DAWN as a tool in scientific projects

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Outline

- The Anticoagulant Clinic
- The "Vitamin K-antagonist" project
- Using DAWN

SYDDANSK UNIVERSITET

The Anticoagulant Clinic at the Hospital of South West Denmark

Staff: Nurses Tanja Graff, Bodil Leed and Pernille Tandrup.
Consulting physician Jørgen Gram

Number of patients: 511

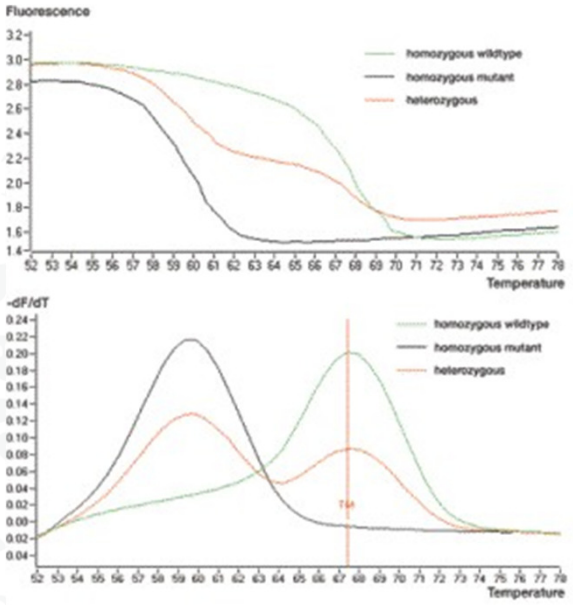
Computer-assisted dosage system: DAWN since 2006

Quality: During the last year, the patients spent 74% of the time in range

Close collaboration with Unit for Thrombosis Research, Institute of Public Health, University of Southern Denmark

Project title

"How to individualise vitamin K-antagonist treatment? A study on the influence of gene-environment interactions on inter- and intra-individual variations in dose-response"



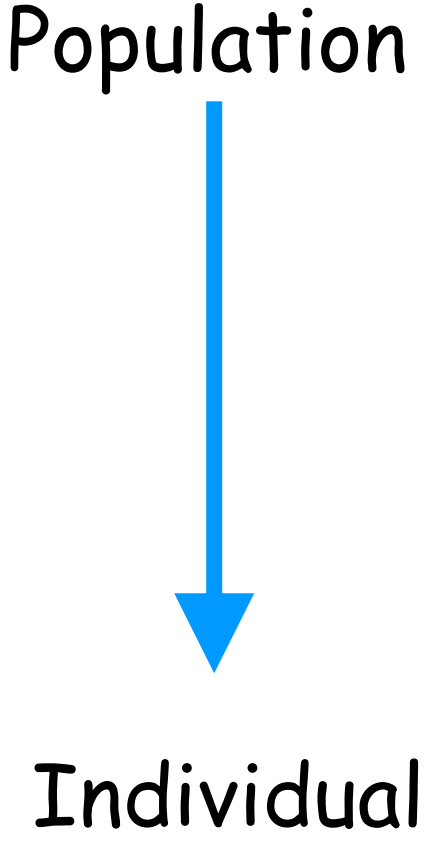
Historical perspective

1998: Computerised anticoagulant dosage improves INR control (Poller, Jespersen et al., Lancet, 1998)

2008: Computerised anticoagulant dosage reduces the number of clinical events (bleeding and thrombosis) (Poller, Jespersen et al., Journal of thrombosis and hemostasis, 2008)

Moving forward

The influence of gene-environment interactions on inter- and intra-individual variations in dose-response of oral anticoagulant therapy



Investigation

The influence of

- **Genetic factors**
  - Polymorphisms in *VKORC1* and *CYP2C9*

- **Environmental factors**
  - Lifestyle (diet, physical activity, smoking, alcohol consumption)
  - Quality of life
  - Socio-demographics
  - Co-morbidity
  - Medicines, including alternative medicine and dietary supplements

on the dose and response (INR) of vitamin K-antagonists

- Patients in the maintenance phase of treatment
- Their fluctuations over time
- Patients with very high or low INRs

Hypothesis

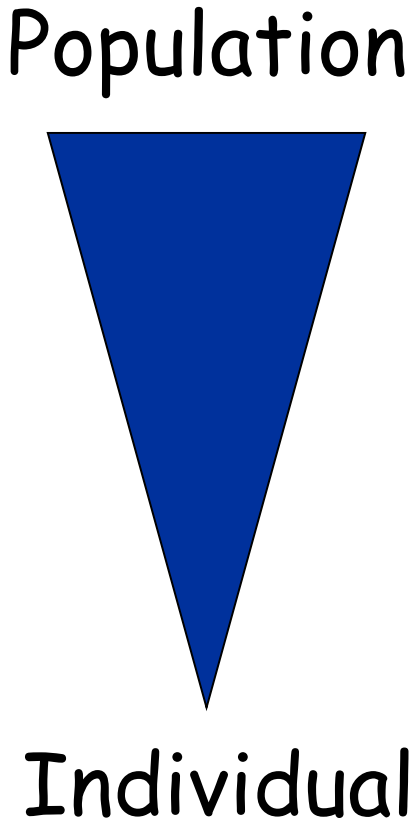
The aforementioned genetic and environmental factors contribute, alone or in combination, to the variation in VKA dose and response.

