DAWN® AC
ANTICOAGULATION SOFTWARE

Using the Variability of INRs to Indicate the Risk of an Event in DAWN AC – Variance Growth Rate (VGR)

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It is widely agreed that neither the INR alone nor the % Time in Therapeutic Range (TTR) are dependable predictors of clinical events in patients receiving oral anticoagulation.

A new study, *'The clinical evaluation of International Normalised Ratio variability and control in conventional oral anticoagulant administration by use of the variance growth rate'* published by Poller, L., Ibrahim, S. and Jespersen, J. in the Journal of Thrombosis and Haemostasis looked at the possible value of an additional calculation (the variance growth rate (VGR)) as an addition to %TTR in predicting clinical events.

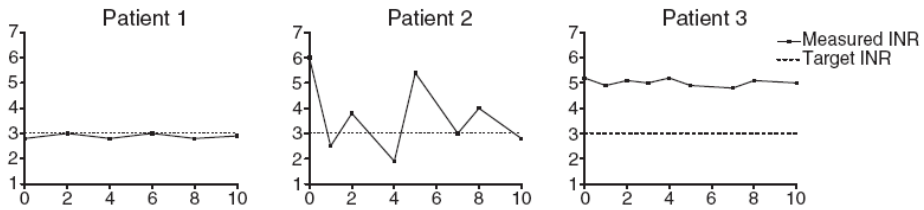
This study took data from a previous prospective multicentre randomised trial comparing DAWN AC computer aided treatment with experienced medical staff (*Poller L, et al. Multicentre randomised study of computerised anticoagulant dosage. Lancet. 1998, 352: 1505-09). In total, 661 control patients were matched to 158 event cases (bleeding, thromboembolism or death). The VGR and %TTR were measured over three time periods, overall follow-up; 6 months; and 3 months before an event.*

The VGR measurements look at the variability between the patient's INR values to determine how 'stable' they are.

Three methods for calculating the VGR were assessed within the study.

Method A measures the degree to which a patient's INR differs from their target INR over a prolonged period, whilst Method B1 measures the degree to which a patient's current INR differs from the previous one. Method B2 is a similar measure to Method B1 but with some minor differences to the denominator value, however, neither Method B1 nor B2 take into account how close the patient is to their target INR.

The following figures graphically illustrate the three methods.



Key Findings:

- %TTR is a reasonable predictor of clinical events only when calculated over the last three or six months of treatment

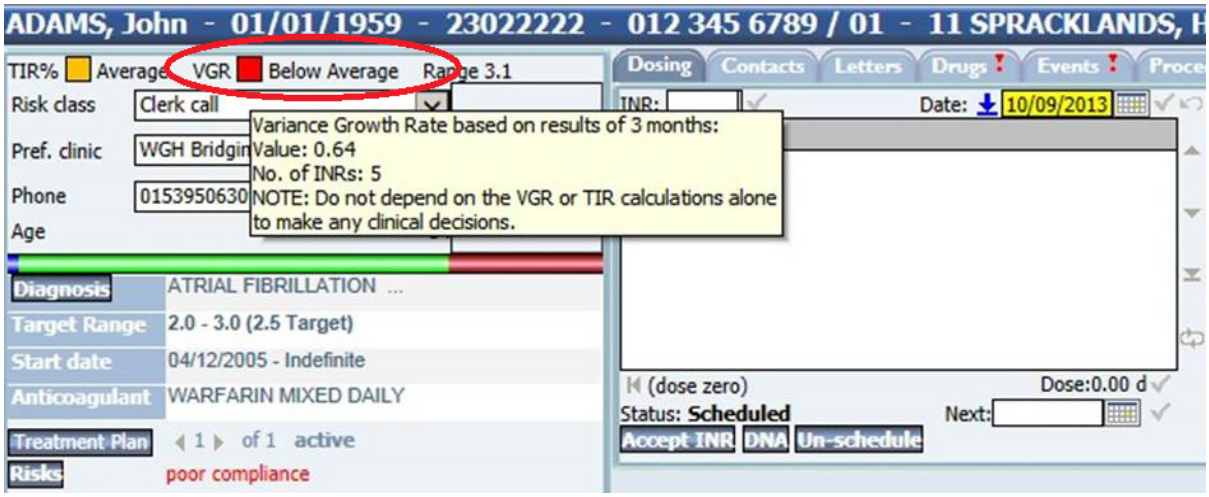
- %TTR showed no correlation with bleeding events when calculated over any period of treatment
- %TTR may be a predictor of thrombotic events when calculated over the last six months of treatment
- The Variance Growth Rate (VGR-A) showed a very strong correlation with clinical events when calculated over the last three or six months of treatment
- The Variance Growth Rate (VGR-A) showed a good correlation with bleeding events when calculated over the last three or six months of treatment
- The Variance Growth Rate (VGR-B1) showed a very strong correlation of bleeding events when calculated over the last three months of treatment
- The Variance Growth Rate (VGR-A) *may be* a reasonable predictor of thrombotic events when calculated over the last three months of treatment

It should be noted that there were very few thrombotic events, which made the prediction of events difficult to measure.

In conclusion, the study determined that INR monitoring with a measure such as the VGR and %TTR, three to six months before the current INR, may offer additional safety by detecting and isolating patients who may be at increased risk of possible adverse episodes.

It should be noted that a large prospective trial is needed to confirm the findings above.

As a result of the findings of the study, the 4S DAWN team have been developing the VGR calculation within DAWN AC as illustrated below:



This is available to customers now and is offered as an option, with users having the choice as to whether the VGR is displayed on the patient records.