MASS SPECTROMETRY TARGETED PROTEOMICS

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Epi-Omics Journal Club

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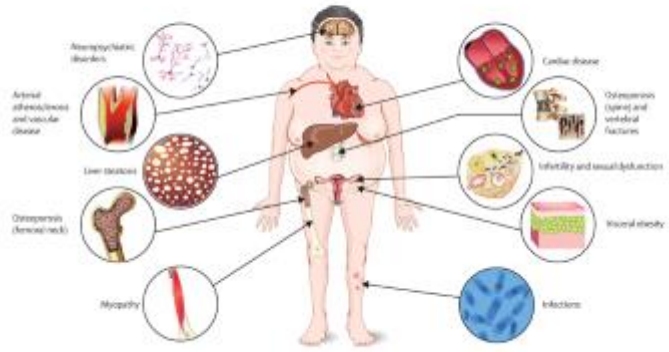
OUTLINE

MASS SPECTROMETRY-BASED TARGETED PROTEOMICS

Relatively novel method to quantitate proteins in plasma

- High level of multiplexation (1-500 proteins)
- Requires only minimal amount of plasma (5µL)

(1) CUSHING DISEASE



Pivonello R. et al. The Lancet. Diabetes & endocrinology 2016

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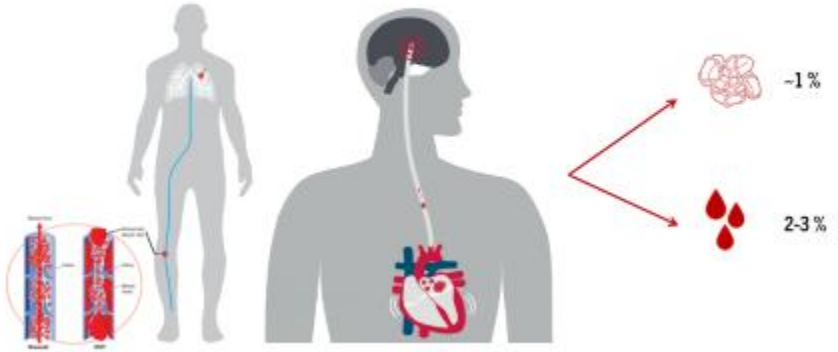
(2) BLEEDING AND THROMBOSIS DURING ANTICOAGULANT TREATMENT

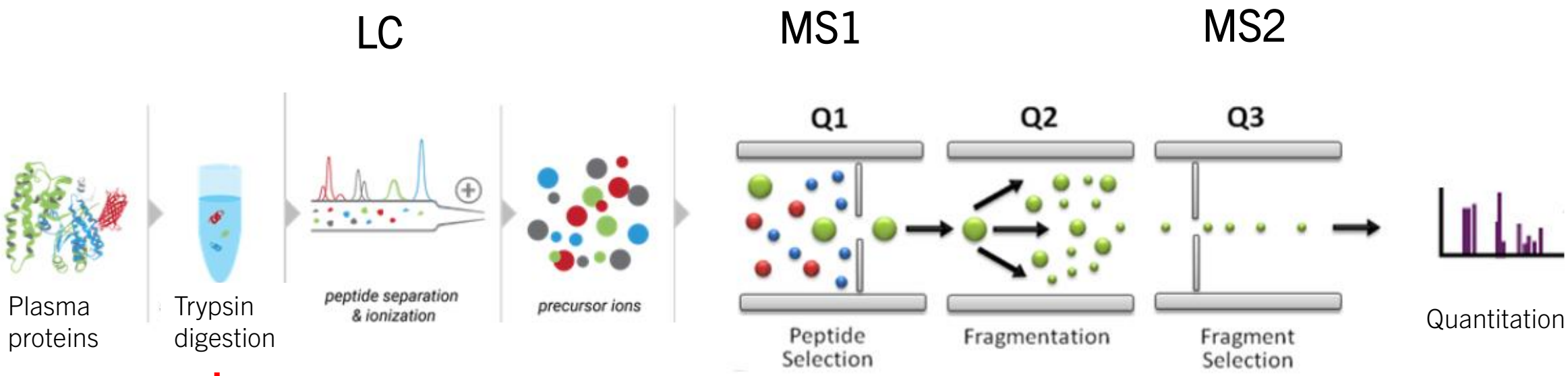


MASS SPECTROMETRY-BASED TARGETED PROTEOMICS

Relatively novel method to quantitate proteins in plasma

- High level of multiplexation (1-500 proteins)
- Requires only minimal amount of plasma (5µL)

HOW DOES IT WORK? (1)



Many proteotypic peptides released like IIPHHNYNAAINK for FIX with m/z = 502.279

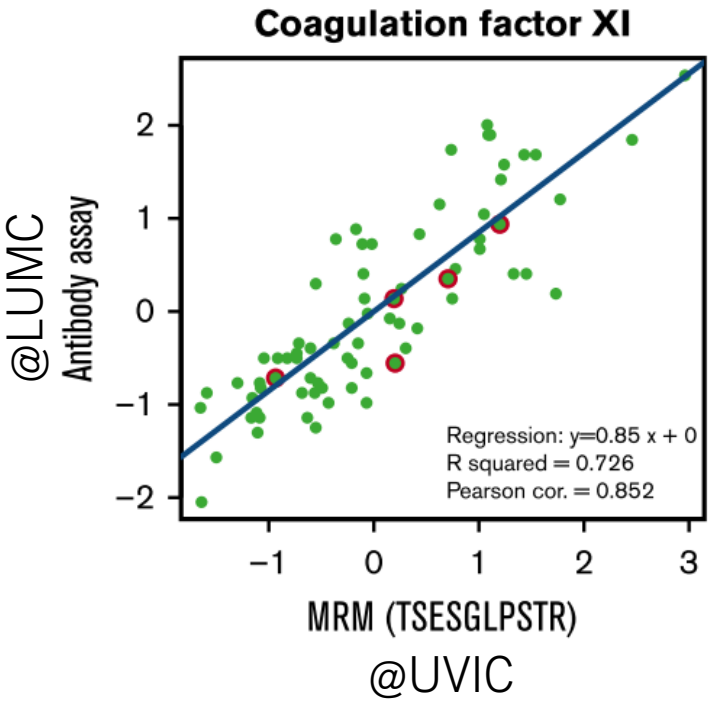
HOW DOES IT WORK? (2)

