

Results of ECAT EQA programme on DOACs

Martine van Essen-Hollestelle and Piet Meijer
ECAT Foundation
The Netherlands

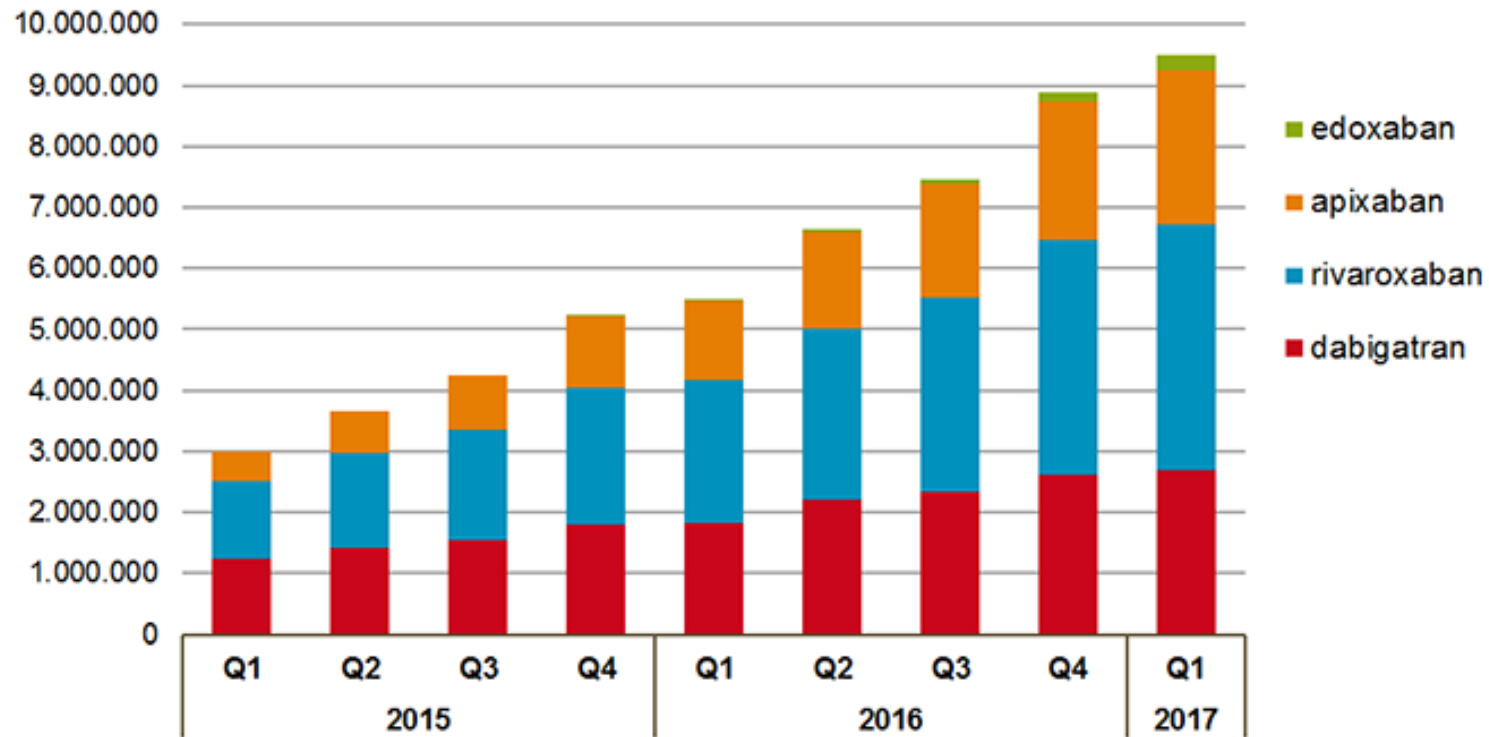


Outline presentation

- **General overview**
- **EQA for Rivaroxaban and Apixaban (2013-2017)**
- **EQA for Dabigatran and Argatroban (2013-2017)**
- **Edoxaban pilot study (2018)**
- **Conclusion**



Increase in number defined daily doses for DOACs in the Netherlands

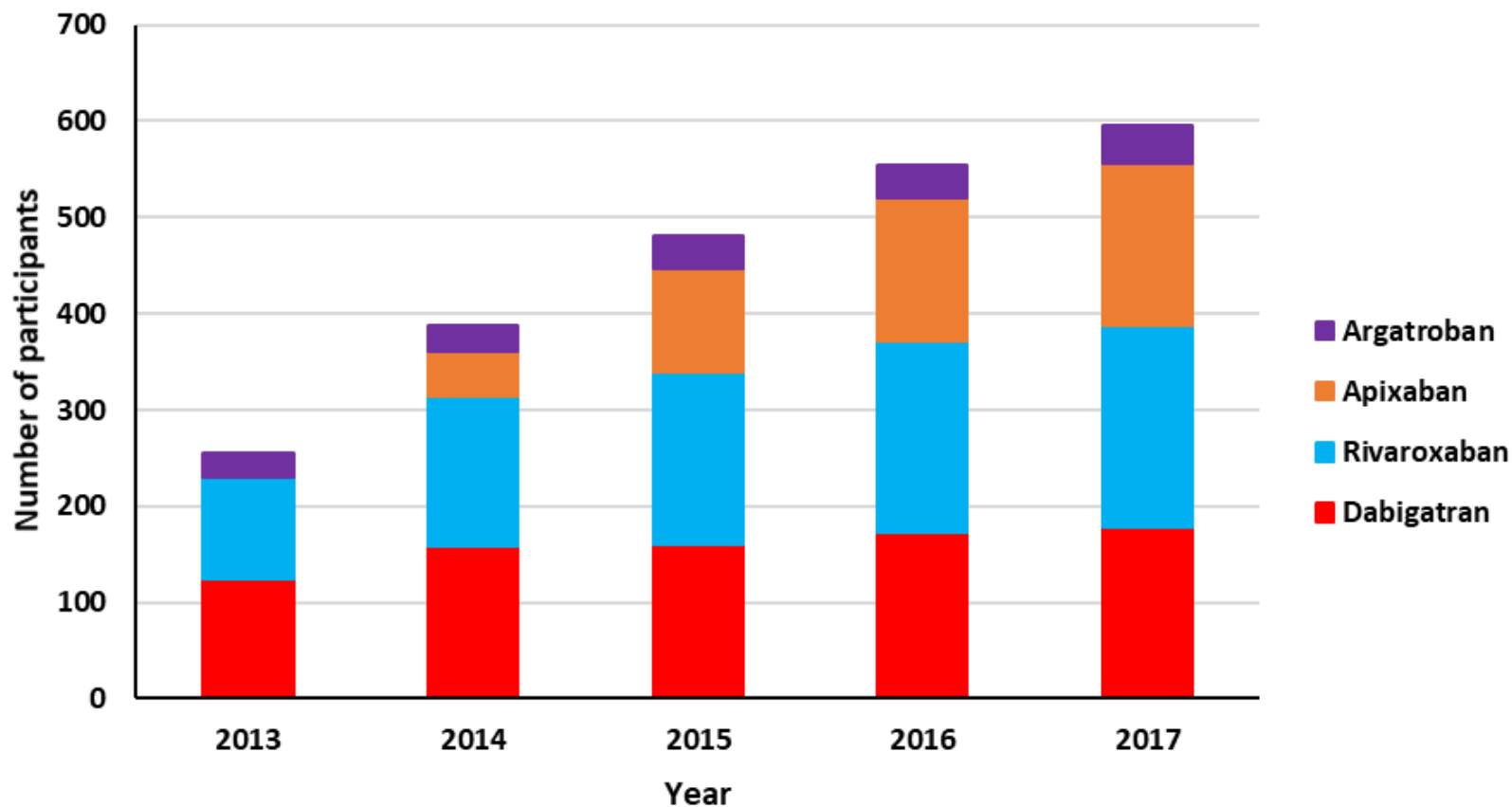


- The Dutch pharmacy delivered 75% more DOACs in 2016 compared to 2015
- Rivaxoban use was the highest



