome risk.**”

At Our Institution...

Implementation at BIDMC

First Step: Identify BIDMC's established transfusion practices

- Define demographic → same as PlaNeT-2
- Policies in place → Standard Operating Procedures

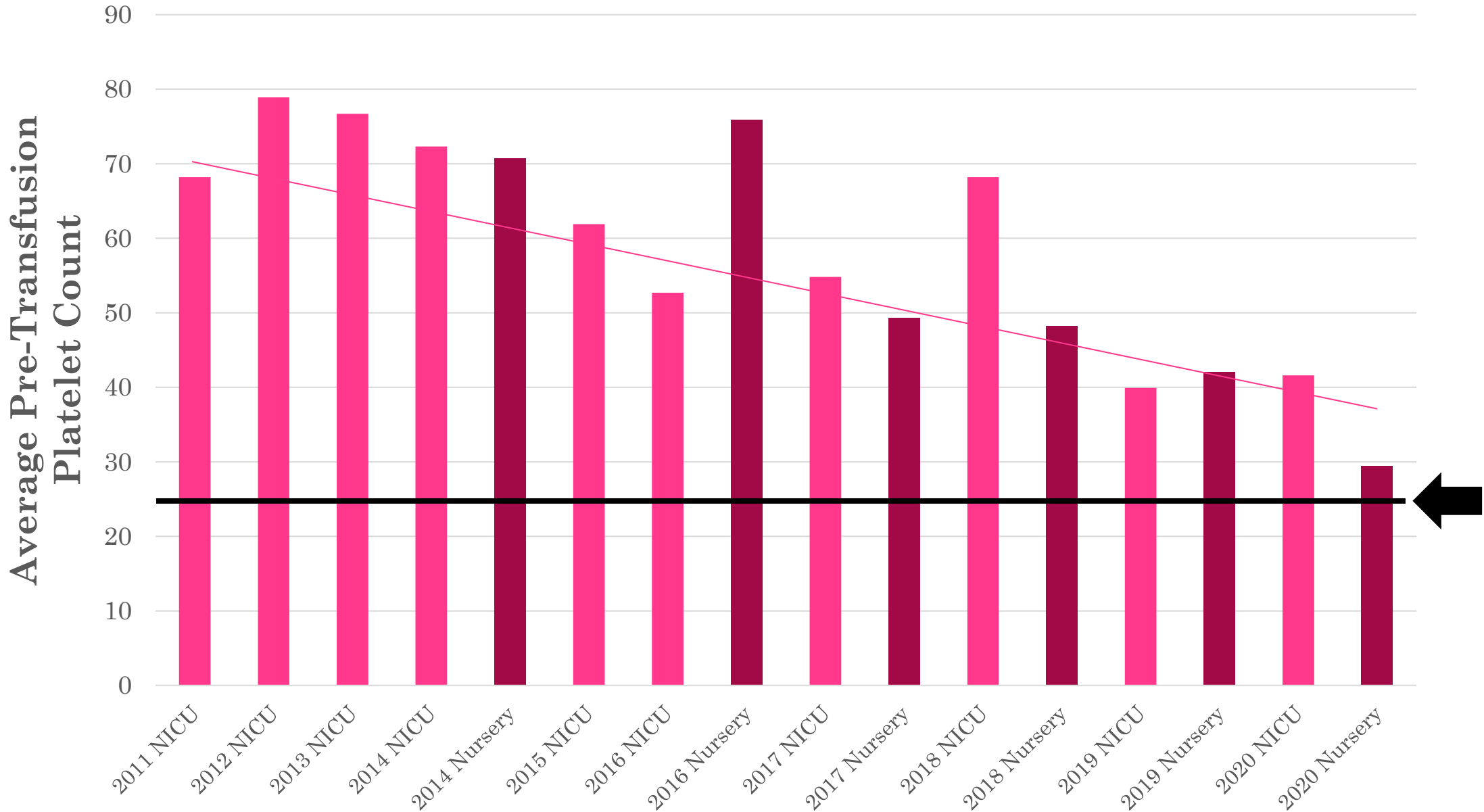
Second Step: Review transfusion data for this demographic

→ Time for a chart review!

