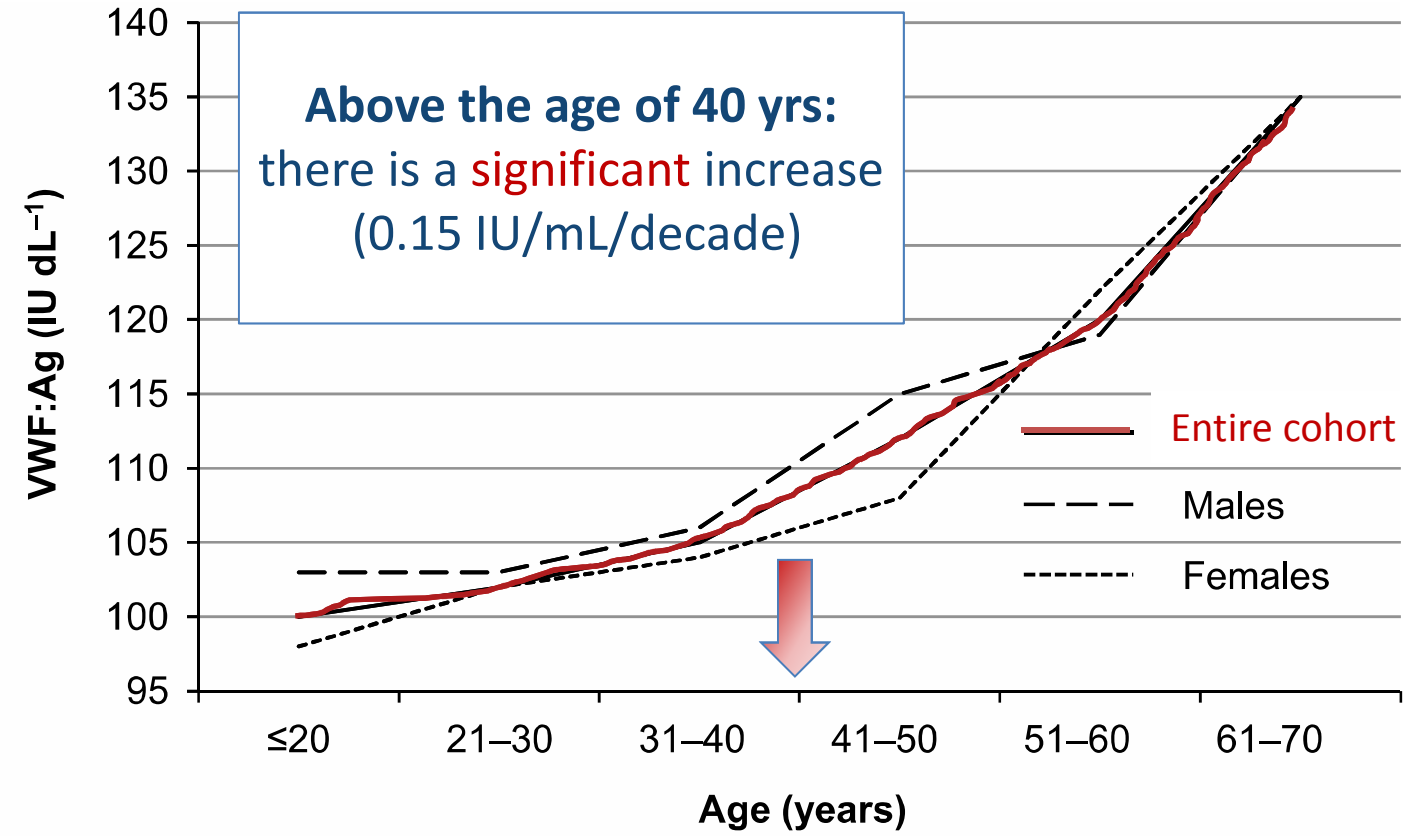
Maladie de Willebrand: effets de l'age

Jenny Goudemand

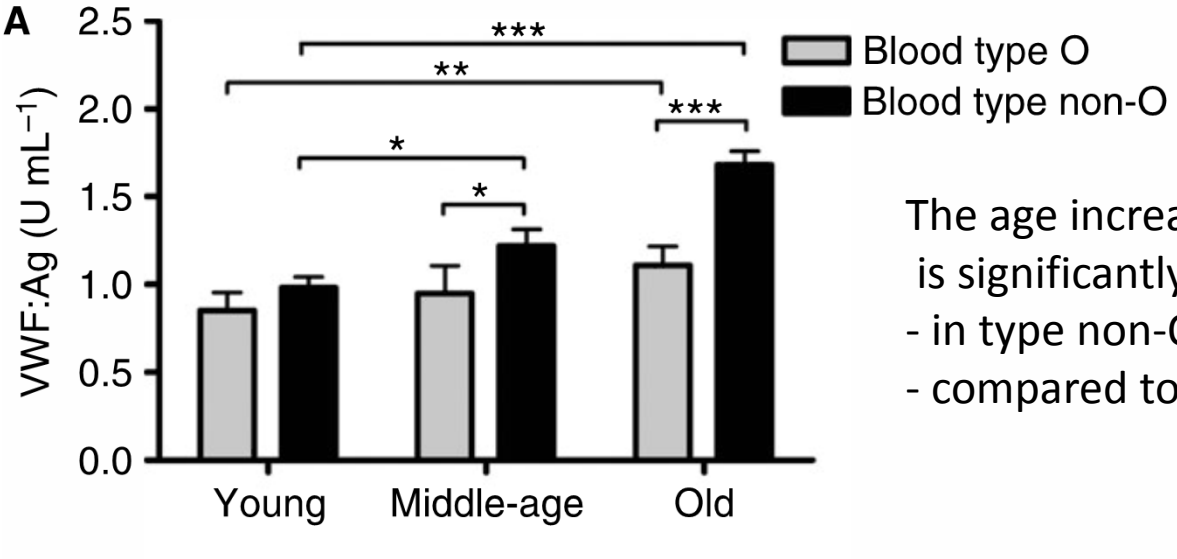
VWF increases with age

5052 normal healthy blood donors (South Wales population of the UK)



