

ATHN
DATA
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The Effect of Age at Diagnosis of Type I Von Willebrand Disease on Diagnostic Lab Values: A Pediatric Perspective

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Project Overview

- Retrospective database review using the American Thrombosis and Hemostasis Network (ATHN) dataset
- Compare age at diagnosis and Ristocetin Cofactor and von Willebrand Antigen levels in patients with Type I von Willebrand disease

Background

- Diagnosis of type I von Willebrand disease can be difficult due to multitude of factors that can affect von Willebrand factor antigen (vWF:Ag) and ristocetin cofactor (vWF:RCo) levels within an individual patient and between lab draws

Background

- The 2008 NHLBI guidelines for diagnosis of von Willebrand Disease recommended the use of the following levels for vWF:Ag and/or vWF:RCo for diagnosis of type I VWD.
 - <30 IU/dL= Type I vWD
 - 30-50 IU/dL= Low von Willebrand Factor

Background

- Prior studies have shown age can affect vWF:Ag and vWF:RCo levels in healthy adults.

1. Gill JC, et al. "The Effect of ABO Blood group on the Diagnosis of von Willebrand Disease". *Blood*. Vol 69, No 6 (1987). pp 1691-1695.
2. Favaloro EJ, et al. "Reassessment of ABO Blood Group, Sex, and Age on Laboratory Parameters Used to Diagnose von Willebrand Disorder". *American Journal of Clinical Pathology*. Vol 124 (2005). pp 910-917.

Background

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

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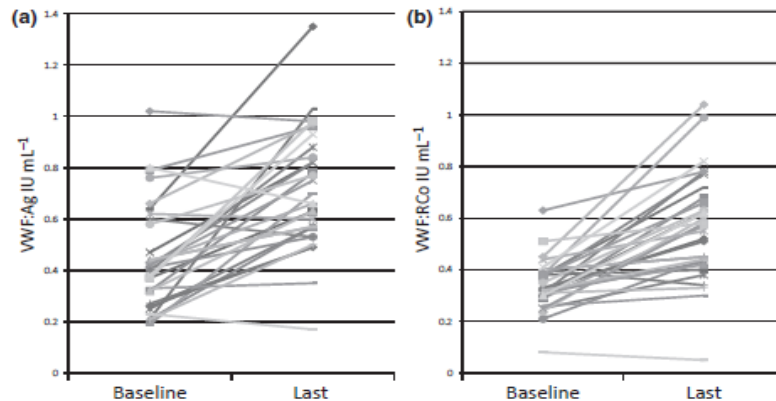
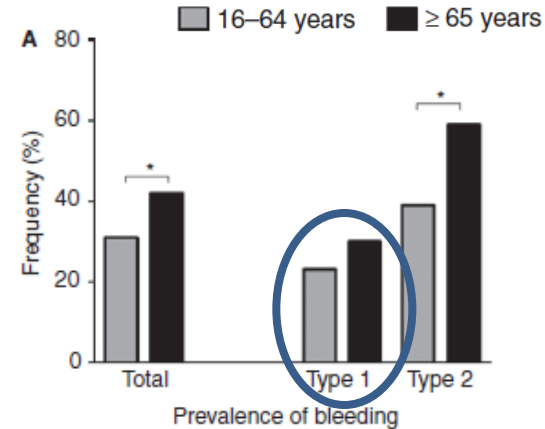
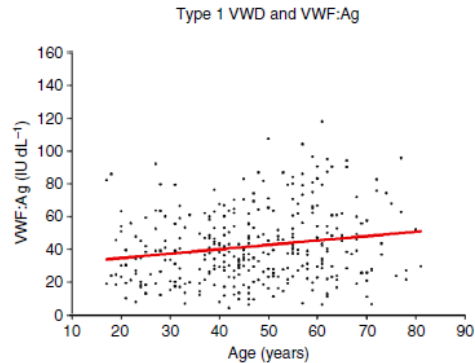


Fig. 1. Baseline and Last VWF:AG, VWF:RCo and FVIII for each patient.

