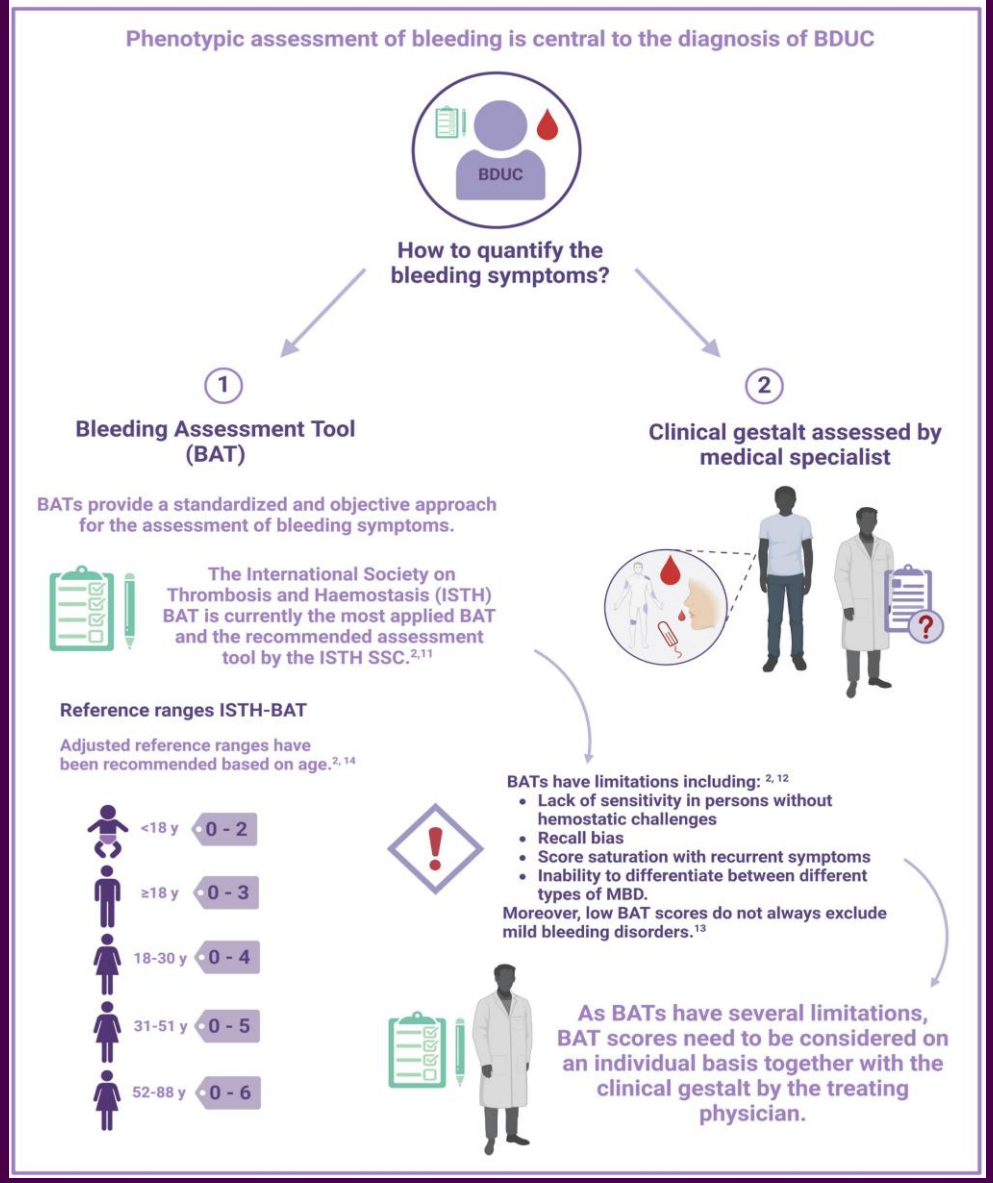

بنام خداوند جان و خرد

Diagnostic work-up of patients with
Increased Bleeding Tendency

M. Ahmadinejad MD. Pathologist
Associate Professor of Blood Transfusion Research Center, High Institute for Research and Education in Transfusion Medicine,
Head of Reference Coagulation Lab of IBTO