Davies et al. Haemophilia 2012; 18:e60-e87

The effect of age is dependent on ABO blood group



7 ± 5 yrs n=52

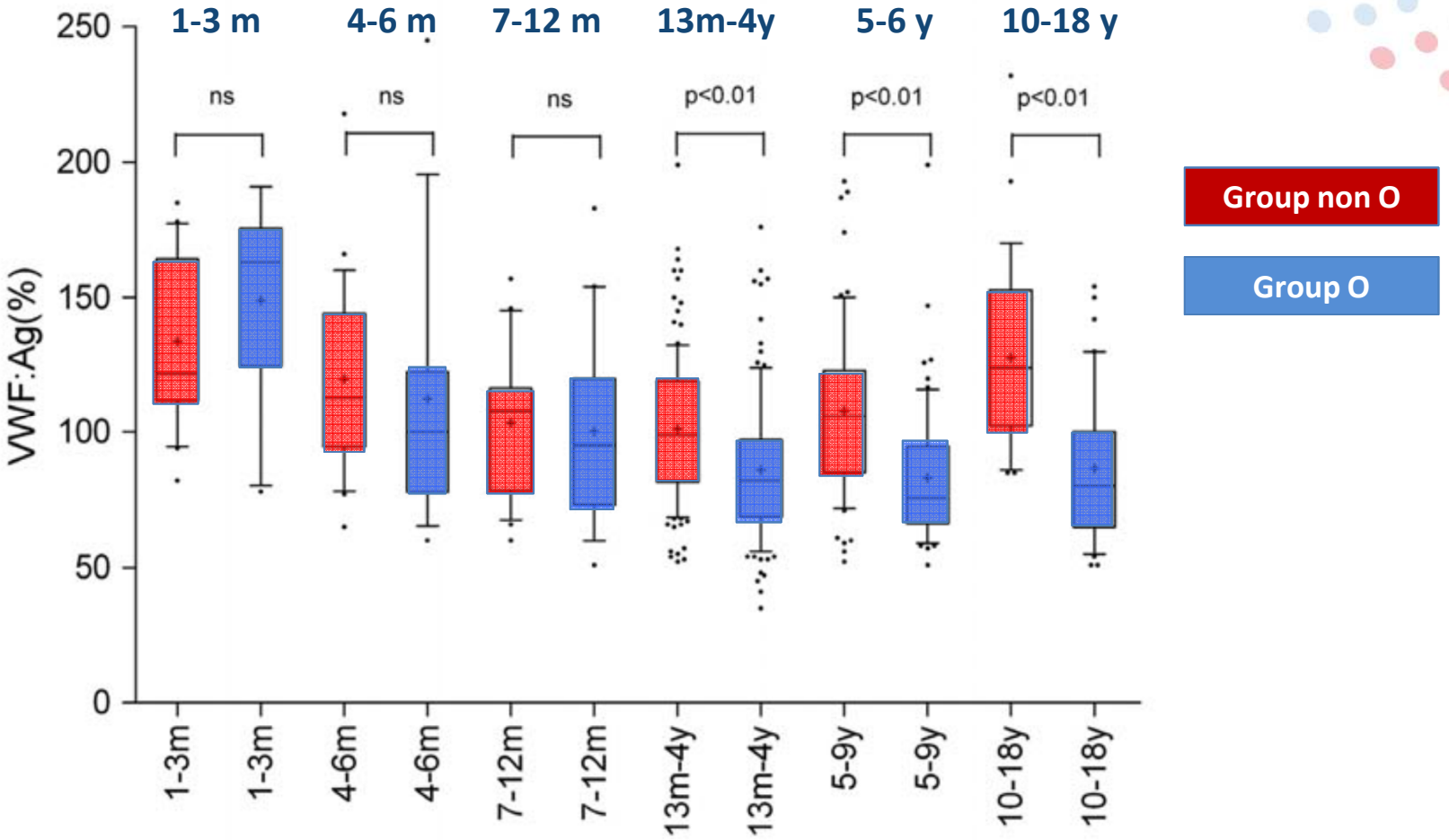
41 ± 6 yrs n=42

71 ± 7yrs n=52

