

INNOVATION IN THE NHS

Implementation of genotype-guided dosing of warfarin

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Background

Warfarin

- the most commonly used oral anticoagulant
- 1% of UK population on warfarin¹
- narrow therapeutic index
- 40-fold interindividual variability in dose requirements²
- INR monitoring required (2-3 target INR)
- indications- atrial fibrillation and venous thromboembolism
- major bleeding rate per 100-person years- 2.6

Genetics of warfarin

- polymorphisms in CYP2C9 and VKORC1 genes - strongly associated with response to warfarin³
- >40% of dose requirements explained by genetic factors⁴
- EUPACT randomised controlled trial findings- genotype guided dosing showed a mean **7% increase in time in therapeutic range**⁵
- Point-of-care genetic testing and algorithms taking into consideration clinical and environmental factors can explain approx **60% of warfarin dose requirement**

Project Overview

Aim- to implement and evaluate genotype guided dosing for patients with AF/VTE who are starting warfarin

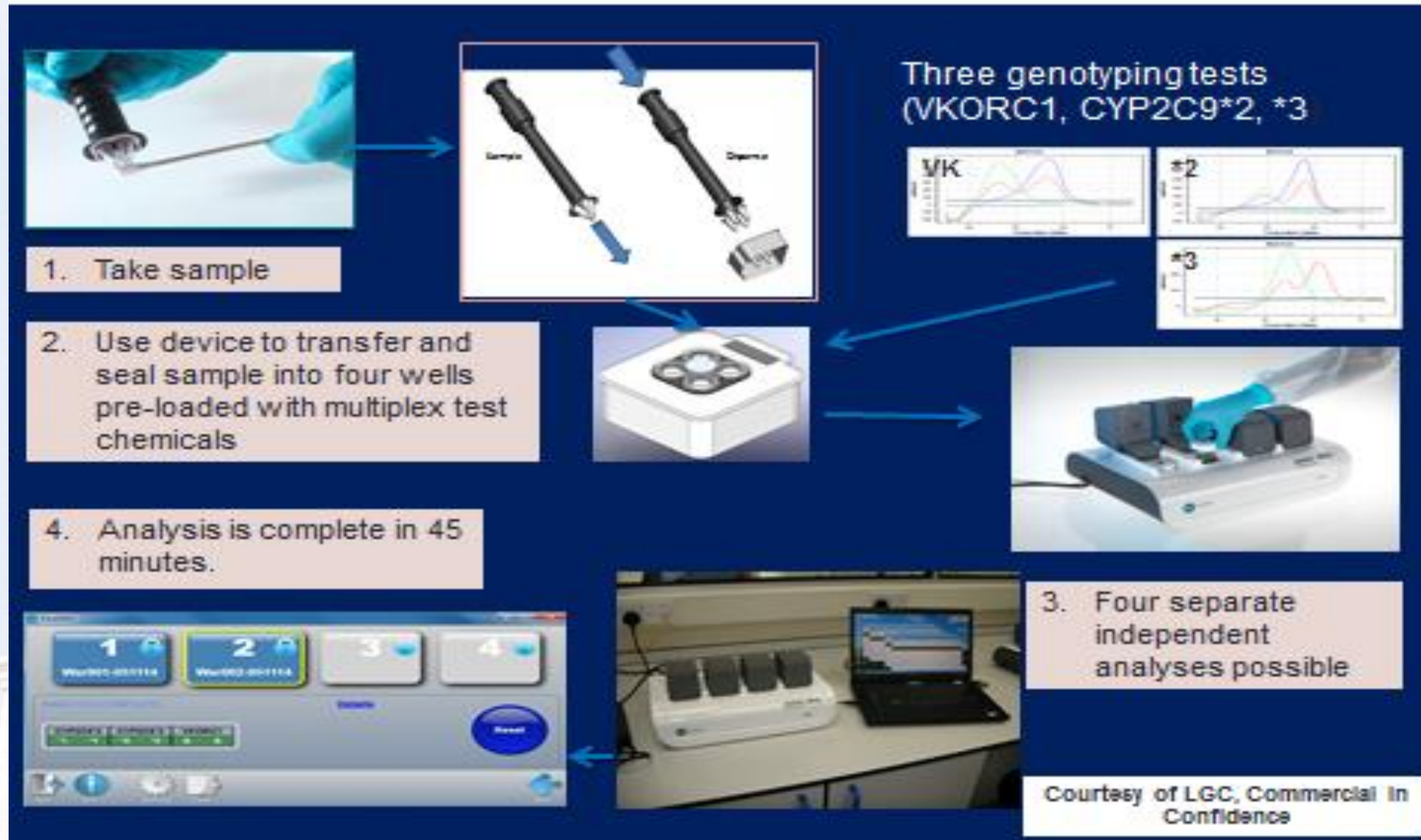
Collaboration

- NIHR CLAHRC North West Coast (NWC) (funding),
- Innovation Agency- Academic Health Science Network
- University of Liverpool
- LGC company provided technology, software and training

Clinical setting –anticoagulant clinics

Genotype guided dosing clinics	Comparator clinics
Royal Liverpool and Broadgreen University Hospitals NHS Trust	St Helens and Knowsley Teaching Hospitals NHS Trust
Warrington and Halton NHS Foundation Trust	Aintree University Hospitals NHS Foundation Trust
Countess of Chester NHS foundation Trust	Lancashire Care NHS Foundation Trust

Technology



Outcomes

Primary Outcome: Time in therapeutic range (INR 2- 3)

Secondary Outcomes:

- INR >4 during the first week of treatment
- INR<2 during the first week of treatment
- Number of visits to the clinic
- Establishment of the dose/ Number of dose changes

- Serious adverse events reported
- Patient acceptability
- Staff acceptability

Longitudinal anonymised data for all patients for 12 weeks

Quality of life survey (EQ5D-5L) collected at baseline and 12 weeks

Patient/staff questionnaires completed at implementation sites

Baseline Characteristics

	Implementation arm (n=133)	Comparator arm (n=92)
Age (mean; (SD)) ¹	72.4 (10.5)	69.4 (14.4)
Gender - male (n; (%))	72 male; 61 female	40 female
- Male	72 (54%)	52 (57%)
- Female	61 (46%)	40 (43%)
Ethnicity (n; (%))		
- Caucasian	130 (100%)	91 (99%)
- Other	0 (0%)	1 (1%)
Indication for warfarin (n; (%))		
-AF	122 (93%)	53 (58%)
-DVT	4 (3%)	17 (19%)
-PE	5 (4%)	21 (23%)

1. Age missing for 2 in implementation arm and 2 in comparator arm

Project Update

- Enrolment stopped in August 2017**
- Final 12 week follow up: October 2017**
- Analysis in progress, preliminary results expected in November 2017**
- If genotype guided dosing is more effective then current practice further discussions with commissioners to adopt this innovation into the NHS will be required**

Summary

Warfarin prescribing is now being challenged by the widespread use of direct oral anticoagulants (DOACs). The choice between **conventional warfarin dosing** vs **genotype guided dosing** vs **DOAC therapy** is dependant on many factors including: **patient choice, patient safety and outcomes, clinician choice, patient/ clinician acceptability** of genotype testing and demonstration of **cost effectiveness**. The capability of the **NHS** to implement and adopt **innovation** will be paramount.