Tehran Heart Center - 1403

5. Assessment of bleeding phenotype



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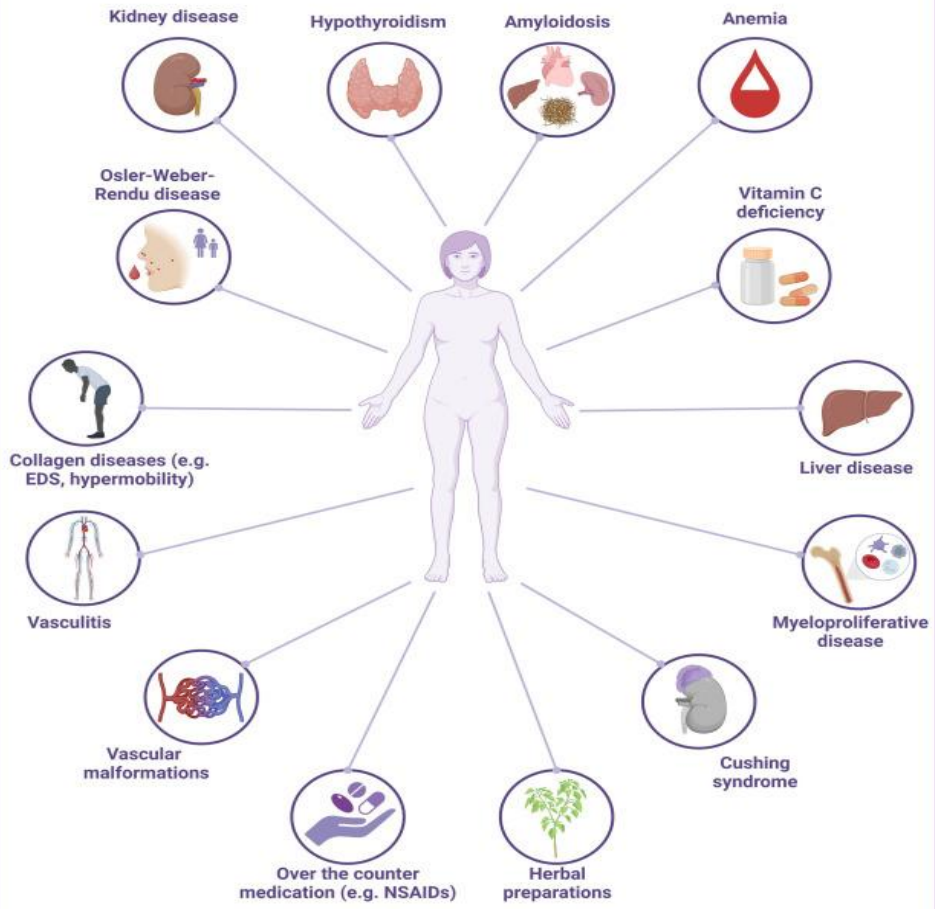
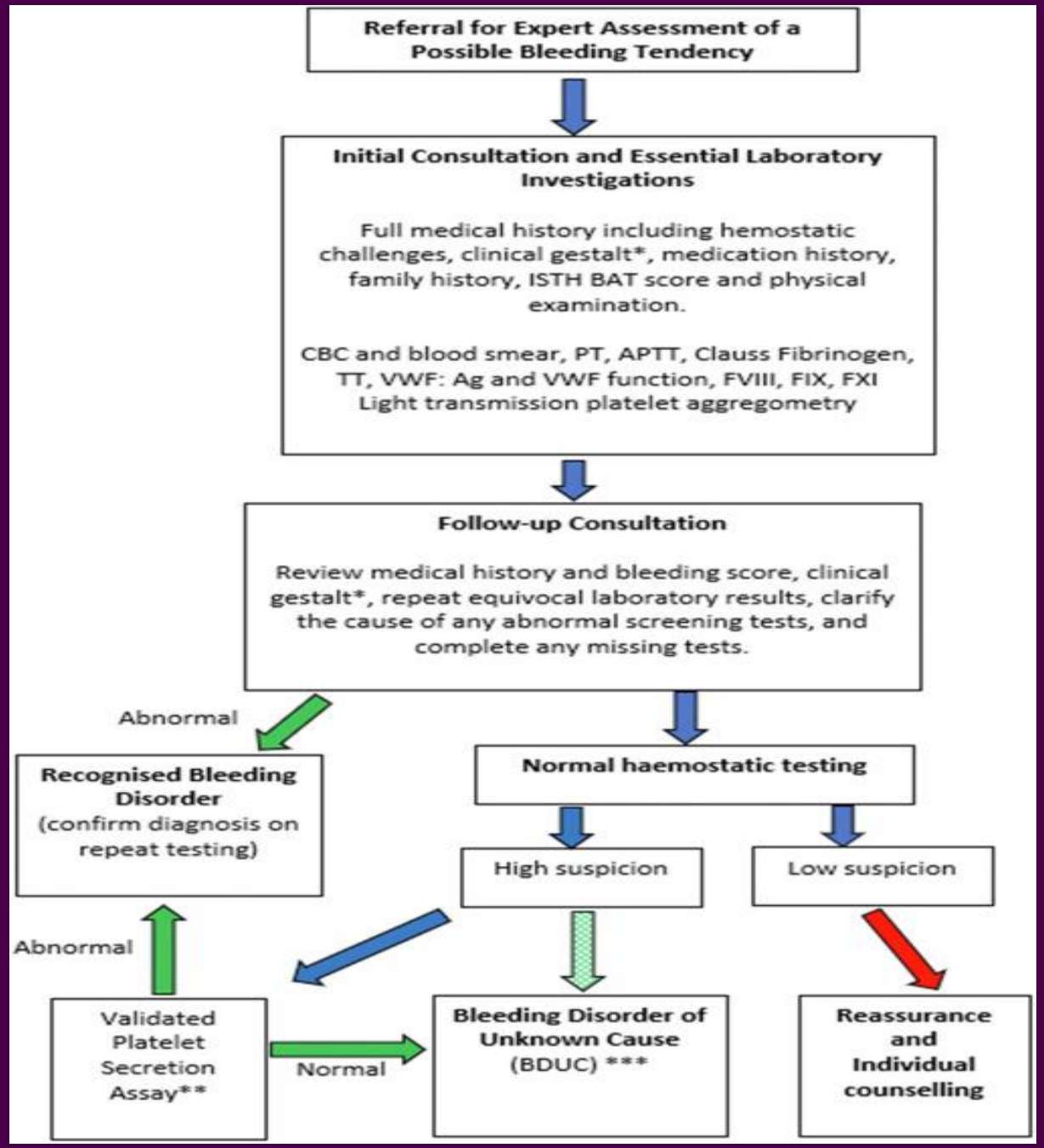
Exclusion of **non-hemostatic causes** for a bleeding tendency*

