KING'S
FORENSICS

Forensic Genetics

Developing an epigenetics-based tool for the inference of chronological age from blood traces

Dr Anastasia Aliferi
Research Associate

DNA Intelligence

DNA

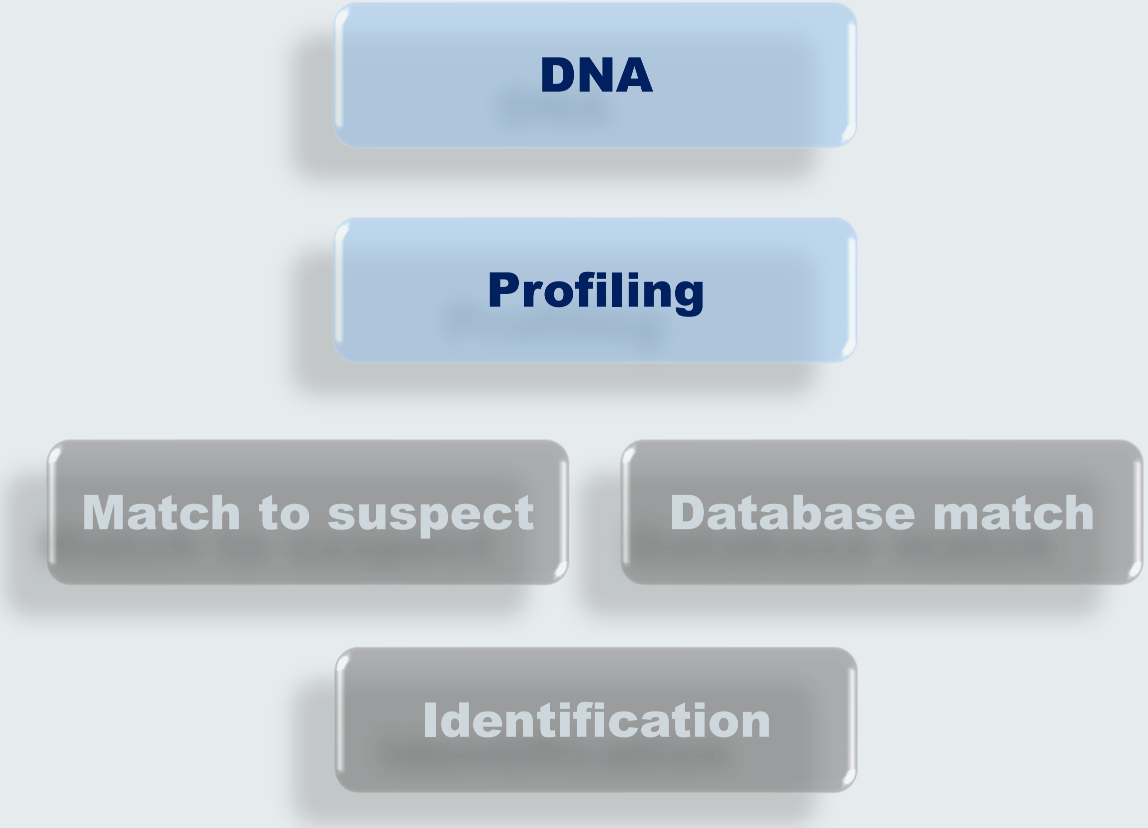
Profiling

Match to suspect

Database match

Identification

DNA Intelligence



DNA

Profiling

Match to suspect

Database match

Identification

DNA Intelligence

DNA

- Eye colour
- Hair colour
- Hair morphology
- Geographical ancestry
- Age

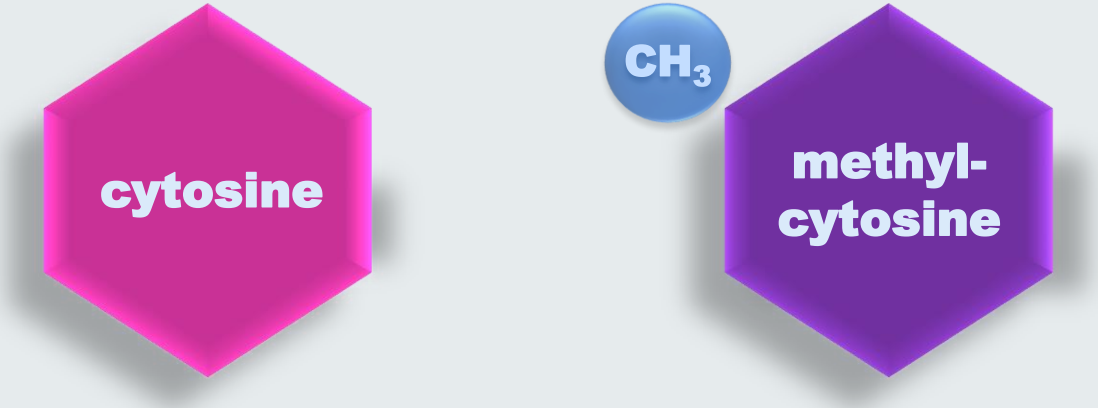
Prioritise suspect pool

Arrest

Identification

DNA methylation-based age estimation

3’ TAATCAGCTGCCACTACATGC 5’
5’ ATTAGTCGACGGTGATGTACG 3’

