ERN-EuroBloodNet Topic on Focus on Inherited Platelet Function Disorders (IPFD)

webinar

HEALTH PROFESSIONALS

Women with Glanzmann thrombasthenia - management of abnormal uterine bleeding (AUB) and pregnancy (maternal and fetal aspects)

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CRPP Centre de Référence Pathologies Plaquettaires
MHEMO La Filière des maladies rares de l'hémostase
ebn ERN | EuroBloodNet

Disclosure for conflict of interest

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Agenda

1 Introduction

2 Abnormal Uterine Bleeding (AUB)

3 Pregnancy

4 Conclusion

Disclaimer

We refer to women and girls in this presentation, but the concepts apply to all menstruating people

01

Introduction

Patient perspective: Life with GT, qualitative results from the GT 360 study

Methods: Self-completion online survey + interviews of affected individuals and carers

14 people with GT (2-78y, mean 32.9y), 5 carers



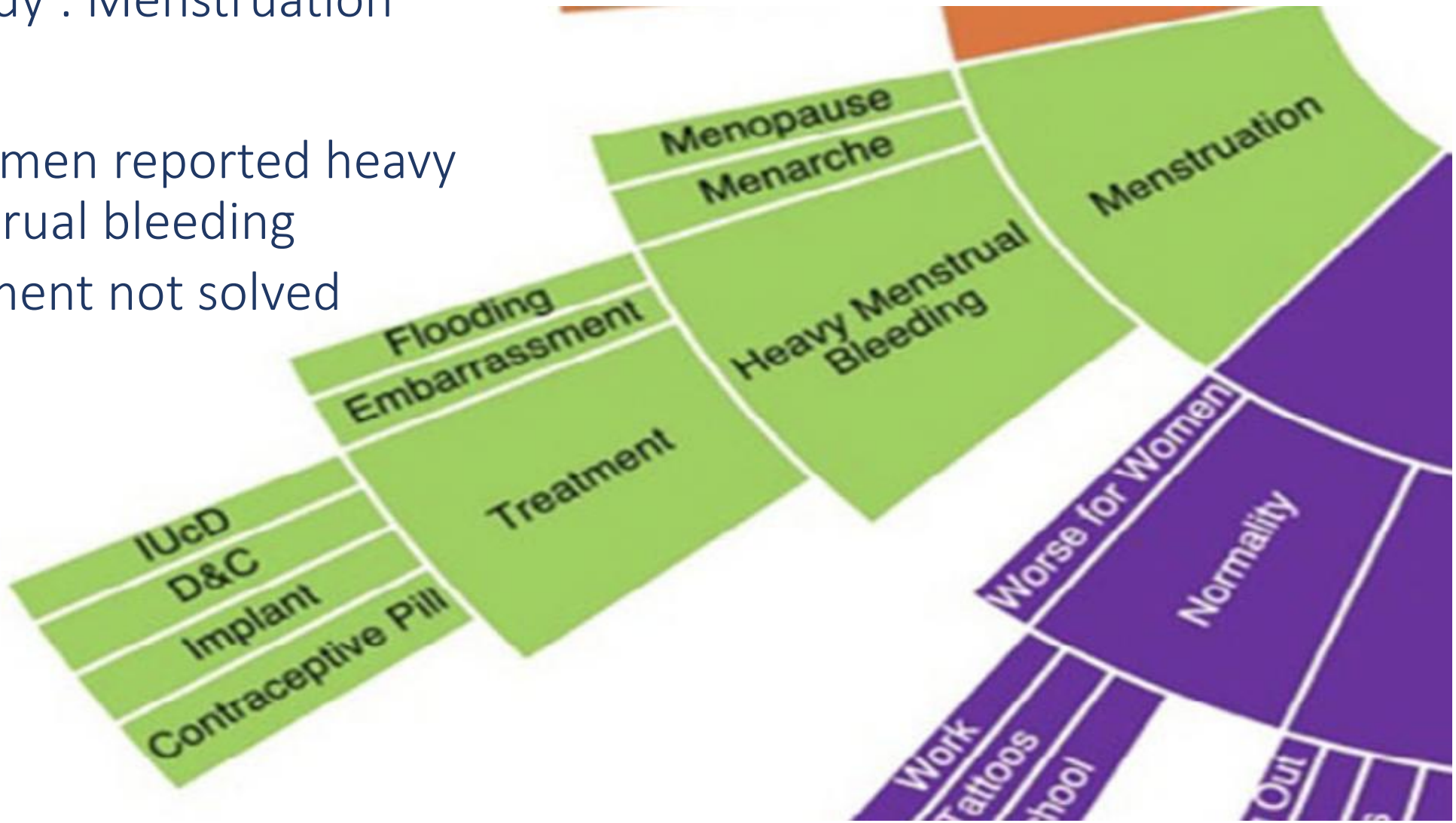
Results, 8 themes emerged

- Abuse
- Bleeding and treatment
- Diagnosis
- Fatigue
- Identity
- Menstruation
- Pregnancy
- The Future

Khair K et al, Haemophilia. 2024;30:1373–1382.

Patient perspective: Life with GT, qualitative results from the GT 360 study : Menstruation

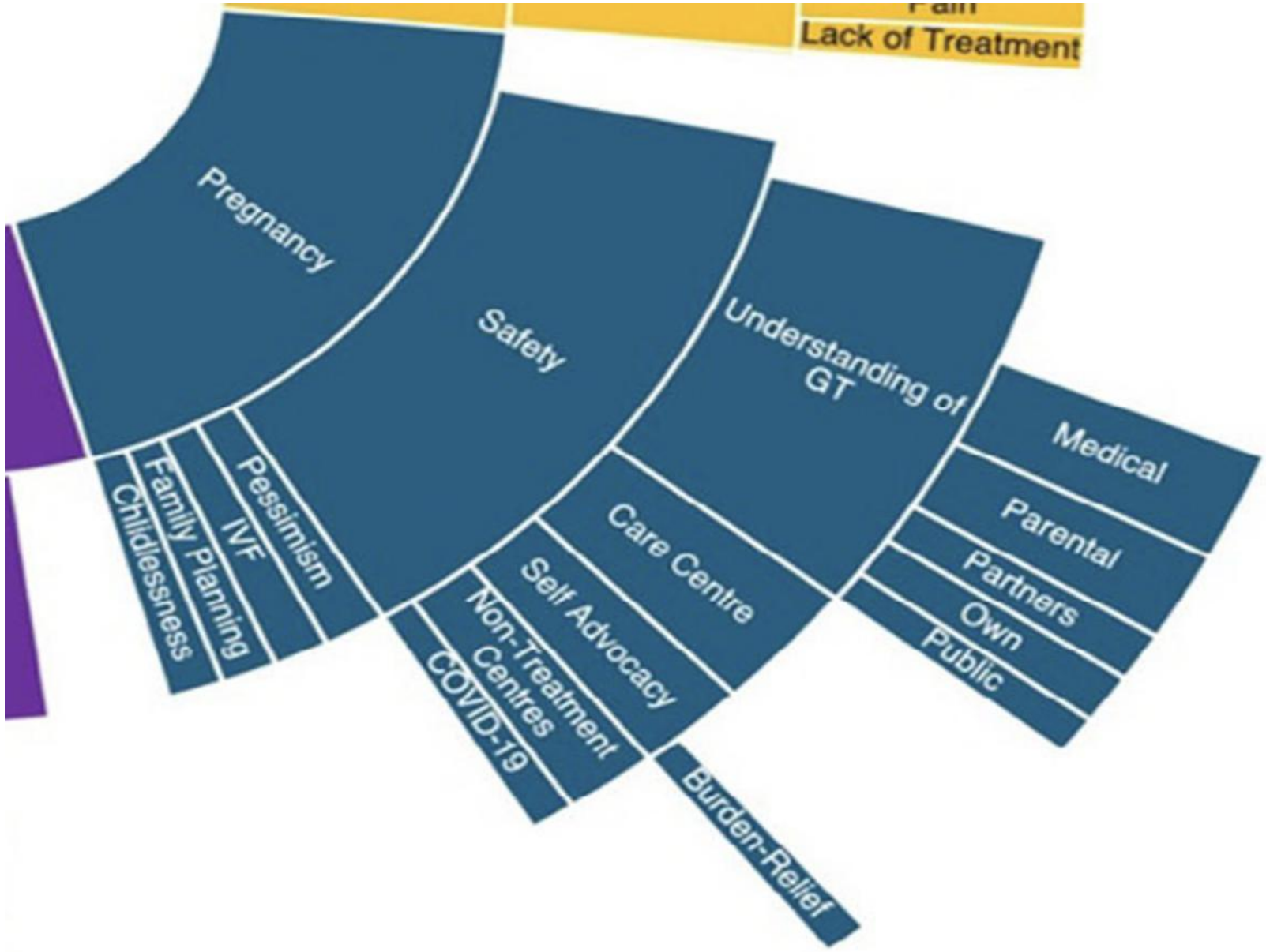
- All women reported heavy menstrual bleeding
- Treatment not solved



Khair K et al, Haemophilia. 2024;30:1373–1382.

Patient perspective: Life with GT, qualitative results from the GT 360 study : Pregnancy

- Safety
- Understanding of GT
- Choices around pregnancy were limited by ‘medical pessimism’



Khair K et al, Haemophilia. 2024;30:1373–1382.

