DAWN® AC

ANTICOAGULATION SOFTWARE

Proceedings of the 26th DAWN AC User Group Meeting

London & Stoke

2018

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Patient questionnaires in referral and review processing

Amanda Pointon, Service Manager, Staffordshire Thrombosis and Anticoagulation Centre (STAC), Royal Stoke University Hospital

STAC is a comprehensive anticoagulation and DVT diagnosis centre that manages over 8000 patients on various forms of anticoagulation. The service offers Inpatient, Outpatient and Community anticoagulation services including DOAC and complex thrombosis clinics and has access to thrombosis and anticoagulation MDT's once a week for carrying out anticoagulation reviews.

STAC has worked closely with DAWN to incorporate two questionnaires into the system to help streamline processes and make them as automated as possible for efficiency and safety:

- New Patient Questionnaire
- Patient Review Questionnaire

QUESTIONNAIRE 1 - New Patient Questionnaire (NPQ)

Referrals are received electronically and the anticoagulation team then carries out additional checks that were previously done on a paper form. The old paper form was incorporated into DAWN as an NPQ questionnaire from January 2017.

For each new referral received, the administration team input the patient details into a new treatment plan in DAWN and then an NPQ is generated in the questionnaires tab on DAWN which gives a more detailed treatment plan for each patient.

Depending on the patient's diagnosis in the treatment plan, different boxes will open in the questionnaire for either: Venous Thromboembolism (VTE); Atrial Fibrillation (AF); Mechanical Heart Valve.

STAC took the current British Society for Haematology (BSH) guidelines for target range and duration and used them in the questionnaires to guide the team when processing a new referral.

The options selected within the questionnaire determine whether, at the end of the questionnaire, an MDT referral is required and, if so, this is automatically set within the DAWN system to prevent any patients who should be referred for an MDT review being missed.

Members of the STAC team can also input relevant clinical information, co-morbidities and document potential problems. The weight of the patient and baseline bloods within the last 8 weeks are required and, if these are not available, they are requested from the referrer.

If a patient is on antiplatelets then information about the indication for antiplatelets is required, if it can be discontinued once the patient is anticoagulated, or if it is to continue then the reason for this needs to be included.

Recommended treatment plan details are then added and the anticoagulation is selected. The team also record whether the patient has been referred to the Thrombosis MDT and the recommended review date which is automatically scheduled in DAWN.

The first section of the questionnaire is different depending on the patient's diagnosis in the DAWN treatment plan:

Diagnosis: VTE

Questionnaire (Pointon Amanda # / 123456789) - New record

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STAFFORDSHIRE THROMBOSIS & ANTICOAGULATION CENTRE

NEW REFERRAL FOR ANTICOAGULATION

Ref Date | Ref Dr | GP/Cons | Ref Loc

Diagnosis: ◉ Venous Thromboembolism ○ Atrial Fibrillation ○ Mechanical Heart Valve ○ Other

Venous Thromboembolism

Select	Site/Provocation	Target	Duration	MDT Referral
○	First Provoked Proximal DVT/PE	2.5	3 months	
○	First Unprovoked DVT/PE	2.5	3 months (consider long-term)	required
○	Recurrent VTE (not on anticoagulation)	2.5	consider long-term	required
○	Recurrent VTE (on therapeutic anticoagulation)	3.5	long-term	required
○	Distal DVT	2.5	3 months	
○	Cancer Associated VTE	Dalteparin preferred		
○	Unusual site thrombosis	Provide clinical details; individualised treatment		required
○	Others	Specify; individualised treatment plan		

Relevant clinical information (including co-morbidities)

Potential Problems

☐ Alcohol or drug abuse ☐ District nurse or transport for blood tests ☐ Dosette box or problems with self-administration

Indication for continuing antiplatelets

Comments

Show Indications

Contraindications and Risks

No contraindication to anticoagulation ☐ Show list Comments

Recommended Treatment Plan

Treatment Plan Date 13/09/2017 Approved by (prescriber only): Reviewed By: Amanda Pointon (BMS)

○ Warfarin ○ Directoral anticoagulant ○ Dalteparin ○ No Anticoagulation

Prescriber instructions / follow-up advice

End date of anticoagulation:

Patient referred to Thrombosis MDT ○ Yes ○ No

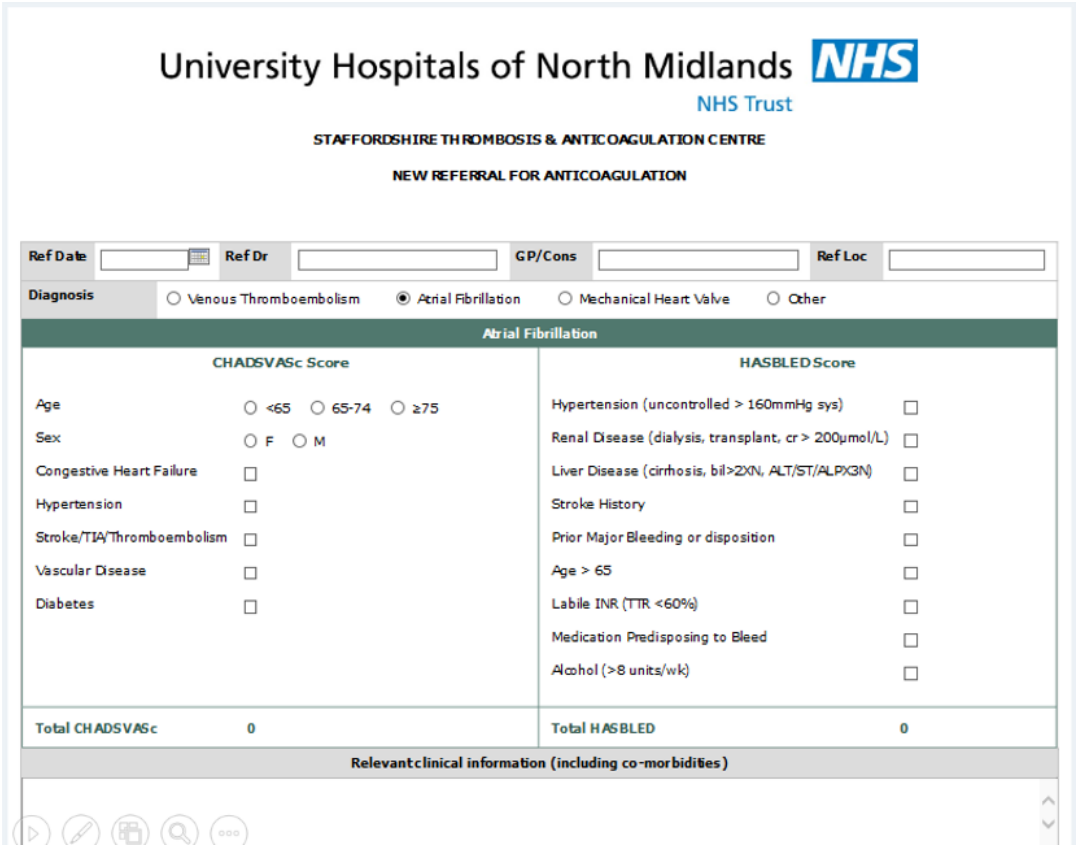
Recommended review date ○ 3 mo ○ 6 mo ◉ 12 mo ○ None
13/09/2018