7. Other causes for bleeding

Other conditions are associated with an increased bleeding tendency, without detectable abnormalities in the coagulation cascade.[15] To exclude other causes, additional (laboratory) tests should be performed when clinically indicated.



1. CBC
2. PT
3. aPTT
4. TT
5. VWF:Ag
6. VWF:activity
7. F VIII, IX, and XI
8. Platelet LTA



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ISTH SSC COMMUNICATION

Standardization of definition and management for bleeding disorder of unknown cause: communication from the SSC of the ISTH

Ross I. Baker[1,2,3,4] | Philip Choi[5,6] | Nicola Curry[7,8] | Johanna Gebhart[9] | Keith Gomez[10] | Yvonne Henskens[11,12] | Floor Heubel-Moenen[13] | Paula James[14] | Rezan Abdul Kadir[15,16] | Peter Kouides[17] | Michelle Lavin[4,18,19] | Marie Lordkipanidze[20,21] | Gillian Lowe[22] | Andrew Mumford[23] | Nicola Mutch[24,25] | Michael Nagler[26,27] | Maha Othman[28,29,30] | Ingrid Pabinger[9] | Robert Sidonio[31] | Will Thomas[32] | James S. O'Donnell[4,18,19] | on behalf of the ISTH SSC Von Willebrand Factor, Platelet Physiology, and Women's Health Issues in Thrombosis and Haemostasis