		Gestational Age at time of Birth	Age at time of Transfusion (day of life)	Transfusion Indication		# of products Transfused	Pre-Count	Post-Count	Bleeding Events/Complications	Disposition	Weight	Additional Information	
Gestational Age at time of Birth	Age at time of Transfusion (day of life)	35w2d	4	Progressive thrombocytopenia iso subplial hemorrhage		1(3 total)	80	209	Subplial hemorrhage discovered on day 1 of life iso thrombocytopenia	Discharged home	1850g at birth	neonatal alloimmune thrombocytopenia. Maternal antiplatelet antibody screen was positive for antibodies against GpA Ia/Ila/HPA 5-b. Ft was Concern for possible NAIT, so patient was given 2 doses of IVIG. Testing of parents recommended	
		36w2d	1	Thrombocytopenia ISO chronic subchorionic hematoma		1(4 total)	73	125	Thrombocytopenia at birth with count of 37k, as well as chronic subchorionic hematoma present throughout	Discharged home	2300g at birth	Concern for possible NAIT, so patient was given 2 doses of IVIG. Testing of parents recommended	
Gestational Age at time of Birth	Age at time of Transfusion (day of life)	36w2d	1	Thrombocytopenia ISO chronic subchorionic hematoma		1(4 total)	65	97	Thrombocytopenia at birth with count of 37k, as well as chronic subchorionic hematoma present throughout	Discharged home	2300g at birth	Concern for possible NAIT, so patient was given 2 doses of IVIG. Testing of parents recommended	
		36w2d	3	Thrombocytopenia ISO chronic subchorionic hematoma		1(4 total)	54	38	Thrombocytopenia at birth with count of 37k, as well as chronic subchorionic hematoma present throughout	Discharged home	2300g at birth	Concern for possible NAIT, so patient was given 2 doses of IVIG. Testing of parents recommended	
Gestational Age at time of Birth	Age at time of Transfusion (day of life)	35w2d	3	Thrombocytopenia ISO chronic subchorionic hematoma		1(4 total)	15	191	Thrombocytopenia at birth with count of 37k, as well as chronic subchorionic hematoma present throughout	Discharged home	2300g at birth	Concern for possible NAIT, so patient was given 2 doses of IVIG. Testing of parents recommended	
		36w2d	0	Platelets dropped to 34k at the end of a double volume exchange transfusion (done for hemolytic anemia iso of antibodies)		1	34	212	None Listed	Transferred to Beverly Hospital on day of life 14	1950g at birth	anti-Kell antibodies and anti-Jka antibodies with fetal hemolytic anemia requiring fetal transfusion. Infant was also given IVIG on day of life 0	
Gestational Age at time of Birth	Age at time of Transfusion (day of life)	36w2d	6	Slow decrease of platelets (167k at birth) to 60k		1	62	132	None listed	Discharged home	1200g at birth	None	
		36w2d	1	Persistent thrombocytopenia and coagulopathy		1(6 total)	57	No post	None listed	Discharged home	2840g at birth	Was twin A of a di-di pregnancy	
Gestational Age at time of Birth	Age at time of Transfusion (day of life)	36w2d	1	Persistent thrombocytopenia and coagulopathy		1(6 total)	89	131 (poor post)	None listed	Discharged home	2840g at birth	Was twin A of a di-di pregnancy	
		36w2d	2	Persistent thrombocytopenia and coagulopathy		1(6 total)	86	91 (next day)	None listed	Discharged home	2840g at birth	Was twin A of a di-di pregnancy	
Gestational Age at time of Birth	Age at time of Transfusion (day of life)	36w2d	3	Persistent thrombocytopenia and coagulopathy		1(6 total)	91	No post	None listed	Discharged home	2840g at birth	Was twin A of a di-di pregnancy	