Recommendation for GP

Print GP and Patient Letter ☐ Blood test prior to review ☐

Approver Feedback/Comments

Diagnosis: Atrial Fibrillation



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NHS Trust

STAFFORDSHIRE THROMBOSIS & ANTICOAGULATION CENTRE

NEW REFERRAL FOR ANTICOAGULATION

Ref Date | Ref Dr | GP/Cons | Ref Loc

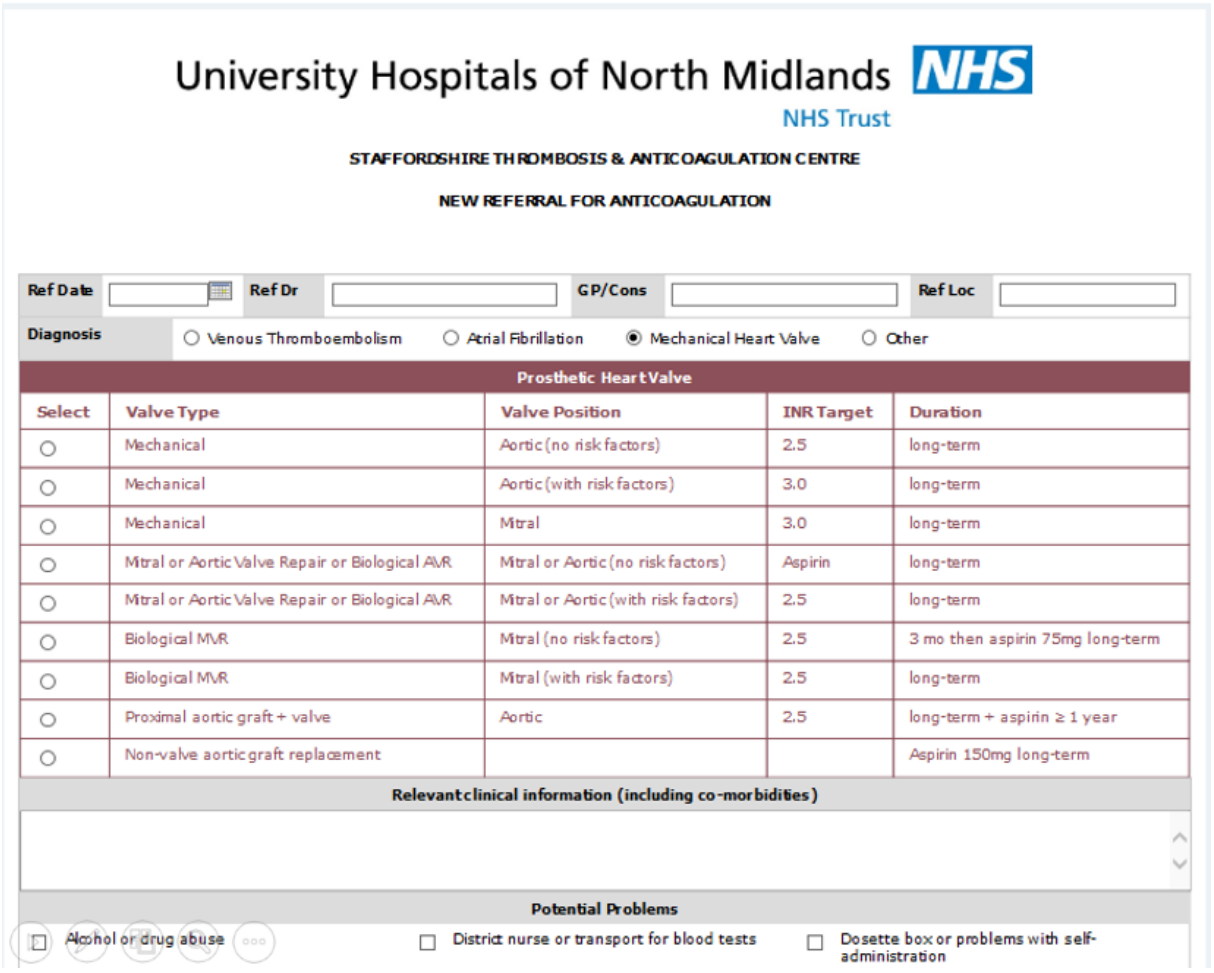
Diagnosis: ○ Venous Thromboembolism ◉ Atrial Fibrillation ○ Mechanical Heart Valve ○ Other

Atrial Fibrillation

CHADSVASc Score		HASBLED Score	
Age	○ <65 ○ 65-74 ○ ≥75	Hypertension (uncontrolled > 160mmHg sys)	☐
Sex	○ F ○ M	Renal Disease (dialysis, transplant, cr > 200µmol/L)	☐
Congestive Heart Failure	☐	Liver Disease (cirrhosis, bil>2XN, ALT/ST/ALPX3N)	☐
Hypertension	☐	Stroke History	☐
Stroke/TIA/Thromboembolism	☐	Prior Major Bleeding or disposition	☐
Vascular Disease	☐	Age > 65	☐
Diabetes	☐	Labile INR (TTR <60%)	☐
		Medication Predisposing to Bleed	☐
		Alcohol (>8 units/wk)	☐
Total CHADSVASc	0	Total HASBLED	0

Relevant clinical information (including co-morbidities)

Diagnosis: Mechanical Heart Valve



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STAFFORDSHIRE THROMBOSIS & ANTICOAGULATION CENTRE

NEW REFERRAL FOR ANTICOAGULATION

Ref Date | Ref Dr | GP/Cons | Ref Loc

Diagnosis: ○ Venous Thromboembolism ○ Atrial Fibrillation ◉ Mechanical Heart Valve ○ Other

Prosthetic Heart Valve

Select	Valve Type	Valve Position	INR Target	Duration
○	Mechanical	Aortic (no risk factors)	2.5	long-term
○	Mechanical	Aortic (with risk factors)	3.0	long-term
○	Mechanical	Mitral	3.0	long-term
○	Mitral or Aortic Valve Repair or Biological AVR	Mitral or Aortic (no risk factors)	Aspirin	long-term
○	Mitral or Aortic Valve Repair or Biological AVR	Mitral or Aortic (with risk factors)	2.5	long-term
○	Biological MVR	Mitral (no risk factors)	2.5	3 mo then aspirin 75mg long-term
○	Biological MVR	Mitral (with risk factors)	2.5	long-term
○	Proximal aortic graft + valve	Aortic	2.5	long-term + aspirin ≥ 1 year
○	Non-valve aortic graft replacement			Aspirin 150mg long-term

Relevant clinical information (including co-morbidities)