The age increase in VWF:Ag is significantly higher
- in type non-O individuals (1.71 fold rise)
- compared to type O (1.25 fold)

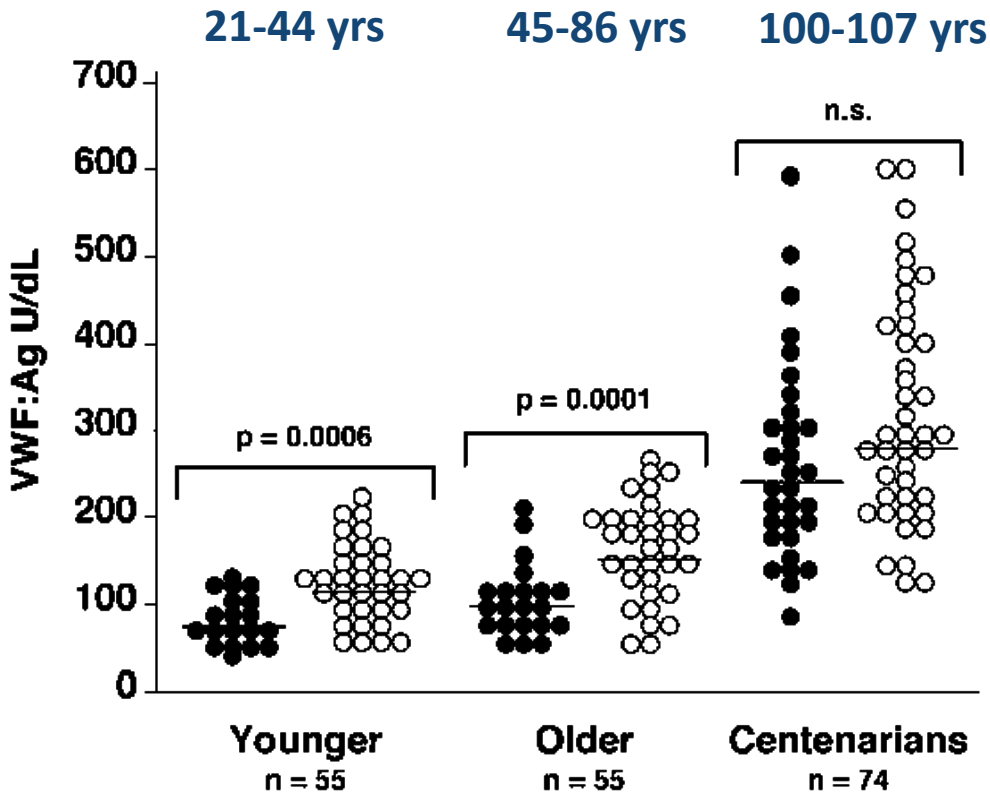
Albanez S et al. J Thromb Haemost 2016; 14:953-63