GT: proportion of women with abnormal uterine bleeding (AUB) and with a history of pregnancy

	George 1990[1]	Toogeh 2004[2]	Vijapurkar 2009[3]	Santoro 2010[4]	Siddiq 2011[5]	Fiore 2012[6]	GTR 2012[8-10]	Civaschi 2015[7]	Tarawah[11] 2023	FranceCoag 2026[12]
All patients	177	382	22	17	35	24	218	10	136	197
Females	102	178	22	9	35	14	127	10	67	103
Females >12 years	na	131	22	9	35	11	83	10	41?	na
Females with menorrhagia	98% (54/55)	13% (17/131)	77% (17/22)	55% (5/9)	68% (17/25)	na	48% (40/83)	na	86% (35/41?)	na
Females with pregnancies	29% 16*/55	7% 9/131	6% 1/17	44% 4**/9	35***	27% 3/11	4.8% 4/83	10***	? (<21%) ? / 28 °	15% 16/103

na, not available

*21 pregnancies

**7 pregnancies

***only patients with pregnancies

°median parity = 2

76 with hormonal cycle
20 pregnancies

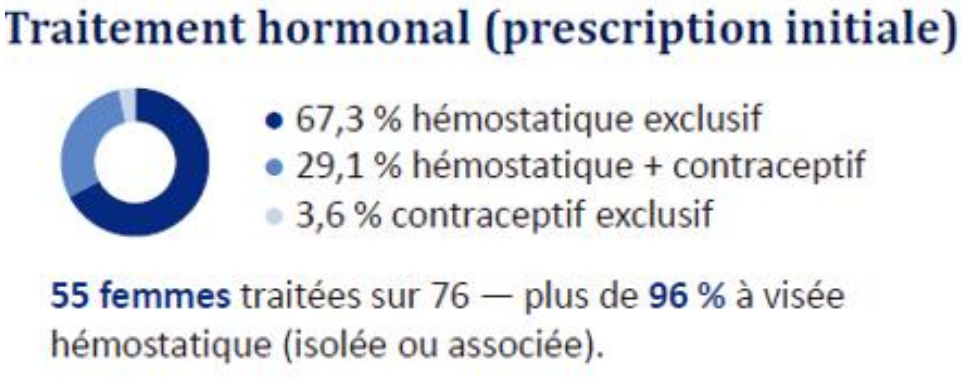
1. George JN et al. Blood 1990;75:1383–95; 2. Toogeh G et al. Am J Hematol 2004;77:198–9
3. Vijapurkar M et al. Haemophilia 2009;15:199–202. 4. Santoro C et al. Haemophilia 2010;16:805–12
5. Siddiq S et al. Haemophilia 2011;1–12; 6. Fiore M et al. Haemophilia 2012;18:e201–9
7. Civaschi E et al. Br J Haematol 2015 [Epub ahead of print]; 8. Poon MC et al. Haematologica [Epub ahead of print]
9. Di Minno G et al. Haematologica 2015 [Epub ahead of print]; 10 d'Oiron R et al, Blood 2012;120:Abstract 2202; 11. Tarawah AM et al, Blood 2023;abstract 396 and 3968; 12. Fropier C et al, SFTH 2026

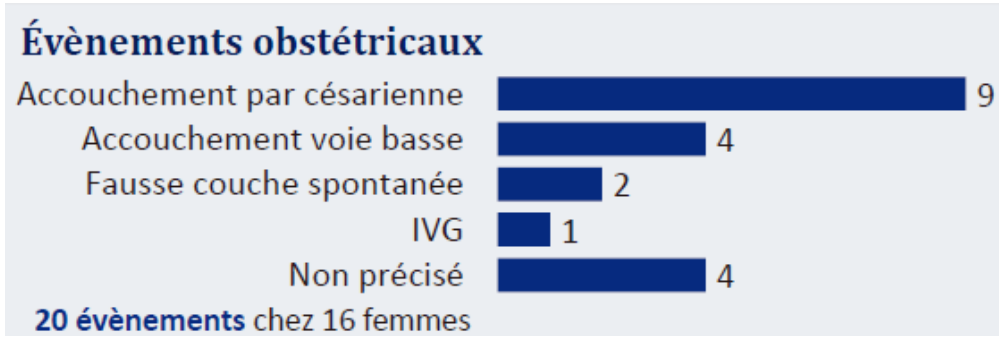
01

Abnormal Uterine Bleeding (AUB)

GT in FranceCoag

- 103 women and girls
  - 76 with menstruations
  - 55/76 treated with hormonal therapy
- Haemostatic purpose of 1st prescription of hormonal therapy in 96%
- 20 Obstetric events in 16 women





Fropier C et al, poster SFTH 2026 Nîmes

GT: AUB treatment principles before rFVIIa era

Adjunctive and/or local measures

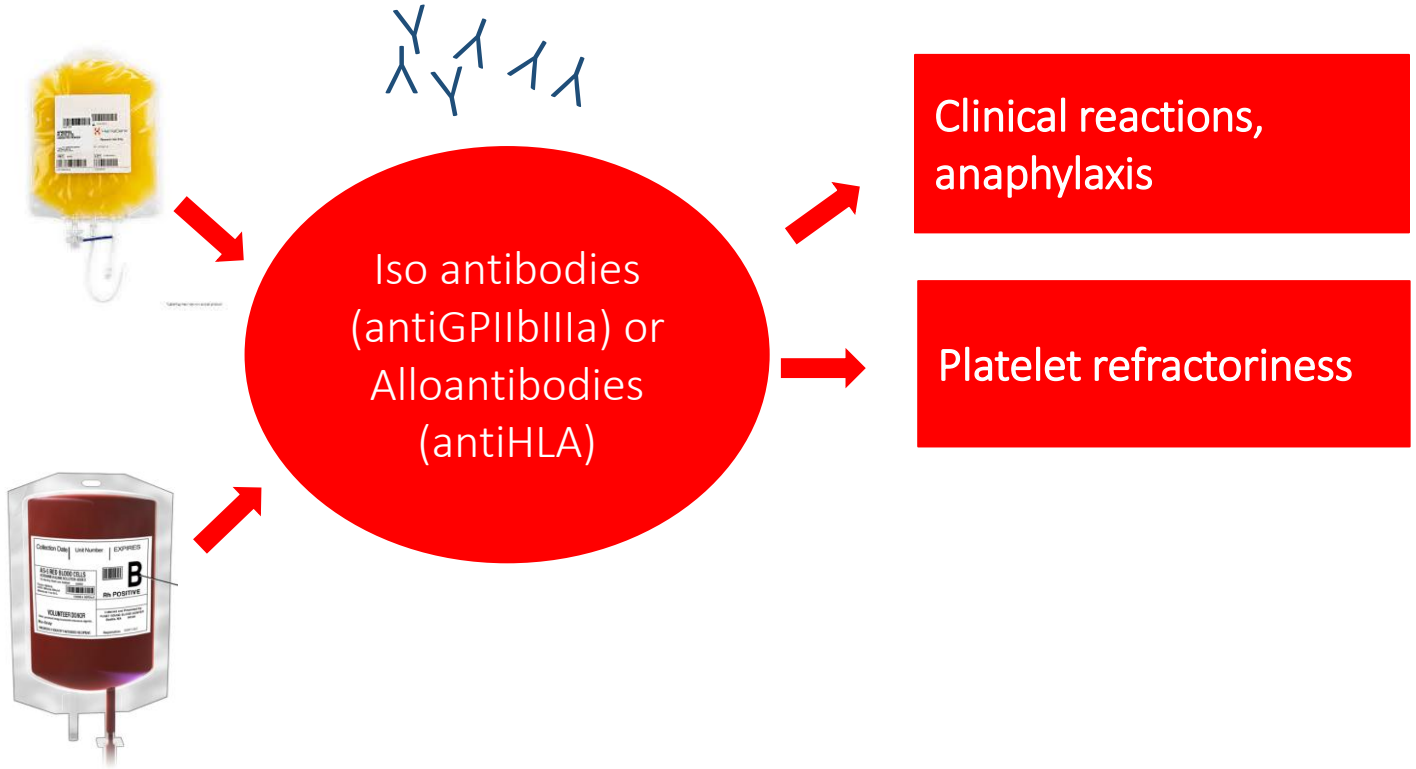
- Antifibrinolytics (mainly for mucosal bleeding)
- Correction of iron deficiency and anaemia
- Hormonal therapy

Platelet transfusions

For acute AUB

- After failure of conservative measures
- Preferentially from single-donor apheresis and HLA-compatible if available

GT and antiplatelet immunisation



GT, Glanzmann's thrombasthenia; HLA, human leukocyte antigens. AUB : Abnormal uterine bleeding

Boval B. *Thromb Haemost* 2001;Suppl.;Abstract P1154; Monrigal C et al. *Ann Fr Anesth Reanim* 2003;22:826-30; Léticée N et al. *Euro J Obstet Gynecol Reprod Biol* 2005;121:139-42; Siddiq S et al. *Haemophilia* 2011;17:e858-69

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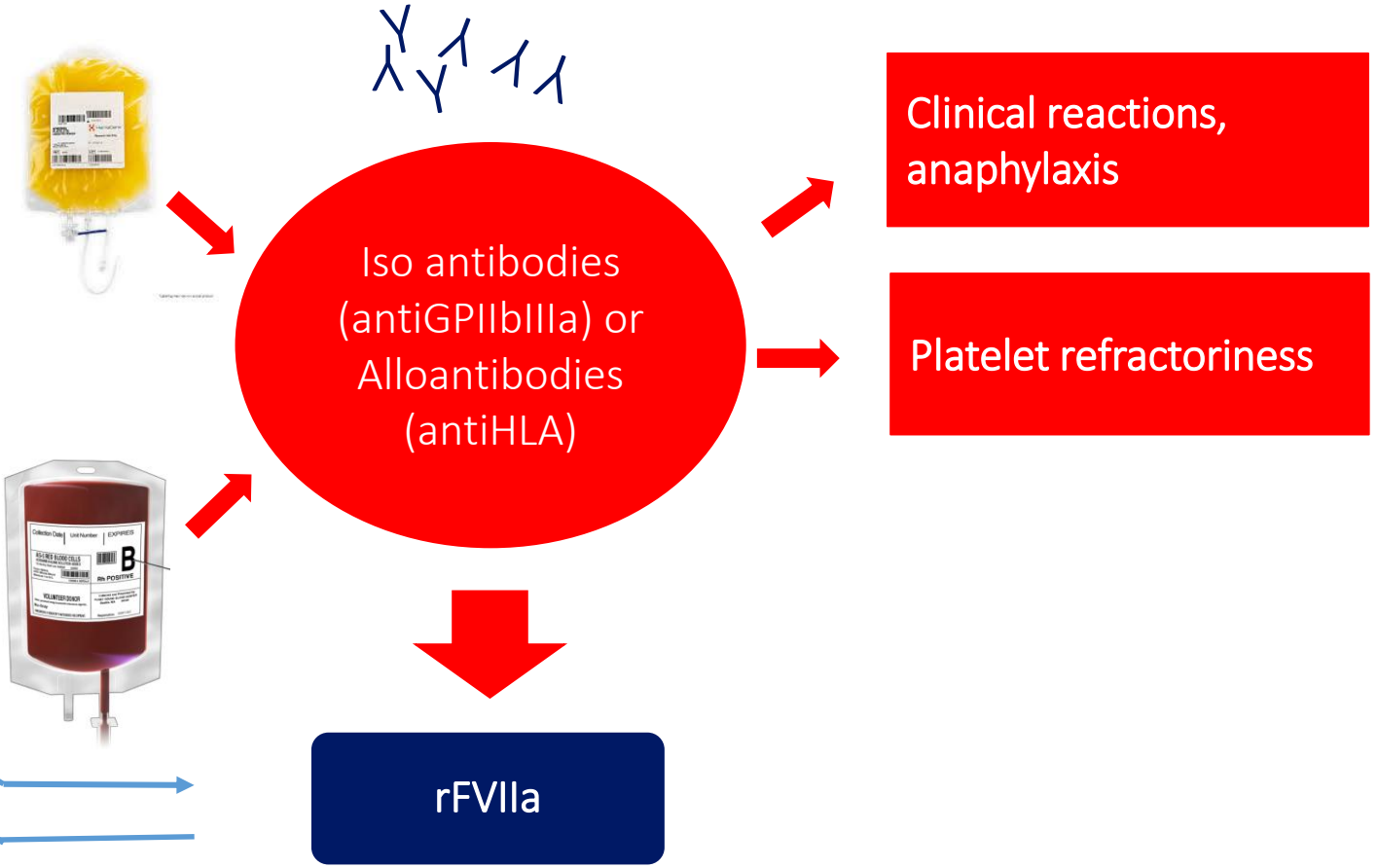
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For acute AUB