		34w1d	5	Persistent thrombocytopenia and coagulopathy		1(6 total)	54	148	None listed	Discharged home	2840g at birth	Was twin A of a di-di pregnancy	
Gestational Age at time of Birth	Age at time of Transfusion (day of life)	36w2d	6	Persistent thrombocytopenia and coagulopathy		1(6 total)	90	183	None listed	Discharged home	2840g at birth	Was twin A of a di-di pregnancy	
		36w2d	6	Persistent thrombocytopenia and coagulopathy		1(6 total)	91	184	None listed	Discharged home	2385g at birth	Born with cardiac anomalies not consistent with life	
Gestational Age at time of Birth	Age at time of Transfusion (day of life)	36w2d	0	Platelets not checked on day of transfusion, before or after		1	720	740g at birth	None	Discharged home	740g at birth	Platelets not checked on day of transfusion, before or after	
		36w2d	0	Severe growth restriction iso twin/twin transfusion syndrome. Prenatal care mostly in		1	320g at birth	None	None	Discharged home	320g at birth	Severe growth restriction iso twin/twin transfusion syndrome. Prenatal care mostly in	
Gestational Age at time of Birth	Age at time of Transfusion (day of life)	36w2d	0	Patient requiring resuscitation at time of birth and did not survive		1	490g	490g	None	Discharged home	490g	Patient requiring resuscitation at time of birth and did not survive	
		36w2d	0	None		1	2300g at birth	None	None	Discharged home	2300g at birth	None	
Gestational Age at time of Birth	Age at time of Transfusion (day of life)	36w2d	0	None		1	520g	520g	None	Discharged home	520g	None	
		36w2d	0	None		1	980g	980g	None	Discharged home	980g	IVF dichorionic-diamniotic twin gestation, complicated by IUFD of Twin A at 24 weeks of IVF dichorionic-diamniotic twin gestation, complicated by IUFD of Twin A at 24 weeks of maternal isoimmunization to the B and C antigens, this is the maternal first pregnancy. Fetus required intra uterine transfusion for fetal	
Gestational Age at time of Birth	Age at time of Transfusion (day of life)	36w2d	11	thrombocytopenia of immaturity		1(total 2)	72	225	None listed	Discharged home	980g	IVF dichorionic-diamniotic twin gestation, complicated by IUFD of Twin A at 24 weeks of IVF dichorionic-diamniotic twin gestation, complicated by IUFD of Twin A at 24 weeks of maternal isoimmunization to the B and C antigens, this is the maternal first pregnancy. Fetus required intra uterine transfusion for fetal	
		36w2d	0	Thrombocytopenia following double volume exchange transfusion		1	66	210	None Listed	Discharged home	2260g	None	
Gestational Age at time of Birth	Age at time of Transfusion (day of life)	36w2d	0	thrombocytopenia iso coagulopathy, subdural hemorrhage, and b/l IVH		1	41	160 (next day)	b/l Intraventricular hemorrhage plus subdural hemorrhage present on day of life 1	Discharged home	1110g	Born with hypothyroidism	
		36w2d	1	thrombocytopenia		1(total 2)	34	no post	None Listed	Deceased	1515g	None	
Gestational Age at time of Birth	Age at time of Transfusion (day of life)	36w2d	2	thrombocytopenia		1(total 2)	88	No post	None Listed	Deceased	1515g	None	
		36w2d	3	Thrombocytopenia iso pulmonary/neuro hemorrhage		1	96	134	Pulmonary hemorrhage plus parenchymar brain hemorrhage	Deceased	601g	Chronic lung disease on ventilator	
Gestational Age at time of Birth	Age at time of Transfusion (day of life)	36w2d	0	Thrombocytopenia following double volume exchange transfusion		1	48	161	None Listed	Discharged home	2440g	Maternal antibody positive for anti-C and anti-D antibodies severe fetal anemia without hydrops, status post PUBS procedure x5 with intrauterine fetal packed red blood cell transfusions. Was	