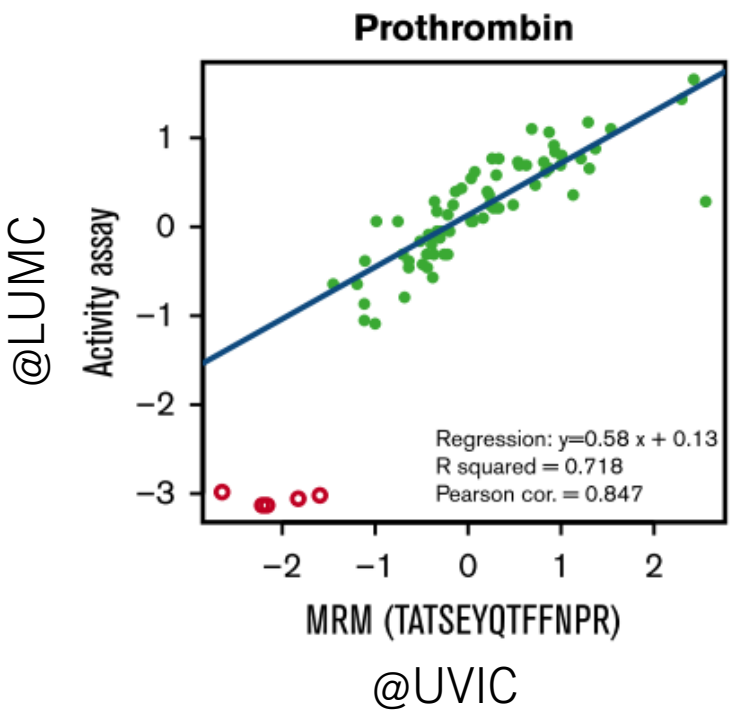
FIX proteotypic peptide
IIPHHNYNAAINK
m/z = 502.279

Example: FIX in plasma

Synthetic IIPHHNYNAAINK-
[13C] m/z = 504.279
spiked in exact amount

MS-QTP in collaboration with Christoph Borchers group at University of Victoria (UViC)