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GT and antiplatelet immunisation





Iso antibodies (antiGPIIbIIIa) or Alloantibodies (antiHLA)

- Clinical reactions, anaphylaxis
- Platelet refractoriness
- Neonatal/foetal thrombocytopenia

rFVIIa

GT, Glanzmann's thrombasthenia; HLA, human leukocyte antigens. AUB : Abnormal uterine bleeding

Boval B. *Thromb Haemost* 2001;Suppl.;Abstract P1154; Monrigal C et al. *Ann Fr Anesth Reanim* 2003;22:826-30; Léticée N et al. *Euro J Obstet Gynecol Reprod Biol* 2005;121:139-42; Siddiq S et al. *Haemophilia* 2011;17:e858-69

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https://doi.org/10.1016/j.rpth.2024.102586

ORIGINAL ARTICLE

rpth research & practice in thrombosis & haemostasis

Bleeding and quality of life in people with Glanzmann thrombasthenia—insights from the Glanzmann's 360 study

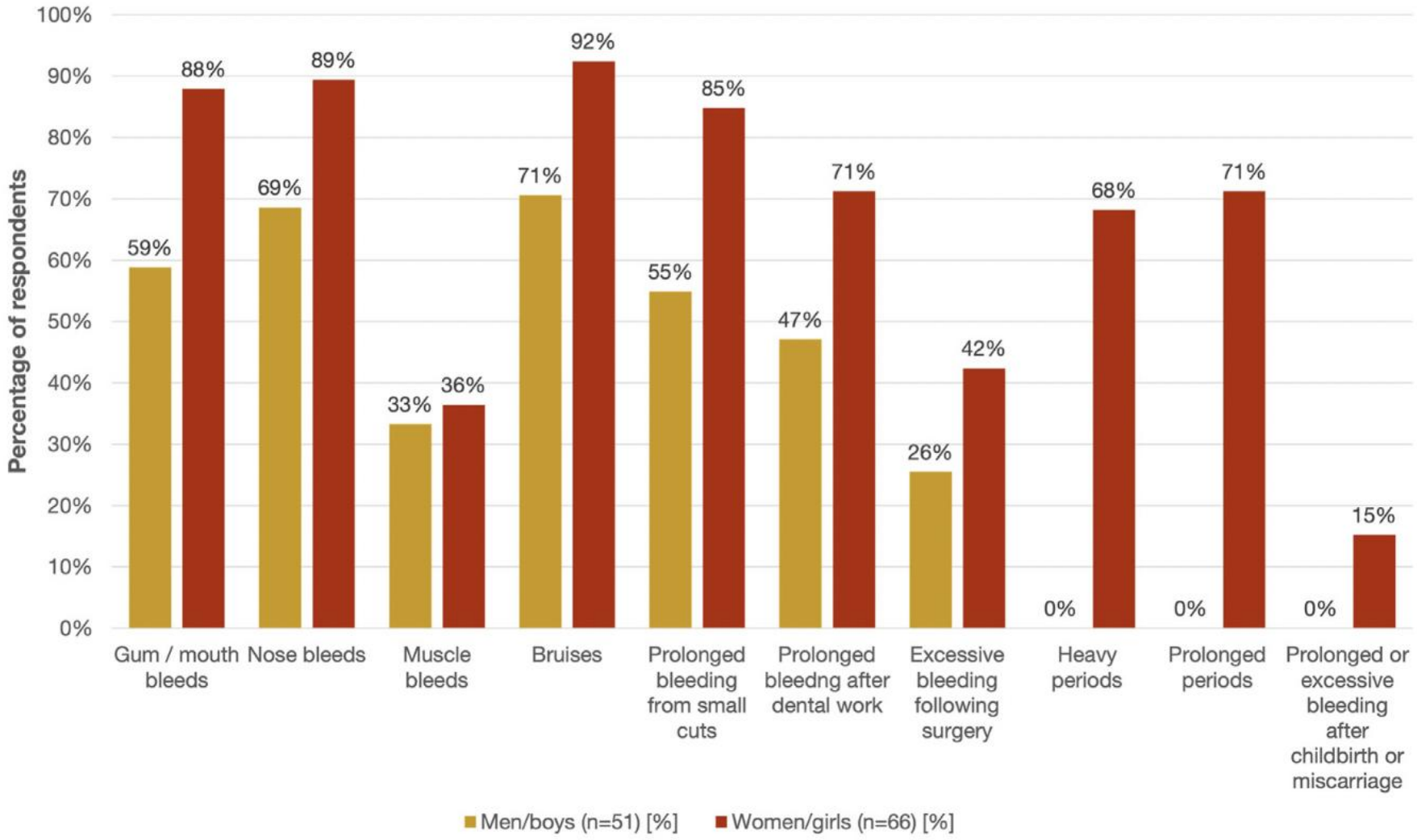
Kate Khair | Simon Fletcher | Matthew Boyton | Michael Holland

Khair K et al, Res Pract Thromb Haemost. 2024;8:e102586

A contemporary snapshot of life with Glanzmann thrombasthenia: GT 360 study

- Methods
  - Self-completion online survey + interviews of affected individuals and carers
- Population
  - **88** people with GT (<2-70y, 56% women or girls)
  - **29** carers of children/young people with GT aged <16 years
- Results
  - 88% experienced at least one bleed in the past week
  - Bleeding disproportionally affected women
  - Bleeds resulted in frequent hospital contact and considerable psychological distress:
    - 26% with low self-esteem,
    - 30% met criteria of symptomatic depression
  - Frequent bleed experiences seemed associated with impaired physical, psychosocial health-related quality of life