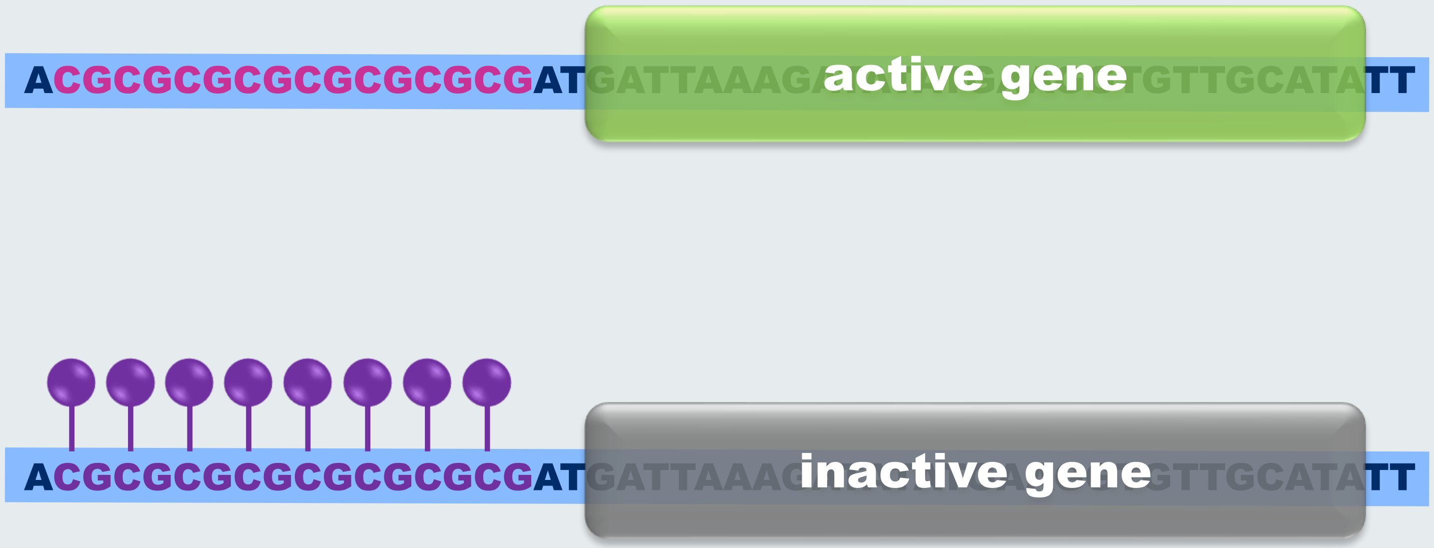


cytosine

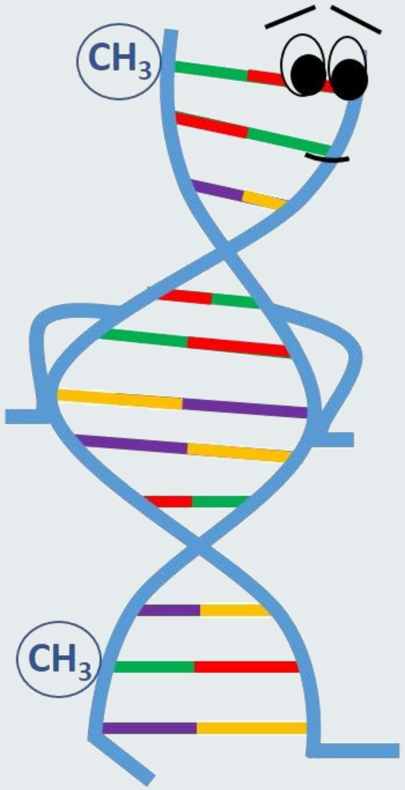
CH_3

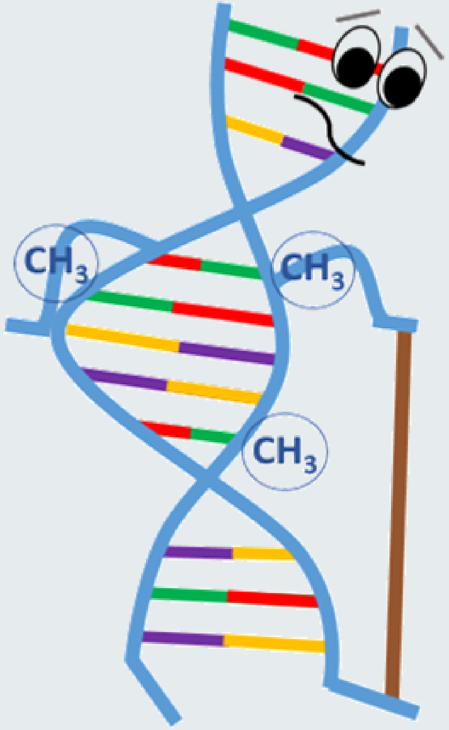
methyl-
cytosine

DNA methylation-based age estimation

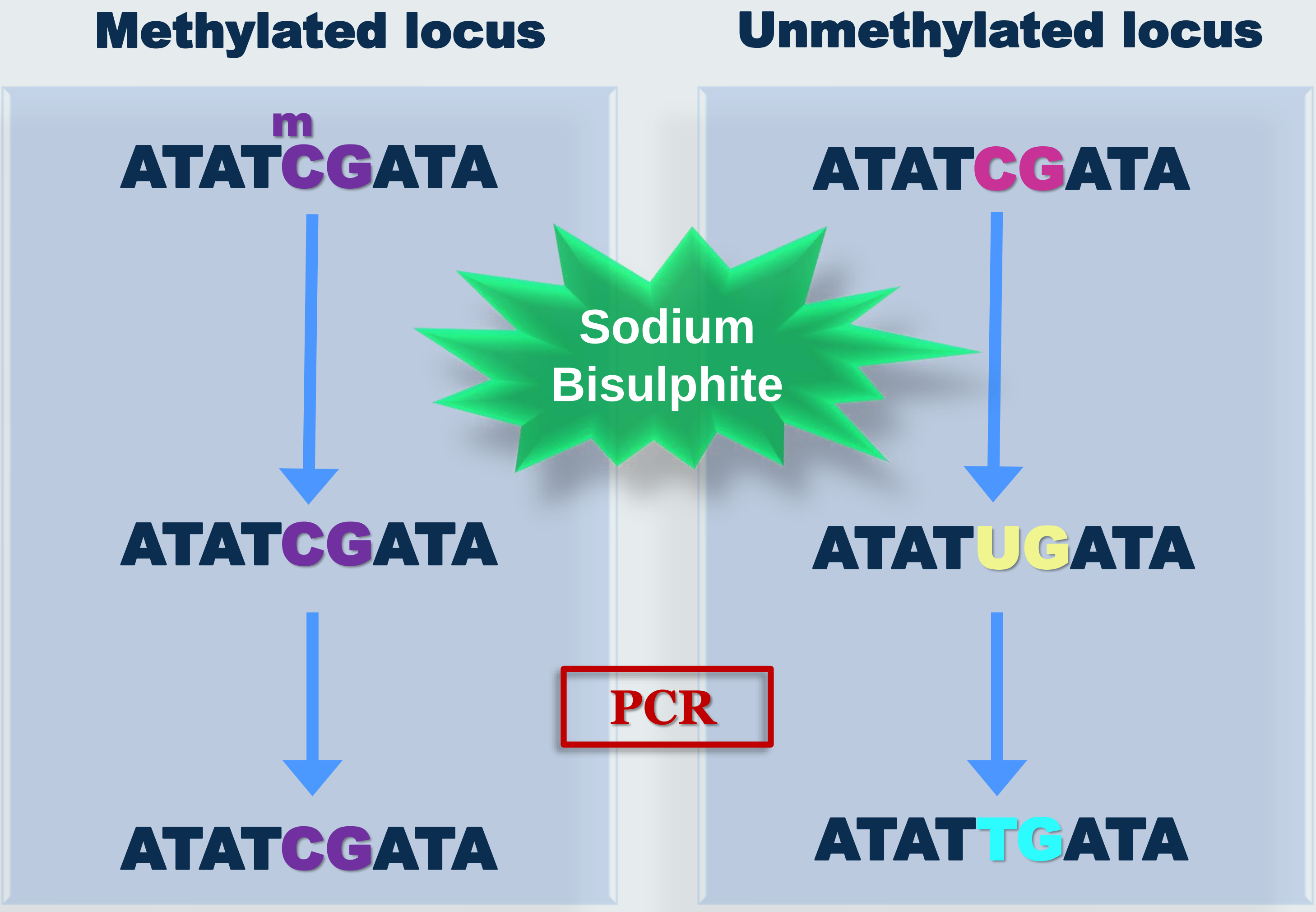


DNA methylation-based age estimation





Targeted DNA methylation quantification



Methylated locus

ATAT^{m}CGATA

ATATCGATA

ATATCGATA

Unmethylated locus

ATATCGATA

ATATUGATA

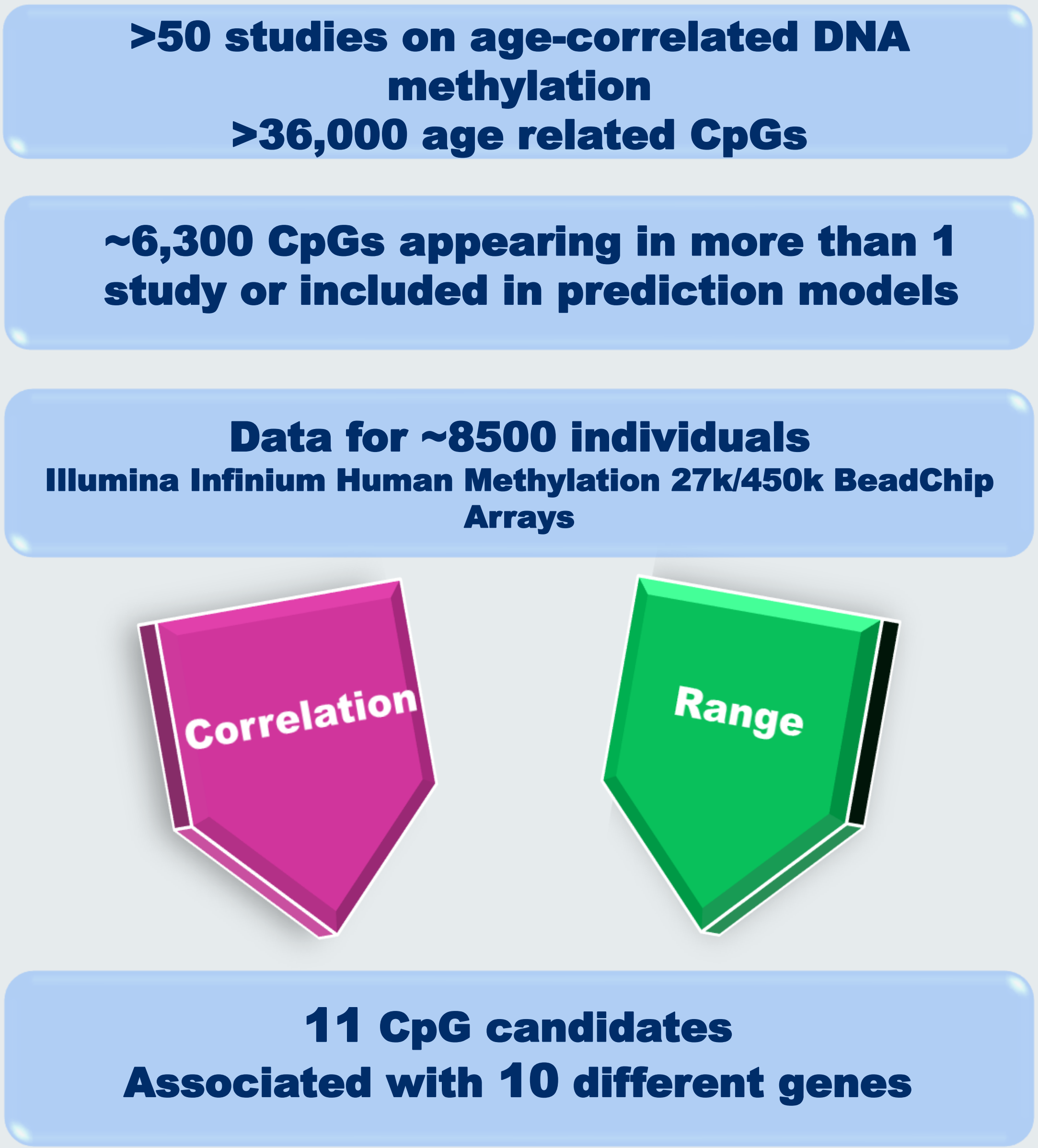
ATATTGATA

Sodium Bisulphite

PCR

Methylation of CpG = C/(C+T)