Background

von Willebrand disease and aging: an evolving phenotype

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GROUP¹



Aims

- **Primary Aim:**

- Determine if age at diagnosis of type I von Willebrand disease correlates with VWF:Ag and VWF:RCo levels at diagnosis.

Aims

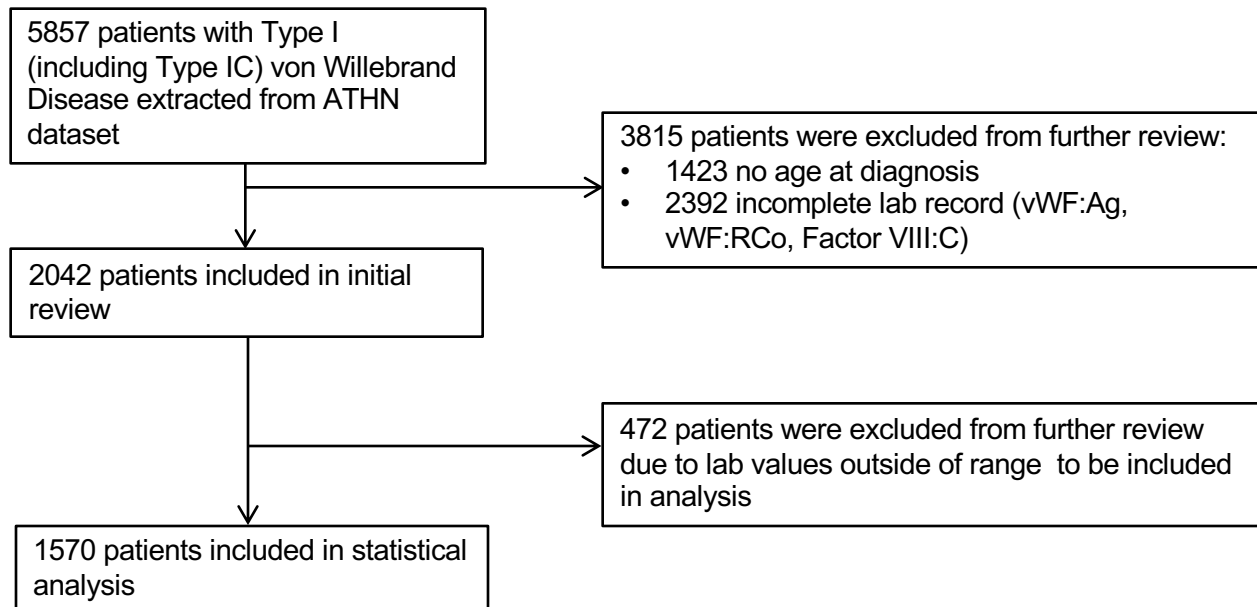
- **Secondary Aims:**

- Determine if there is a difference in reason for testing (i.e. bleeding symptoms vs family history) between age strata
- Number of patients that would be reclassified as low von Willebrand Factor according to the NHLBI 2008 guidelines titled “*The Diagnosis, Evaluation and Management of von Willebrand Disease*”

Methods

- **Inclusion Criteria**
 - Diagnosis (Type I vWD)
 - Sex
 - Age at diagnosis
 - Diagnostic Lab Values
 - vWF: Ag
 - vWF:RCo
 - Factor VIII:C