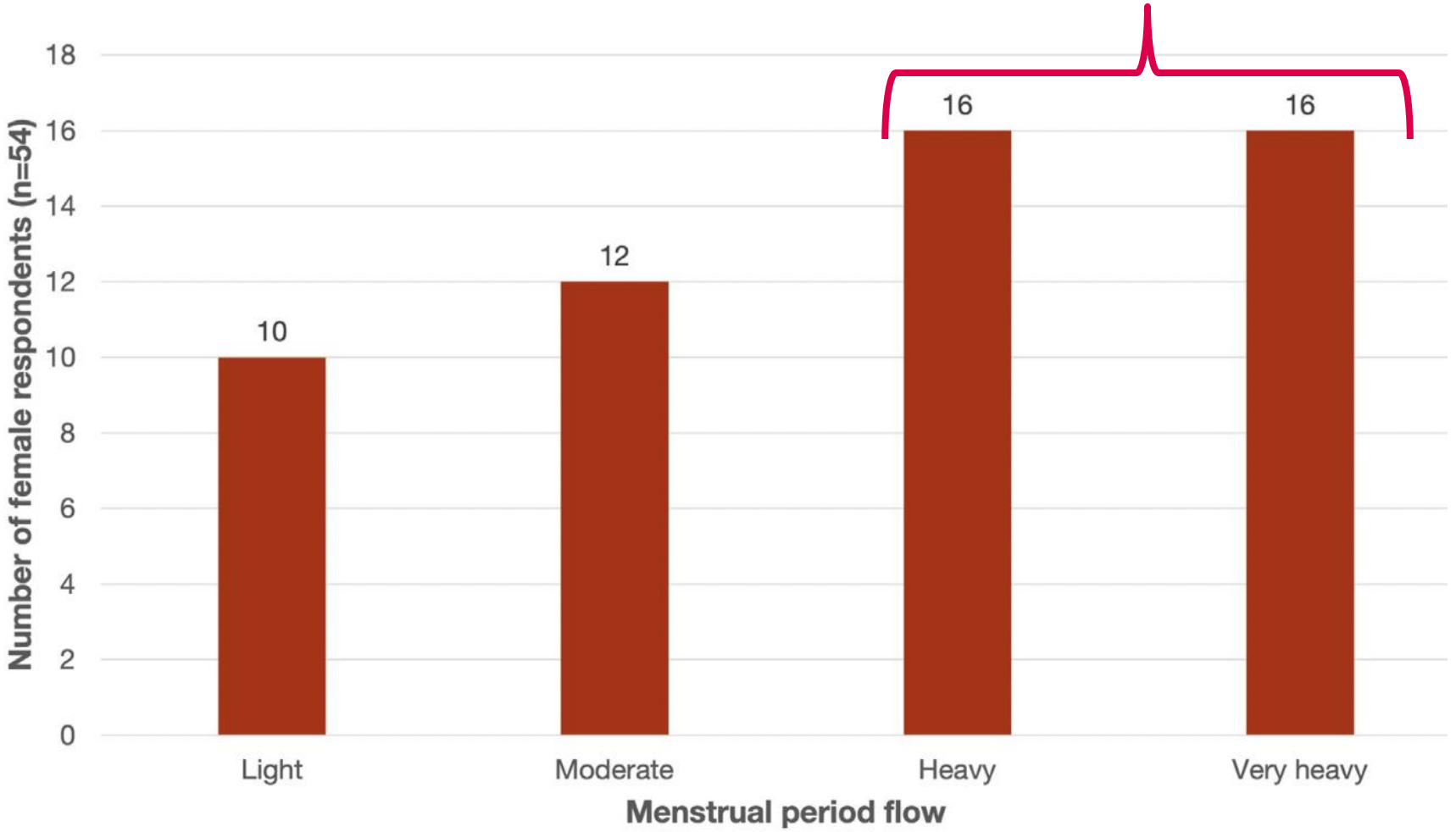
Self-reported bleed sites



Khair K et al, Res Pract Thromb Haemost. 2024;8:e102586

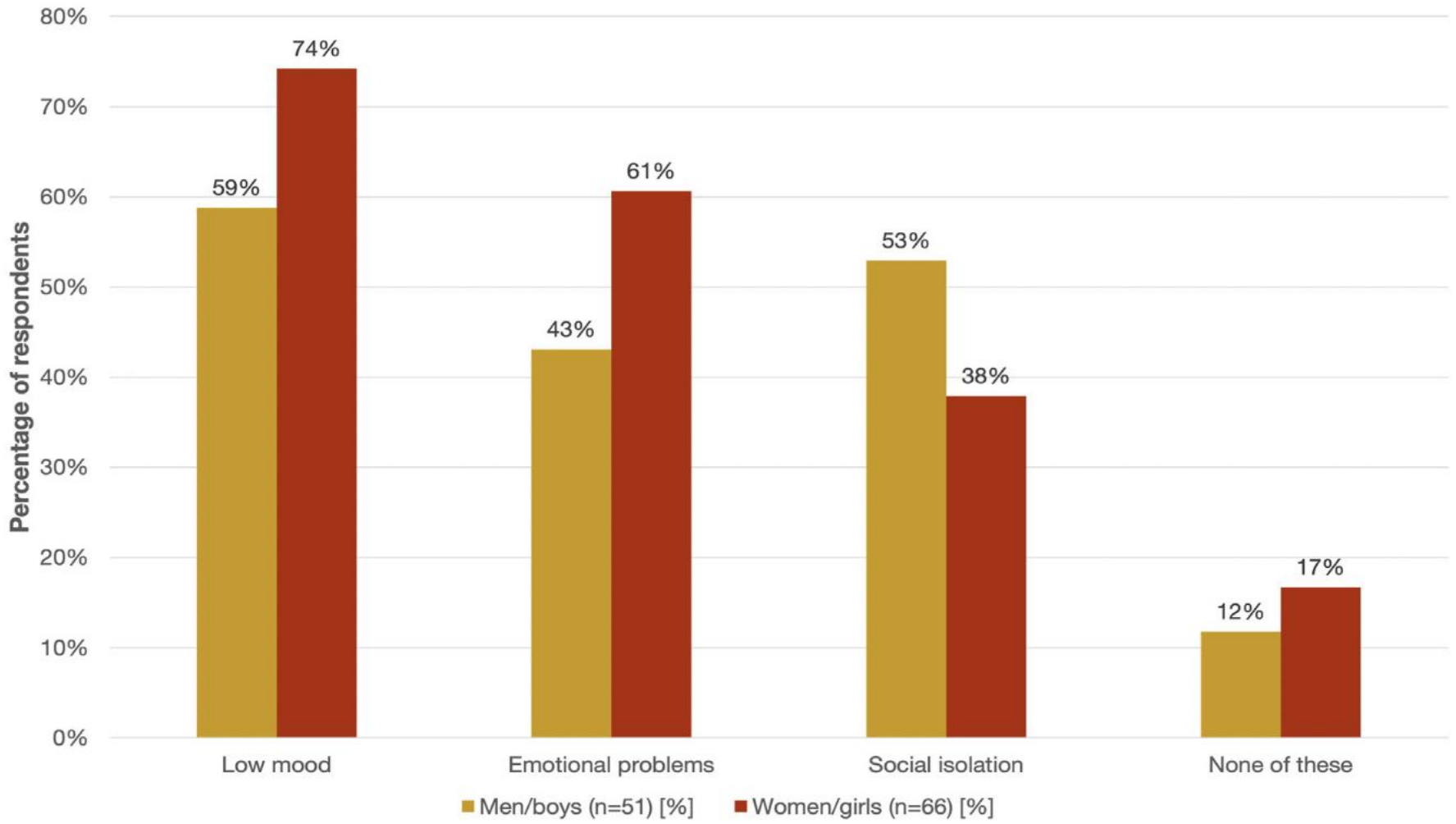
Blood loss in most recent menstrual period, using the Menstrual Impact Questionnaire

32 of 54 (**59%**) described blood loss in their most recent menstrual period as “heavy” or “very heavy



Khair K et al, Res Pract Thromb Haemost. 2024;8:e102586

Psychological impact of bleeding
data are presented as frequency (%) for categorical variables



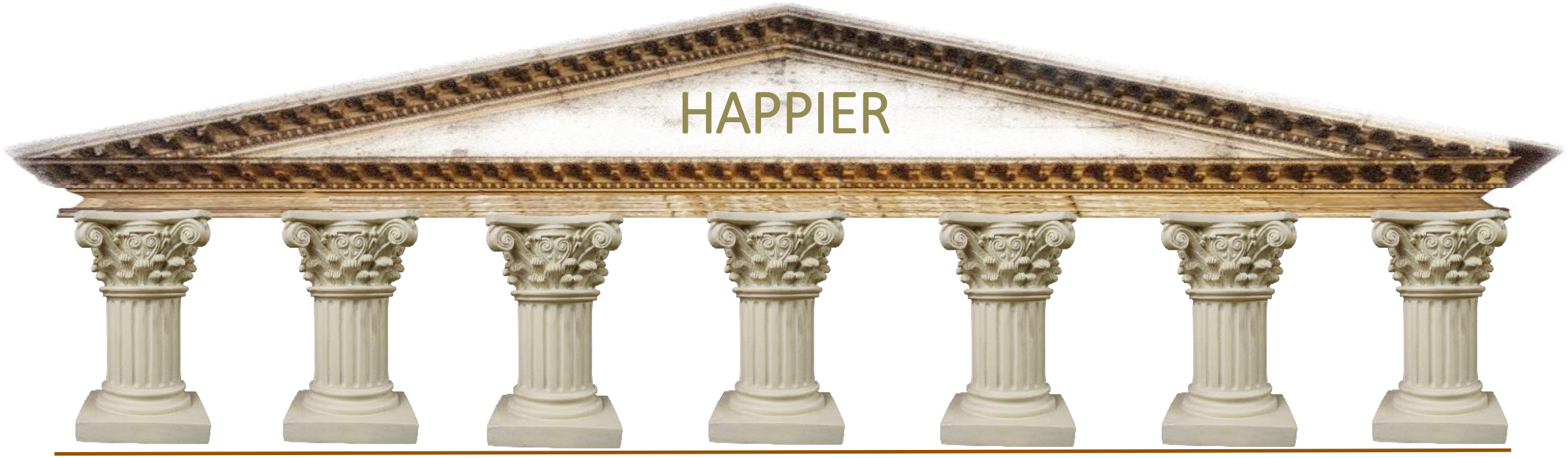
Khair K et al, Res Pract Thromb Haemost. 2024;8:e102586

Participants' psychological responses stratified by bleed data responses: Lower EQ-5D-5L mean score in bleeders

Patient reported outcome tool	Bleeds in past week		Bleed requiring hospital contact in the past week		Bleed requiring a hospital visit in the past 6 mo	
	0	>1	0	>1	0	>1
EQ-5D-5L index score, mean (SD)	0.833 (0.217) n = 11	0.672 (0.282) n = 74	0.730 (0.254) n = 59	0.514 (0.377) n = 26	0.793 (0.212) n = 33	0.582 (0.338) n = 52
	$P < .05$		$P < .05$		$P < .01$	

Khair K et al, Res Pract Thromb Haemost. 2024;8:e102586

The 7 pillars of symptomatic treatment for abnormal uterine bleeding for improved quality of life of GT women and girls



Hormonal treatment

Tranexamic **A**cid

Pain killers

Psy support

Iron

Education

Regular Follow-up

Alone or in combination ± specific treatments (platelets, rFVIIa)

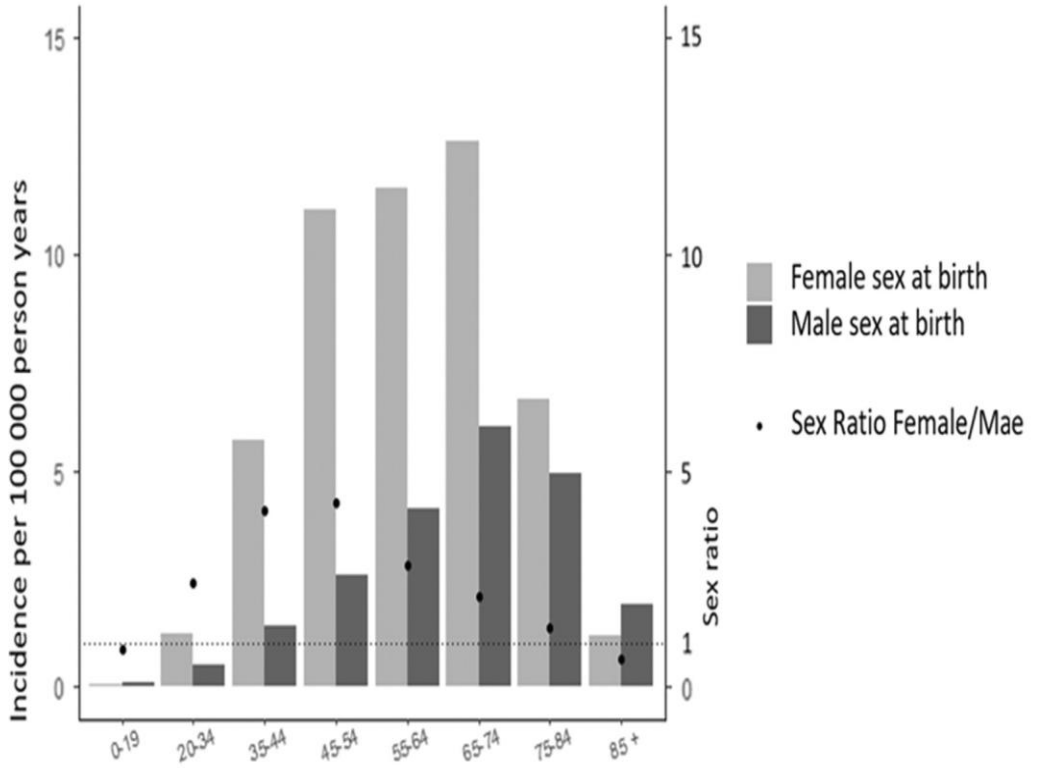
Dose-dependent association between progestins use and surgery for meningioma