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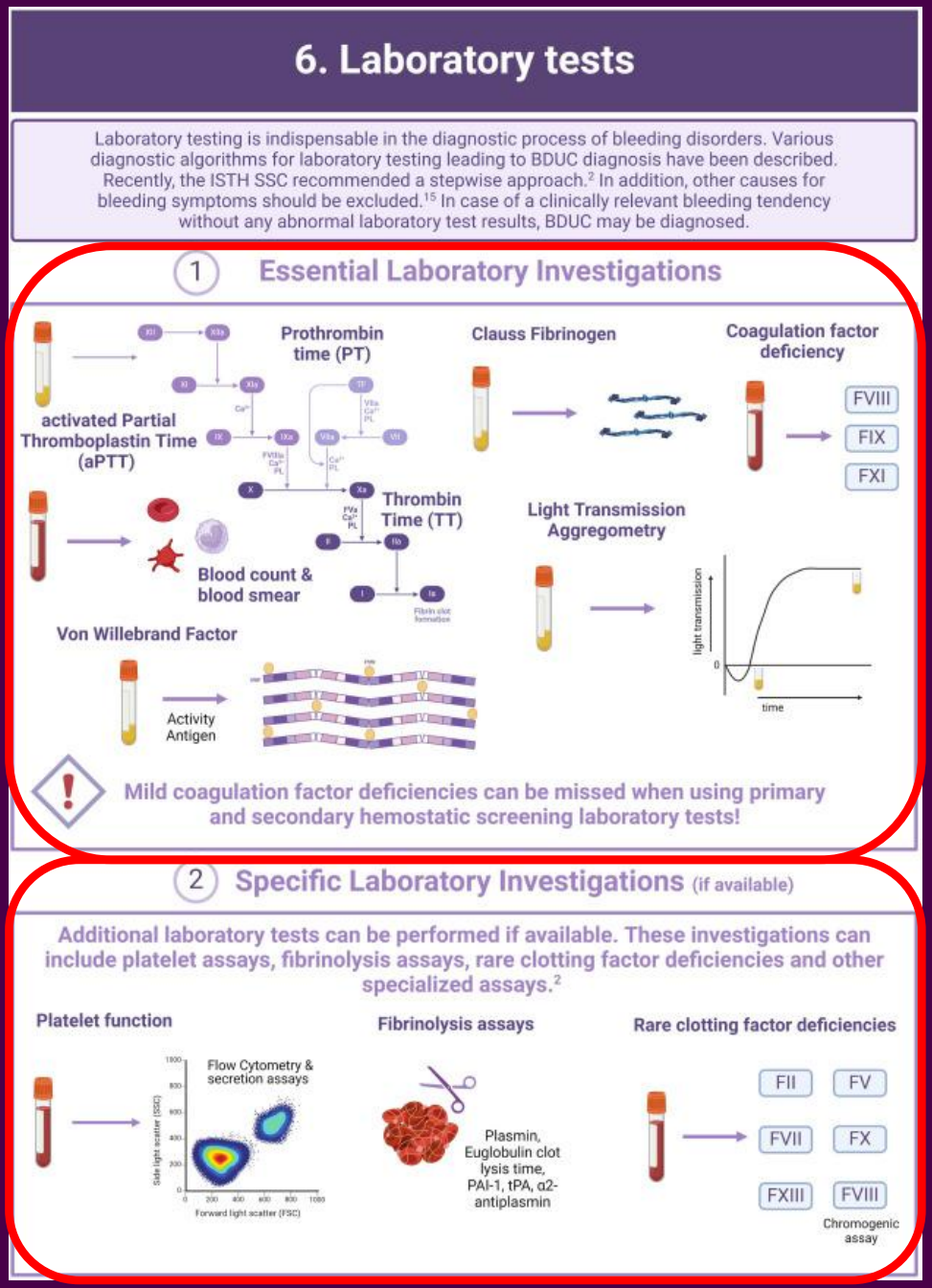
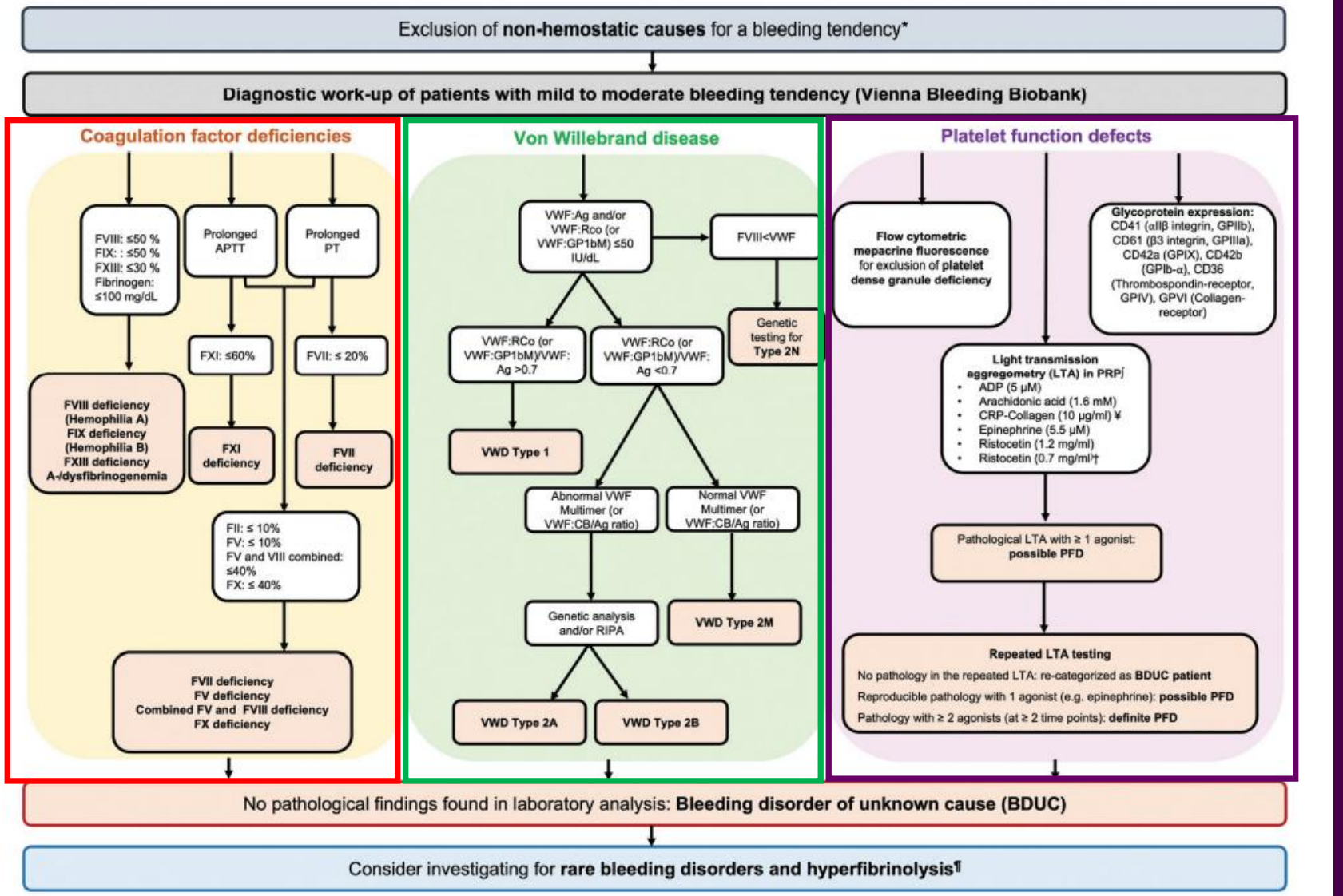