Inclusion/Exclusion Flow Diagram

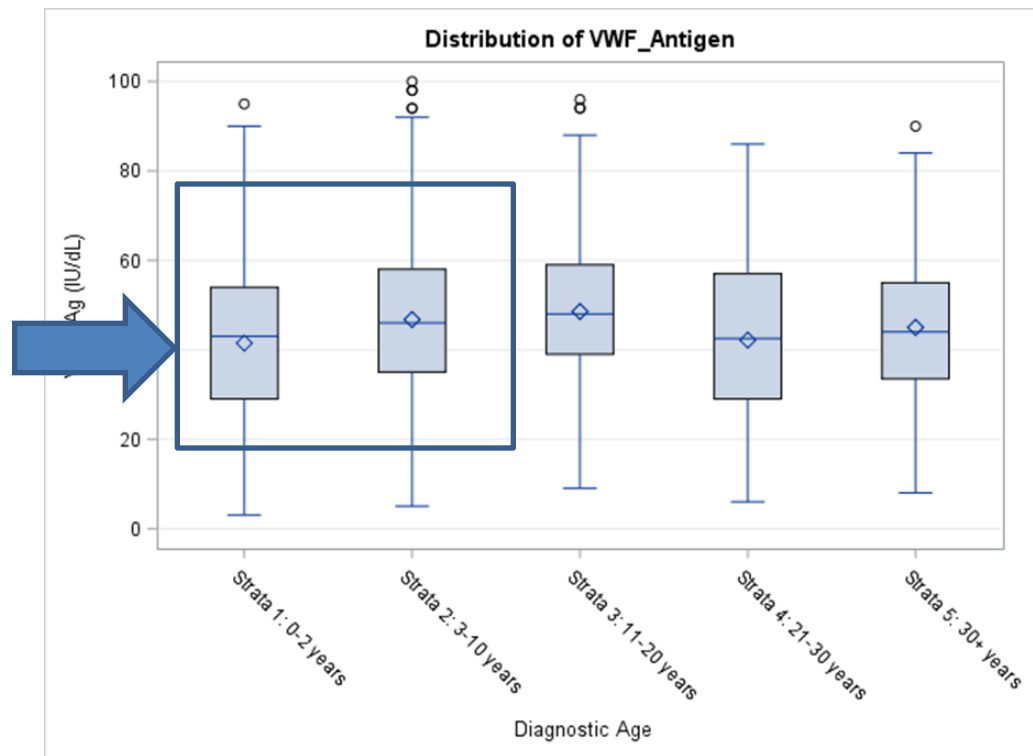


Results

- An ANOVA (Analysis of variance) was completed to determine if there is a statistically significant difference between the mean vWF:Ag and vWF:RCo across the diagnosis age strata
- The null hypothesis that the mean vWF:Ag levels were homogenous across diagnosis age strata was rejected ($p < 0.001$)
- The null hypothesis that the mean vWF:RCo levels were homogenous across diagnosis age strata was rejected ($P = 0.001$)
- A post-hoc analysis was then performed comparing all possible pairs of means to determine if there is a statistically significant difference in mean vWF:Ag and vWF:RCo between strata