Reference: Foundation Farmaceutische Kengetallen

Overview number of participants in the DOAC programme from 2013-2017



- Increasing interest in EQC of specific DOAC tests
- Since 2018 pilot for EQC of Edoxaban



Important issues when measuring DOACs (1)

- **Peak level between 1-4 h -> important to know time between sampling and DOAC intake**
- **Half life 5-17 h**
- **Function of liver and kidney important**
- **Dabigatran predominantly (80%) degraded via kidney**
- **Rivaroxaban and apixaban largely metabolised via the liver (respectively, 65 & 73%)**

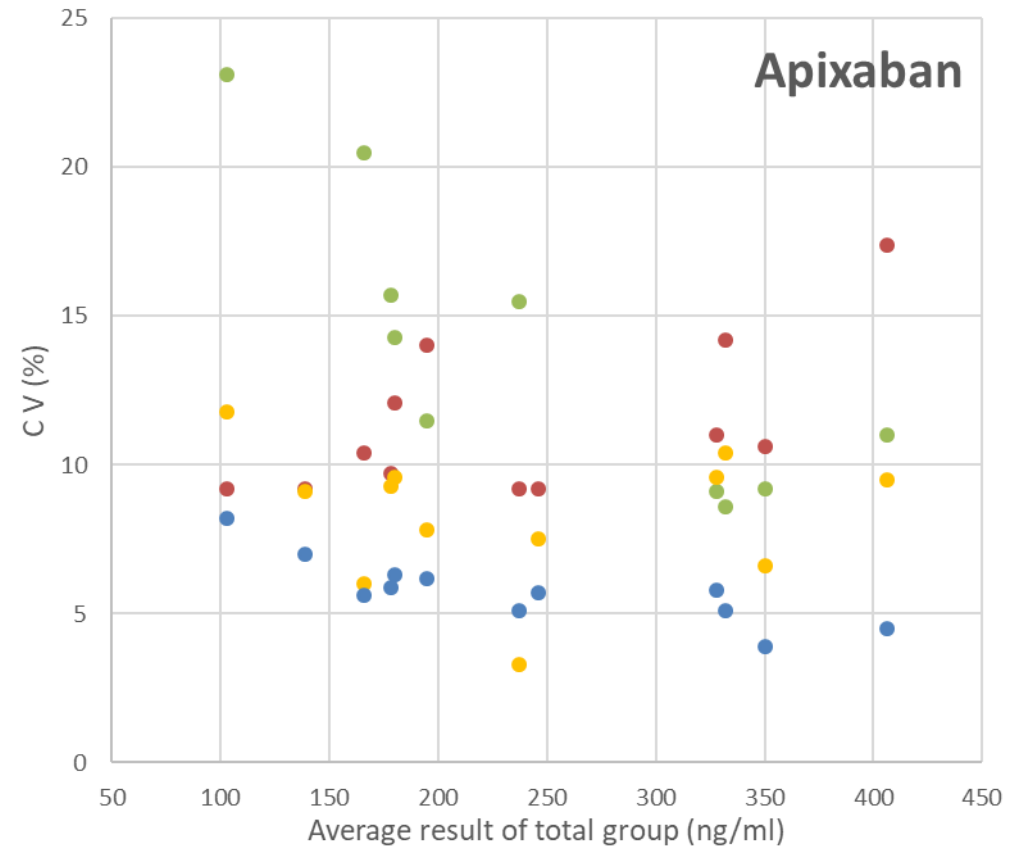
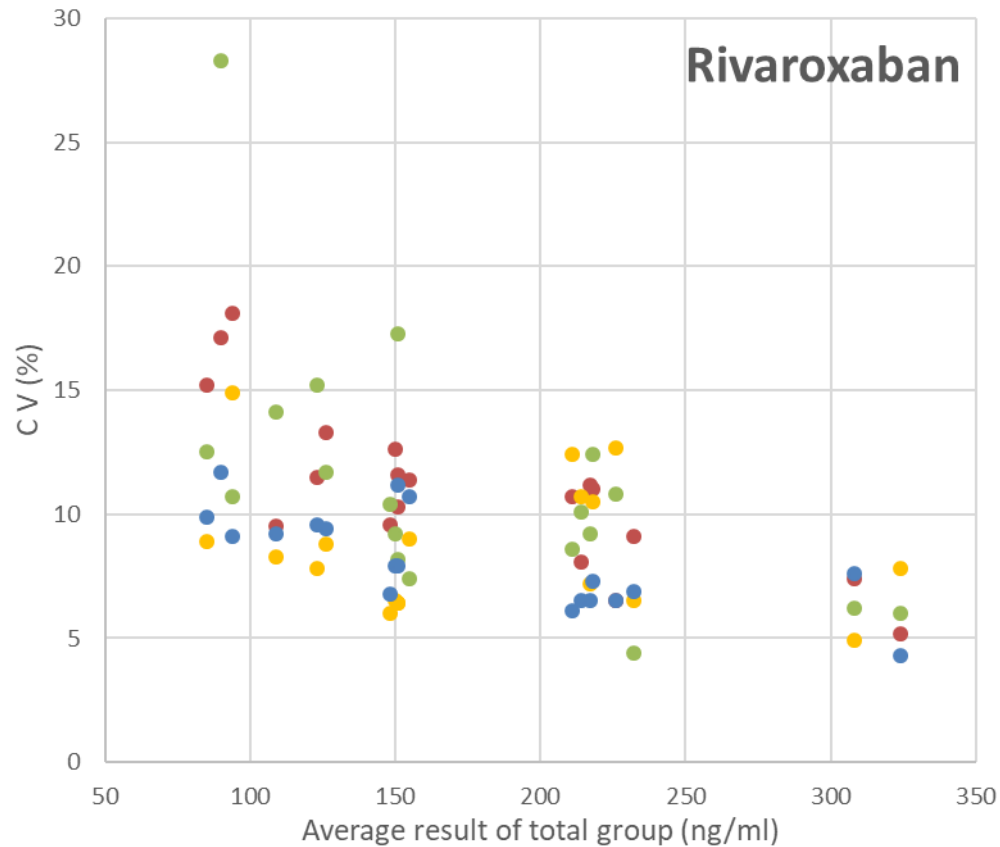


Important issues when measuring DOACs (2)

- **Guidance from the SSC of the ISTH:**
 - **Patients with serious bleeding: antidote administration considered if DOAC concentration > 50 ng/mL**
 - **Patient requiring urgent intervention with high bleeding risk: antidote administration considered if DOAC concentration > 30 ng/mL**