		36w2d	12	Thrombocytopenia iso IVH and sepsis		1(total 2)	42	no post	Grade 1 IVH (discovered day of life 11)	Transferred to Children's Hospital	1720g	None	
Gestational Age at time of Birth	Age at time of Transfusion (day of life)	36w2d	13	Thrombocytopenia iso IVH and sepsis		1(total 2)	77	No post	Grade 1 IVH (discovered day of life 11)	Transferred to Children's Hospital	1720g	None	
		36w2d	16	Progressive thrombocytopenia iso pulmonary/neuro hemorrhage		1	108	No post	"Mild" pulmonary hemorrhage (developed day of life 9)	Discharged home	680g	None	
Gestational Age at time of Birth	Age at time of Transfusion (day of life)	36w2d	3	Thrombocytopenia iso pulmonary/neuro hemorrhage		1	96	194	Pulmonary hemorrhage plus parenchymar brain hemorrhage	Deceased	601g	Chronic lung disease on ventilator	
		36w2d	0	Thrombocytopenia following double volume exchange transfusion		1	48	161	None Listed	Discharged home	2440g	Maternal antibody positive for anti-C and anti-D antibodies severe fetal anemia without hydrops, status post PUBS procedure x5 with intrauterine fetal packed red blood cell transfusions. Was	
Gestational Age at time of Birth	Age at time of Transfusion (day of life)	36w2d	12	Thrombocytopenia iso IVH and sepsis		1(total 2)	42	no post	Grade 1 IVH (discovered day of life 11)	Transferred to Children's Hospital	1720g	None	
		36w2d	13	Thrombocytopenia iso IVH and sepsis		1(total 2)	77	No post	Grade 1 IVH (discovered day of life 11)	Transferred to Children's Hospital	1720g	None	
Gestational Age at time of Birth	Age at time of Transfusion (day of life)	36w2d	16	Progressive thrombocytopenia iso pulmonary/neuro hemorrhage		1	108	No post	"Mild" pulmonary hemorrhage (developed day of life 9)	Discharged home	680g	None	
		36w2d	0	Thrombocytopenia iso coagulopathy		1	53	121	pulmonary hemorrhage	deceased	1380g	None	
Gestational Age at time of Birth	Age at time of Transfusion (day of life)	36w2d	49	thrombocytopenia iso NEC		1	66	no post	none	transferred to Boston Children's Hospital	580g	None	

→ A lot of chart review...

NICU/Nursery Platelet Pre-Transfusion Averages 2011-2020



PlaNeT-2 Recommendation

What We Determined

- Platelet transfusion thresholds trended down over time

~However~

- The “**restrictive**” threshold recommended by the PlaNeT-2 Trial data was never achieved

-
- These data were presented to the BIDMC NICU and Neonatology teams

Outcomes

Formal Guidance Document Created

- Establishes protocols for platelet transfusion in this demographic

Baseline Data Available

- Foundation for ongoing review process
- QA/QI value

Increased Visibility of BB Team to Clinicians

Return to Case

Baby Boy AZ/ZA:

- 31 1/7 week male
- Pregnancy c/b growth restriction, gHTN, GDM
- Urgent C/S for NRFHT → Now in NICU

NICU Course:

- Prematurity/SGA, ?sepsis
- Platelets: downtrend from 73 to 46 → **Transfusion Indicated?**

→ Would not recommend transfusion at this time

Take-Home Points

- Specific demographics may require individualized transfusion management
- Platelet transfusion at a restrictive threshold of $<25\text{K}$ reduces composite risk of death or major bleeding in preterm neonates
- Understanding your institution's guidelines can help you to implement evidence-based practices

Works Cited

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Questions?