Potential Problems

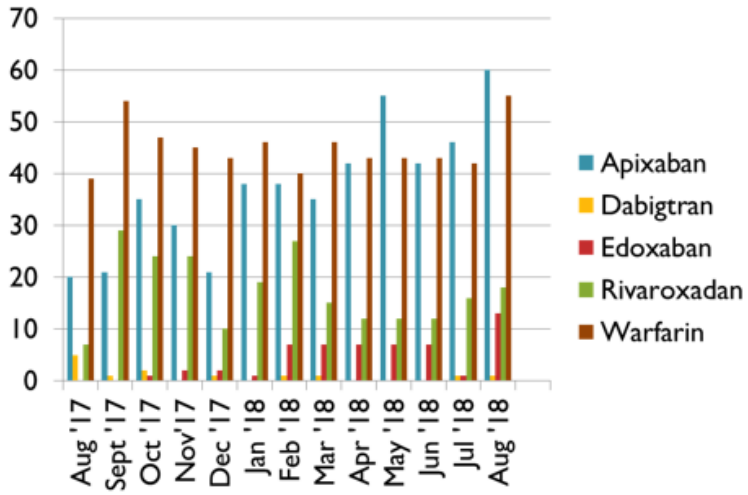
☐ Alcohol or drug abuse ☐ District nurse or transport for blood tests ☐ Dosette box or problems with self-administration

Once the anticoagulation nurse has completed the NPQ they tick the 'Referred for Approval' tab at the end of the questionnaire and this then gets added to a 'Status - For Approval' list view in DAWN that either the Haematology Consultant or Registrar works through to approve the treatment plans and add comments where necessary.

Approved NPQs are then automatically moved to a 'Status – New Referral Approved' list view for the nurses who can make amendments to the treatment plan based on any approver comments and make a counselling appointment for the patient.

A new patient letter is then generated automatically in DAWN that pulls the relevant information from the NPQ and sends it to both the patient and their GP.

A report in DAWN collates the information in the NPQs for data analysis, e.g. Anticoagulation type:



QUESTIONNAIRE 2 - Patient Review Questionnaire

Two years ago, STAC were tasked with completing the anticoagulation annual reviews for all the patients under the service, as per NICE recommendations. Prior to this, the annual reviews were completed by the GPs.

Around 15 GPs deliver anticoagulation services under a subcontract arrangement with STAC and access the DAWN system to manage their patients including their annual reviews, approximately 2000 patients. This left STAC with 6,000 patients that now needed an annual review.

With such a large undertaking, STAC worked with DAWN to develop a questionnaire template to streamline and document the annual review process.

For most patients, telephone reviews are held, however face to face reviews are available for any patients who don't want a telephone review.

Prior to the telephone review:

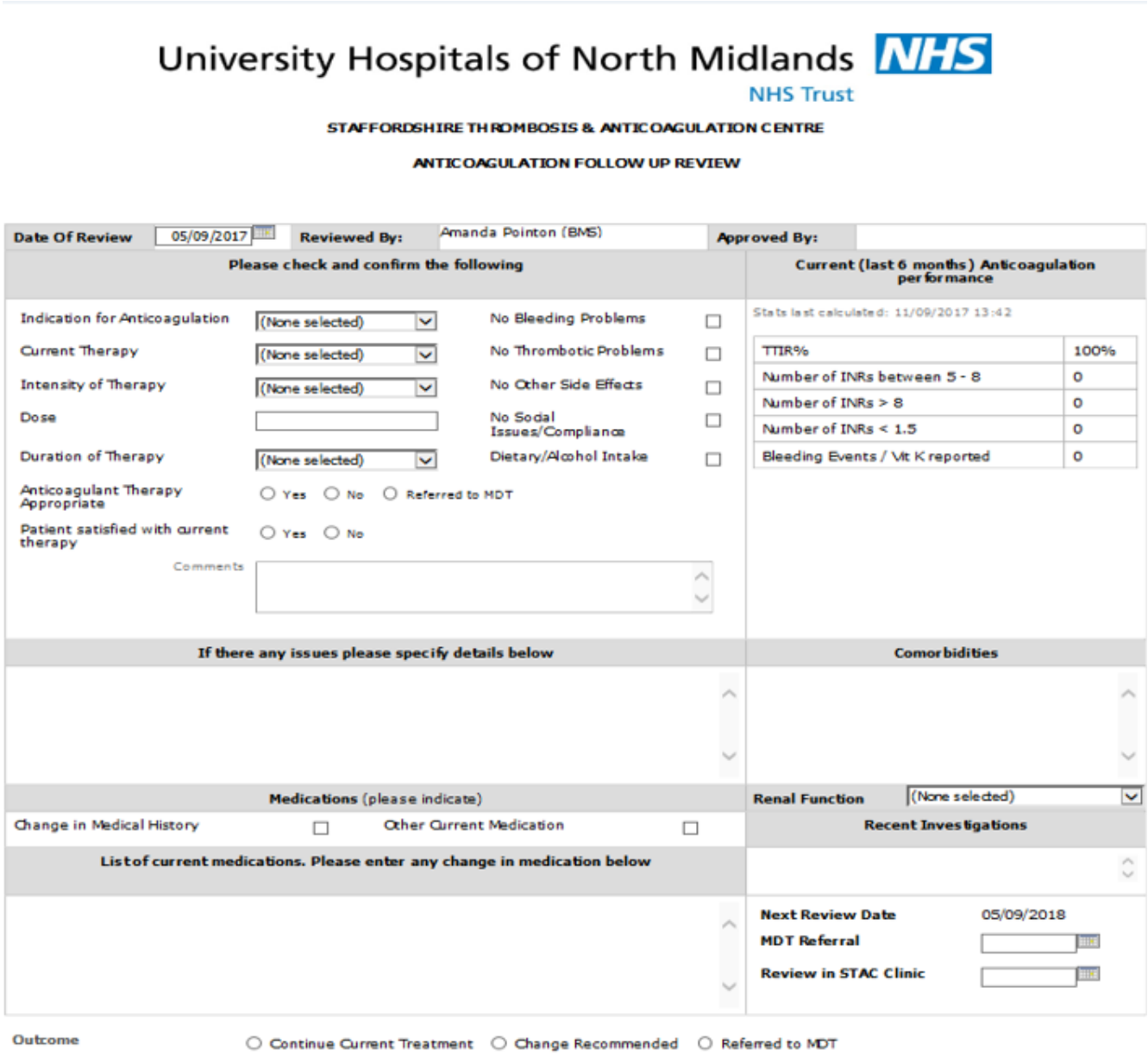
- The clerical team schedule the review, working through the review tab in DAWN that shows all patients with a follow up review due in the next 4 weeks
- A letter is sent to the patient with a blood test form for FBC, LFT and CRE and a date and 3-hour time window for the telephone review
- A letter also goes to the patient's GP requesting an up to date list of medication and Co-Morbidities to be sent for new patients
- The follow up review in DAWN is then changed to Telephone Annual review AM or PM and the date that this review is scheduled for. This informs the team that the patient has had a letter regarding their review and one is scheduled
- The nursing team perform 20 reviews in the morning and 20 in the afternoon

Checks before the telephone review:

- One week before the telephone review, the clerical team check the patient has had their bloods done and updates DAWN with drugs and co-morbidities from the GP.
- If this information is not available, it is chased up by the team via a phone call
- The Follow Up Review Questionnaire is then opened in DAWN and this automatically imports any drugs and co-morbidities directly into the questionnaire
- A few days before the review the Nursing team input the blood results onto the Follow Up Review Questionnaire – only those that are abnormal/out of range are input into the questionnaire

On the day of the review:

- Anticoagulation Nurse Specialists (ANS) work through the list view review tab for Telephone reviews due on that day
- For each patient, the nurse opens the Follow Up Review Questionnaire and works through it with the patient.