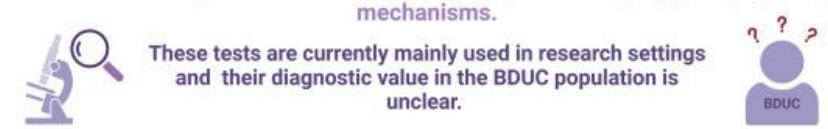
Platelet LTA should be performed as a minimum assessment of platelet function and, if possible, platelet-dense granule assessment. Further specialized platelet investigations in expert laboratories will identify additional rare IPFD in some MBD patients.


Exclusion of non-hemostatic causes for a bleeding tendency*
Diagnostic work-up of patients with mild to moderate bleeding tendency (Vienna Bleeding Biobank)
Coagulation factor deficiencies
FVIII: ≤50 %
FIX: : ≤50 %
FXIII: ≤30 %
Fibrinogen: ≤100 mg/dL
Prolonged APTT
Prolonged PT
FXI: ≤60%
FVII: ≤ 20%
FVIII deficiency (Hemophilia A)
FIX deficiency (Hemophilia B)
FXIII deficiency
A-/dysfibrinogenemia
FXI deficiency
FVII deficiency
FII: ≤ 10%
FV: ≤ 10%
FV and VIII combined: ≤40%
FX: ≤ 40%
FVII deficiency
FV deficiency
Combined FV and FVIII deficiency
FX deficiency
Von Willebrand disease
VWF:Ag and/or VWF:Rco (or VWF:GP1bM) ≤50 IU/dL
FVIII<VWF
Genetic testing for Type 2N
VWF:RCo (or VWF:GP1bM)/VWF: Ag >0.7
VWF:RCo (or VWF:GP1bM)/VWF: Ag <0.7
VWD Type 1
Abnormal VWF Multimer (or VWF:CB/Ag ratio)
Normal VWF Multimer (or VWF:CB/Ag ratio)
Genetic analysis and/or RIPA
VWD Type 2M
VWD Type 2A
VWD Type 2B
Platelet function defects
Flow cytometric mepacrine fluorescence for exclusion of platelet dense granule deficiency
Glycoprotein expression: CD41 (αIIβ integrin, GPIIb), CD61 (β3 integrin, GPIIIa), CD42a (GPIX), CD42b (GPIb-α), CD36 (Thrombospondin-receptor, GPIV), GPVI (Collagen-receptor)
Light transmission aggregometry (LTA) in PRP
ADP (5 µM)
Arachidonic acid (1.6 mM)
CRP-Collagen (10 µg/ml) ¥
Epinephrine (5.5 µM)
Ristocetin (1.2 mg/ml)
Ristocetin (0.7 mg/ml)†
Pathological LTA with ≥ 1 agonist: possible PFD
Repeated LTA testing
No pathology in the repeated LTA: re-categorized as BDUC patient
Reproducible pathology with 1 agonist (e.g. epinephrine): possible PFD
Pathology with ≥ 2 agonists (at ≥ 2 time points): definite PFD
No pathological findings found in laboratory analysis: Bleeding disorder of unknown cause (BDUC)
Consider investigating for rare bleeding disorders and hyperfibrinolysis¶

11. Advanced hemostatic laboratory testing

Besides the broadly available hemostatic laboratory tests, additionally more advanced hemostatic laboratory tests can be used to investigate underlying pathophysiological mechanisms.