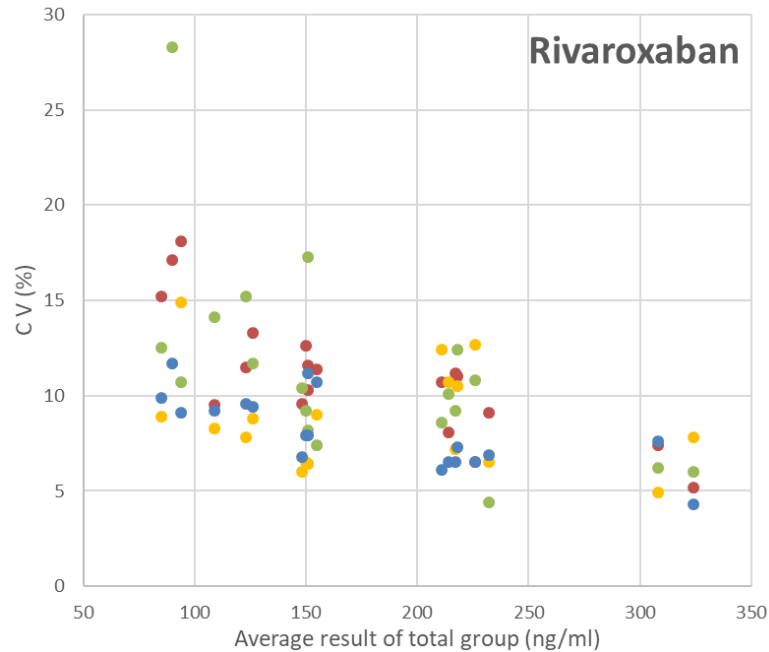
Between laboratory variation per assay



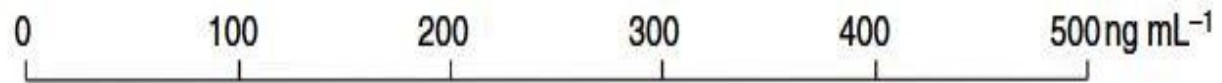
- Hyphen Biomed Biophen (LRT&Heparin)
- Hyphen Biomed DiXa
- IL HemosIL Liquid anti-Xa
- Stago Liquid anti-Xa



Peak and trough levels compared to imprecision results



- Hyphen Biomed Biophen (LRT&Heparin)
- Hyphen Biomed DiXa
- IL HemosIL Liquid anti-Xa
- Stago Liquid anti-Xa



RIVAROXABAN 20 mg OD

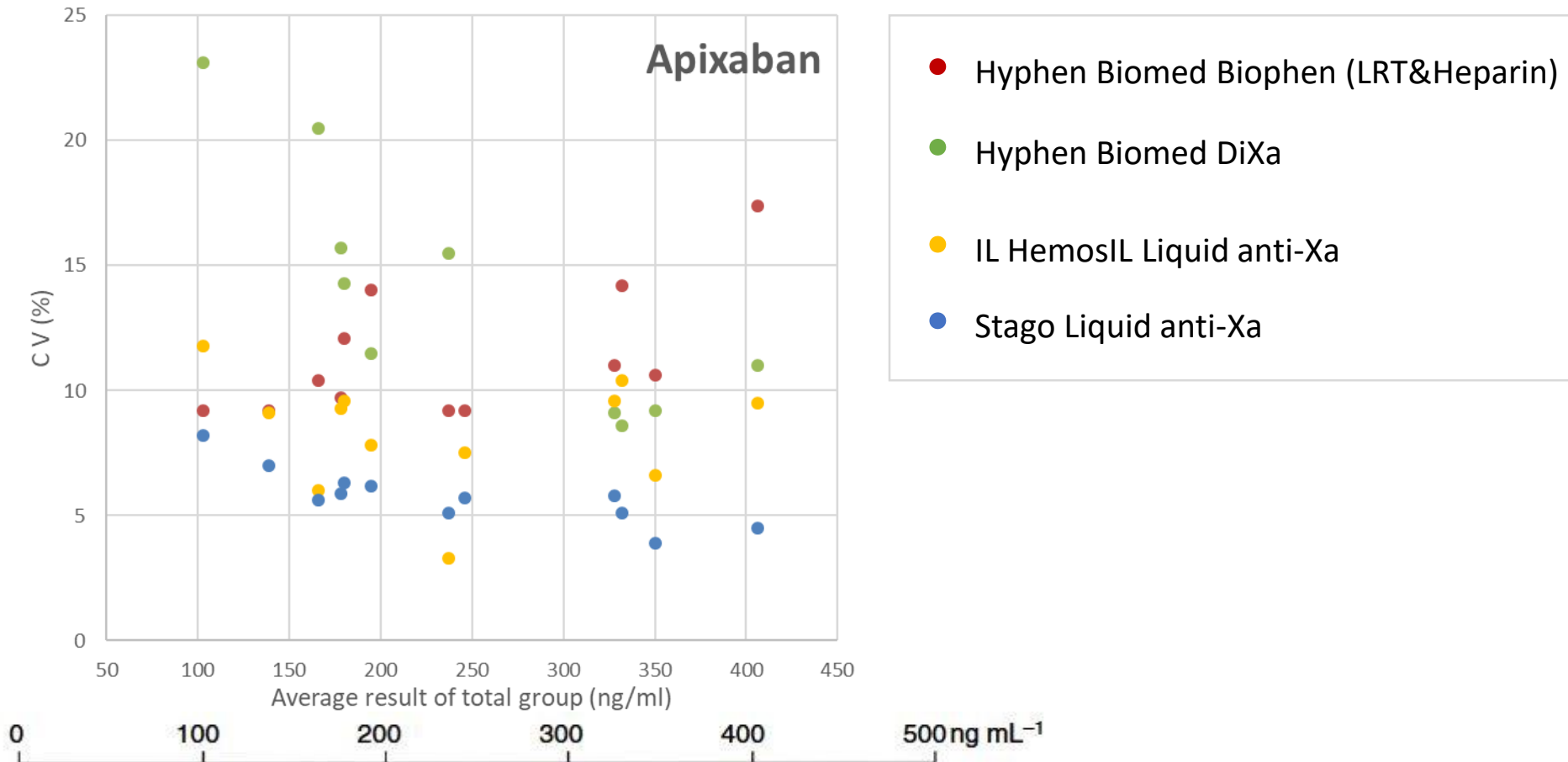


NVAf C_{TROUGH} : 44 (12 – 137 ng mL⁻¹) – mean (5th – 95th percentile)
 NVAf C_{MAX} : 249 (184 – 343 ng mL⁻¹) – mean (5th – 95th percentile)
 VTE C_{TROUGH} : 26 (6 – 87 ng mL⁻¹) – mean (5th – 95th percentile)
 VTE C_{MAX} : 270 (189 – 419 ng mL⁻¹) – mean (5th – 95th percentile)