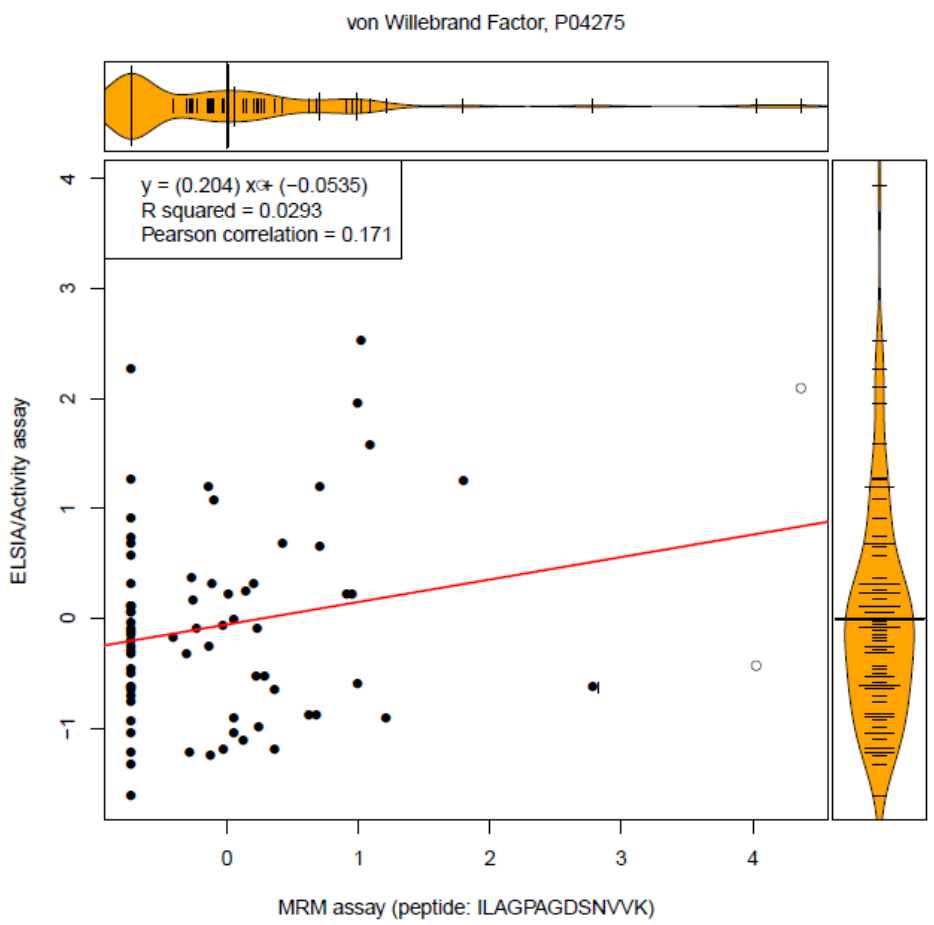




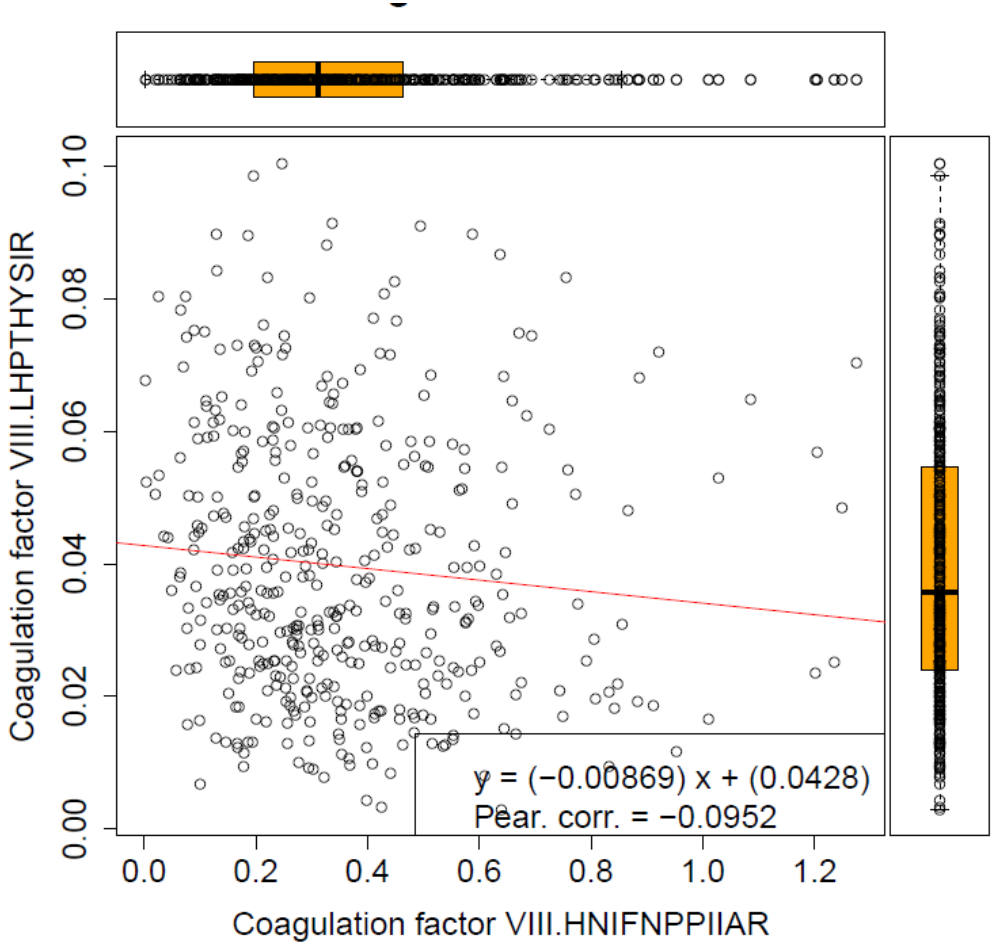
MS-QTP successfully determined plasma levels of
31 coagulation (-related) factors <u>in multiplex in one single run</u>

MS-QTP in collaboration with Christoph Borchers group at University of Victoria (UViC)