- A case–control study investigating the association between intracranial meningioma surgery and exposure in France, from 2009 to 2018, to 3 different progestins
- Each case was matched to 5 controls by sex, year of birth, and region of residence

- Results
  - A total of 25,216 cases (75% women; median age, 58 years)
  - Progestogen exposure in 9.9% of cases and 1.9% of controls, with an OR of 6.7 (95% CI, 6.3–7.1).
    - OR 1.2 (95% CI, 1.0–1.4) for short-term use (<1 year)
    - **OR 9.5 (95% CI, 8.8–10.2) for long-term use**
  - A strong association was identified:

	Association between long term exposure to progestins use and surgery for meningioma
Cyproterone acetate (CPA; ≥25 mg/day)	22.7 (95% CI, 19.5–26.4)
Nomegestrol acetate (NOMAC; 3.75–5mg/day)	6.5 (95% CI, 5.8–7.2)
Chlormadinone acetate (CMA; 2–10 mg/day)	4.7 (95% CI, 4.5–5.3)

  - Observed across all histological grades and anatomical locations
  - Estimated number of attributable cases was 2,124 (95% CI, 2,028–2,220), corresponding to 212 cases per year



Hoisnard et al; Eur J Neurol. 2022;29:2801–2809

Still NO prophylactic approach approved in GT

Restriction of inclusion criteria of innovative therapies may not solve these issues promptly for women and girls with GT

03

Pregnancy

Pregnancy and GT

- Pregnancy and childbirth present significant challenges for mother and child
- Extremely low amount of data available
- The 3 main contributors to the high level of clinical challenge are
  - The rarity of GT
  - The bleeding complication
    - following hormonal treatment arrest, leading to recurrence of abnormal uterine bleeding (AUB) and ovarian cyst haemorrhage
    - of delivery and post partum period
  - The consequences of antiplatelet antibodies on management of delivery and neonatal/fetal immune thrombocytopenia

GT: before pregnancy

Hormone therapy*



In vitro fertilisation?[1]

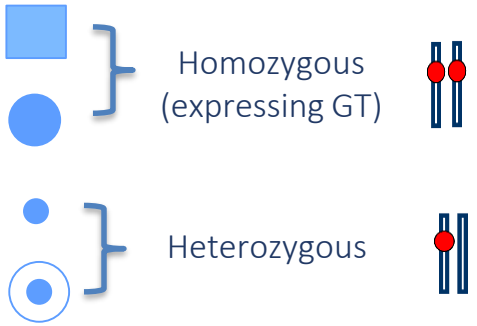
Hormone therapy discontinuation

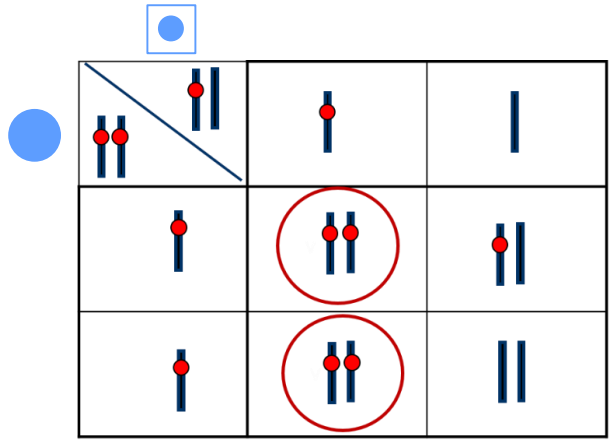
Abnormal Uterine Bleeding, Ovarian haemorrhage

*Regularly tailored hormone therapy according to bleeding profile

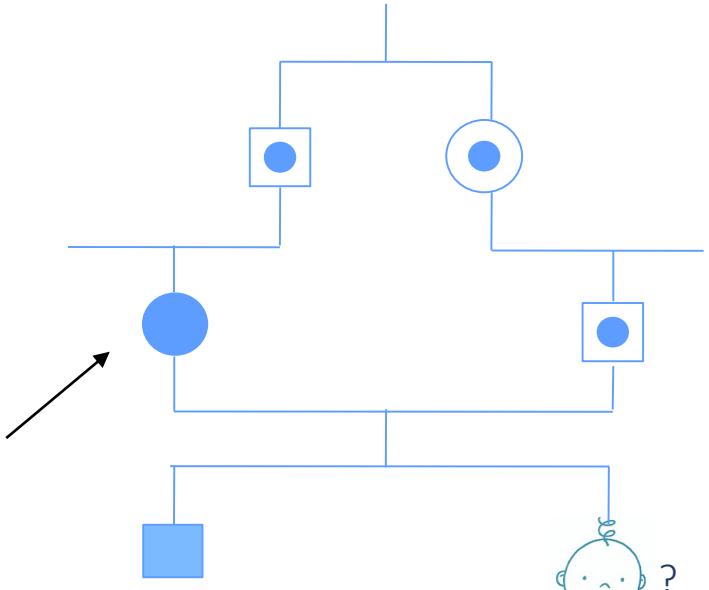
GT : Glanzmann Thrombasthenia ; Domschke C et al. *Haemophilia* 2012;18:e380–1

GT: genetic counselling if consanguineous partners, mother with GT

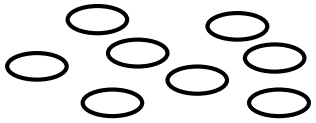




Autosomal recessive :
Risk of GT is 1/2



GT fetal platelets ?



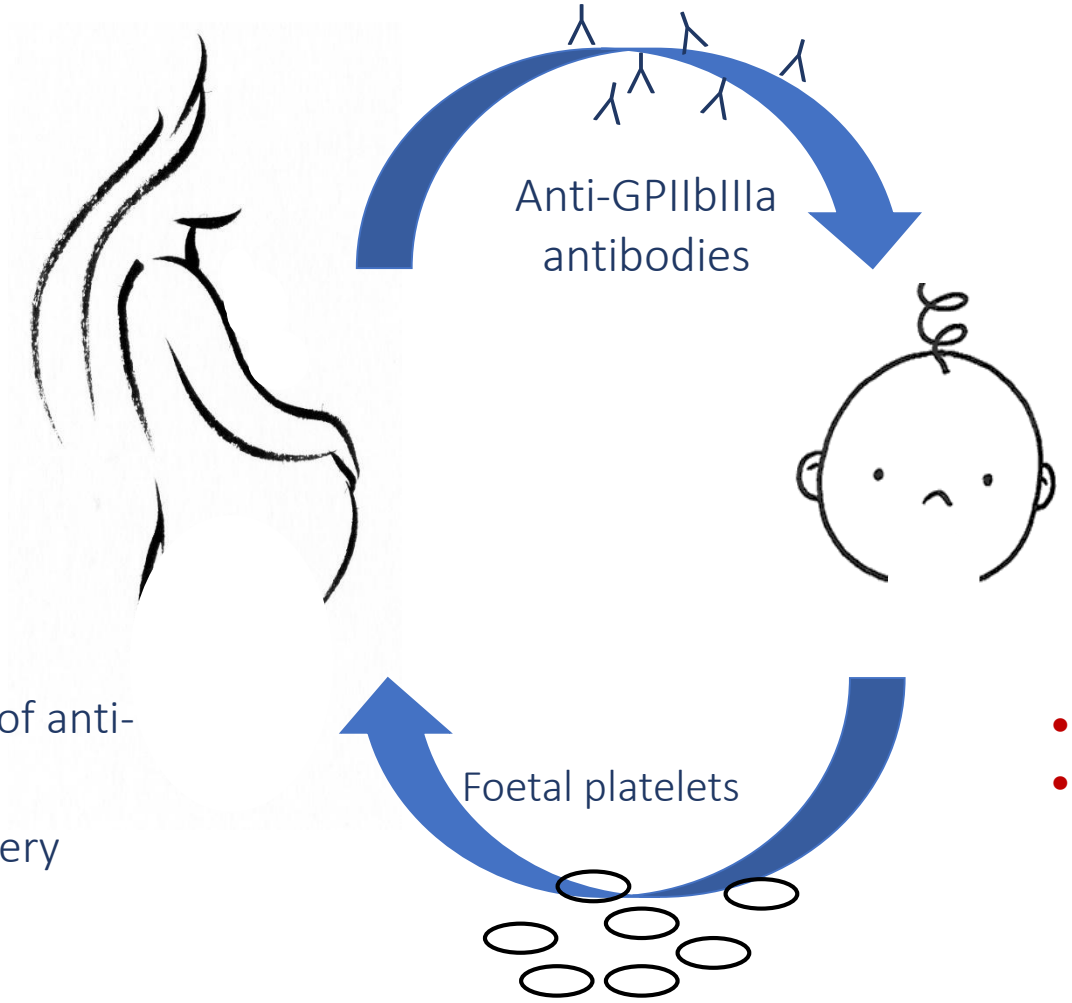
- Risk of GT affected child?
- Discuss options for pregnancy
  - prenatal (PND)
  - and/or preimplantation diagnosis (PGD)

1. Siddiq S, et al. Haemophilia 2011;1-12. 3.*Boval B. Thromb Haemost 2001; suppl);4.* Monrigal C, Ann Fr Anesth Reanim. 2003;
5. Léticée N, Euro J Obstet GynecolReprod Bio. 2005; 6. Siddiq S, et al. Haemophilia 2011

GT : Glanzmann thrombasthenia
PND : prenatal diagnosis

GT and pregnancy: maternal and foetal/neonatal risks

Transfusions



- Risk of severe form[1]
  (if consanguinity between parents)

- Appearance or anamnesis of anti-GPIIbIIIa[1]
- Difficult bleeding and delivery management

- Thrombocytopenia[1,2]
- Intracranial bleeding[1,3]
  (Prognostic factors and preventive strategies currently unknown)

1. Siddiq S et al. *Haemophilia* 2011;17:e858–69; 2. Monrigal C et al. *Ann Fr Anesth Reanim* 2003;22:826–30; 3. Léticée N. *Euro J Obstet Gynecol Reprod Bio* 2005;121:139–42.