These tests are currently mainly used in research settings and their diagnostic value in the BDUC population is unclear.



In the next four capsules current research and knowledge gaps on advanced hemostatic laboratory testing in BDUC are highlighted.

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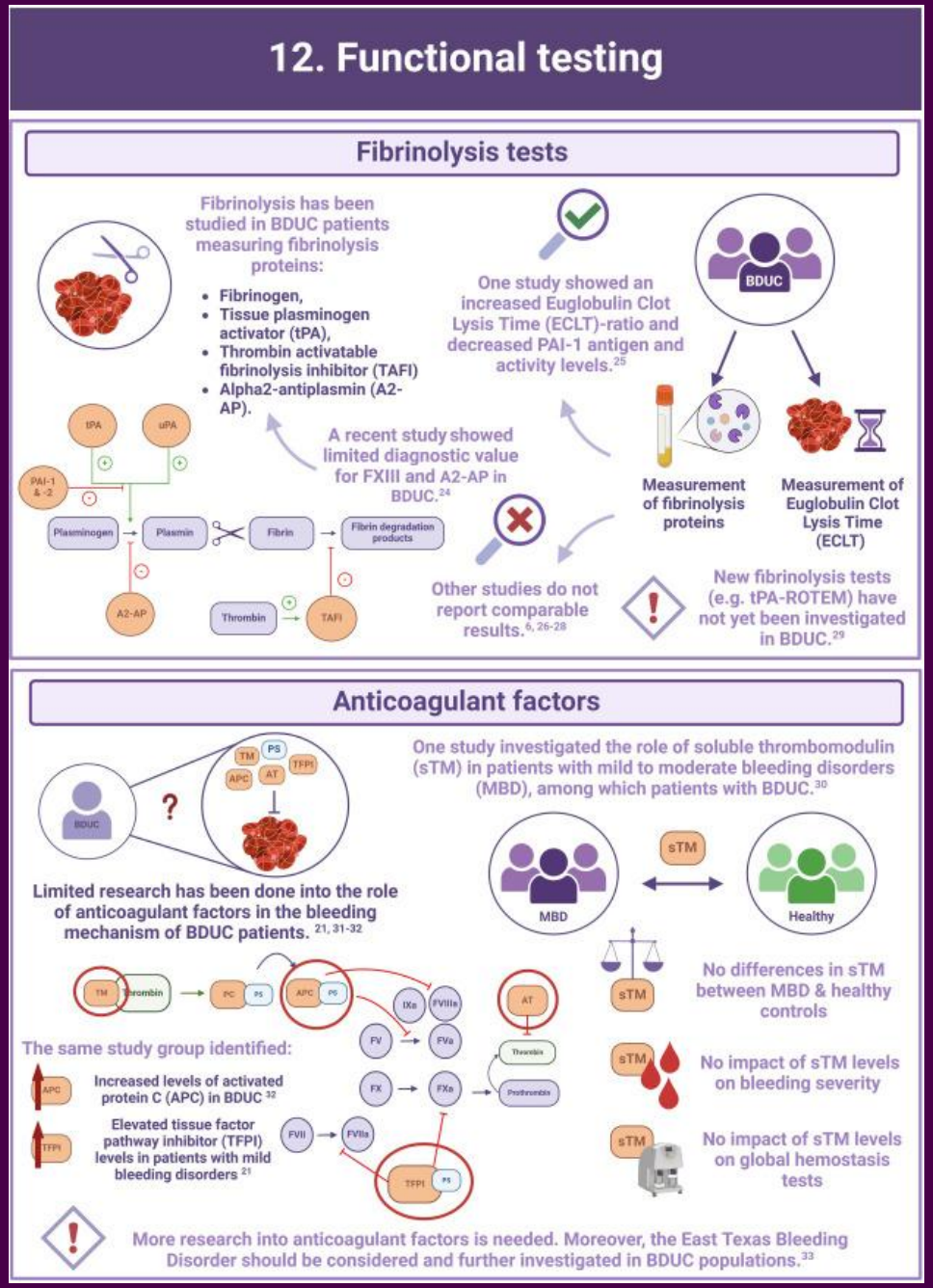