vWF

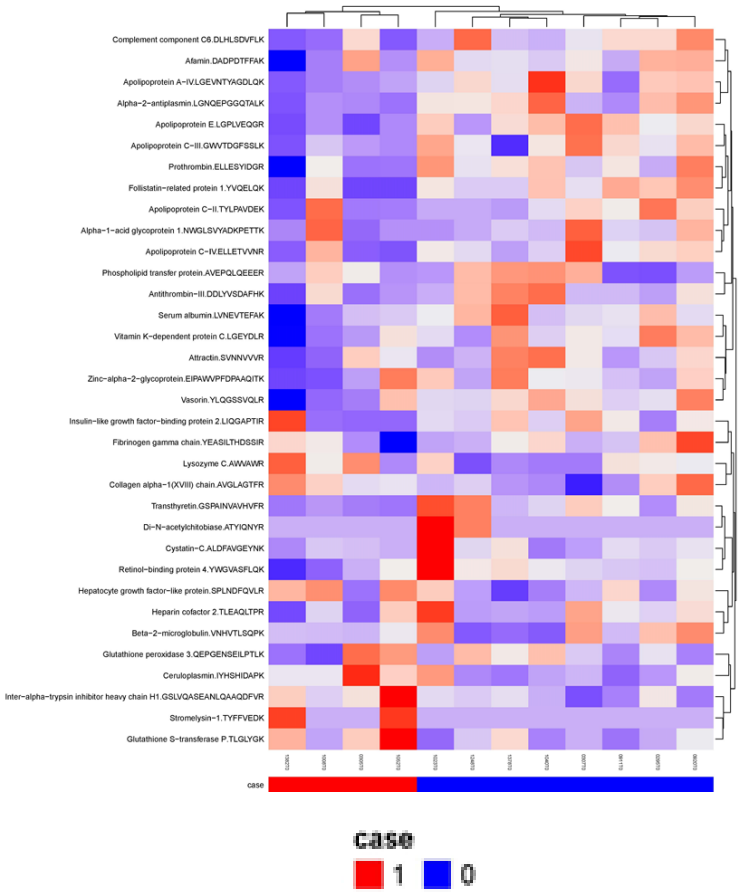


FVIII

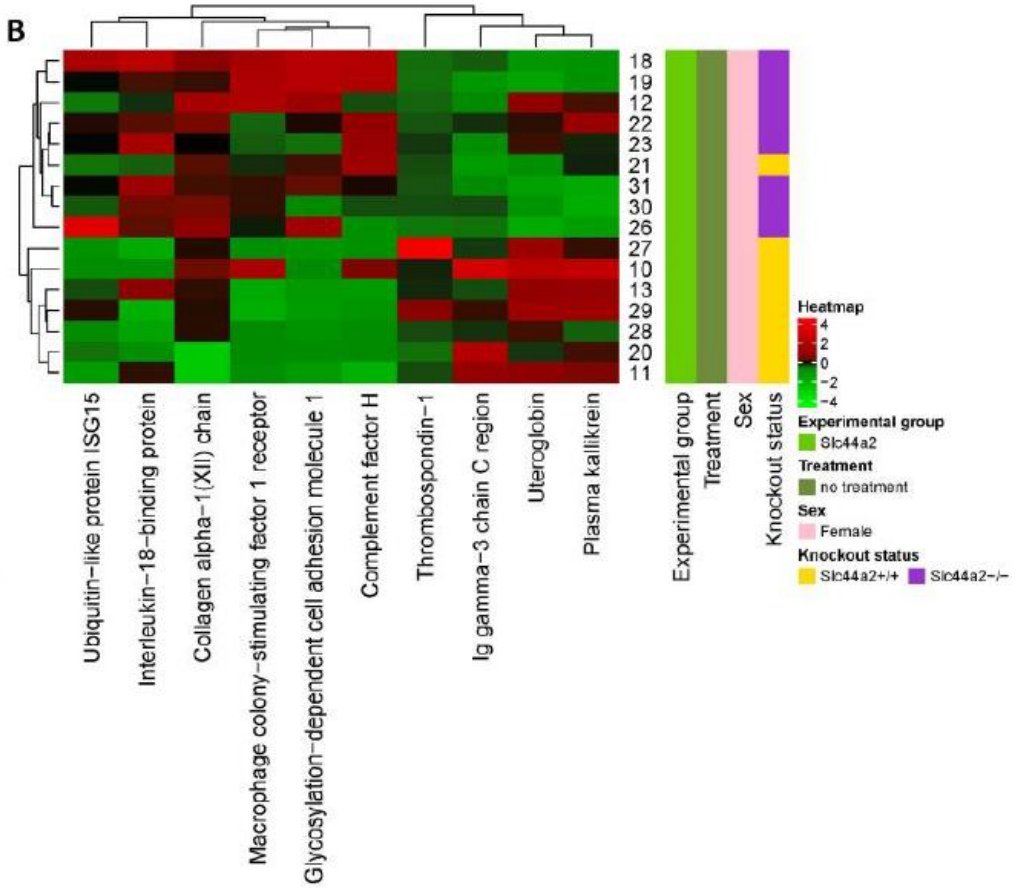


LATEST STUDIES WITH UVIC USING 'DISCOVERY' PANELS

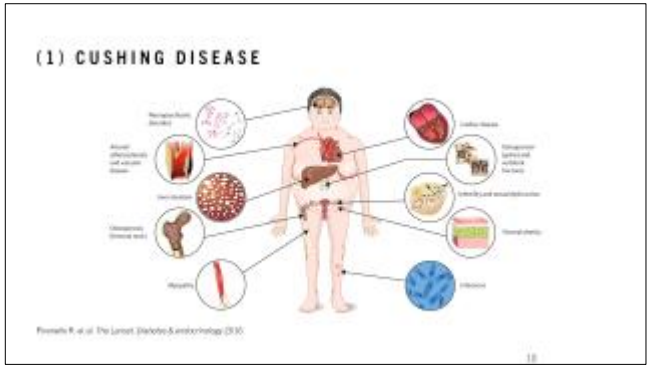
Signature' VTE in POT-(K)CAST



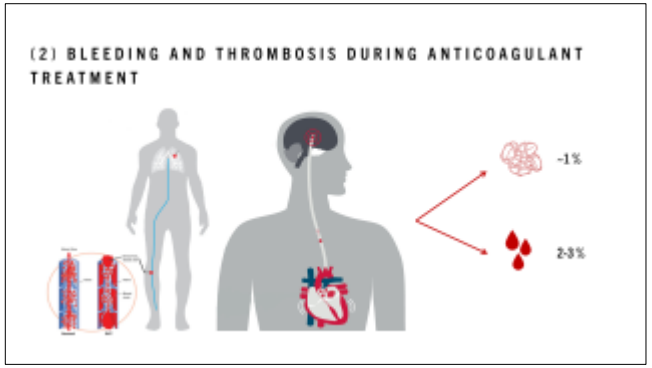
'Signature' *Slc44a2* deficiency in



CURRENT PROJECTS

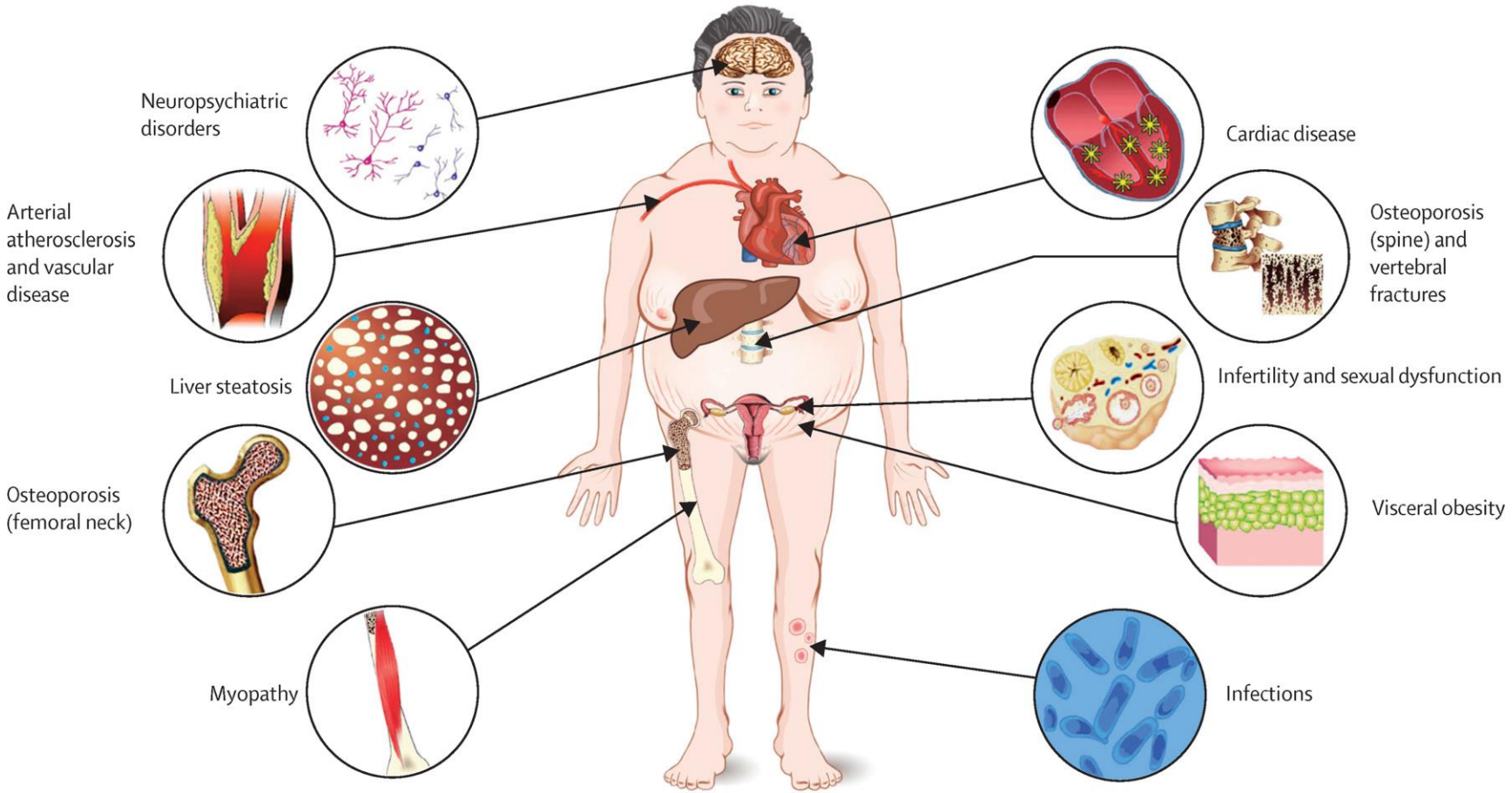