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STAFFORDSHIRE THROMBOSIS & ANTICOAGULATION CENTRE

ANTICOAGULATION FOLLOW UP REVIEW

Date Of Review 05/09/2017 Reviewed By: Amanda Pointon (BMS) Approved By:

Please check and confirm the following

Indication for Anticoagulation (None selected)
Current Therapy (None selected)
Intensity of Therapy (None selected)
Dose
Duration of Therapy (None selected)
Anticoagulant Therapy Appropriate Yes No Referred to MDT
Patient satisfied with current therapy Yes No
Comments

No Bleeding Problems
No Thrombotic Problems
No Other Side Effects
No Social Issues/Compliance
Dietary/Alcohol Intake

Current (last 6 months) Anticoagulation performance

Stats last calculated: 11/09/2017 13:42

TTIR%	100%
Number of INRs between 5 - 8	0
Number of INRs > 8	0
Number of INRs < 1.5	0
Bleeding Events / Vit K reported	0

If there any issues please specify details below

Comorbidities

Medications (please indicate)

Change in Medical History Other Current Medication

List of current medications. Please enter any change in medication below

Renal Function (None selected)

Recent Investigations

Next Review Date 05/09/2018
MDT Referral
Review in STAC Clinic

Outcome Continue Current Treatment Change Recommended Referred to MDT

The patient's anticoagulation performance is pulled in automatically from DAWN. If the TTR is <65% with no clear reason for this then DOACs are discussed, if they are licensed for the indication. Information is sent to the patient regarding DOACs and an appointment to switch is made if the patient requests this.

Co-morbidities and drugs are also automatically imported straight from the tabs in DAWN into the questionnaire.

The next review interval is set for either 3, 6 or 12 months and this automatically sets a review date in DAWN for the follow up review and the process is repeated.

Letters are then generated in DAWN and sent to the patient and the GP informing them that their patient has had an anticoagulation review and a copy of the questionnaire is included.

To conclude:

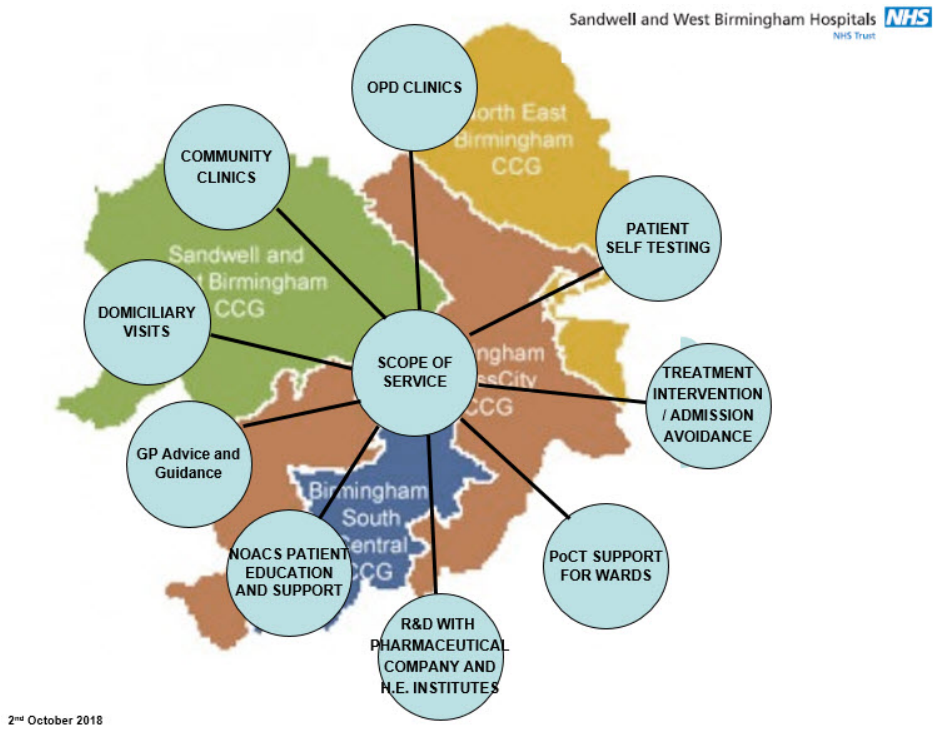
- By working closely with DAWN to develop these 2 bespoke questionnaires it has enabled streamlining of the processes, making them safe and auditable
- DAWN have developed reports which collate all the information from the NPQ and follow up review and these can then be imported into an excel spreadsheet for data analysis
- The service perform approximately 700 follow up reviews each month and receive just over 100 new anticoagulation referrals each month
- A change in anticoagulation is recommended for approximately 10% of patients
- The term ‘annual review’ is no longer used as over 50% of patients are reviewed more frequently

Tendering for a new contract and anticoagulation at the drop of a hat

Joanne Malpass & Victoria Atherton, Anticoagulation Services, Sandwell and West Birmingham Hospitals NHS Trust (SWBH)

The anticoagulant service at SWBH looks after around 5,000 patients and is made up of a multidisciplinary team of Biomedical Scientists (BMS), Nurses, Senior Assistant Technical Officers (SATO) and Administrators, with a Consultant Lead. Previously the service sat under Pathology but now sits under primary care.

Scope of SWBH Anticoagulant Service:



Funding

Most services are funded through Nationally Agreed tariffs (PbR) that were set up in 2003 with the government promoting choice and more competition within the NHS.

Services are also funded through Locally Agreed Tariffs and SWBH get paid on a cost per case basis, so payment by activity – every time the service sees a patient, they get a payment – and there are different

tariffs for different types of patient contact e.g. new patient, follow-up, whether prescribing was involved etc. This approach still has tolerances and caps associated with it to ensure that services stay within a budget.

Any Qualified Provider (AQP)

A 2012 NHS initiative saw Local Enhanced Services (LES) withdrawn as CCGs became active and searched for new ways to commission services. One of the options was the concept of AQP.

What are the aims of AQP?

- Improve choice and access to services – non-NHS providers were encouraged to bid for contracts
- Improve quality and outcomes
- Drive innovation and efficiency – by incentivising the competition

What does AQP mean for providers?

- Must meet rigorous quality requirements
- Terms and conditions of NHS contract all have to be met
- Accept tariff for service – no negotiation – set figure per patient per year regardless of whether they attend twice or fifteen times each year
- Price is the same for all providers
- Provide assurances of delivery of service specification – each provider has to meet the service specification
- A no volume and no income guarantee contract

A local engagement event hosted by the CCG invited AQPs to attend and provide feedback on where the process failed previously. Following this, the CCG announced that the next round of AQP contracts were due.