This project will, by increasing our knowledge of these interactions, help us to:

1) Individualise anticoagulant therapy
2) Identify patients at risk for complications (bleeding and thrombosis)
3) Reduce the number of complications

Elements

- Cross-sectional study
- Longitudinal study
- Case-control study



Design

Follow-up for 12 months
Less than 4 weeks between INR measurements
Same treatment as non-project patients

Inclusion
•Interview (185 questions)
•Blood samples (DNA analyses, D-dimer, vWF, CRP, fibrin structure etc.)
•Height, weight, girth and blood pressure was measured

Out-of-range INR?
The patient can be included in the case-control study (phone interview, 48-hour diet registration)

Who are involved in the project?

Managing group,
Chairman Professor Jørgen Jespersen

Who are involved in the project?

Anticoagulant nurses,
biomedical laboratory technicians
and secretaries

Who are involved in the project?

Postdoctoral researchers

Using DAWN

- **Cross-sectional study:**

Extracting information about duration of treatment, clinical indication and co-morbid conditions

- **Longitudinal study:**

Gathering data (INR and dose at each visit to the clinic)

- **Case-control study:**

Before phoning the patients, we checked previous INR measurements, dosage changes and whether there were any special considerations (eg. impaired hearing, history of stroke)

How DAWN improved the project

- Making it easy to check that protocols were followed when selecting patients for the case-control study

- Saving time for the anticoagulant nurses (I was able to acess information about the patients without asking them)

- Saving time and leg-work for me (I did not have to localize hospital charts all the time)

- Preparing me before phoning patients

Status

- 250 patients have been included in the cross-sectional study, a database has been created and data analysis is ongoing
  - Multivariate statistics
- One year follow-up is ongoing
- About 70 cases and controls have been interviewed, a database is under construction

Study population (n = 250)

Median age (25-75 percentile)	65 (59 - 75)
Number of males	163 (65.2%)
Living alone	62 (24.8%)
Still working (including part-time)	64 (25.6%)

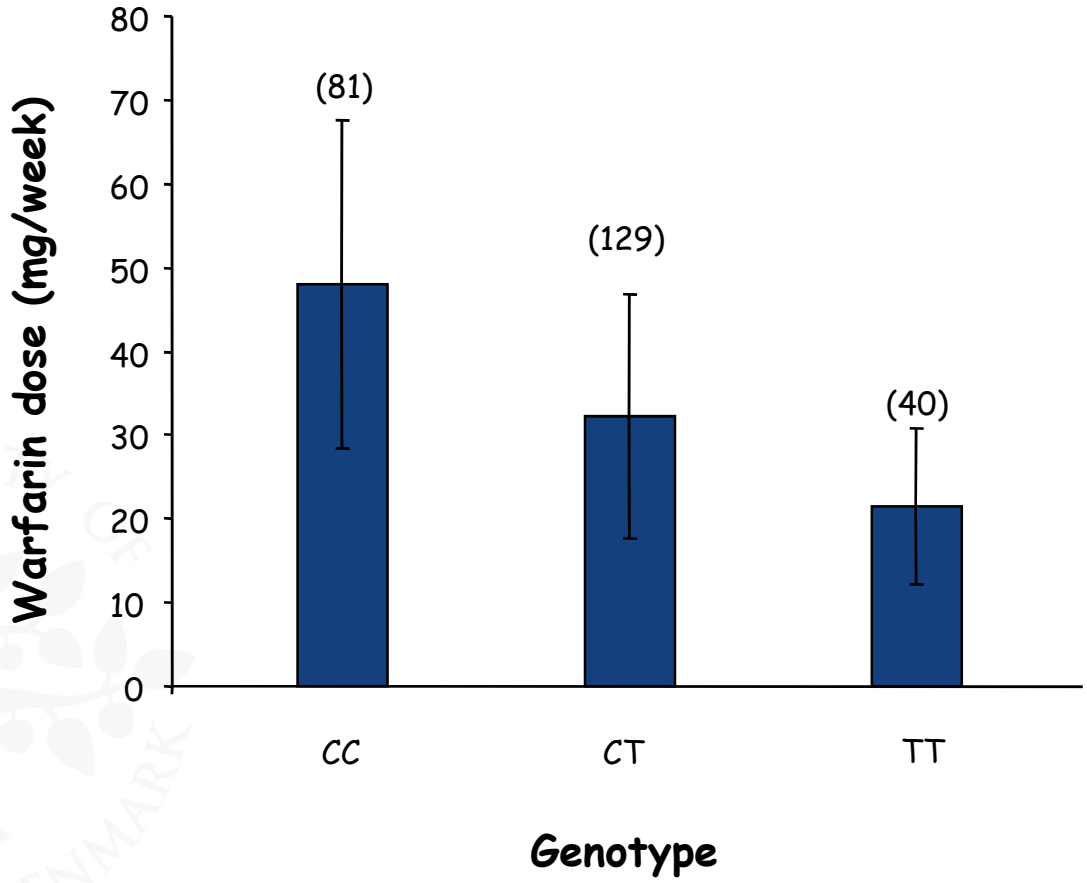
Number of patients by clinical indicatior

Atrial fibrillation	143 (57.2%)
Mechanical heart valve	30 (12%)
Deep vein thrombosis	43 (17.2%)
Pulmonary thromboembolism	26 (10.4%)
Other indications	8 (3.2%)

Number of patients by duration of treatment at the time of inclusion

Less than 3 months	34 (13.7%)
3 - 6 months	26 (10.4%)
6 – 12 months	50 (20.1%)
More than 12 months	139 (55.8%)

VKORC1 1173 and warfarin dose



Could DAWN be improved?

As a scientific tool:

- Enable us to search patients by project number
- Project information and treatment information in separate fields

In general

- Addition of information about genotype and co-medications

Acknowledgements

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