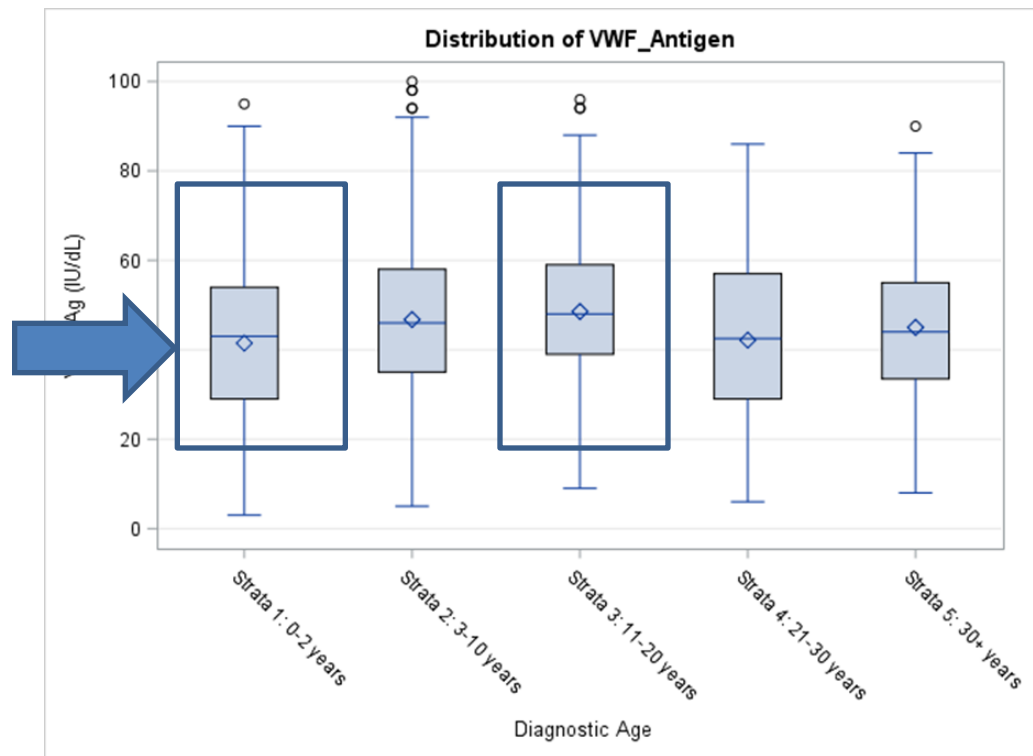
Results

Mean Difference=
5.3 (CI 2.0-8.6)



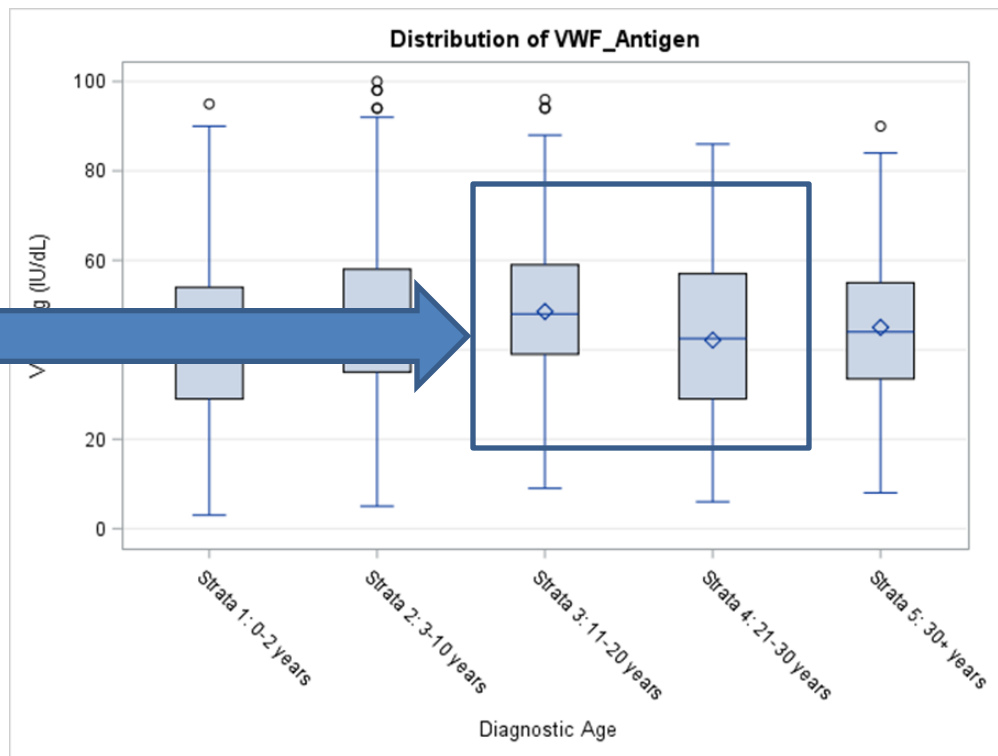
Results

Mean Difference=
7.1 (CI 3.6-10.5)