Step 1: Expressions of Interest were requested for AQP provision
Step 2: Complete Submission and provide questions to show that the service meets the specifications
- Responses around Workforce, Licensing and regulations, Clinical Governance pathway etc

Step 3: Review by CCG

Timeline

Task	Complete by
AQP published	01st June 2018
Deadline for receipt of clarification questions from bidders	1700hrs 20th June 2018
Deadline for submission of AQP response	1700hrs 02nd July 2018
ITT Evaluation (inc CCG Approval)	31st July 2018
Notification of outcome to bidders	01st August 2018
Standstill period	13th August 2018
Contract award & Agreement	31st August 2018
Service start	01st December 2018

As of the beginning of October 2018, there is still no confirmation as to who the providers are.

What did SWBH learn?

1. **Support and expertise required as no longer directly part of the Trust**
   - Business Development Team – helped with contract and finding information
   - Specialist knowledge – called upon within the Trust to assist with responses to contract requirements and tender submission
   - Interpretation of service specification – help with understanding exactly what the specification was asking of the service to ensure accurate responses in place
   - Expectations of CCG
   - TIME – biggest factor – getting through the process and completing relevant documentation

2. **Large financial risk associated with AQP contracts**
    - No guarantee of activity or income – have to go out and find the work for the service
    - Set up costs included in the contract – no additional money
    - Business case was required for moving forward as an AQP
    - Accurate capture of activity – due to the service having a range of different contracts across different CCGs, all of them want different information about their patient population
    - Marketing costs – posters, business cards etc to attract patients into clinics – no additional money for promoting the service
    - Loss of income – patient could easily change provider – possibly move to a closer GP surgery who has started offering a service as part of the AQP scheme
    - Administration costs – the service wants patient numbers to increase but at the same time, this attracts substantial administrative work. No money allocated for that under the AQP contract

3. **Operational Considerations**

    Fragmented care
    - Differing care pathways **across** consortia – which CCG you are covering and what they are expecting from you as this differs across territories
    - Differing care pathways **within** consortia – AQP contracts in place but the SWBH service also still have a standard contract in place for complex patients because AQPs were aimed at non-complex patients

    Workforce
    - Skill mix – prior to AQP the service was mainly run by biomedical scientists and due to prescribing issues, the service now employs more nurses
    - Resilience built into the service – to take account of staff turnover and the difficulty in attracting non-medical prescribers. 5 nurses now trained to prescribe.
    - Lots of administration work – apprentices to help with the admin workload

    Change management has been the biggest issue
    - Service users
    - Workforce

    Capacity and Demand
    - No guarantees of income or activity and no idea how many patients the service will attract but need to ensure that the service can handle the demand should it grow.

Anticoagulation at the Drop of a Hat

During preparation of the tender response for the CCG's AQP specification, the current provider served a one month notice to stop their anticoagulation service. An expression of interest to provide an intermediate Anticoagulant Service was sent out from the CCG that outlined the clinic locations, number of patients and a very short timeline, only two months to complete the process and start delivering the intermediate service.

SWBH were interested in providing the intermediate service but first had to consider a number of key factors:

- Location of clinics
    - Could the service cover the clinics, some were 40-50 minutes from where the service is based
- Staffing – TUPE of Staff
    - A requirement to take on some of the staff from the previous provider. A new area of legalities that the service had to consider
- Number of patients
    - Approximately 900 more patients to take on within two months
- Days and times of clinics
    - Previous AQP provider was non-NHS and ran clinics 9-5, Mon-Fri. SWBH service as an NHS provider with other patient cohorts to serve couldn't commit to this and so had to look at changing days and times
- Dosing software and patient data
    - Previous provider used a different software to SWBH so there was the logistics of moving the data across to the DAWN system.

- Communication to patients and stakeholders
    - How would SWBH service communicate to all stakeholders regarding a new provider, new dates and times for clinics etc

What happened next?

SWBH's expression of interest was submitted to the CCG and they were awarded the intermediate contract. A patient data transfer agreement was drawn up and patients and service users were notified of the change in provider through letters sent from the CCG and the current provider.

Clinic locations and times were then agreed for the service and the data transfer began which involved data moving from the current provider to SWBH Anticoagulation service, pathology IT and then onto DAWN. There were differences between the two pieces of dosing software and so the data transfer was not a simple process:

- Creation of a patient record in DAWN
- Spreadsheets galore!
- Clinic changes, appointments and patient choice

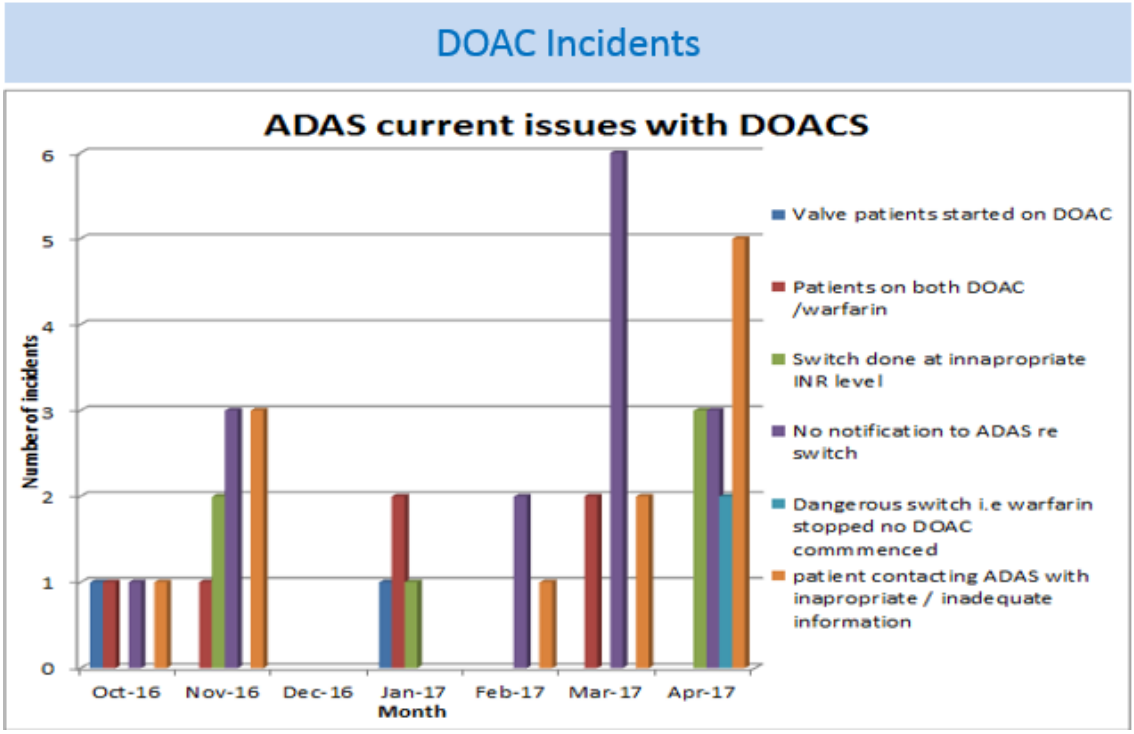
Learning curve…..

- What have we learnt from the process?
    - Communication is key! Between SWBH, current service provider and stakeholders from the very beginning
    - Cross reference everything
    - Production plans … now attend Trust meetings to discuss planned care once a week
    - Legalities
    - Patience!