Marker selection



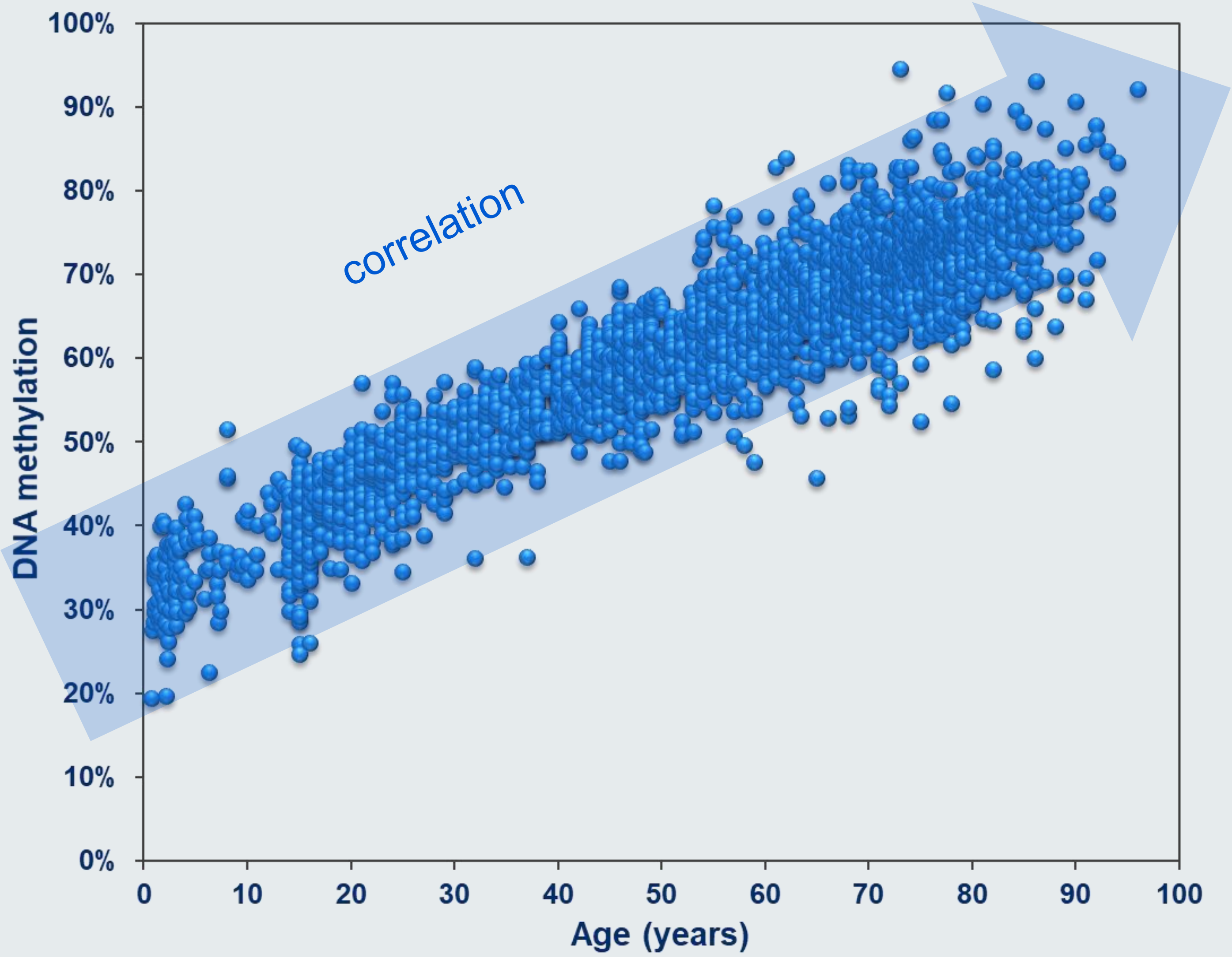
>50 studies on age-correlated DNA methylation
>36,000 age related CpGs

~6,300 CpGs appearing in more than 1 study or included in prediction models

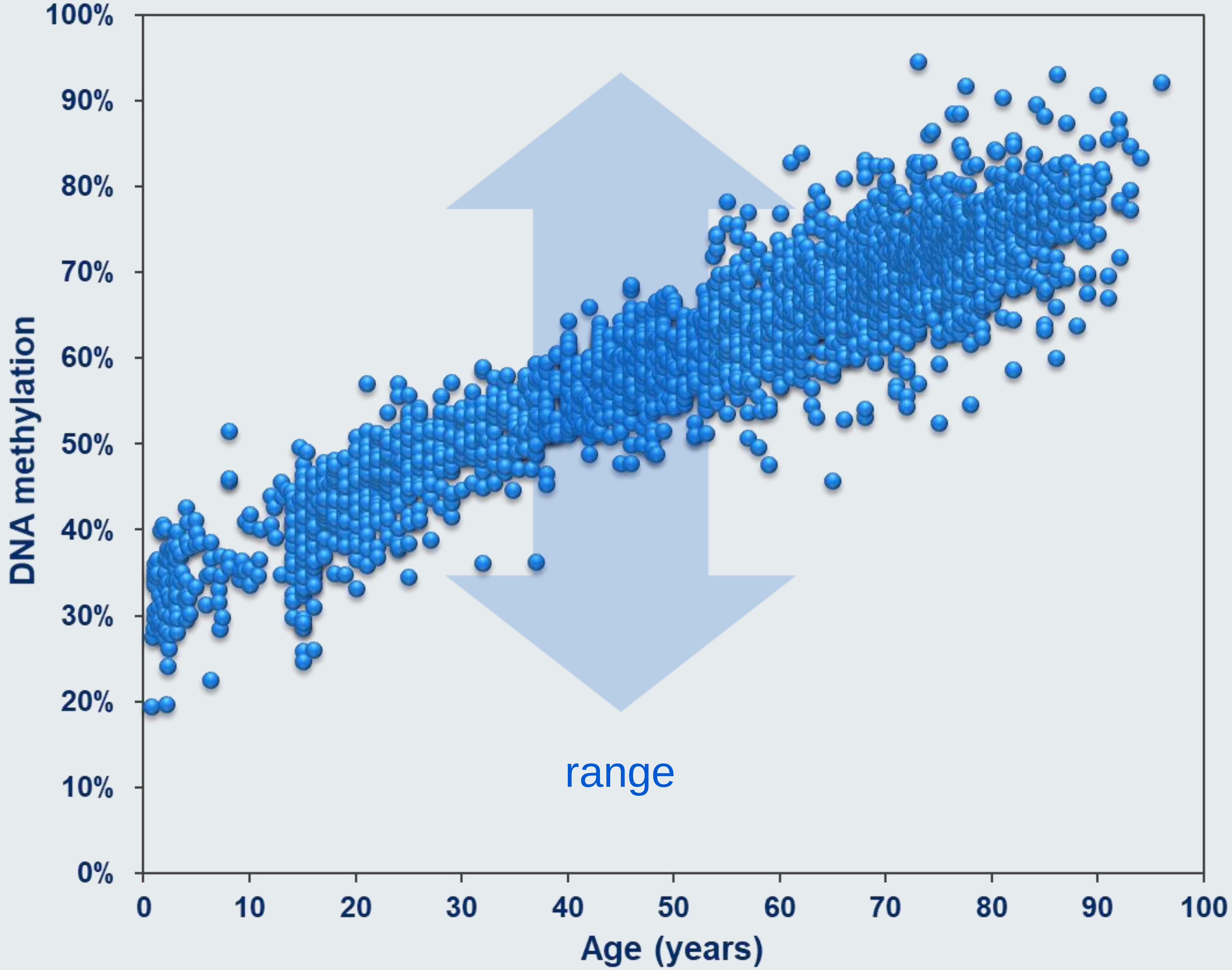
Data for ~8500 individuals
Illumina Infinium Human Methylation 27k/450k BeadChip Arrays