- **Plasma profiling of Cushing patients**
  - Changes before-after treatment
  - Biomarkers for remission



- **Plasma profiling of patients with major bleeding & thrombosis during anticoagulation**
  - Novel biomarkers for bleeding &thrombosis
  - Prediction model

(1) CUSHING DISEASE



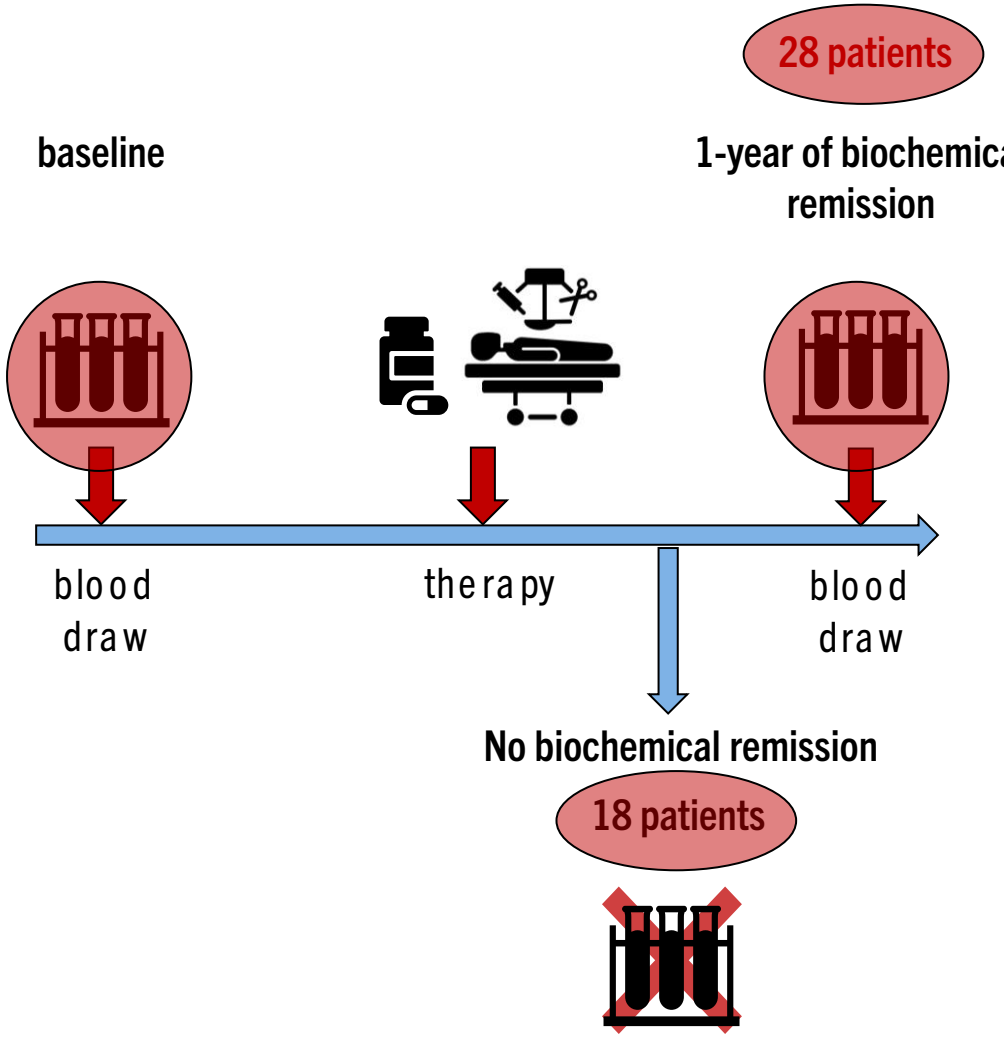
Pivonello R. et al. *The Lancet. Diabetes & endocrinology* 2016