Abnormalities in the fibrinolytic pathway may be identified in some BDUC patients, but the clinical utility for diagnosis remains unclear and not routinely recommended for diagnosis of BDUC

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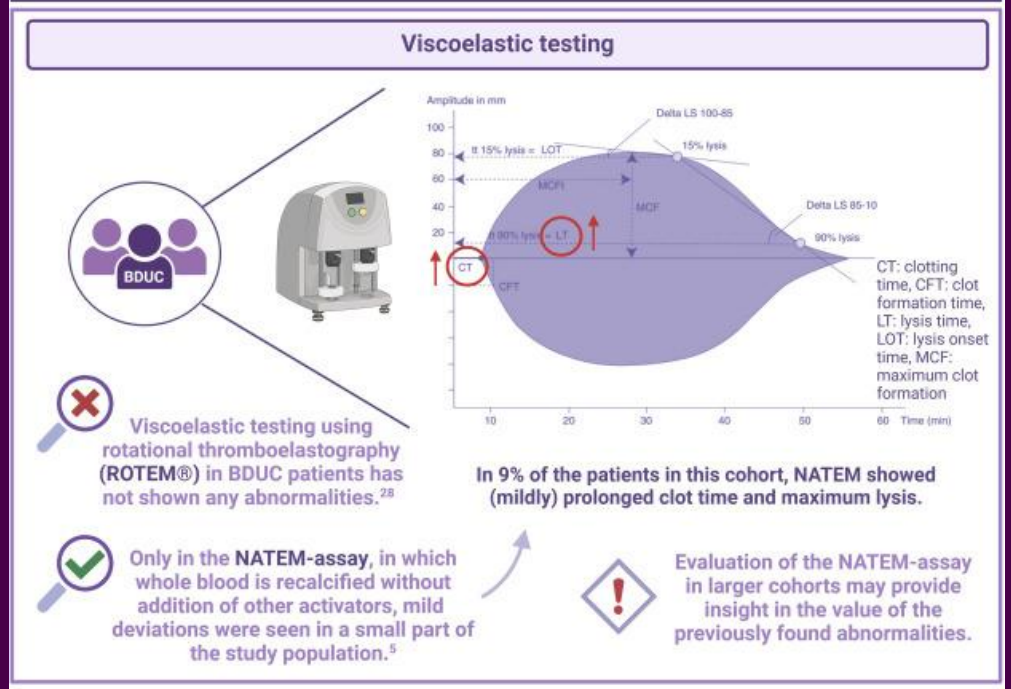
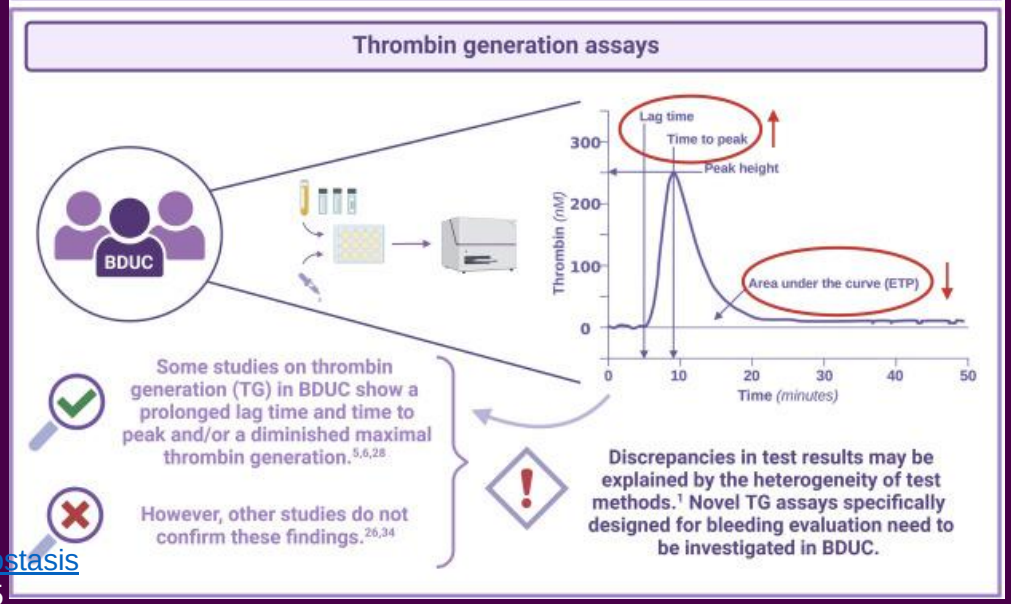
13. Global hemostasis