11 CpG candidates
Associated with 10 different genes

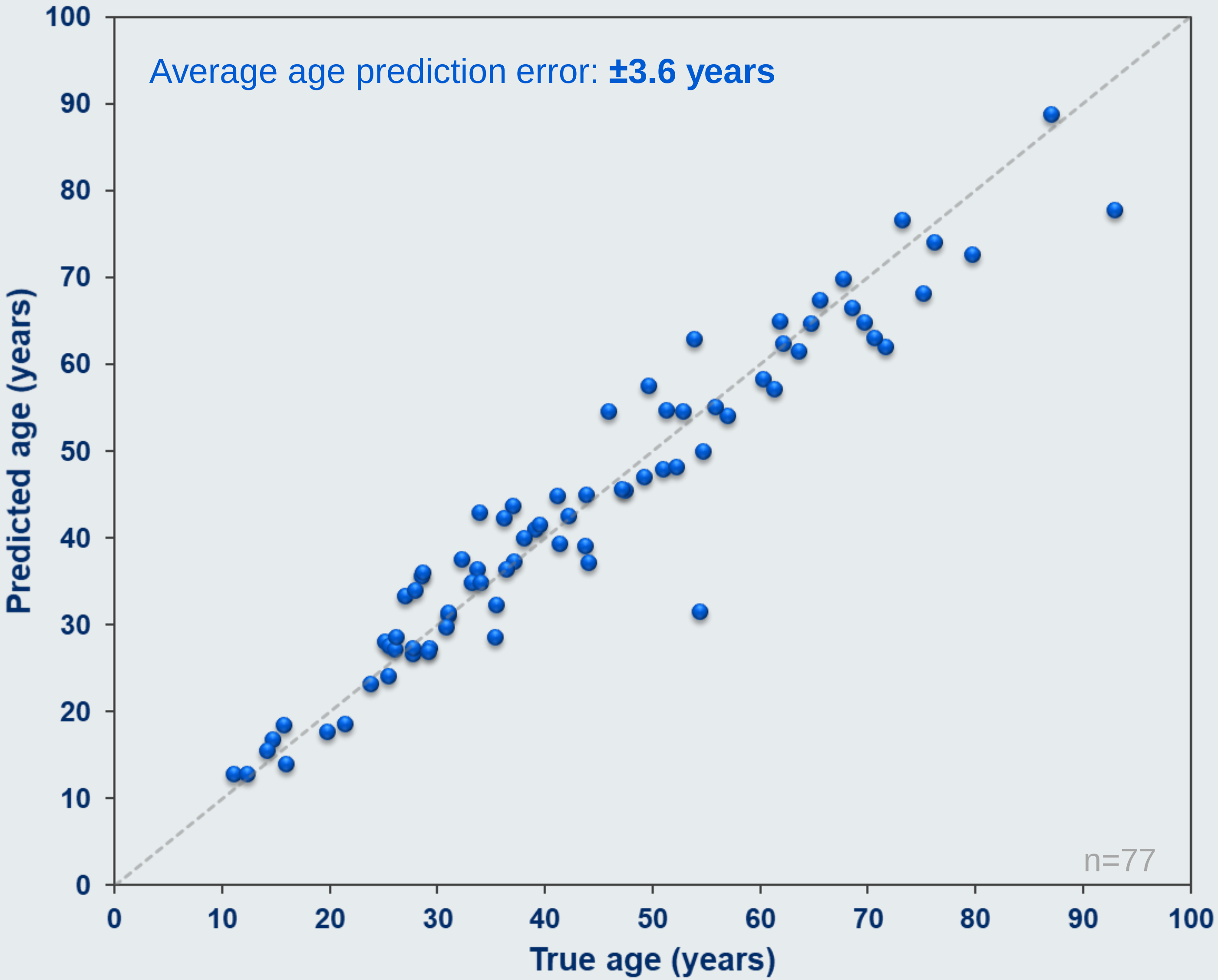
Marker selection



Marker selection

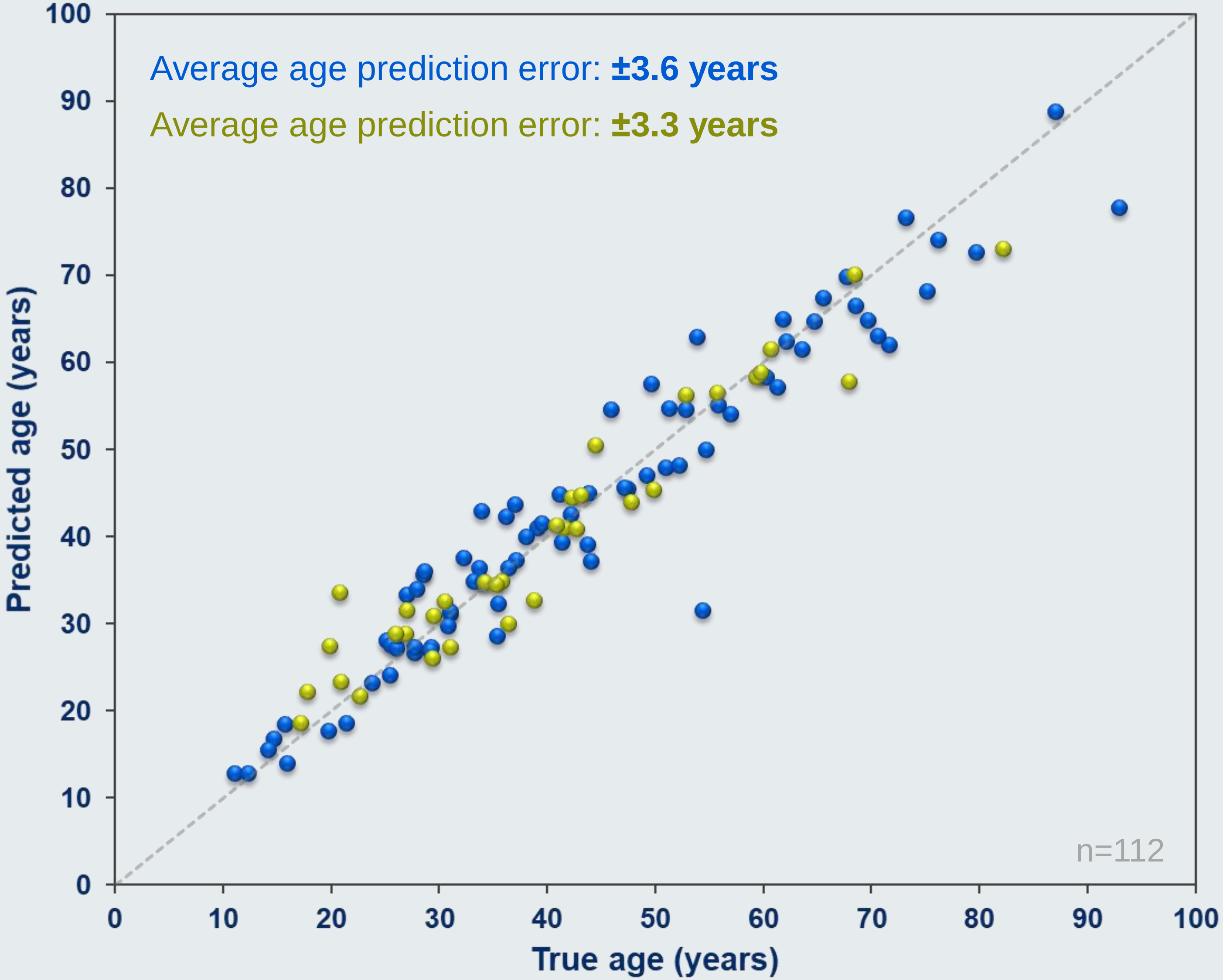


Prediction accuracy



Training dataset

Prediction accuracy



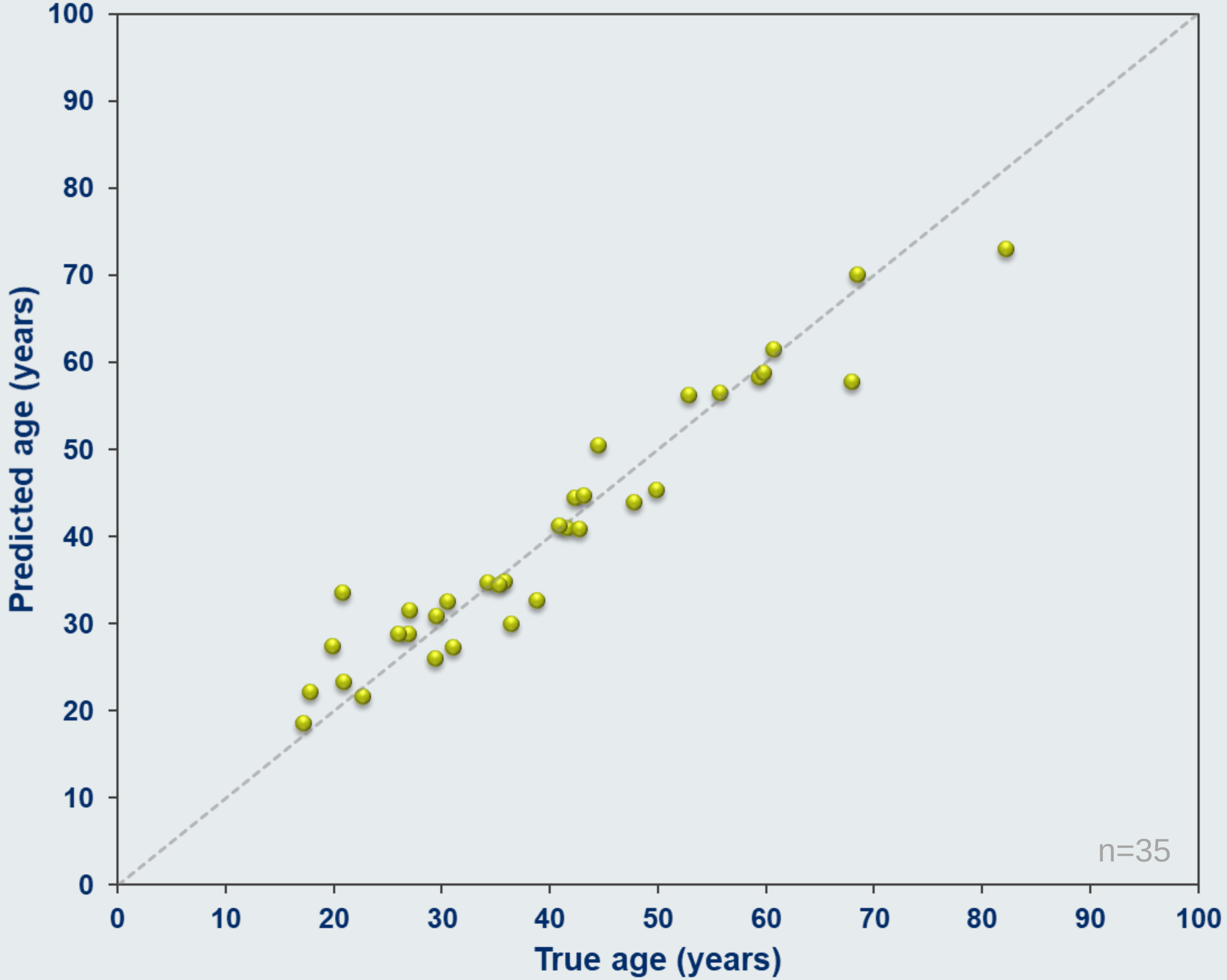
Average age prediction error: **±3.6 years**