STUDY DESIGN AND METHODS

46 patients

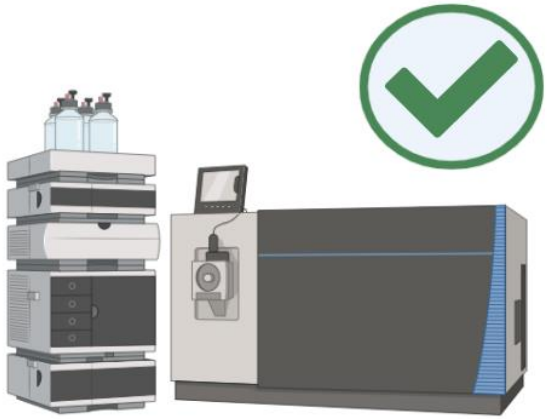
Cushing disease

Erasmus MC
Universitair Medisch Centrum Rotterdam



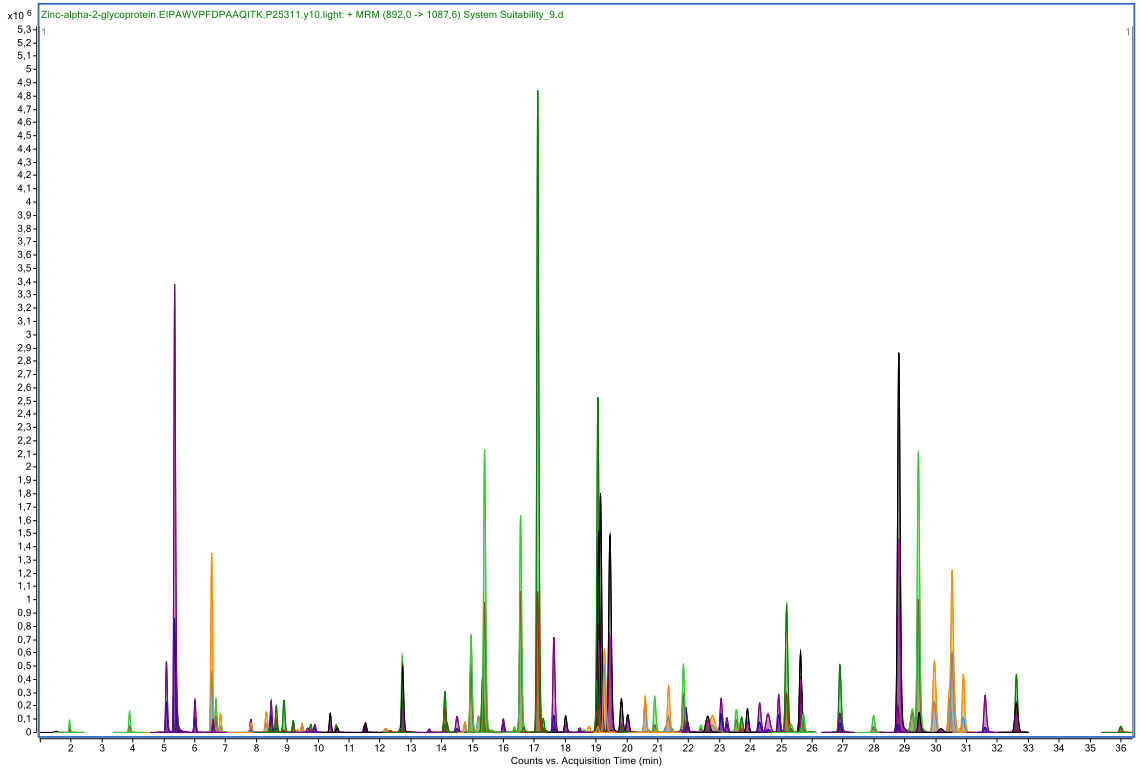
125-assay

QUALITY CHECKS



System suitability