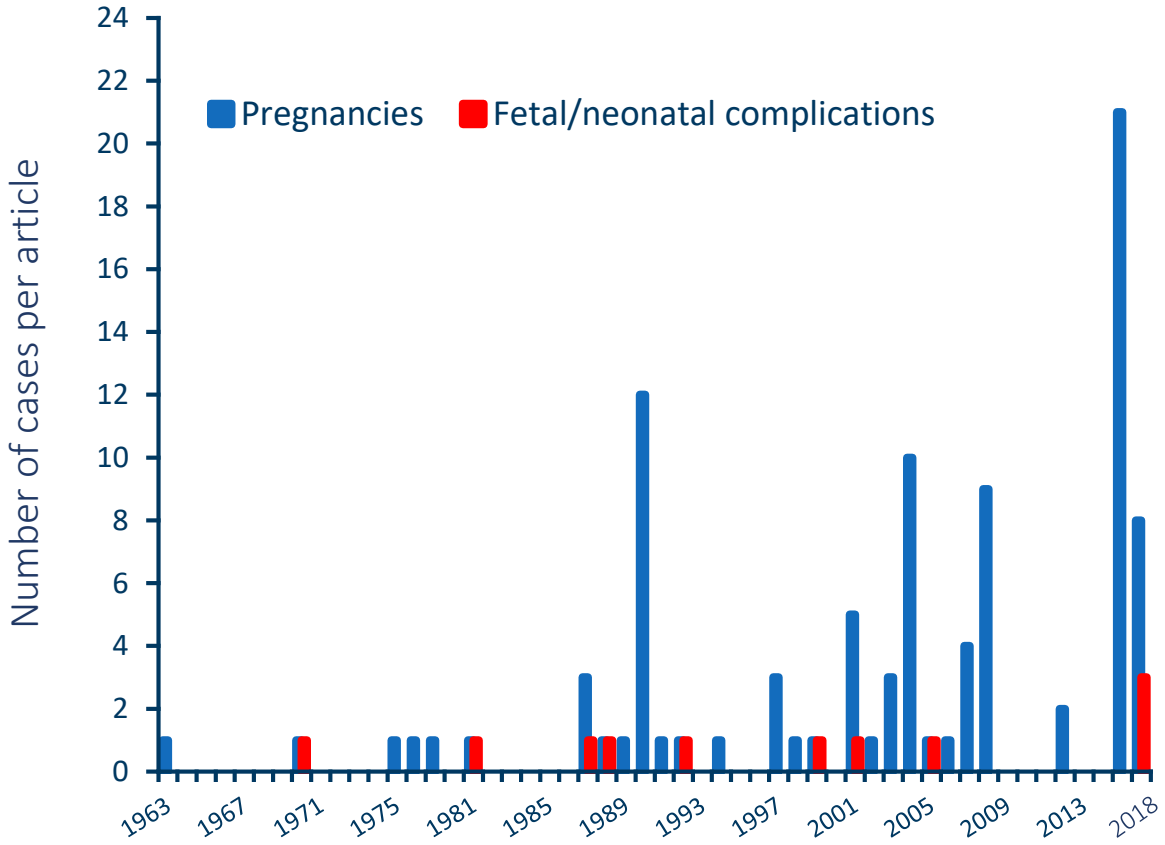
GT : Glanzmann Thrombasthenia

GT and pregnancy review (2011)

- 35 TG mothers:
  - Increased risk of HPP I and II
  - No maternal deaths
  - Multiple hemostatic strategies during delivery
  - Documented maternal immunization status:
    - 10/22 positive at the beginning of pregnancy
    - 3 with increased antibodies during pregnancy
- 41 fetuses/neonates
  - 2 documented deaths at 24 and 31 weeks of gestation (ICH, mothers with strong anti-GPIIbIIIa immunization)
  - 2 other more ambiguous deaths
    - Spontaneous miscarriage at 9 weeks,
    - Severe Hemolytic disease of the newborn and thrombocytopenia 40 G/L, death at 48 hours (mother with anti-Rh, anti-GPIIbIIIa, anti-HLA)
- Platelet count documented in 4 newborns
  - 2/4 with thrombocytopenia

Siddiq S et al. Haemophilia 2011;17:e858–69

GT: reports of pregnancies and neonatal/foetal complications over time[1-11]



Fetal/Neonatal complications occurred in highly immunized GT mothers

1. Léticée N, et al. Eur J Obstet Gynecol Reprod Biol 2005;121:139–42. 2. Boval BBS et al. Thromb Haemost 2001;85 (Suppl).1154. 3. Sundqvist SB, et al. Scand J Haematol 1981;27:159–64.
4. Kiefel V, et al. Beitr Infusionsther 1992;30:450–3. 5. Pico MRA, et al. Thromb Haemost 1987;58:475. 6. Payne PR, et al. Proc R Soc Med 1970;63:56–7. 7.Siddiq S, et al. Haemophilia 2011;17:e858–69. 8. Civaschi E, et al. Br J Haematol 2015;170(4):559-63. 9. Di Minno G, et al. Haematologica 2015;100(8):1031-7. 10. Poon MC, et al. Haematologica 2015 100(8):1038-44. 11. Santoro C, et al. Haemophilia 2010;16:805–12. 12. Barg et al, Pediatr Blood Cancer 2018: e27376. 13 Presenter's summary

May IVIg during pregnancy of GT immunised mothers contribute to limit fetal/neonatal thrombocytopenia?

- Monocentric study, files from 1999 to 2017
  - **5 women** with GT
  - **9 newborns**

- **3/9 newborns had severe thrombocytopenia**
  - Platelets 18, 16 and 52 G/L
  - all 3 were offspring of 2 GT mothers who were positive for antiplatelet antibodies
  - all 3 newborns, treated with IVIg + random platelets
  - none experienced severe bleeding episodes

- Mother 1:
  - 1st pregnancy
    - **2 twins with low platelets at birth (18 and 16 G/L)**
    - Mother discovered positive for antiplatelets post natally
  - 2nd pregnancy
    - Positive for antiplatelets pre natally
    - **Received IVIg**
    - **Neonate with normal platelet count at birth (282 G/L)**

- Mother 2 :
  - 1st pregnancy uneventful
  - 2nd pregnancy
    - Discovered positive for antiplatelets post natally
    - Neonate with 53 then 10 G/L

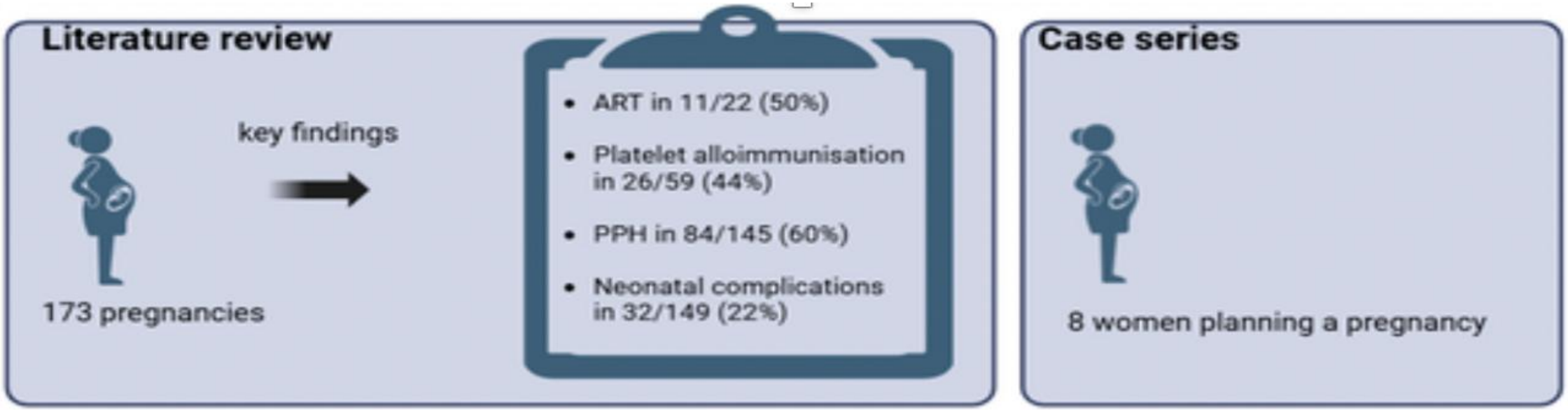
Barg AA et al. Pediatr Blood Cancer.2018;65:e27376.

RESEARCH LETTER

BJHaem
BRITISH JOURNAL OF HAEMATOLOGY

Management of pregnancy and childbirth in Glanzmann thrombasthenia: A case series and review

- 8 cohort studies, 1 systematic review, + 24 case reports + 8 new case reports
- important items/knowledge gaps



Rutten K et al. Br J Haematol. 2025;207:1702–1708 (review on studies published up to 22 May 2025)
ART, assisted reproductive therapy; PPH, post-partum haemorrhage;

RESEARCH LETTER

BJHaem
BRITISH JOURNAL OF HAEMATOLOGY

Management of pregnancy and childbirth in Glanzmann thrombasthenia: A case series and review

- 143 pregnancies
  - ART in 11 (50%) of 22 pregnancies in which the mode of conception described
    - 1/3 with bleeding (where bleed was documented)
  - increased incidence of ovarian haemorrhage and endometriosis in GT
  - Screening for platelet antibodies was carried out in only 59/173 pregnancies (34%) :
    - Positive in 26/59 (44%) : HLA 15% , αIIbβ3 12% or both 8%, NA 8%
    - Negative 56%,
  - 53% VD, 47% CS
  - 91% general anesthesia (11 documented)
  - TP 73% (platelets 64%, rFVIIa 10%, both 19%; TXA 24%)
  - PPH primary 31%, secondary 14%, both 6%
  - Treatment PPH I : RBC 56%, platelets 42%, rFVIIa 22%

Rutten K et al. Br J Haematol. 2025;207:1702–1708 (review on studies published up to 22 May 2025)
ART, assisted reproductive therapy; PPH, post-partum haemorrhage; rFVIIa, recombinant activated factor VII. FNAIT: fetal neonatal alloimmune thrombopenia, ICH intracranial hemorrhage

RESEARCH LETTER

BJHaem
BRITISH JOURNAL OF HAEMATOLOGY

Management of pregnancy and childbirth in Glanzmann thrombasthenia: A case series and review