Average age prediction error: **±3.3 years**

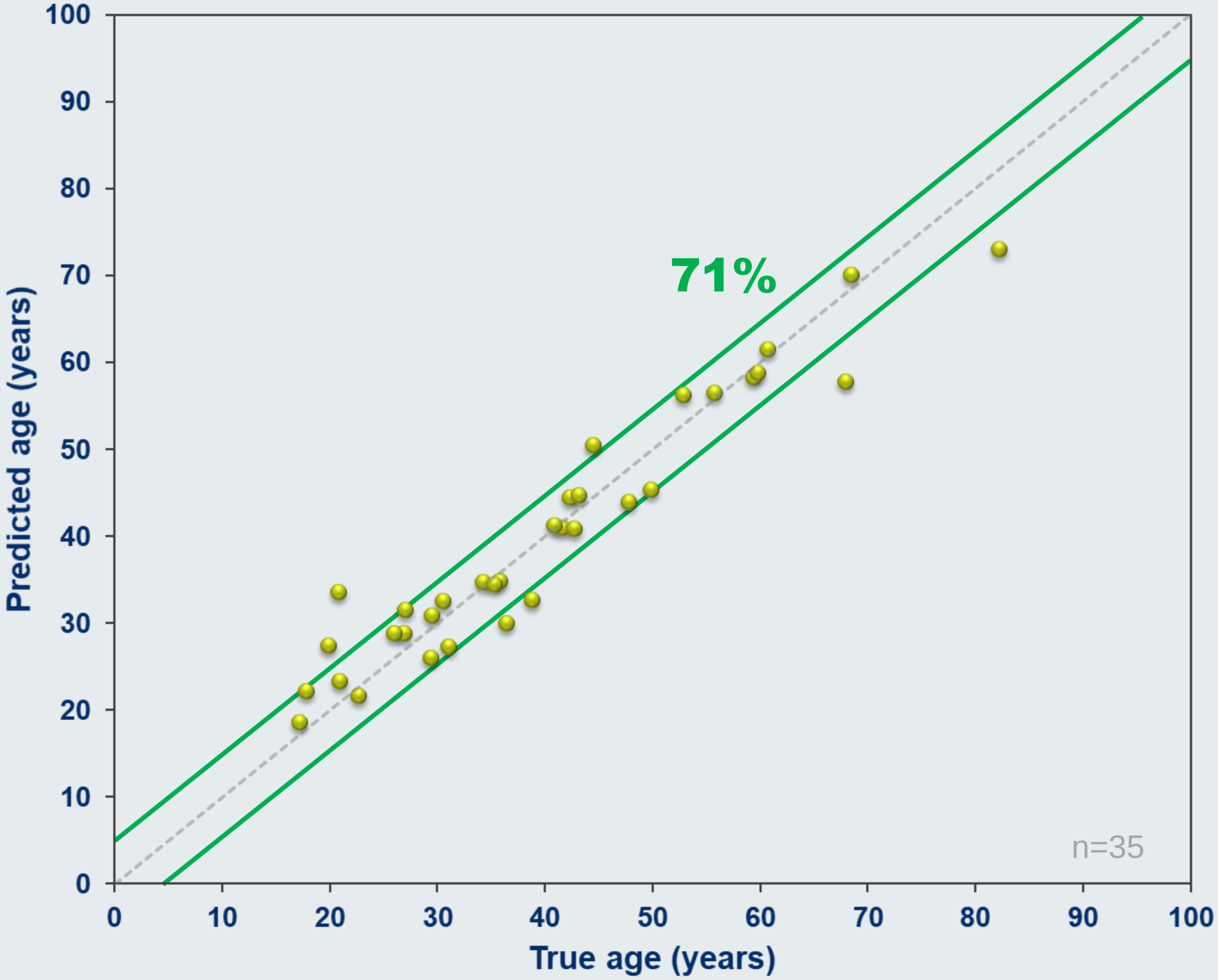
Training dataset

Test dataset

Prediction accuracy

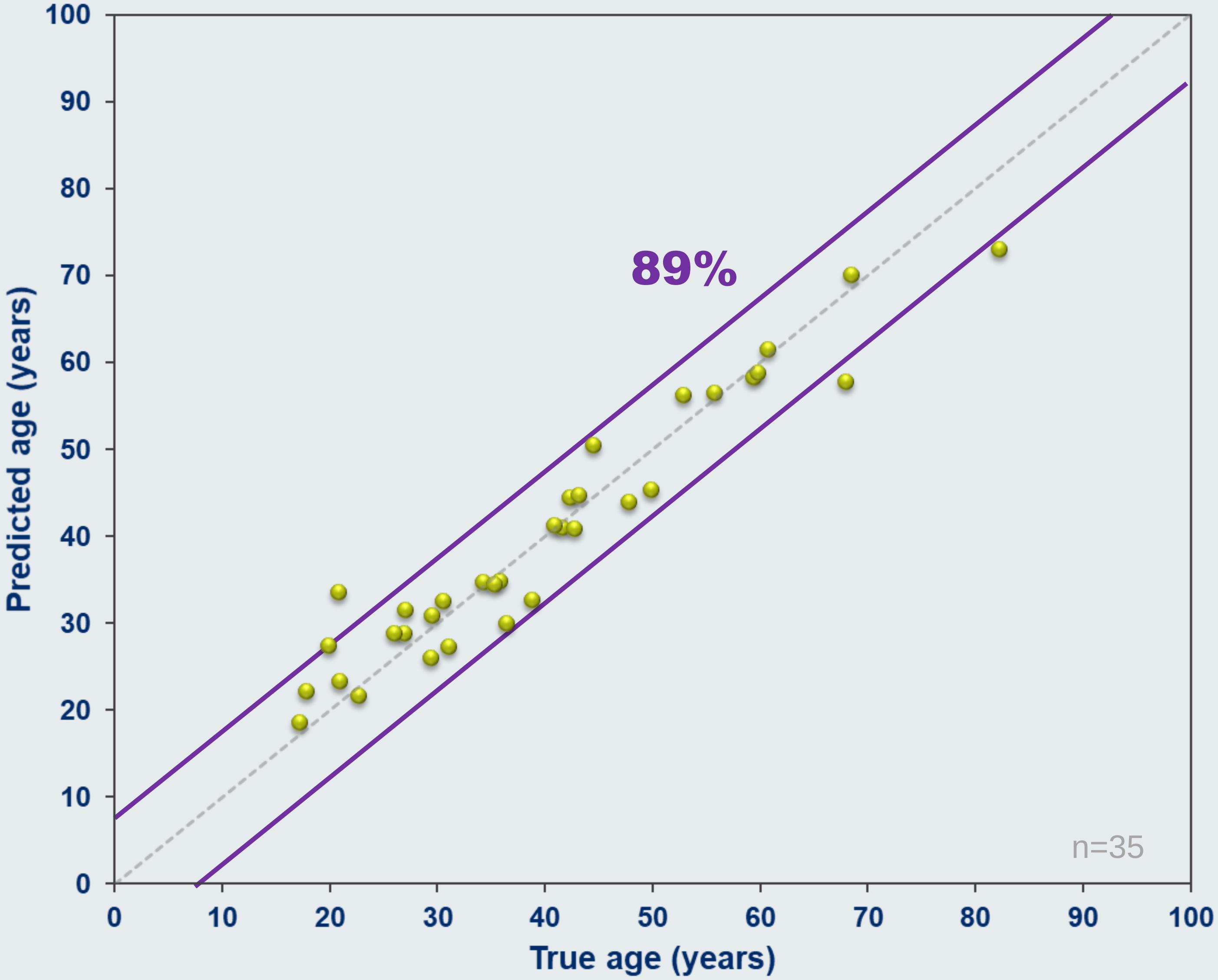


Prediction accuracy



71% of the test samples predicting with an **absolute error of less than 4 years**