VWF level is increased during childhood



Klarmann D et al. Transfusion 2010 50: 1571-80

VWF level is increased also in very old individuals



Blood group O

Blood group non O

Coppola R. et al. Haematologica 2003; 88: 39-43

The age increase in VWF: multifactorial mechanisms

- Increase in secretion
  - significant only in the **oldest age** and **non-O** individuals
  - due to vascular damage, inflammation…
- Progressive reduction of clearance
  - more significant in **non-O** individuals
- ADAMTS 13 activity decreases with age

►combined to the increase in VWF this could be involved in the prothrombic state of elderly individuals

Albanez S et al. J Thromb Haemost 2016; 14:953-63
Kokame K et al. J Thromb Haemost 2011; 9: 1426-8

Which consequences for patients with VWD ?

von Willebrand disease and aging: an evolving phenotype

Y. V. SANDERS,* M. A. GIEZENAAR,* B. A. P. LAROS-VAN GORKOM,† K. MEIJER,‡ J. G. VAN DER BOM,§¶ M. H. CNOSSEN,** M. R. NIJZIEL,†† P. F. YPMA,‡‡ K. FIJNVANDRAAT,§§ J. EIKENBOOM,¶¶ E. P. MAUSER-BUNSCHOTEN,*** and F. W. G. LEEBEEK,* FOR THE WIN STUDY GROUP[1]

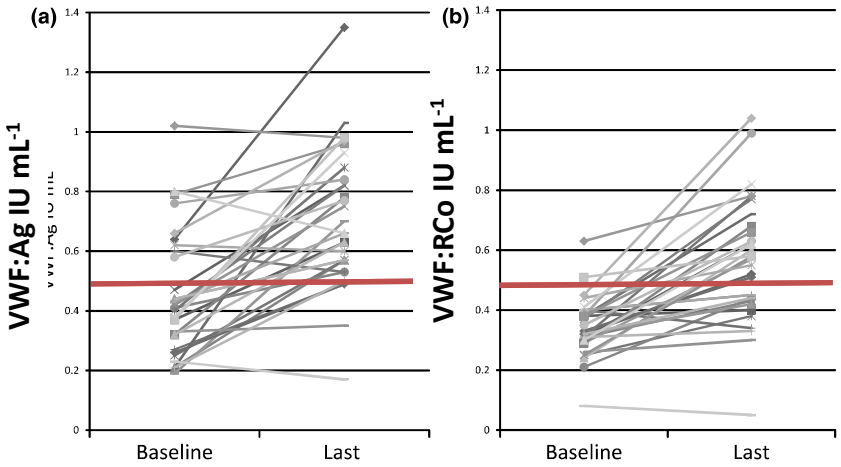
- WiN study
  - 71 patients aged 65-85 yrs (61% type 1 VWD)
  - 593 patients aged 16-64 yrs (58% type 1 VWD)
- In type 1: significant increase (per decade) in:
  - VWF:Ag 2.7 IU/dL
  - VWF:Act 4.1 IU/dL
  - FVIII:C 3.7 IU/dL
- But not in type 2

J Thromb Haemost 2014; 12: 1066-75

Changes in von Willebrand factor level and von Willebrand activity with age in type 1 von Willebrand disease

N. RYDZ,* J. GRABELL,† D. LILLICRAP* and P. D. JAMES†
*Department of Pathology and Molecular Medicine, Queen's University, Kingston, ON, Canada; and †Department of Medicine, Queen's University, Kingston, ON, Canada

- 31 pts with **type 1** VWD aged 30-74 yrs
- Mean follow up: **11 years** (5-26 yrs)



18 (58%) normalized (≥ 0.50 IU/ml) both VWF:Ag and VWF:RCo

Haemophilia 2015; 21: 636-641

Outgrowing the laboratory diagnosis of type 1 von Willebrand disease: A two decade study