- 149 fœtus/neonates, 6 twins
  - 32 NN with complications (22%)
    - 5 stillbirth (4 HIC), 1 NN death
    - 17 FNAIT, 9 with bleeding
  - 45% of NN complications occurred in 22 immunized mothers
  - No NN complication in non immunized mothers
  - 5 pregnancies with use of gestational IVIG
    - 5 five healthy NN
    - 1 NN with FNAIT without bleeding complications

Rutten K et al. Br J Haematol. 2025;207:1702–1708 (review on studies published up to 22 May 2025)
ART, assisted reproductive therapy; NN: neonatal; PPH, post-partum haemorrhage; rFVIIa, recombinant activated factor VII. FNAIT: fetal neonatal alloimmune thrombopenia, ICH intracranial hemorrhage



PLATELETS AND THROMBOPOIESIS

How I manage pregnancy in women with Glanzmann thrombasthenia

Mathieu Fiore,[1,2] Loïc Sentilhes,[3] and Roseline d'Oiron[4,5]

[1]Hematology Laboratory, Reference Center for Inherited Platelet Disorders, University Hospital of Bordeaux, Pessac, France; [2]Biology of Cardiovascular Diseases, INSERM U1034, Pessac, France; [3]Department of Obstetrics and Gynecology, University Hospital of Bordeaux, Pellegrin Hospital, Bordeaux, France; [4]Reference Center for Hemophilia and Other Rare Inherited Bleeding Disorders, Bicêtre Hospital APHP, Le Kremlin-Bicêtre, France; and [5]Hemostasis, Inflammation, and Thrombosis (HITh), UMR_S1176, INSERM, Paris-Saclay University, Le Kremlin-Bicêtre, France

Preconception

Gestation/Antenatal

Delivery

Postpartum

Fiore M, Senthiles L and d'Oiron R, Blood 2022;139:2633-41

Pregnancy in GT?

GO

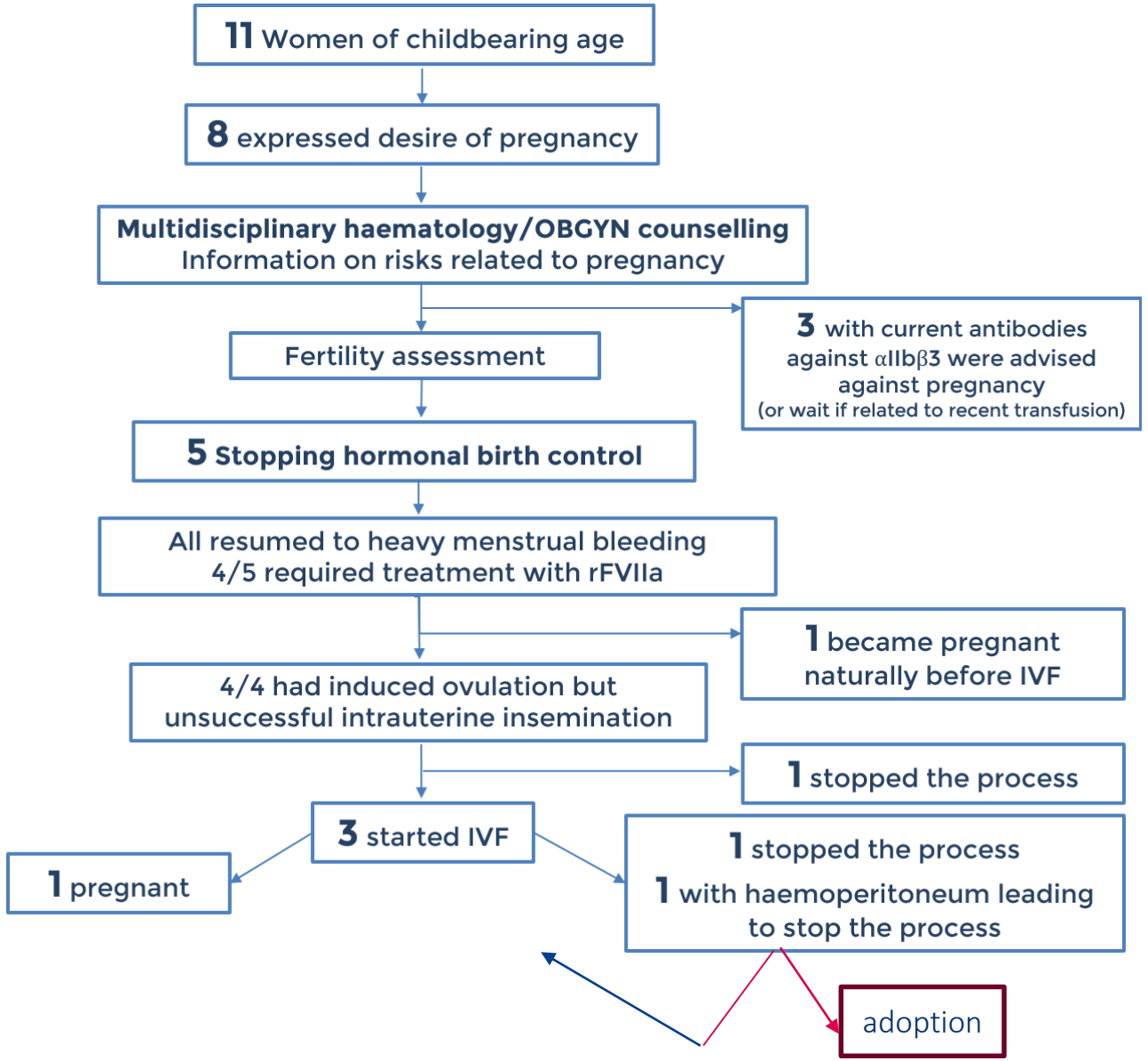
?

NO GO

?

Obtain a pregnancy in GT: a monocentric cohort

- Cohort of women with type 1 GT seen in Bicêtre hospital from 2006 to 2021
- Observational study on eligibility assessment and support for obtention of pregnancy
- Result :
  - Access to pregnancy remains rare and complex
  - Very few eligible women without significant antiplatelets antibodies and preserved couple fertility
  - A vigorous frame of evaluation and a combined expertise of the haematology and gynaecology teams is mandatory



Morelle et al. EAHAD 2022. e-poster PO106

GT initiatives

- 2 EAHAD Working Groups
  - Women and Girls with Bleeding Disorders (WGBD^{+}-WG)
  - Glanzmann Thrombasthenia (GT-WG)

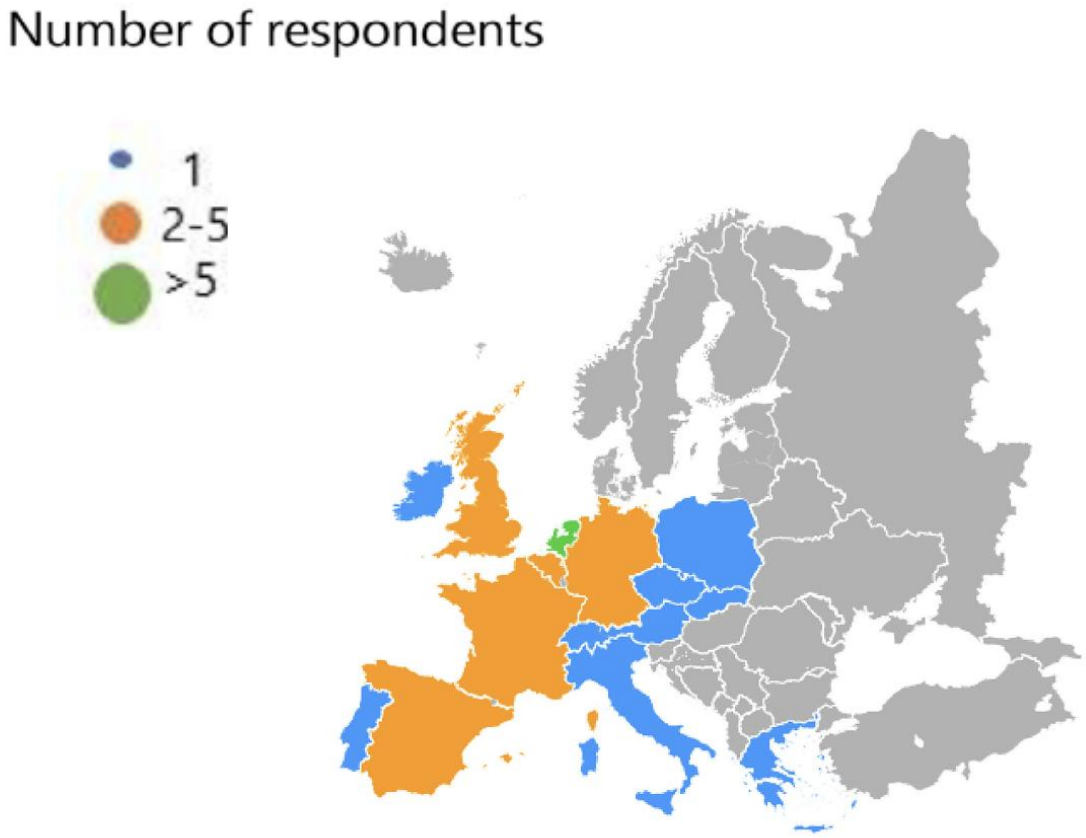
- GT :
  - European Survey on current clinical practice[1]
    - Some consensus
    - A lot of heterogeneity between respondents (immunization screening, duration of hemostatic coverage across treatments,…)
    - Highlighted the needs for in-depth study on specific topics, including pregnancy in GT

- Joint project of WGBD^{+}-WG and GT-WG following the general practice survey:
  - in-depth survey on pregnancy, 30 questions

1. Fiore M et al. Haemophilia, 2025; 31:1261–1270

GT/pregnancy European survey: respondents

Geographical distribution



Respondents

- 37 responses, 18 countries
  - 73% haematologists treating adults
  - 68% took care of a woman with GT with a pregnancy wish
  - **35% managed a pregnancy in a woman with GT in the last 10 years**

- **Mean number of women with GT with an active wish to become pregnant that the responders took care of in the past 10y**

  = 1.6 (range 0-8)