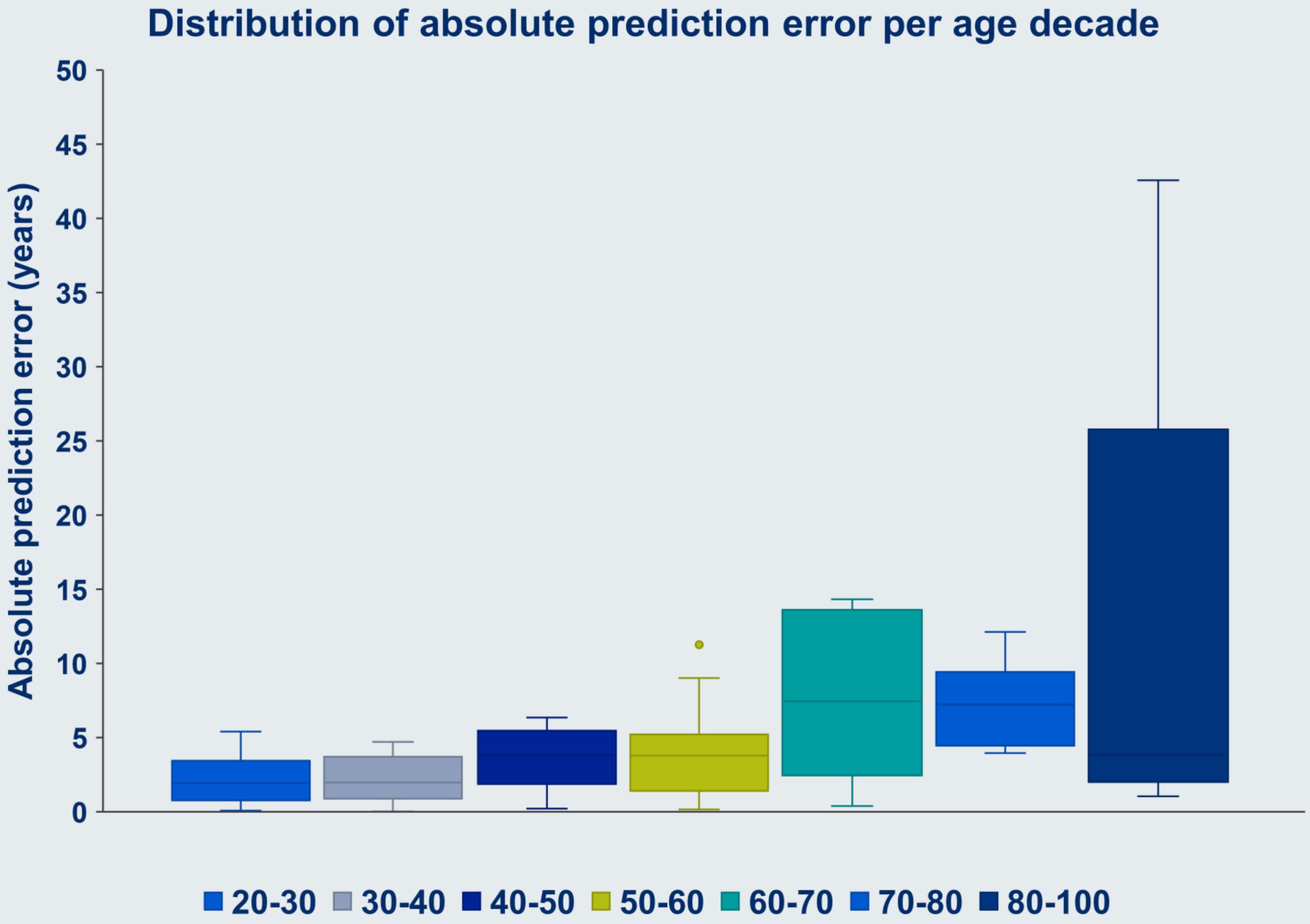
Prediction accuracy



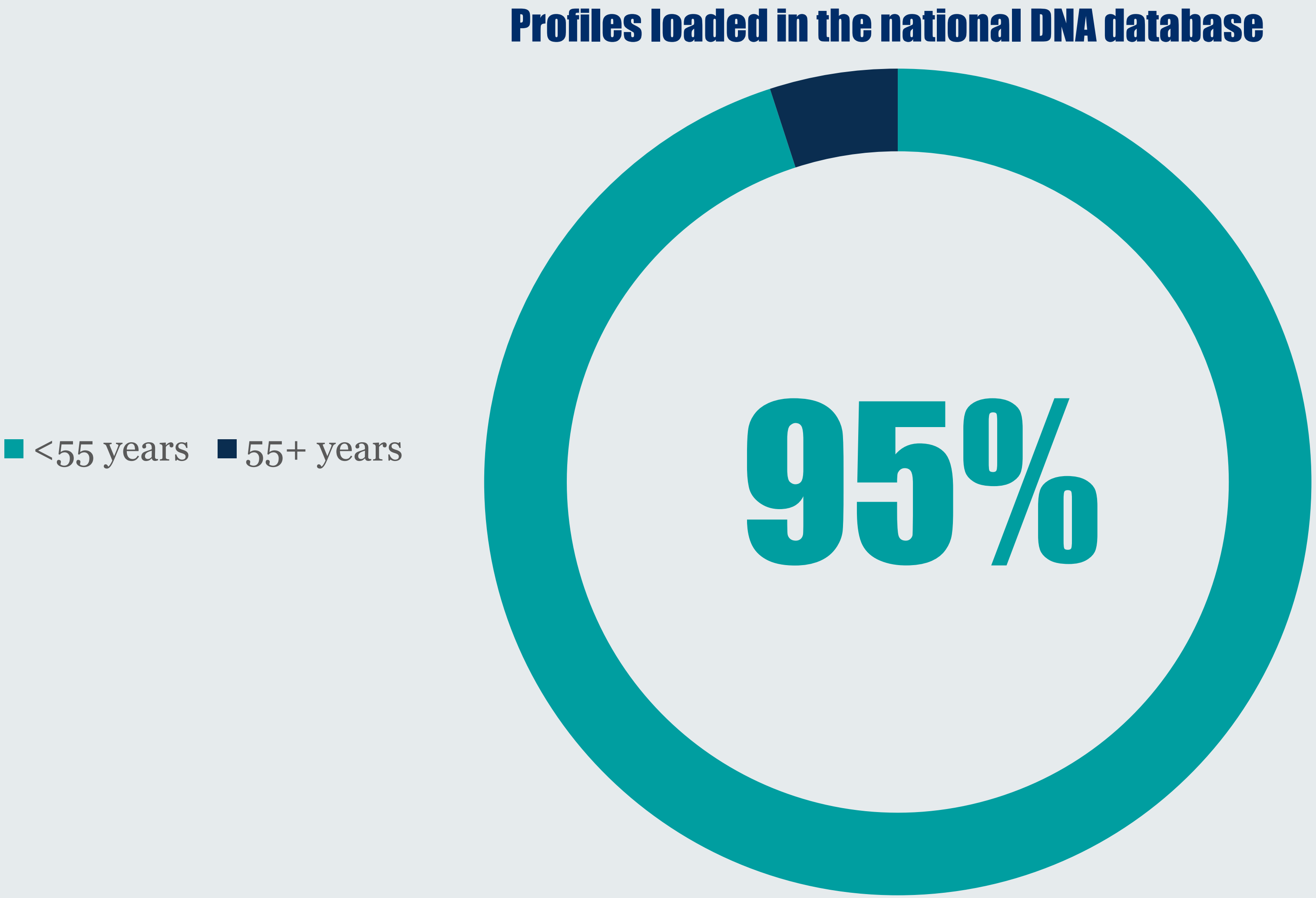
89% of the test samples predicting with an **absolute error of less than 7 years**