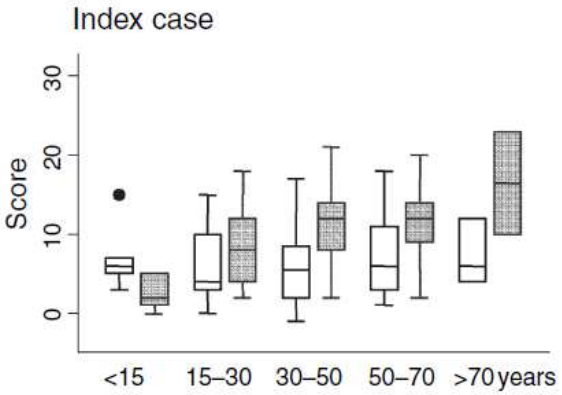
Mouhamed Yazan Abou-Ismail[1] | Gbolahan O. Ogunbayo[1] | Michelle Secic[2] | Peter A. Kouides[1,3]

- 126 pts with type 1 VWD aged 27.7 ± 16.2 yrs at diagnosis
- Mean follow up: **10.5 ± 3.7 yrs** (5-20 yrs)
- Complete* (or possible**) normalization : **55%**

*Complete N: VWF:Ag and VWF:RCo > 50 IU/dL at least twice
**Possible N: VWF:Ag and VWF:RCo > 50 IU/dL only once

Am J Hematol 2018; 93: 232-237

Is it associated with a decreased bleeding risk ?



Tosetto et al. J Thromb Haemos 2006; 4: 766-73

The BS increases with age

BUT

BS is cumulative based on lifetime bleeding symptoms and may not reflect the current bleeding risk

Seaman CD et al. Clin Appl Thromb/Hemost 2017

39 patients with type 1 VWD (VWF:Ag or RCo <0.50 IU/dL) aged 19 to 85 yrs

BS (ISTH BAT) measured for the **3 previous years**

BS inversely associated with age

Sanders Y et al. J Thromb Haemost 2014; 12:1066-75

WiN study: 71 elderly (>65 yrs) and 593 younger (16-65) pts with VWD (Type 1: 58%)

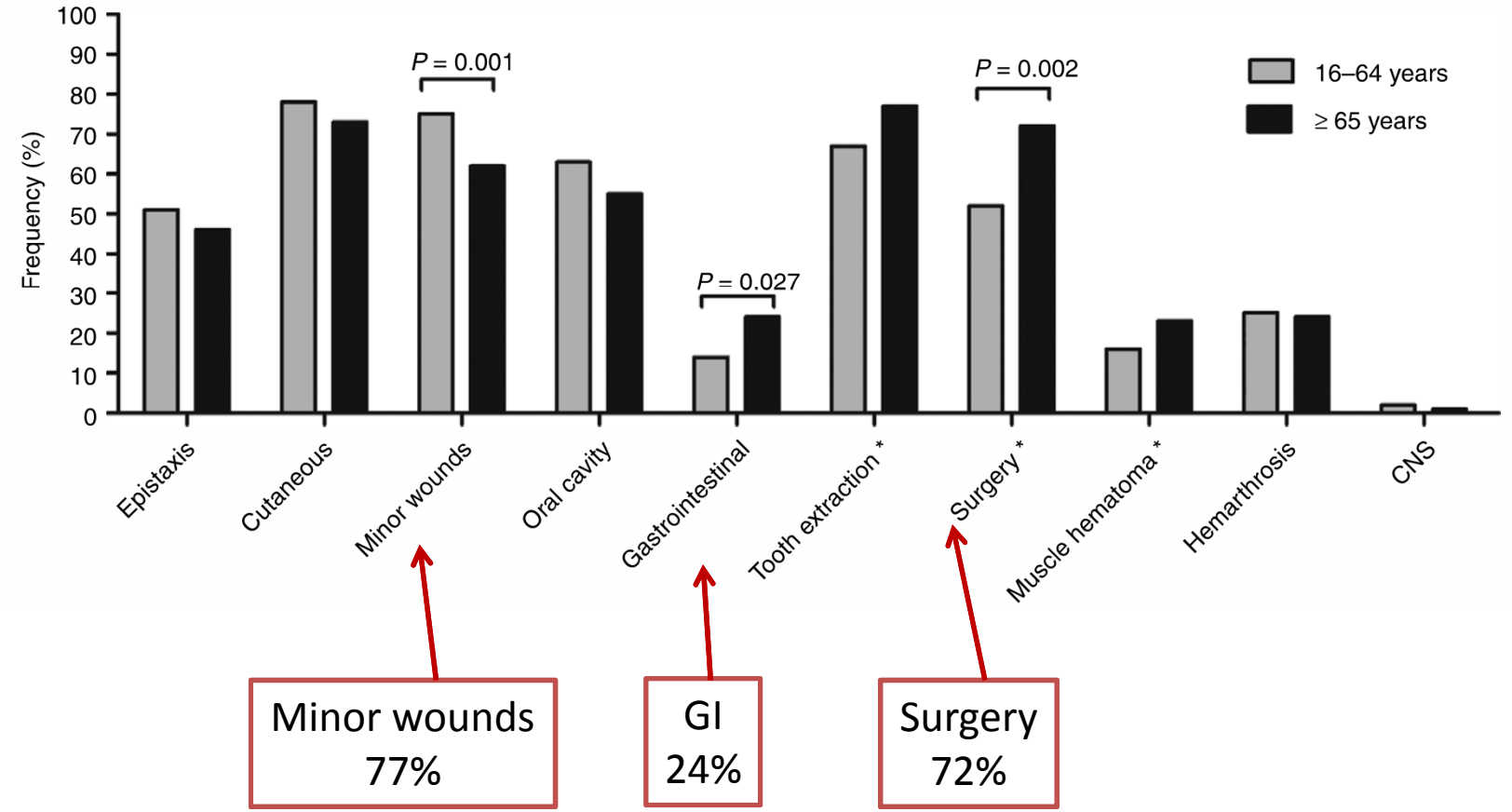
BS analyzed in the **preceeding** year:

BE requiring treatment in the oldest population: ↗ in type 2 but not in type 1

von Willebrand disease and aging: an evolving phenotype

Y. V. SANDERS,* M. A. GIEZENAAR,* B. A. P. LAROS-VAN GORKOM,† K. MEIJER,‡ J. G. VAN DER BOM,§¶ M. H. CNOSSEN,** M. R. NIJZIEL,†† P. F. YPMA,‡‡ K. FIJNVANDRAAT,§§ J. EIKENBOOM,¶¶ E. P. MAUSER-BUNSCHOTEN,*** and F. W. G. LEEBEEK,* FOR THE WIN STUDY GROUP[1]

The bleeding phenotype



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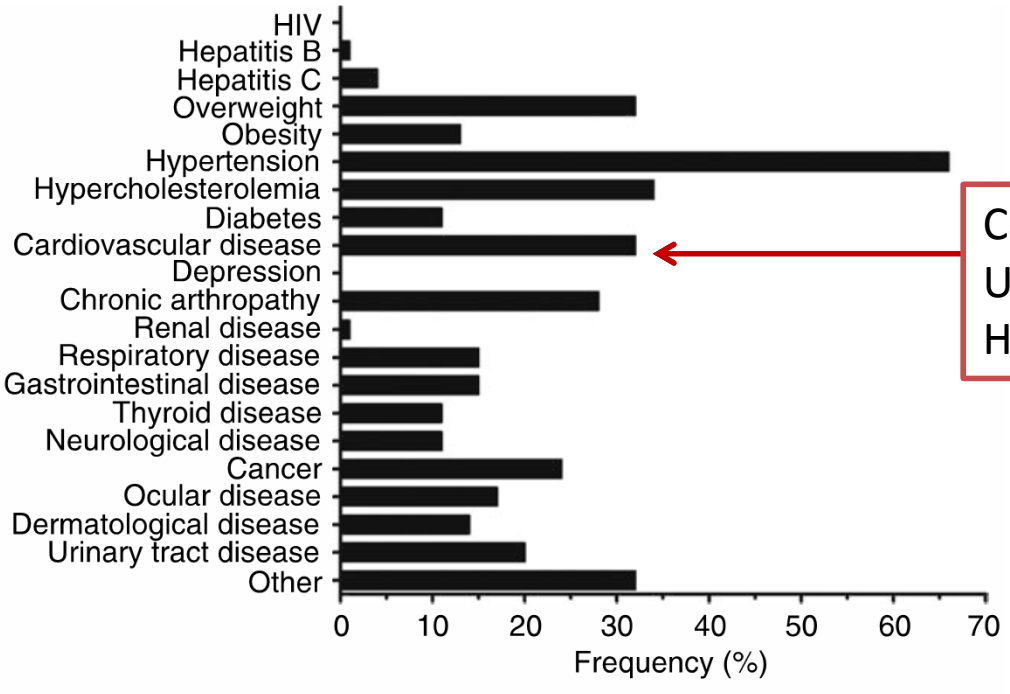
von Willebrand disease and aging: an evolving phenotype