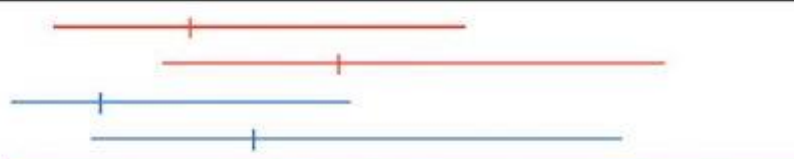
Calibrated chromogenic anti-Xa assays



Peak and trough levels compared to imprecision results



APIXABAN 5 mg BID

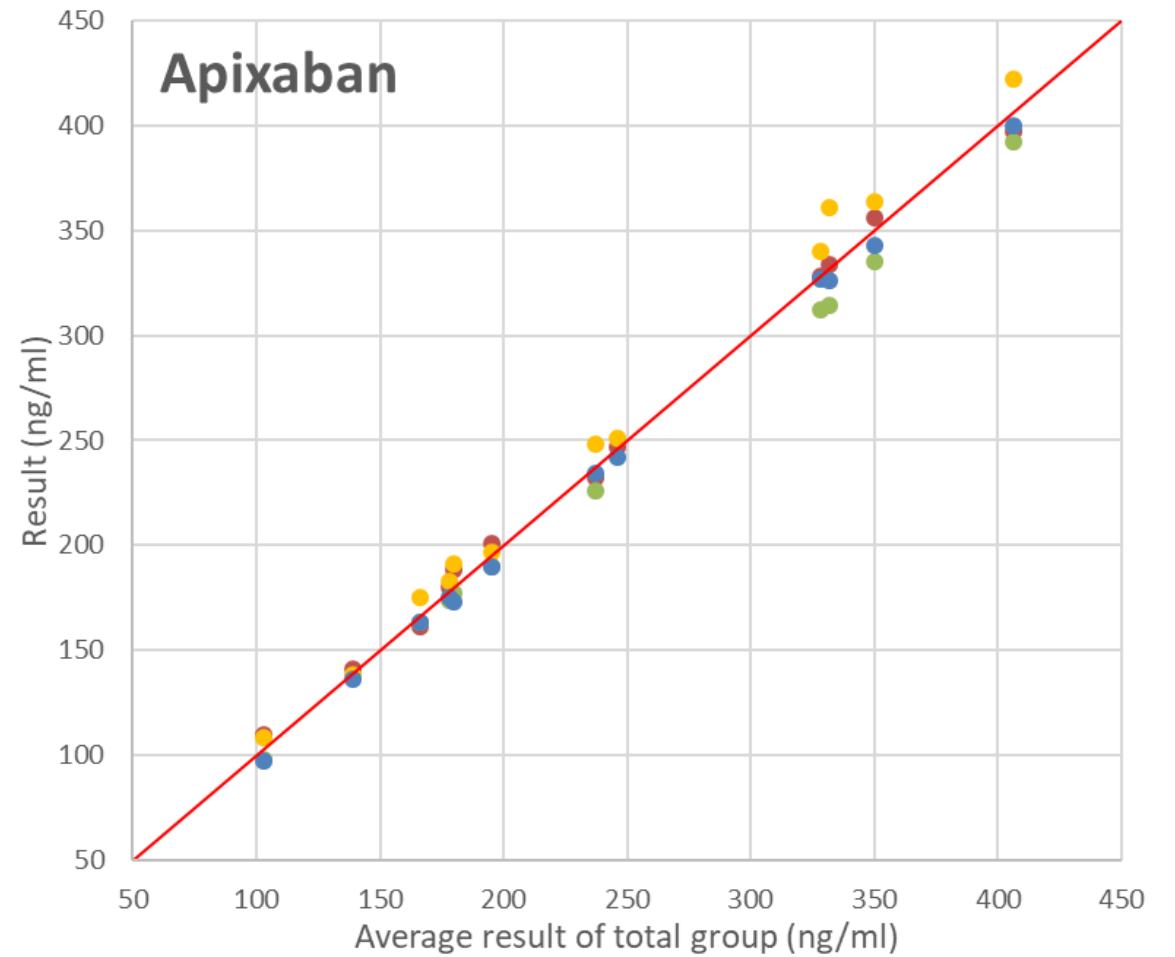
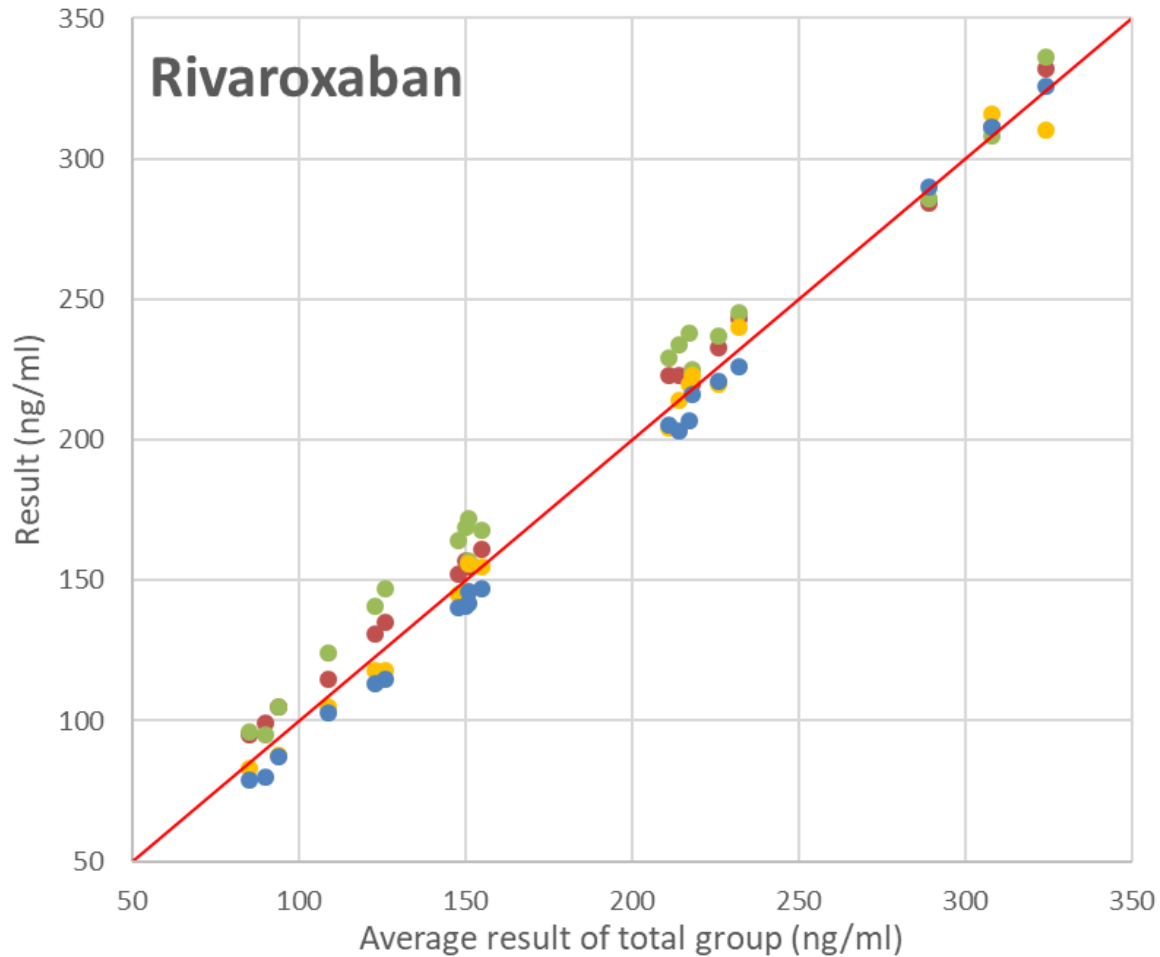


NVAF C_{TROUGH} : 103 (41 – 230 ng mL⁻¹) – median (5th – 95th percentile)
 NVAF C_{MAX} : 171 (91 – 321 ng mL⁻¹) – median (5th – 95th percentile)
 VTE C_{TROUGH} : 63 (22 – 177 ng mL⁻¹) – median (5th – 95th percentile)
 VTE C_{MAX} : 132 (59 – 302 ng mL⁻¹) – median (5th – 95th percentile)