Although global hemostatic tests may demonstrate variable abnormaliti in
a minority of BDUC patients, they are r recommended for routine diagnosis or management

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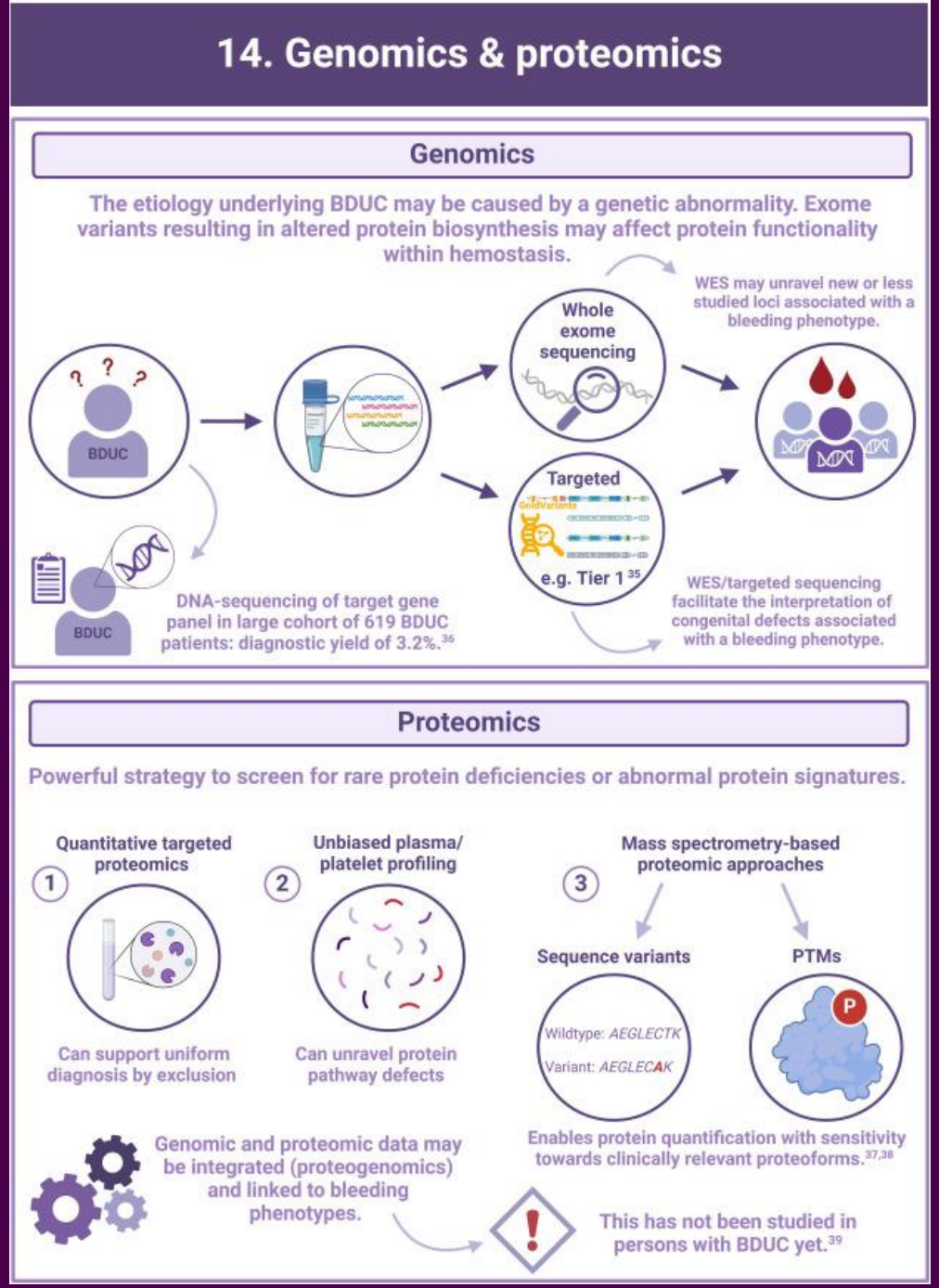

- **Routine** genetic testing **is not indicated** for BDUC
- Patients **should be considered for enrolment in research studies** that enable more expansive phenotypic and genomic testing.

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Bleeding Disorder of Unknown Cause (BDUC)

- We recommend :

"*Bleeding disorder of unknown cause*" be used

1- in preference to other terminology for classification f

2- patients with a bleeding phenotype in whom hemostatic investigations are normal

IRSTH

Iranian Society of Thrombosis and Hemostasis

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