DAWN of the DOACs: Part II

Bev Straker-Bennett & Sean O'Brien, Senior Anticoagulation Practitioners, Anticoagulation Dosing Advice Service (ADAS), Blackpool Teaching Hospitals NHS Foundation Trust

At the 2017 DAWN AC UK User Group, ADAS presented on the issues that they had come across with DOACs being prescribed to the patient population by primary care and other hospital departments, and their subsequent plan and approach to the CCG for ADAS to take on the secondary care prescribing of DOACs.



The uptake of DOACs in the Fylde Coast was very slow initially but eventually saw sudden growth in DOAC prescribing which led to patients turning up at ADAS clinics not knowing why they had been switched and with various other issues that ADAS struggled to deal with due to their full capacity warfarin clinics.

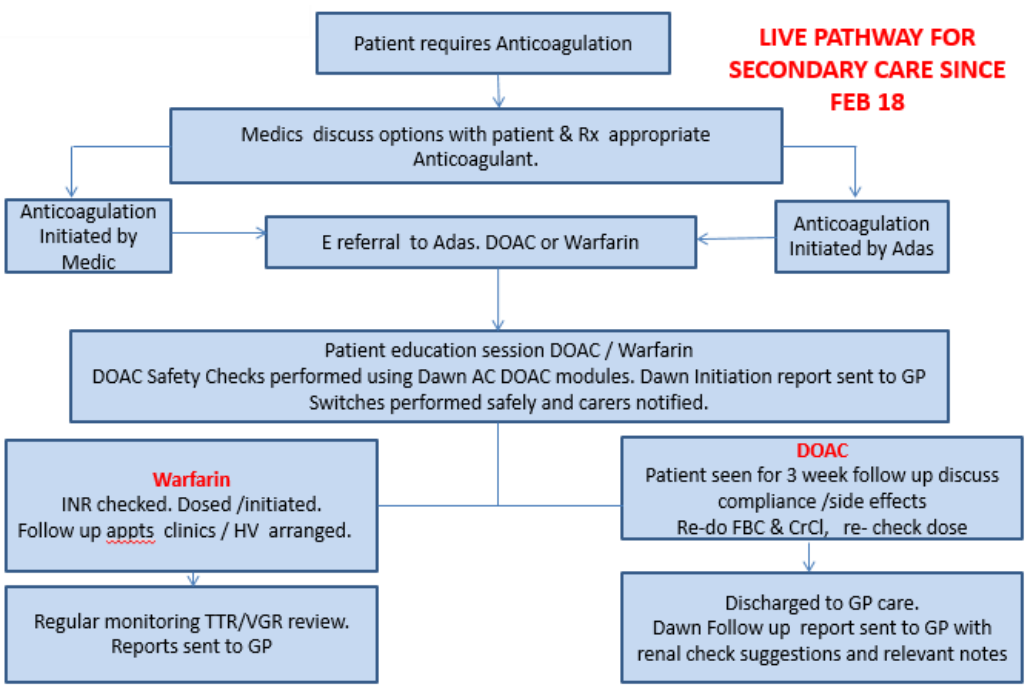
After a patient attended clinic who, as an inpatient, had been prescribed 15mg Rivaroxaban and discharged without education, then continued to take it after being discharged along with 15mg of warfarin that they were taking prior to being an inpatient, ADAS decided it was time to add DOACs to the Trust's risk register and began to highlight other recurring issues to the Trust:

- Variation in initiation between medics both primary and secondary care.
- Inconsistent levels of education provided to patients.
- Patients presenting at ADAS clinics asking for advice.
- Patients prescribed a DOAC with contraindications.
- Patients taking both warfarin and a DOAC.
- Switches done without renal bloods or INR checks. NICE guidance not followed.
- Switches done when INR is above recommended level, introducing bleeding risks.
- Patients on the wrong doses of DOACs with no follow up checks.
- GP's / nurses phoning ADAS for DOAC advice and switch assistance.

As a result, ADAS produced a pathway that was then presented to secondary care initially so that the issues within secondary care could be dealt with first.

The ADAS service is all BMS run so there are no prescribers. As such, ADAS patients are those who have already gone through the process of being started on Warfarin or a DOAC.

This pathway was presented to secondary care and has now been running since the start of February 2018.



These changes were a complete shift in what ADAS was currently used to in terms of dosing warfarin patients, educating them and managing them via the DAWN AC software.

Incorporating DOAC management into the service's remit was also a big training curve for the ADAS team with a lot to learn. There is now a specialist team of 5 trained anticoagulant practitioners with a variety of protocols in place. Training for the team included Warwick Anticoagulant Masterclasses / in house training and Pharma company presentations at training mornings.

The DAWN DOAC modules were installed onto the system in preparation for the new pathway starting.

As the ADAS Service weren't aware how many referrals would be received, this pathway was started with secondary care only to avoid an unmanageable influx of DOAC referrals and to deal with the issues and risks that were highlighted in secondary care.

An e-referral app within the Trust's hospital system enabled ADAS to add a 'DOAC e-referral form' that mirrors the DAWN DOAC modules so that all of the required information is provided as part of the referral. ADAS decide when to see the patients, medics do not book appointments, and patients are currently seen within 1 week of the referral being made. These patients have already been initiated on their DOAC treatment.

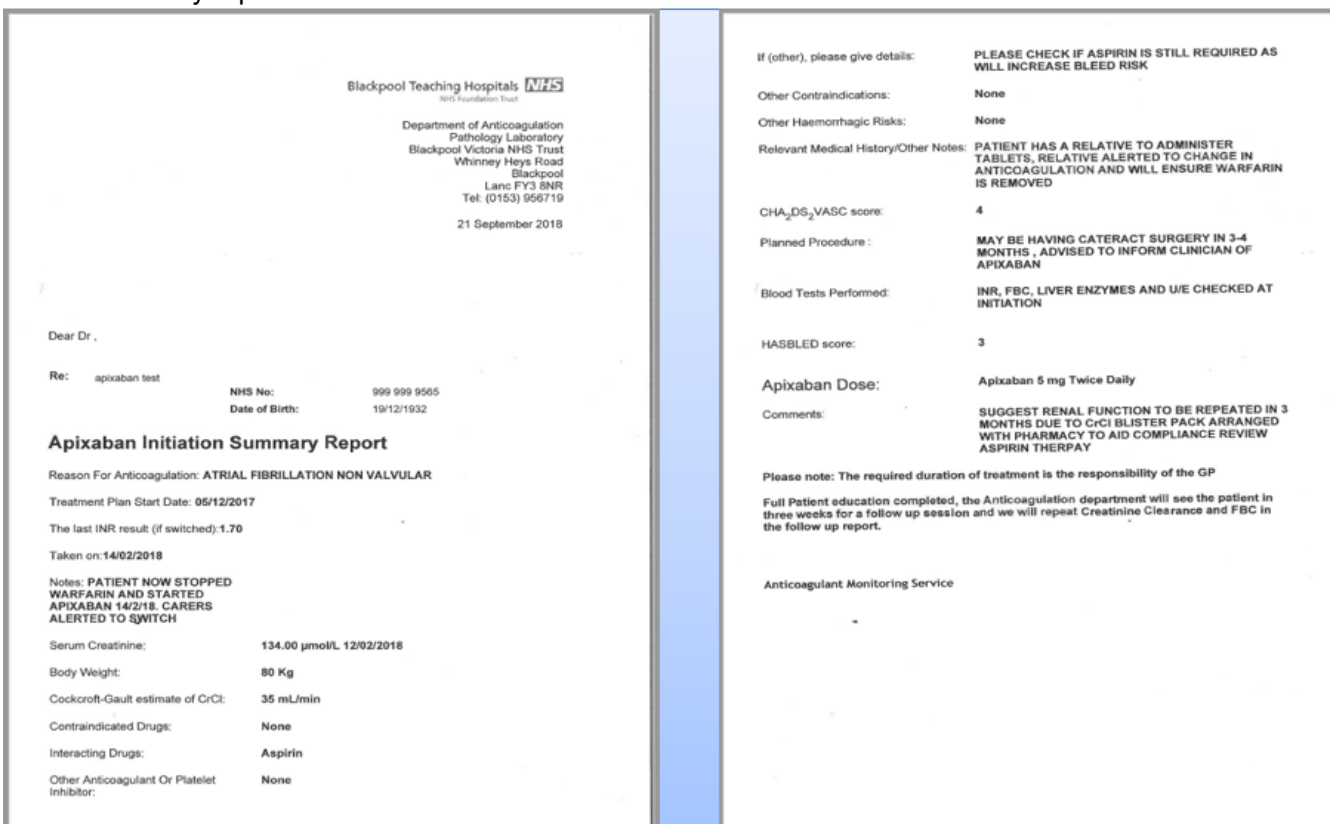
The DOAC sessions run 3 days per week at a Primary Care centre and provide 30-minute sessions for DOAC initiation that includes a lot of safety work and the DAWN modules are used during each of these sessions. DOAC diaries are managed via a DOAC specific list view in DAWN.