Calibrated chromogenic anti-Xa assays



Overall results of Rivaroxaban and Apixaban

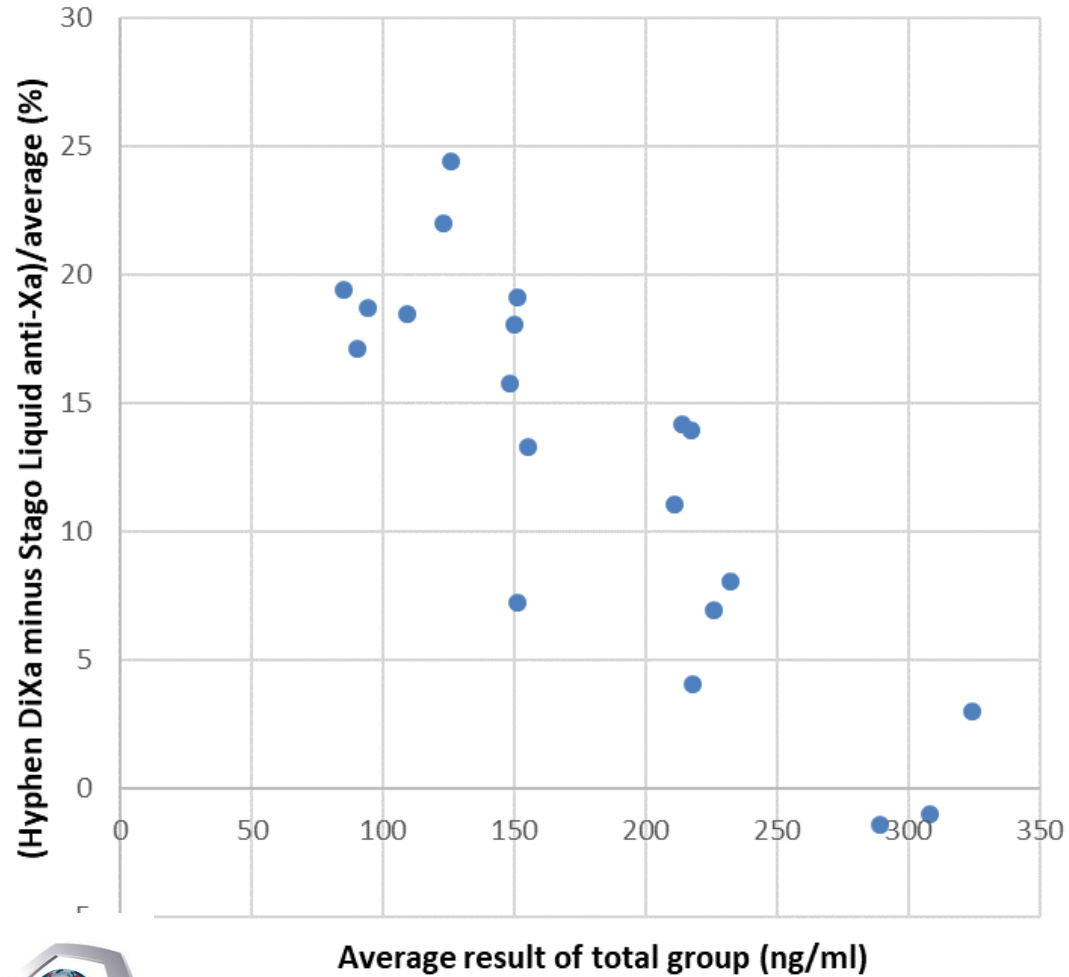


- Hyphen Biomed Biophen (LRT&Heparin)
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- Stago Liquid anti-Xa