Prediction accuracy – Spanish cohort

Prediction accuracy – Spanish cohort

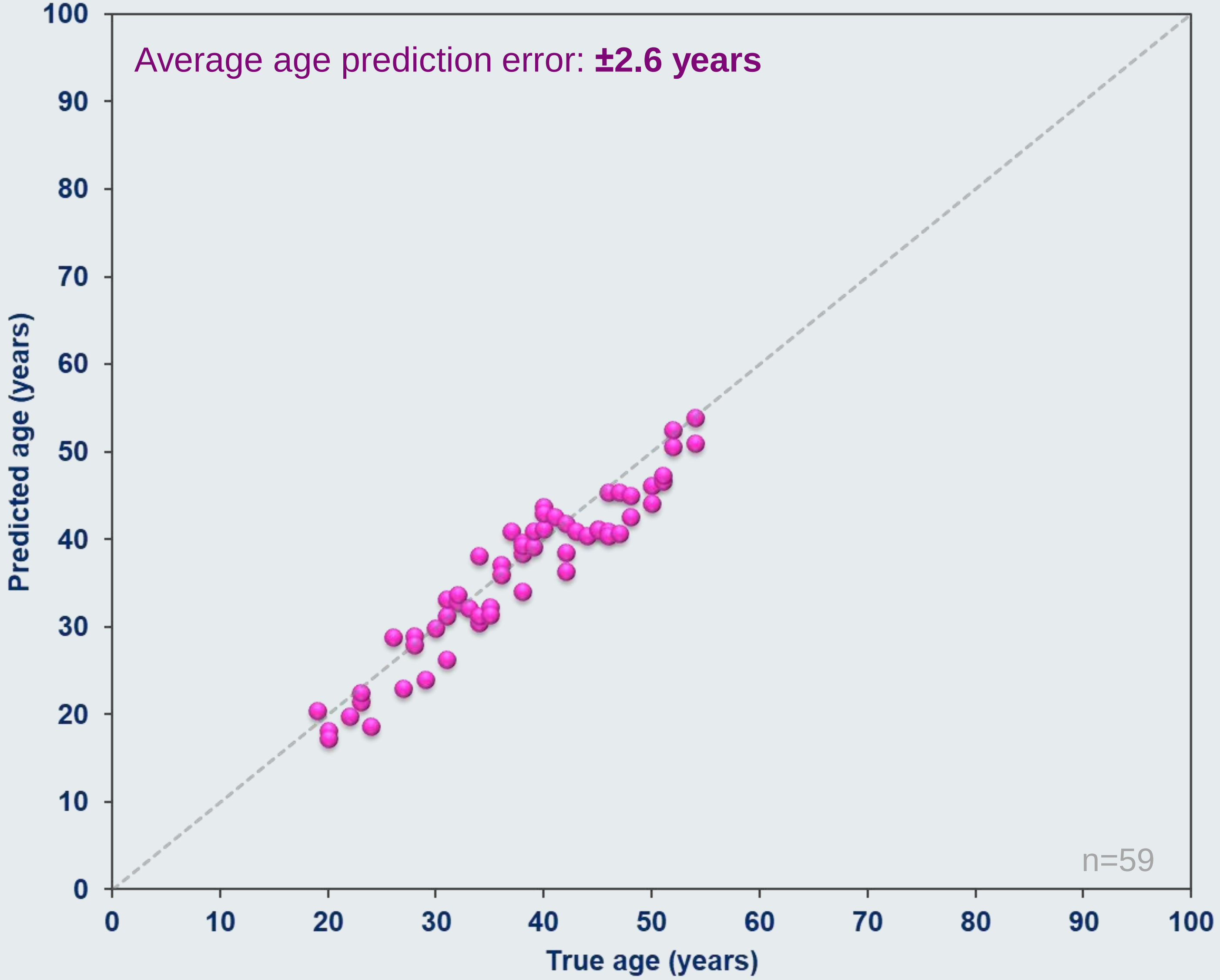


DNA database statistics

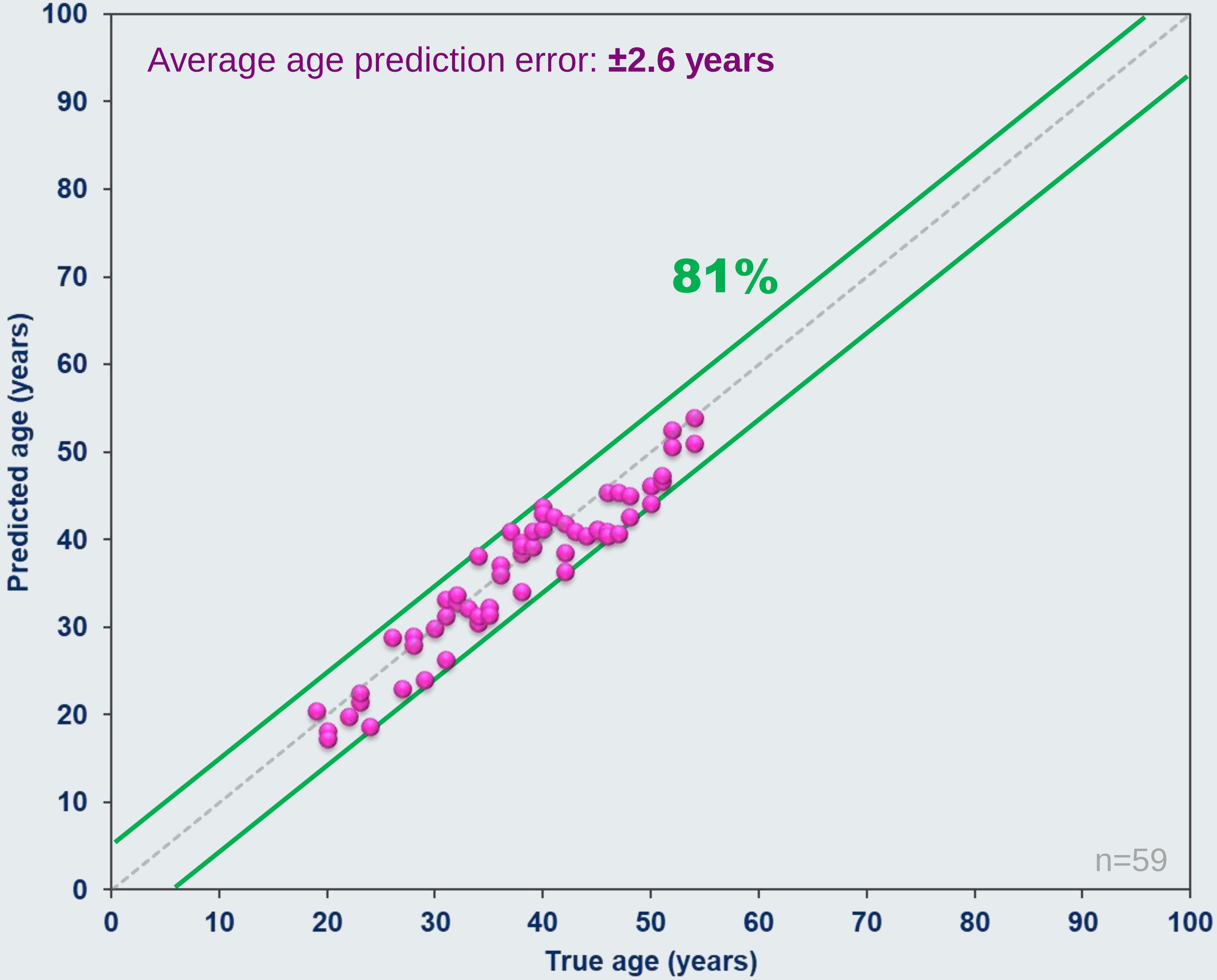


*19/06/19 – England, Wales and the British Transport Police

Prediction accuracy <55 years

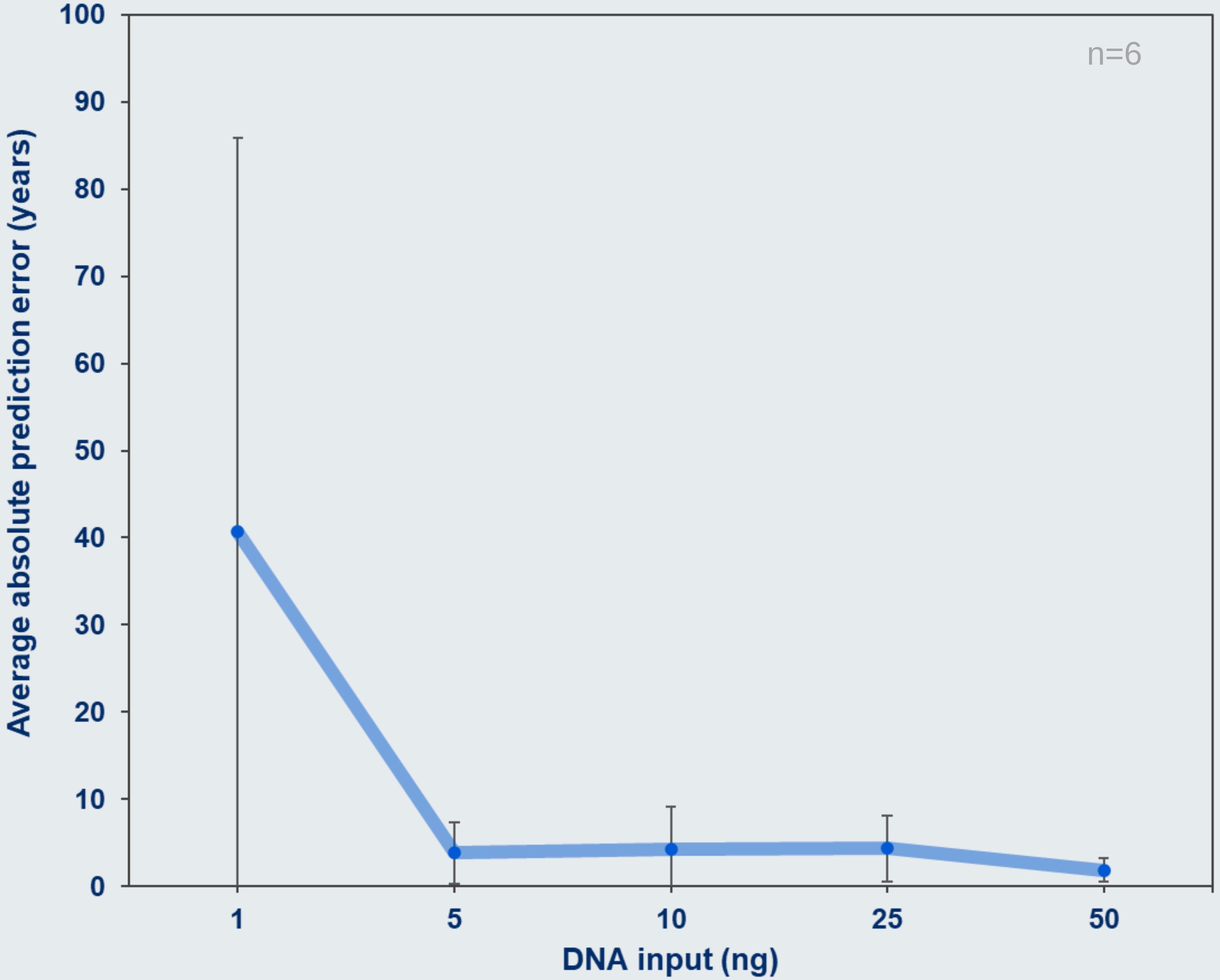


Prediction accuracy <55 years

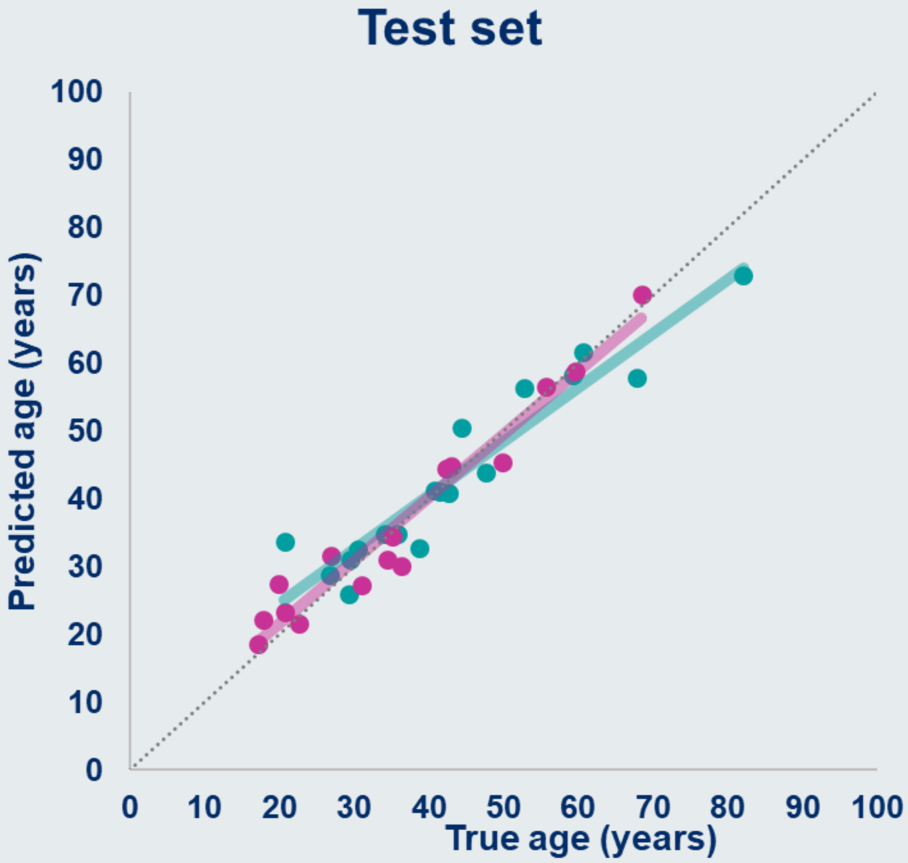


81% of the test samples predicting with an **absolute error of less than 4 years**

Sensitivity



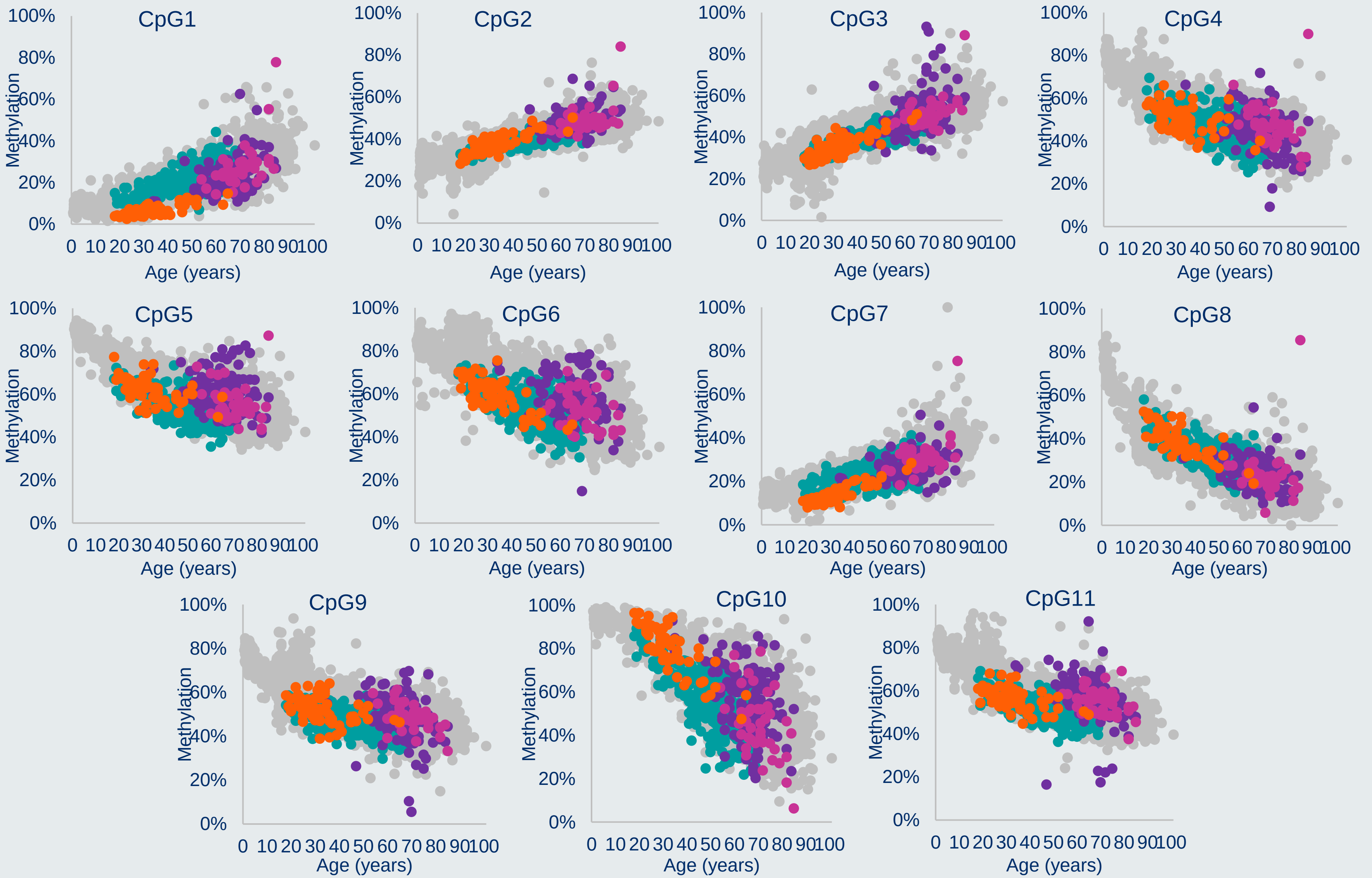
Sex-related bias



No significant difference observed in the age estimation for **male** and **female** donors

Disease-related bias

Schizophrenia Rheumatoid arthritis Frontal temporal dementia Progressive supranuclear palsy



Conclusions

11 CpG markers associated with **10 different genes**

Targeted methylation sequencing using a benchtop instrument

Average prediction error of **±3.3 years** in the KCL test set and **±3.8 years** in the USC set

Average prediction error of **±2.6 years in under 55 year olds**, while:

- **81%** predicting with an absolute error of less than **4 years**
- **59%** predicting with an absolute error of less than **3 years**
- **44%** predicting with an absolute error of less than **2 years**

High prediction accuracy retained down to **5ng of initial DNA input** (~1ng in the PCR)

No evidence of **sex** or **disease** status affecting the final model

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Thank you

Dr Anastasia Aliferi

Email: anastasia.aliferi@kcl.ac.uk

Twitter: @anastasialiferi