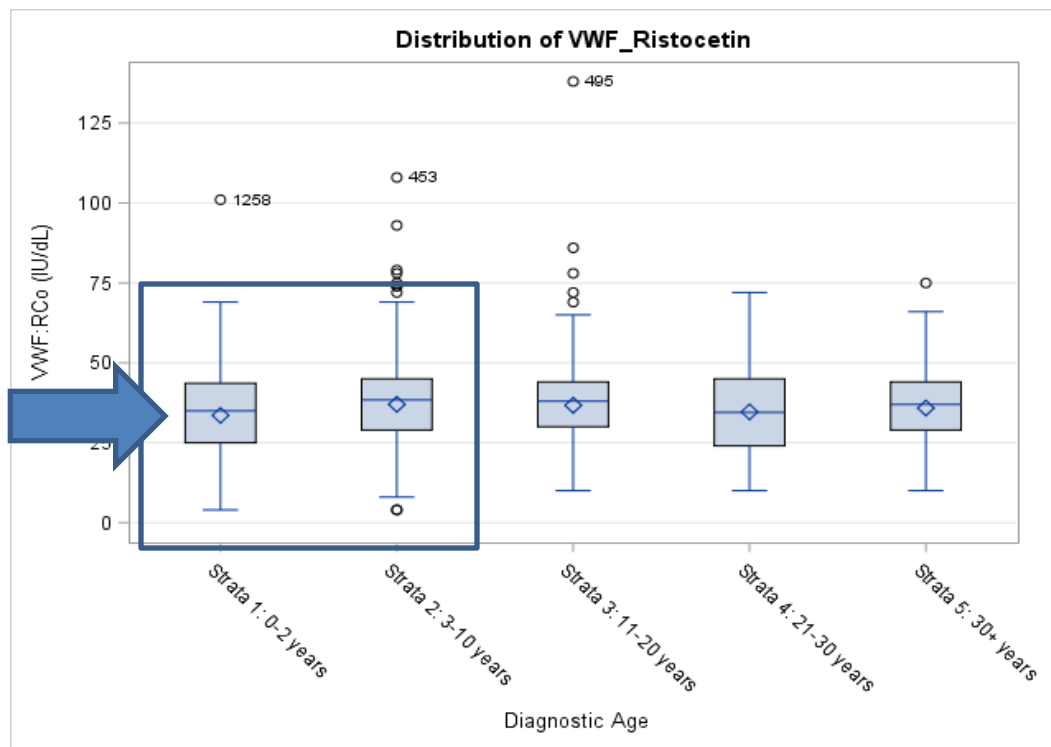
Results

Mean Difference=
5.4 (CI 1.0-11.8)



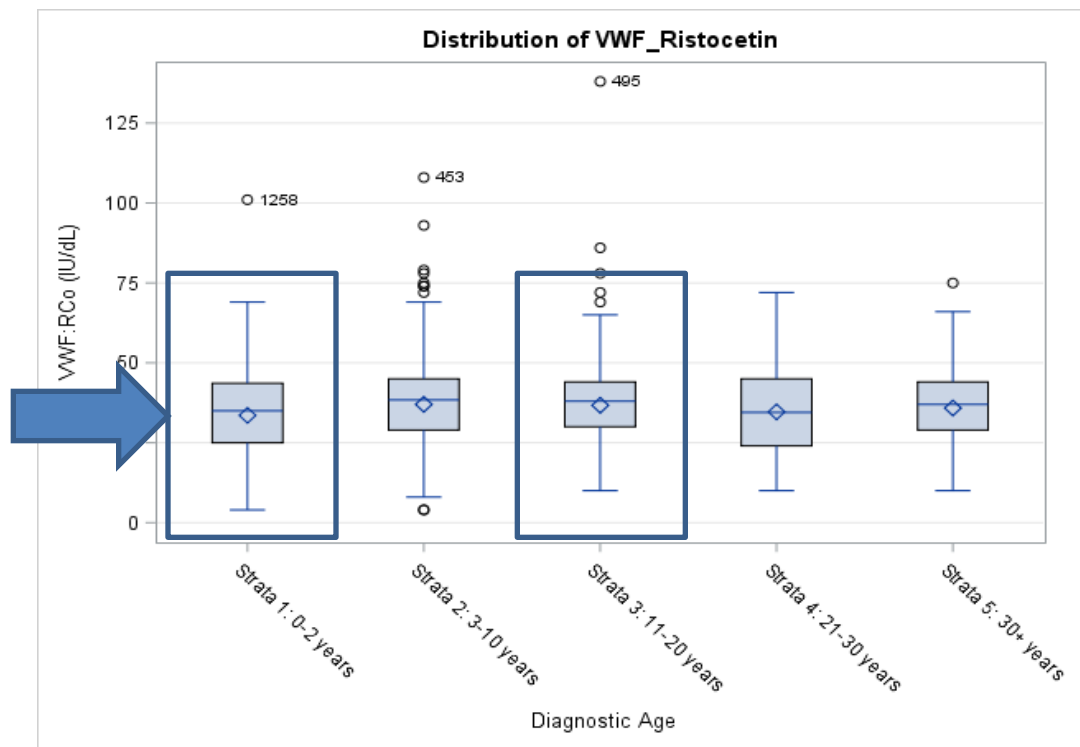
Results

Mean Difference=
3.4 (CI 1.1-5.8)