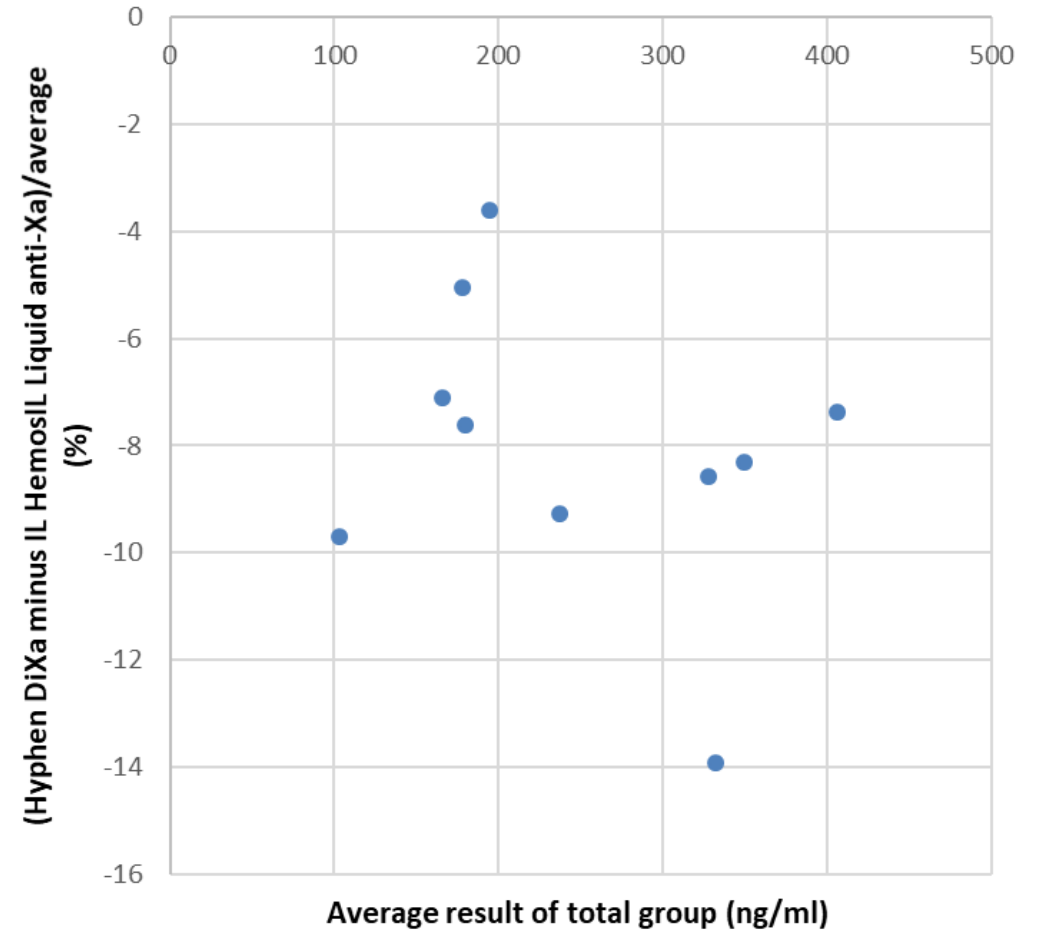
Rivaroxaban

Comparing Hyphen vs Stago



Apixaban

Comparing Hyphen vs IL

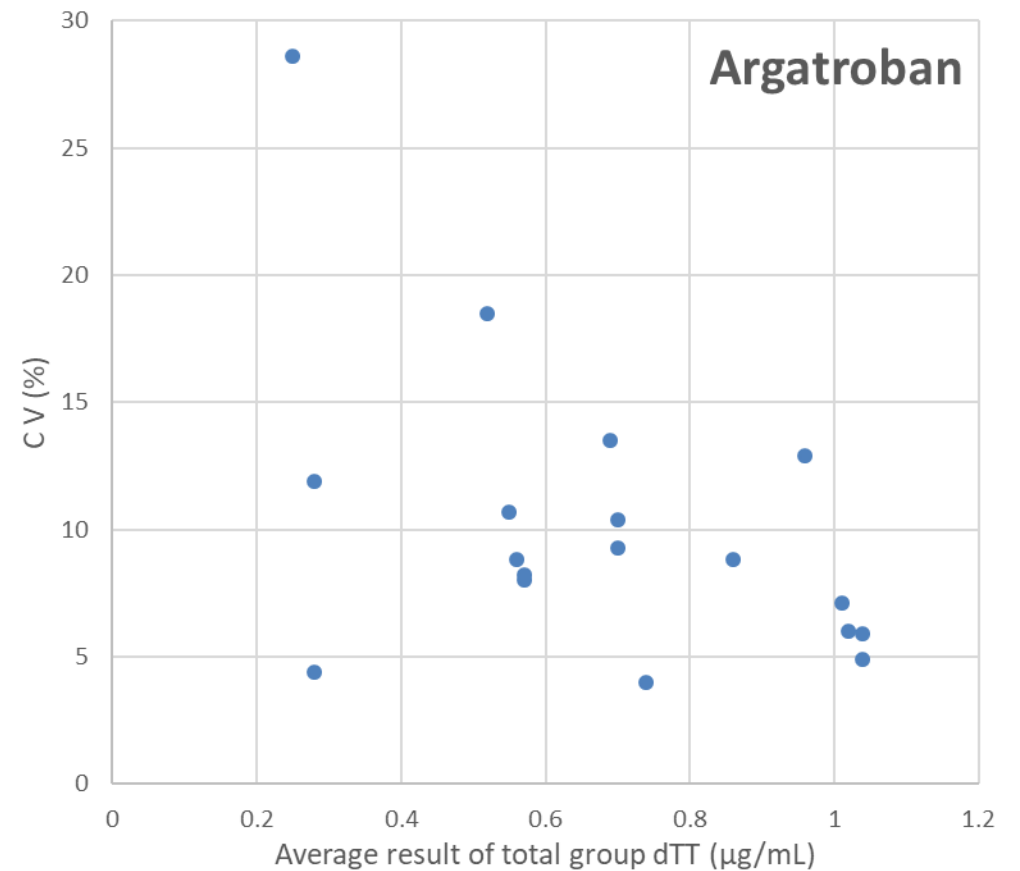
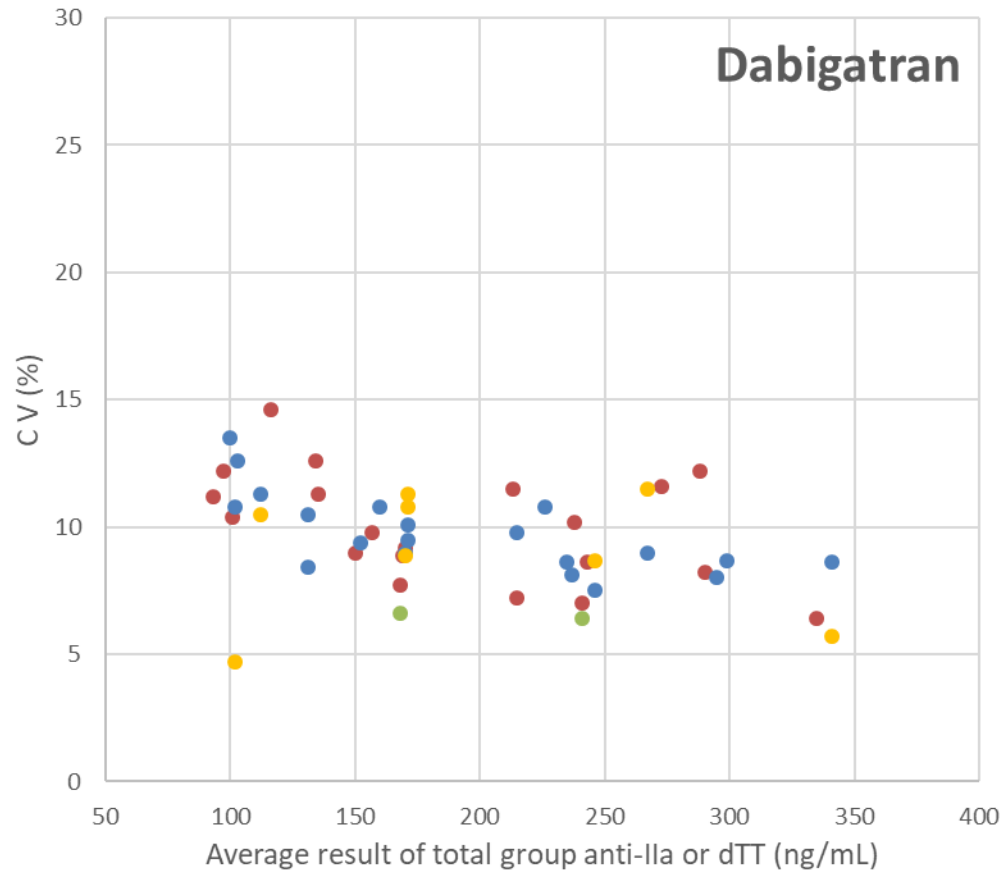


Summary Rivaroxaban and Apixaban

- **No significant difference in imprecision for rivaroxaban methods**
- **Significant difference in imprecision between methods for apixaban measurements**
- **No large difference between absolute values for apixaban**
- **Up to 20% difference between the absolute measured values for rivaroxaban**
- **Important to know specifications of the method for interpretation of the results**



Between laboratory variation per assay



Anti-IIa assays:

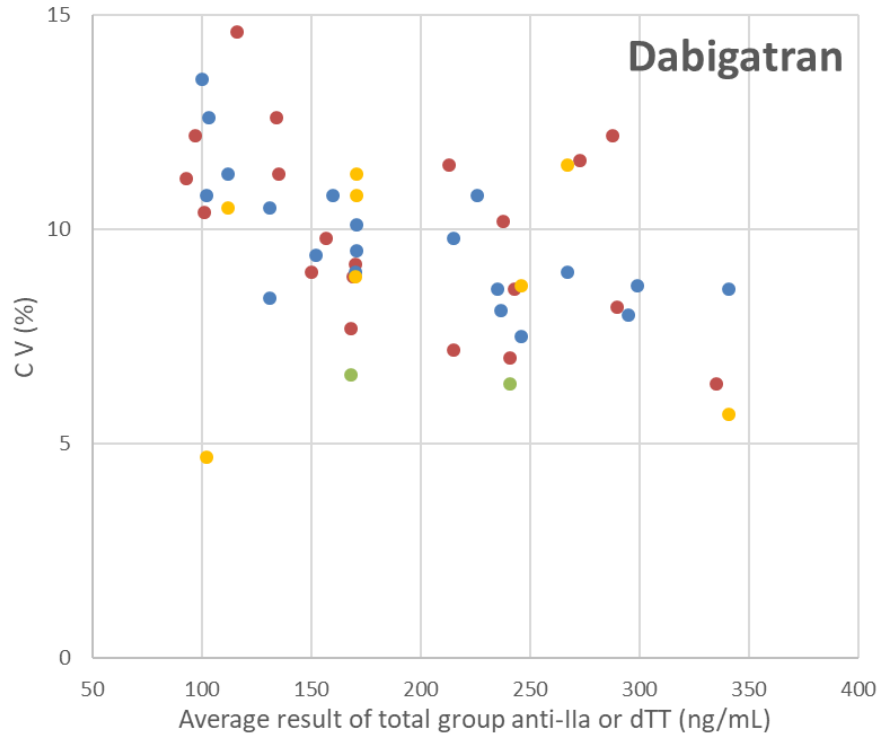
- Hyphen Biomed DTI
- Siemens Innovance DTI

dTT assays:

- IL HemosIL DTI
- Hyphen Hemaclot DTI



Peak and trough levels compared to imprecision results



Anti-IIa assays:

- Hyphen Biomed DTI
- Siemens Innovance DTI

dTT assays:

- IL HemosIL DTI
- Hyphen Hemaclot DTI

0 100 200 300 400 500 ng mL⁻¹

DABIGATRAN 150 mg BID

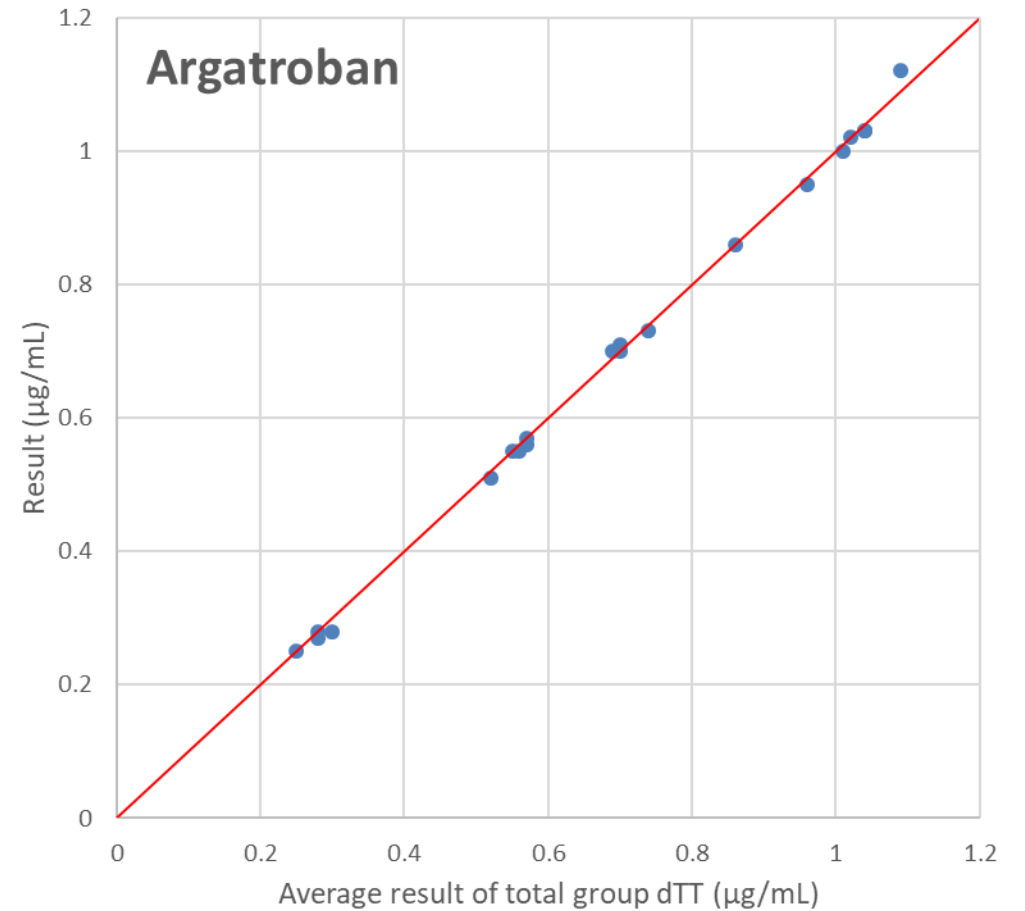
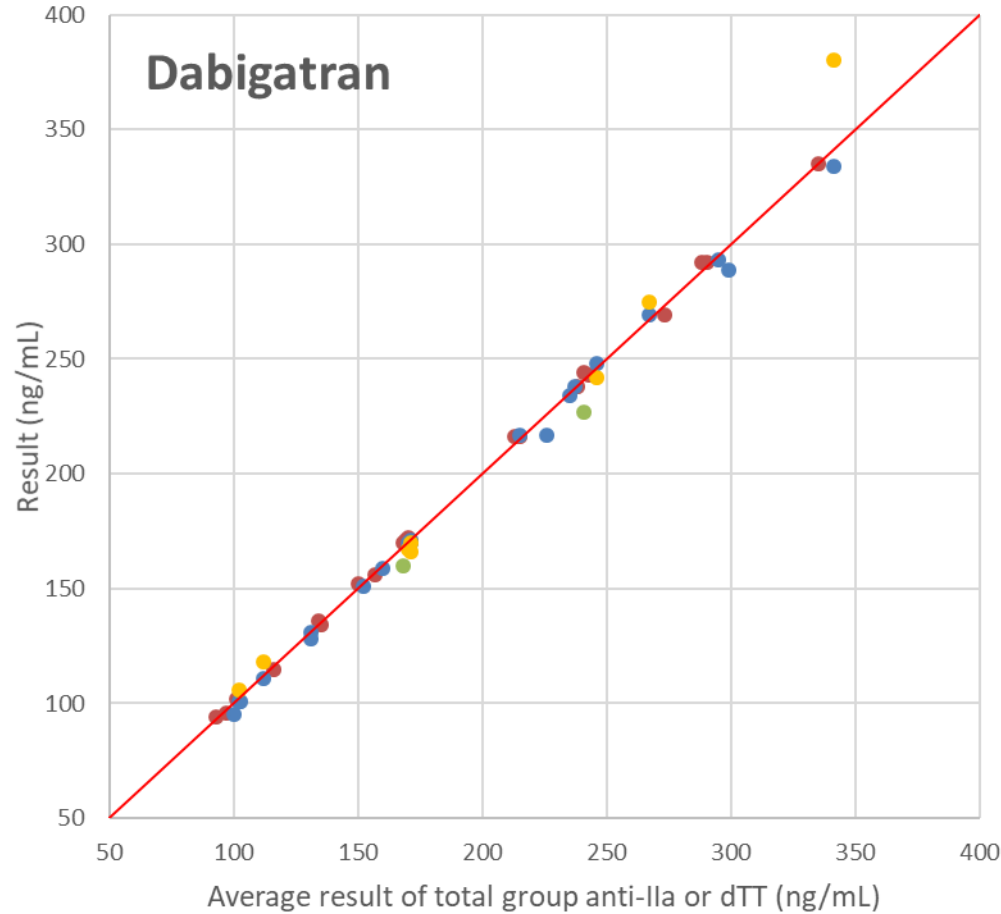


NVAF C_{TROUGH} : 91 (61 – 143 ng mL⁻¹) – mean (25th – 75th percentile)
 NVAF C_{MAX} : 175 (117 – 275 ng mL⁻¹) – mean (25th – 75th percentile)
 VTE C_{TROUGH} : 60 (39 – 95 ng mL⁻¹) – mean (25th – 75th percentile)
 VTE C_{MAX} : 175 (117 – 275 ng mL⁻¹) – mean (25th – 75th percentile)

dTT[†] - ECA



Overall results of Dabigatran and Argatroban



Anti-IIa assays:

- Hyphen Biomed DTI
- Siemens Innovance DTI

dTT assays:

- IL HemosIL DTI
- Hyphen Hemaclot DTI

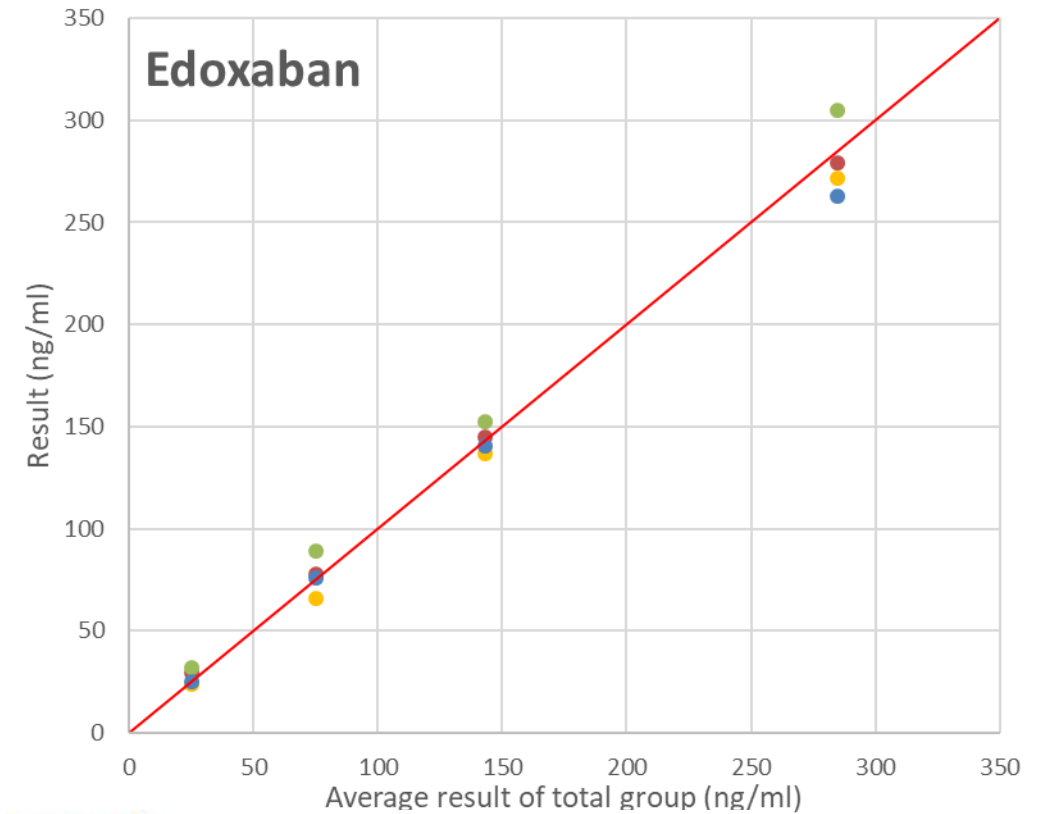
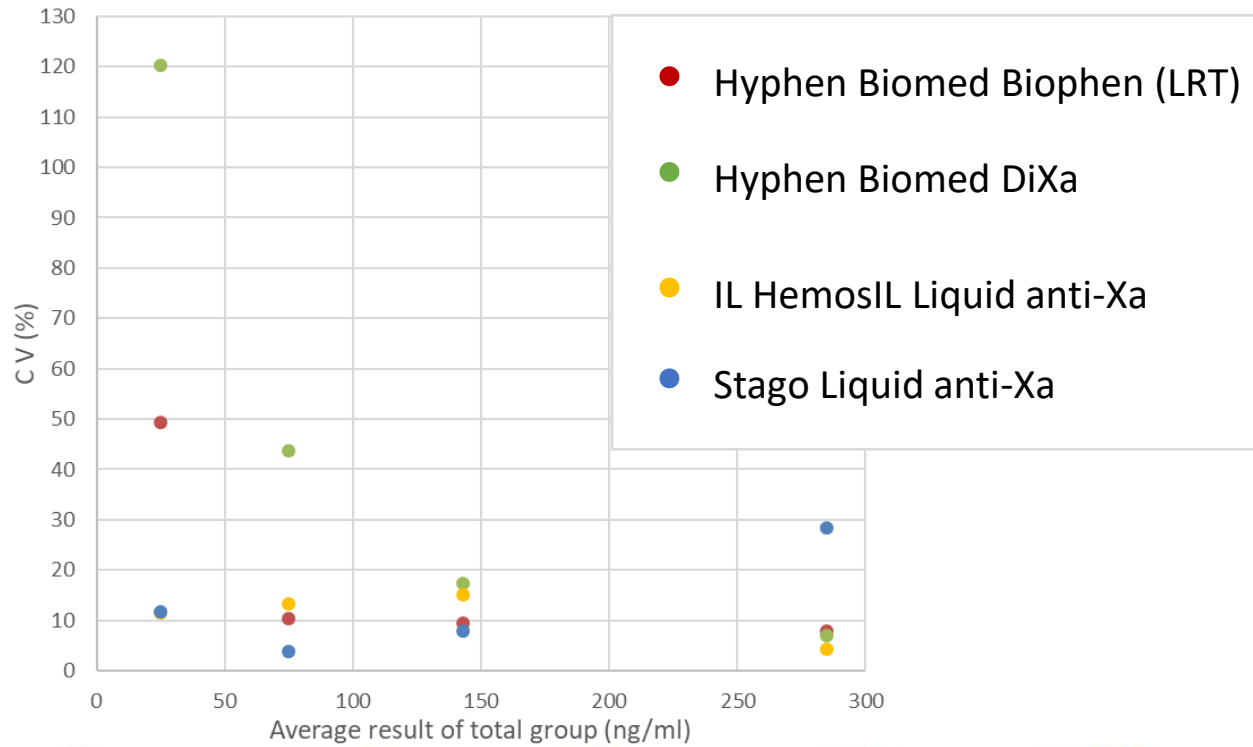


Summary Dabigatran and Argatroban

- **Only one main method group is seen for argatroban measurements**
- **For both dabigatran and argatroban the average imprecision is approximately 10%**
- **No large difference between the methods to measure dabigatran are observed for absolute measured values and imprecision of the assays**

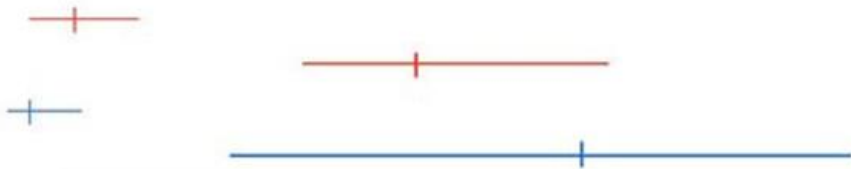


Results of the pilot of Edoxaban



0 100 200 300 400 500 ng mL⁻¹

EDOXABAN 60 mg OD



NVAf C_{TROUGH} : 36 (19 – 62 ng mL⁻¹) – median (IQR)
 NVAf C_{MAX} : 170 (125 – 245 ng mL⁻¹) – median (1.5 × IQR)
 VTE C_{TROUGH} : 19 (10 – 39 ng mL⁻¹) – median (IQR)
 VTE C_{MAX} : 234 (149 – 317 ng mL⁻¹) – median (IQR)

Calibrated chromogenic anti-Xa assays



Take home message

- **Important to know specification of the method for interpretation of the results**
- **Method differences should be taken into account when determining decision limits**
- **Analytical performance below 50 ng/ml are lacking in the EQA programme**