Y. V. SANDERS,* M. A. GIEZENAAR,* B. A. P. LAROS-VAN GORKOM,† K. MEIJER,‡ J. G. VAN DER BOM,§¶ M. H. CNOSSEN,** M. R. NIJZIEL,†† P. F. YPMA,‡‡ K. FIJNVANDRAAT,§§ J. EIKENBOOM,¶¶ E. P. MAUSER-BUNSCHOTEN,*** and F. W. G. LEEBEEK,* FOR THE WIN STUDY GROUP[1]

- Elderly patients with VWD
  - co-morbidities present in 93%
  - 86% had ≥ 2 co-morbidities



Cardiac arythmia
Unstable angina pectoris
Heart valve disease

J Thromb Haemost 2014; 12: 1066-75

Comorbidities associated with higher von Willebrand factor (VWF) levels may explain the age-related increase of VWF in von Willebrand disease

Atiq et al. Br J Haemat 2018 (in press)

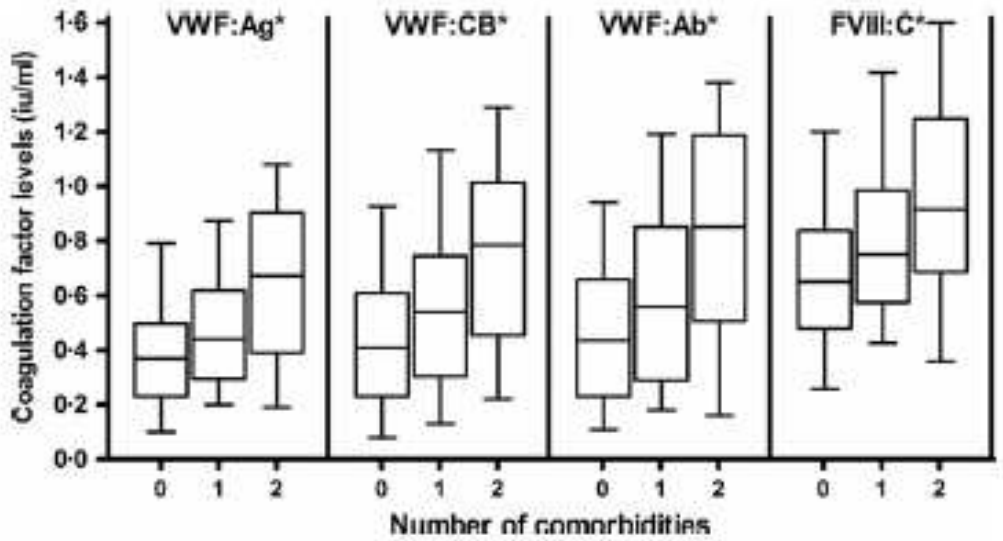
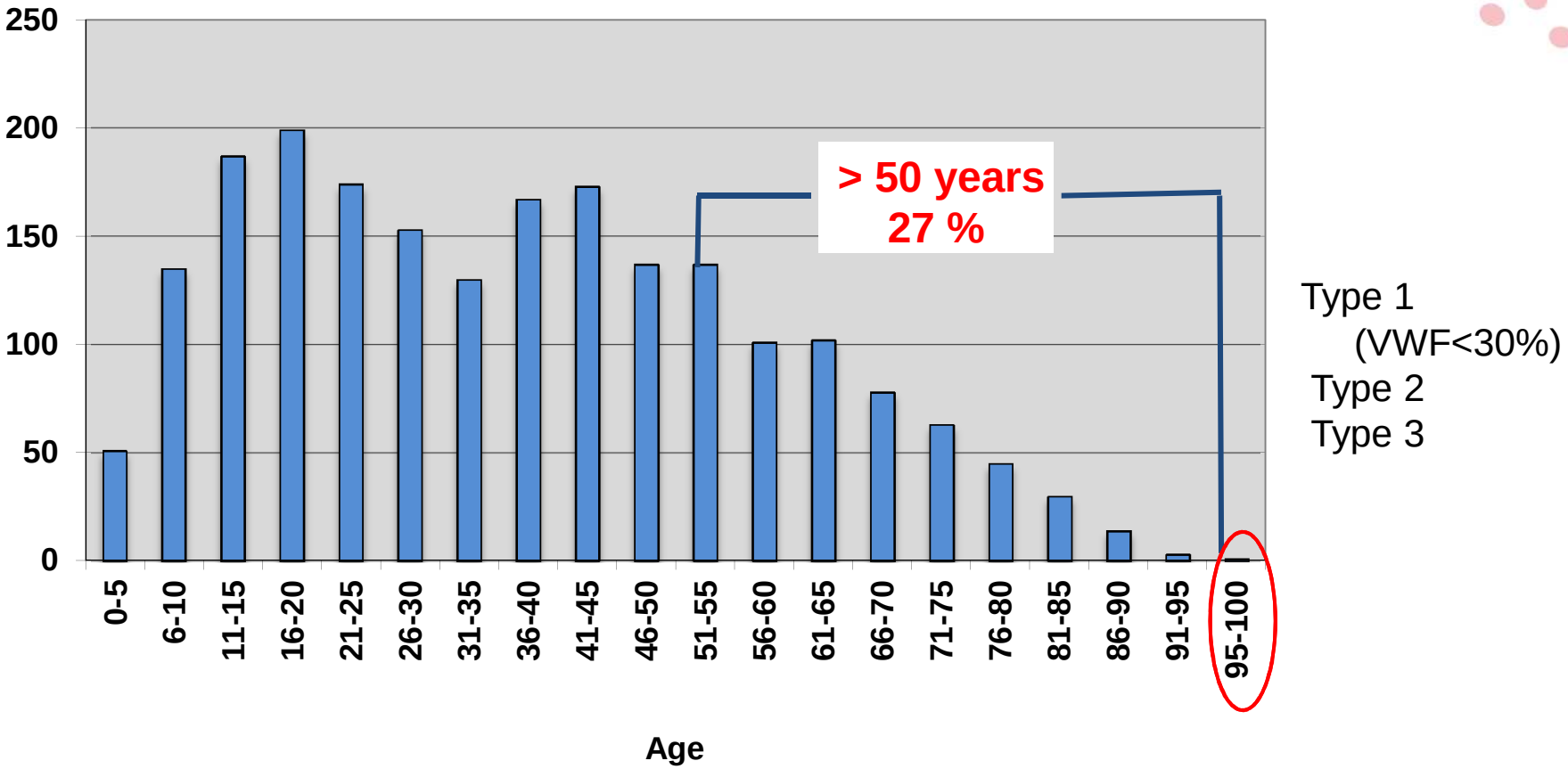


Fig 6. The number of comorbidities and VWF and FVIII levels in type 1 VWD. There were 236 patients with 0 relevant comorbidities, 77 patients with 1 relevant comorbidity and 18 patients with two relevant comorbidities. Only 2 patients had three relevant comorbidities and are excluded from the figure. Data presented as boxplots with median and interquartile ranges, and 5–95 percentiles. *$P < 0{\cdot}001$, Multiple regression outcomes corrected for age, sex and blood group. FVIII:C, factor VIII coagulant activity; VWD, von Willebrand disease; VWF:Ab, von Willebrand factor activity as measured by a monoclonal antibody assay; VWF:Ag, von Willebrand factor antigen; VWF:CB, von Willebrand factor collagen binding capacity.

Elderly patients with VWD

- The age increase in VWF may be protective at least in the less severe forms of type 1 VWD
- Probably less post trauma bleedings
- Less epistaxis, less bleedings from minor wounds
- No longer menorrhagia or post partum bleedings
- More GI bleedings +++
- More and more co morbidities ►anticoagulant, anti platelets, chemotherapy, surgery that increase the bleeding risk
- On the other hand, the thrombotic risk may be also increased: cardio vascular pathologies, obesity …
- Desmopressin can become contra indicated

French registry of haemorrhagic disease in 2017: 2080 patients with von Willebrand disease



Réseau FranceCoag

CRMW