Results

Mean Difference=
3.1 (CI 0.7-5.6)



Results

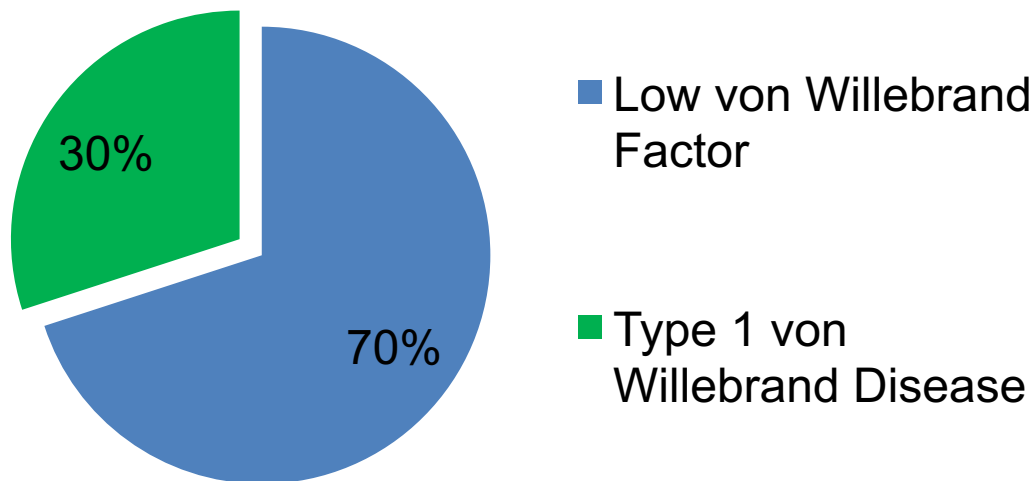
Table 1: Association between testing reason and age at diagnosis

Testing Reason	Strata 1 (0-2 years)	Strata 2 (3-10 years)	Strata 3 (11-20 years)	Strata 4 (21-30 years)	Strata 5 (30+ years)	Total
Bleeding Symptom	33 (10.8%)	117 (20.2%)	152 (33%)	13 (14.4%)	14 (10.6%)	329 (21.0%)
Family History	49 (16.0%)	62 (10.7%)	29 (6.3%)	5 (5.6%)	13 (9.9%)	158 (10.1%)
Lab Screening	2 (0.7%)	9 (1.6%)	3 (0.7%)	1 (1.1%)	2 (1.5%)	17 (1.1%)
Other	4 (1.3%)	7 (1.2%)	5 (1.1%)	1 (1.1%)	1 (0.8%)	18 (1.1%)
Unknown	219 (71.3%)	385 (66.4%)	272 (59.0%)	70 (77.8%)	102 (77.3%)	1048 (66.8%)
Total	307	580	461	90	132	1570

Chi-Squared Test: $p < 0.001$

Results

Diagnostic Classification of Patients According to the 2008 NHLBI Guidelines



Limitations

- **Core Data Elements**

- Required data fields are minimal
- Elements may have more than 1 way of entering the data

- **Discrepancy of Data Entered**

- Several patients had diagnostic lab values entered that were not reflective of their diagnosis of Type I von Willebrand Disease

Future Research

- Should age at diagnosis be considered in the diagnosis of Type I vWD?
 - Will need large prospective study evaluating vWF:Ag and vWF:RCo levels as patients increase in age (include pediatric patients)

Future Research

- Does puberty correlate with increased levels of vWF:Ag and vWF:RCo?