- 3 retention time check
- 3 before run
- 3 after run



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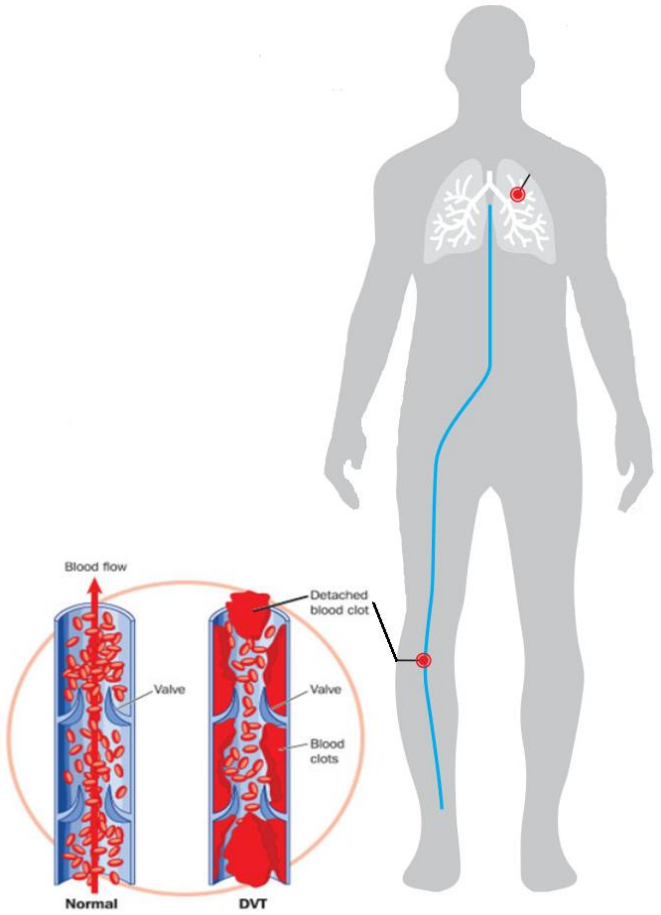
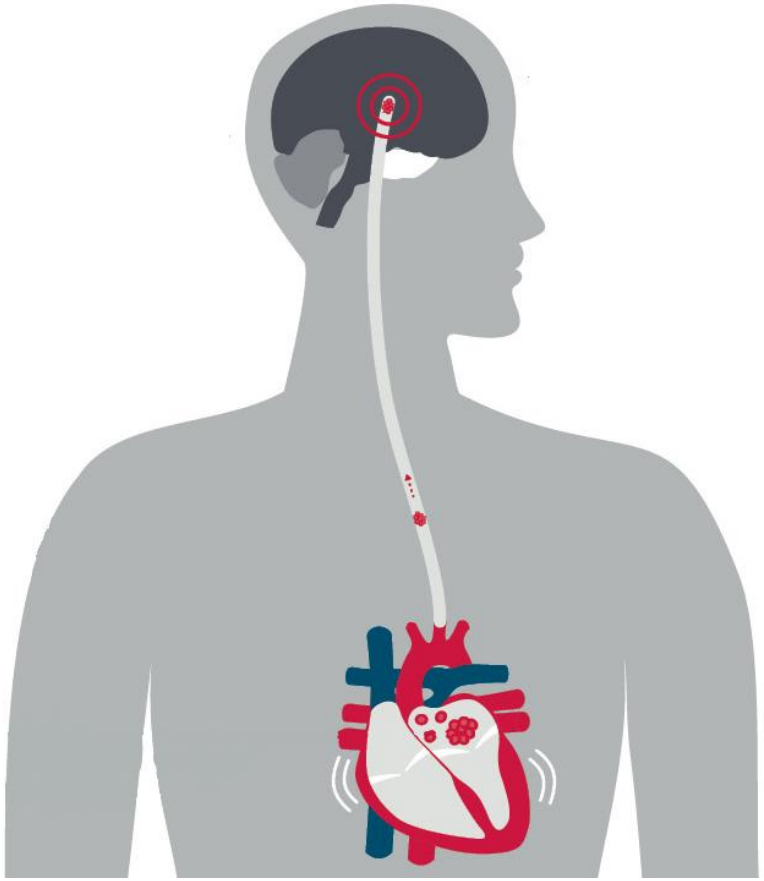
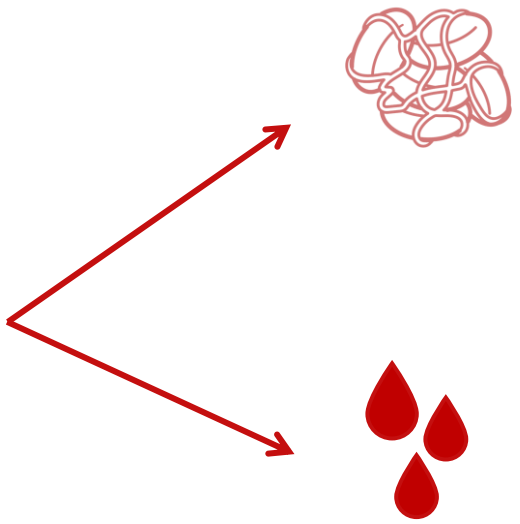