Rutten K et al. EAHAD 2026, PO243 and Haemophilia, 2025; 0:1–7

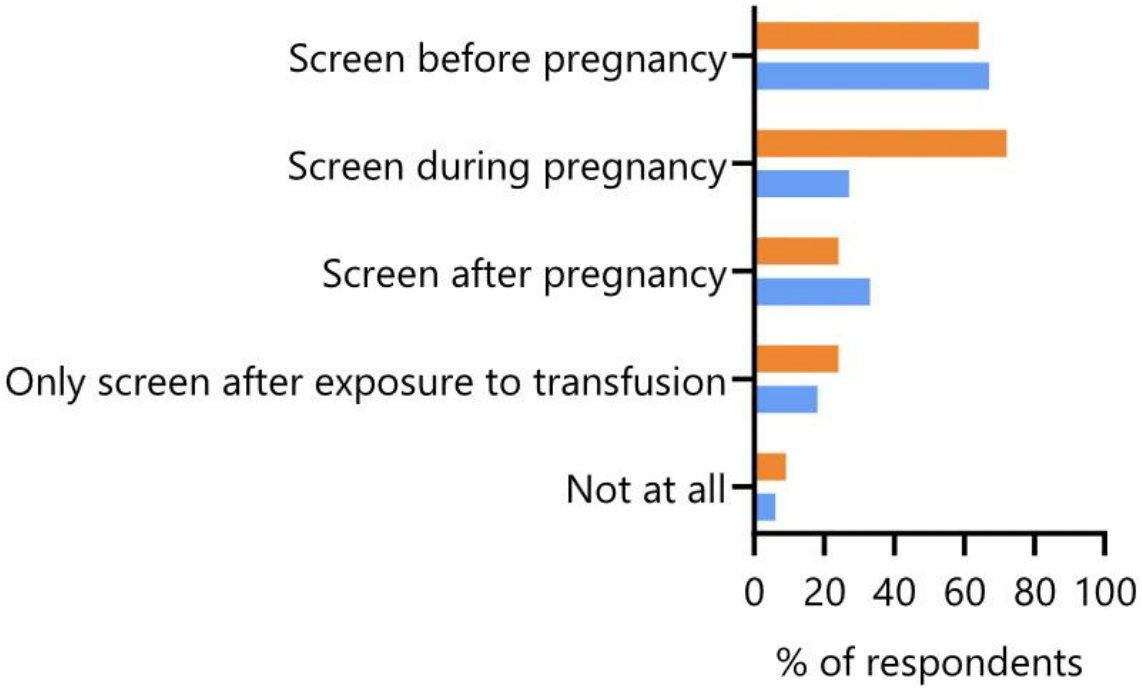
GT/pregnancy European survey: Main results

- 62% reported delay in conceiving
- Almost all respondents recommended multidisciplinary approach and preconception counselling
- 91% would screen for platelet alloimmunisation; however, the timing of screening varied
- 75% would advise a mode of delivery as per obstetric indication
- 69% would recommend to avoid neuraxial anaesthesia
- 50% would add pharmacological thromboprophylaxis

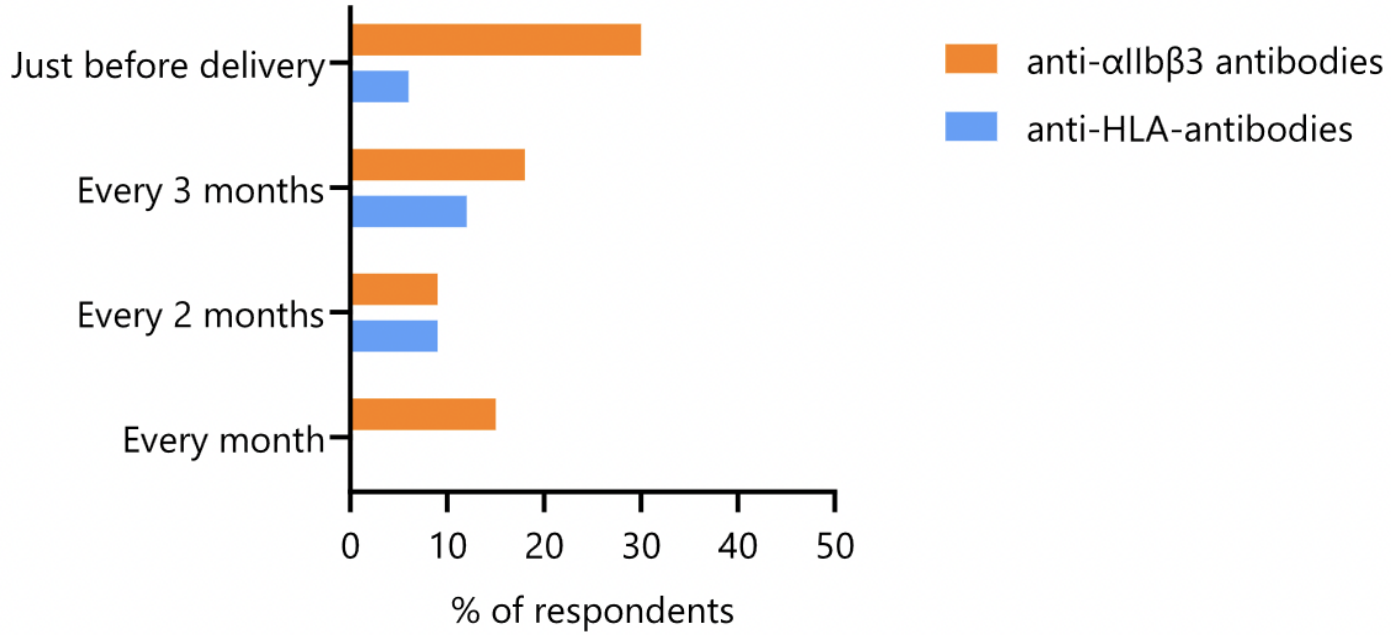
Rutten K et al. EAHAD 2026, PO243 and Haemophilia, 2025; 0:1–7

GT/pregnancy European survey: Current practice regarding maternal anti-HLA and anti-αIIbβ3 antibody screening.

(A) Timing of screening during different phases of pregnancy.

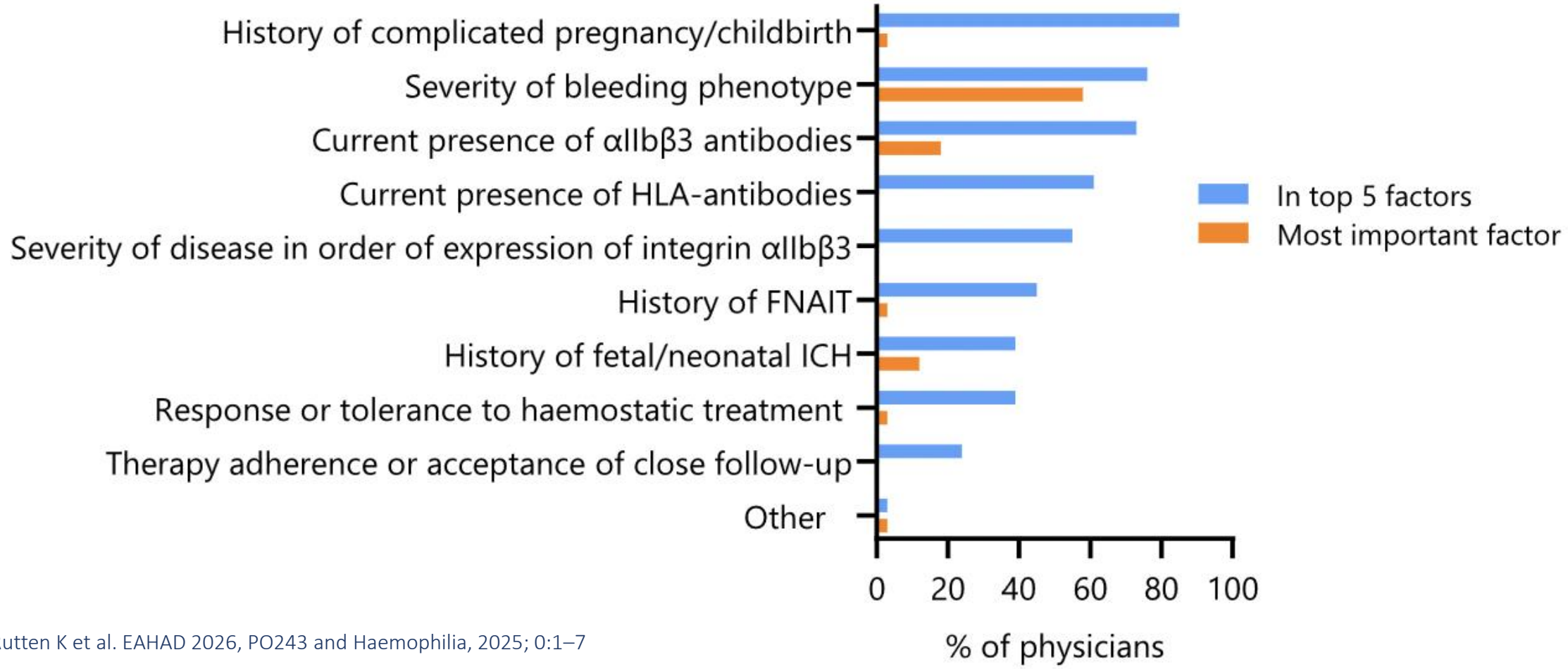


(B) Frequency of screening during pregnancy.



Rutten K et al. EAHAD 2026, PO243 and Haemophilia, 2025; 0:1–7

GT/pregnancy European survey: Healthcare professional responses on when they may advise against pregnancy



Rutten K et al. EAHAD 2026, PO243 and Haemophilia, 2025; 0:1–7

Impact of evolution of care for women with Glanzmann Thrombasthenia



Low chance of pregnancy

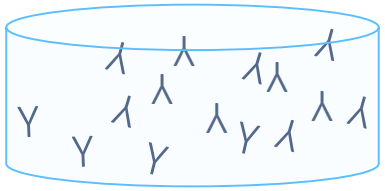
High risk of uncontrolled bleeding and foetal complication



Safer hormonal discontinuation?

In vitro fertilisation for selected patients?

Increased confidence in ability to stop or prevent acute bleeding



1990



2026

Platelets

rFVIIa

Platelets or rFVIIa*

04

Conclusion

Closing message

- The ultra-rare nature of the condition greatly limits available evidence
- Highly fragmented expertise, as most clinicians encounter very few cases, if any
- AUB and pregancy remain key issues in GT girls/women
- Variability in practice, access and consideration given to immunization status
- New ethical challenges emerge as disparities in expertise drive inconsistent clinical decisions across centers and specialists
- We need to further explore the go/no-go criteria for pregnancy and IVF in GT women, including ethics

THANK YOU

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