A training proforma is used to provide a scripted standard approach to patient education so that each patient receives the same level and quality of education regarding DOACs. The training proforma is signed by the patient, scanned into the DAWN system and added to the patient record to provide an auditable record of training.

Follow up appointments are then set for 3 weeks after the initiation session to check compliance issues and that patients are OK on the DOACs.

ADAS are seeing around 15 new DOAC referrals per week and currently, after the 3 week follow up, patients are discharged to their GPs care along with a DOAC report which contains a summary of the key elements of the DAWN DOAC questionnaire and any issues or concerns. Again, this provides an auditable record of the communication with the GP.

DOAC summary report:



Blackpool Teaching Hospitals NHS
NHS Foundation Trust

Department of Anticoagulation
Pathology Laboratory
Blackpool Victoria NHS Trust
Whinney Heys Road
Blackpool
Lanc FY3 8NR
Tel: (0153) 956719

21 September 2018

Dear Dr ,

Re: apixaban test
NHS No: 999 999 9565
Date of Birth: 19/12/1932

Apixaban Initiation Summary Report

Reason For Anticoagulation: **ATRIAL FIBRILLATION NON VALVULAR**

Treatment Plan Start Date: **05/12/2017**

The last INR result (if switched):**1.70**

Taken on:**14/02/2018**

Notes: **PATIENT NOW STOPPED WARFARIN AND STARTED APIXABAN 14/2/18. CARERS ALERTED TO SWITCH**

Serum Creatinine:	**134.00 µmol/L 12/02/2018**
Body Weight:	**80 Kg**
Cockcroft-Gault estimate of CrCl:	**35 mL/min**
Contraindicated Drugs:	**None**
Interacting Drugs:	**Aspirin**
Other Anticoagulant Or Platelet Inhibitor:	**None**

If (other), please give details:	**PLEASE CHECK IF ASPIRIN IS STILL REQUIRED AS WILL INCREASE BLEED RISK**
Other Contraindications:	**None**
Other Haemorrhagic Risks:	**None**
Relevant Medical History/Other Notes:	**PATIENT HAS A RELATIVE TO ADMINISTER TABLETS, RELATIVE ALERTED TO CHANGE IN ANTICOAGULATION AND WILL ENSURE WARFARIN IS REMOVED**
CHA_2DS_2VASC score:	**4**
Planned Procedure :	**MAY BE HAVING CATERACT SURGERY IN 3-4 MONTHS , ADVISED TO INFORM CLINICIAN OF APIXABAN**
Blood Tests Performed:	**INR, FBC, LIVER ENZYMES AND U/E CHECKED AT INITIATION**
HASBLED score:	**3**
Apixaban Dose:	**Apixaban 5 mg Twice Daily**
Comments:	**SUGGEST RENAL FUNCTION TO BE REPEATED IN 3 MONTHS DUE TO CrCl BLISTER PACK ARRANGED WITH PHARMACY TO AID COMPLIANCE REVIEW ASPIRIN THERPAY**

Please note: The required duration of treatment is the responsibility of the GP

Full Patient education completed, the Anticoagulation department will see the patient in three weeks for a follow up session and we will repeat Creatinine Clearance and FBC in the follow up report.

Anticoagulant Monitoring Service

Since starting the new pathway in February, ADAS have made 36 interventions where patients were at risk and the issues potentially wouldn't have been picked up by anyone outside of ADAS.

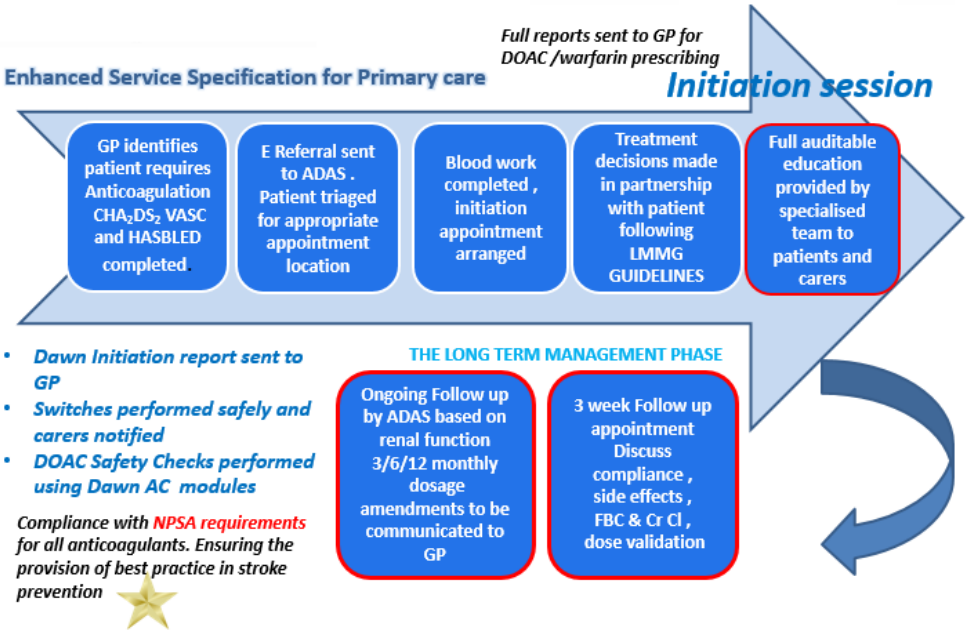
Patient Satisfaction

At the end of each follow up session, patients receive a feedback form so that ADAS can measure how they are doing. Given that this element of the service is new, the feedback received from patients is very positive.