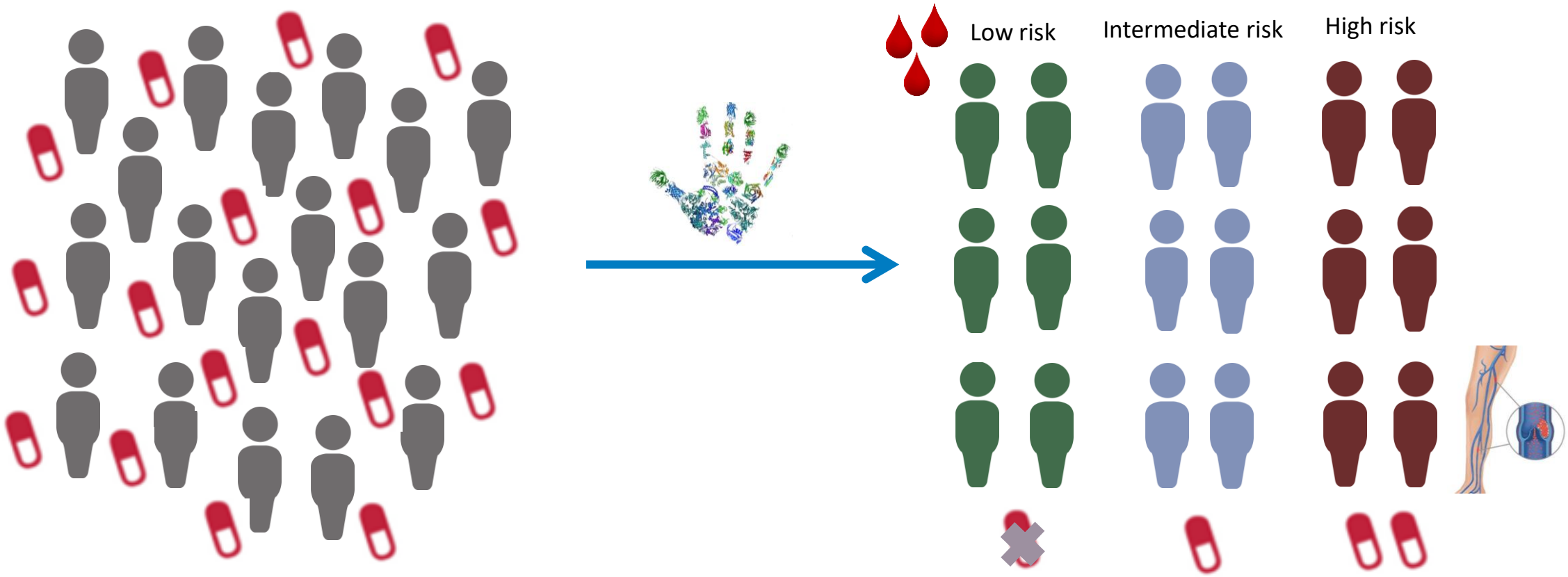




~1 %

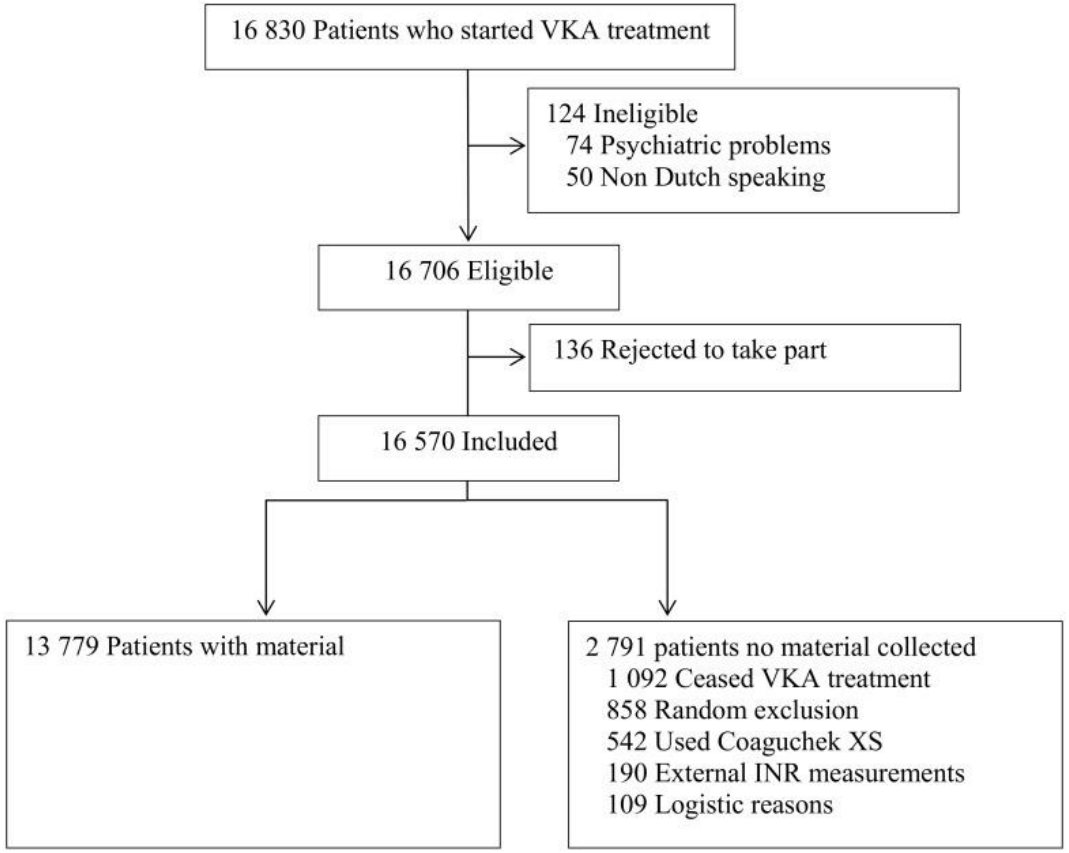
2-3 %

CURRENT APPROACH VS IDEAL APPROACH



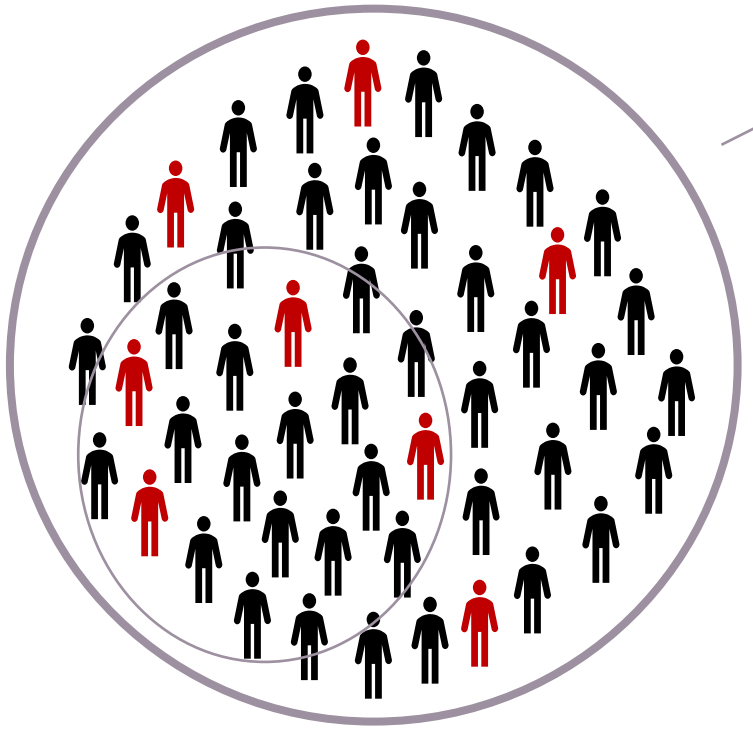
BLEED STUDY

16,570 patients who started treatment with Vitamin K antagonists (2012-2014)

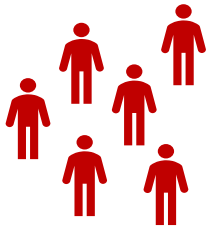


van Rein N, Lijfering WM, Bos MH, et al. *PLoS One*. 2016

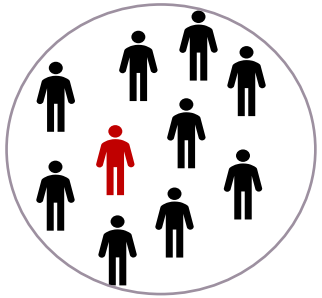
CASE-COHORT FROM THE BLEED STUDY



Cases
Major bleeding/thrombosis



Subcohort
Random sample at baseline



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UVic Genome BC PROTEOMICS CENTRE