	Definitely helped	Already understood condition/ medication	Didn't really help
Q1. Do you feel the DOAC education session helped you to understand your condition better?	96%	4%	0
Q2. Do you feel the DOAC education session helped you to understand your anticoagulant medication better?	100%	0	0
	Yes	Not Sure	No
Q3. Did you find the follow up session useful and feel reassured about your therapy?	100%	0	0
	Very Satisfied	Satisfied	Dissatisfied needs improvement
Q4. Could you rate your level of satisfaction on the ADAS staff, were they polite, efficient and helpful at your visit?	100%	0	0

ADAS Action Plan

- All interventions are monitored and audited so that ADAS can report back to the Trust who want to know how ADAS are progressing with the pathway.
- Continuing medic training for the pathway to raise awareness internally with doctors to increase referrals.
- The risk assessment was initially scored at 15 and was added the Trust's risk register. This has now reduced and will reduce further if primary care are included in the next stage of the pathway.
- Request from CCG for ADAS to revise the current service specification to include primary care referrals based on current service.
- CCG options appraisal to include ADAS to provide initial discussion and suggest appropriate anticoagulant based on CCG AF guidelines.
- The image below shows what ADAS have put together at the request of the CCG for a fully managed, comprehensive DOAC service in the future, covering both primary and secondary care



A year in quality management: applying principles of ISO15189 to anticoagulant services

Brad Dickinson, Advanced Biomedical Scientist, The Leeds Teaching Hospitals NHS Trust

The Anticoagulation Service was originally under the umbrella of Pathology but now sits under Clinical Haematology as a nurse-led service. Having worked across both Anticoagulation and Quality it was clear that many of the ISO standards for medical laboratories, could be applied to anticoagulation services.

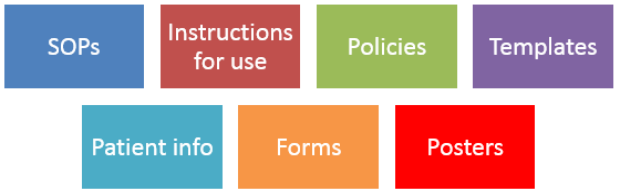
> "Medical laboratory services are essential to patient care and therefore have to be available to meet the needs of all patients and the clinical personnel responsible for the care of those patients.
>
> Such services include arrangements for examination requests, patient preparation, patient identification, collection of samples, transportation, storage, processing and examination of clinical samples, together with subsequent interpretation, reporting and advice, in addition to the considerations of safety and ethics in medical laboratory work."

Elements of ISO15189 / ISO9001 are applicable to good practice in Anticoagulant Services:

- Document control
- Identifying and controlling non-conformities
- Equipment, reagents and consumables
- Laboratory information management

Document Control

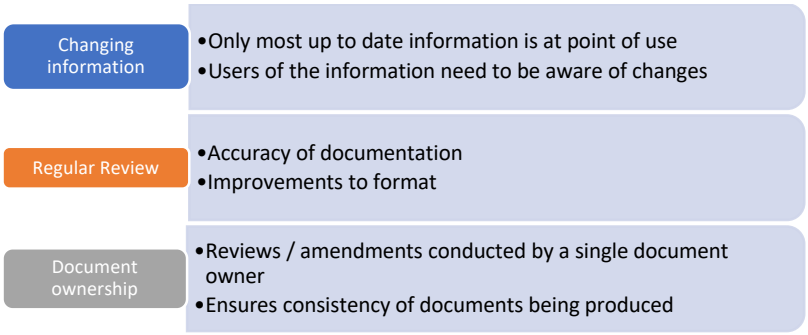
The laboratory shall control documents required by the quality management system and shall ensure that unintended use of any obsolete document is prevented.



This means that documents need to be reviewed regularly to ensure they are still suitable and anything that is out of date/obsolete should be removed from use. All documents must reflect current practice, be authorised for use by a qualified member of personnel and be made available at the point of use and accessible as required.

Document control systems need to be in place for both hard copy and electronic documents with any hard copies being manually collected and replaced when updated or removed.

Review dates should also be stated for all documents including having in place a way of monitoring these reviews. In addition, SOP folders should contain signed, authorised versions of procedures, whilst there also needs to be a means of communicating changes.



Identification and Control of Non-Conformities

These are not just issues with procedures, they can cover a range of topics:

The system at Leeds for controlling non-conformities is quite complex with a number of different forms that need to be completed depending on where the non-conformity is found e.g. whether it was highlighted in an audit, whether it came from quality assurance and control, staff, health & safety, risk assessments etc. Work is ongoing to improve the system and condense it into a single report.

For anything that affects patient safety and patient care, a system is in place (DATIX) that can be accessed from any primary care facility or hospital within the Trust so that incidents can be reported and go to a named person to review it accordingly.

Key functions of the DATIX system:

Non-Conformance Report Forms are based around the DATIX structure and are used for items such as problems with deliveries, IT issues, processing within the laboratory etc. These forms include a summary of what went wrong, what remedial action was taken to fix the issue at the time, a risk score and a basic root cause analysis. Identification of a root cause then prompts the completion of what corrective action is required to address the root cause.

Evaluations and audits are also able to highlight non-conformances and, within the ISO standards, the following is expected:

- Demonstrate that the pre-examination, examination and post-examination and supporting processes are being conducted in a manner that **meets the needs and requirements of users**
- Ensure conformity to the quality management system
- **Continually improve** the effectiveness of the quality management system.

Meeting these expections and requirements can include:

Identifying and controlling non-conformances allows a formal record of incidents and non-conformances to be kept and can be used to monitor and address trends or recurrent issues. It also provides evidence of issues to encourage positive change and evidence of action being taken to correct issues and improve services whilst demonstrating continual improvement.

Equipment, Reagents and Consumables

ISO requires the laboratory to verify upon installation and before use, that the equipment can achieve the necessary performance and that it complies with requirements relevant to any examinations concerned. Importantly, it is ensuring that the equipment does what it is supposed to do taking into account that Manufacturer Quality Control is not perfect and can fail, damage/changes can occur in transit and also that there are environmental factors – Your environment with Your staff using Your procedures.

As such, the ISO standards specify:

- Reception and storage
    - The laboratory shall store received reagents and consumables according to manufacturer's specifications
    - Ensures the best results from the reagent / consumables
- Acceptance testing
    - Each new formulation of examination kits with changes in reagents or procedure, or a new lot or shipment, shall be verified for performance before use in examinations
    - Consumables that can affect the quality of examinations shall be verified for performance before use in examinations
- Inventory management
    - The laboratory shall establish an inventory control system for reagents and consumables
    - The system for inventory control shall segregate uninspected and unacceptable reagents and consumables from those that have been accepted for use
- Instructions for use
    - Instructions for the use of reagents and consumables, including those provided by the manufacturers, shall be readily available
- Adverse incident reporting
    - Adverse incidents and accidents that can be attributed directly to specific reagents or consumables shall be investigated and reported to the manufacturer and appropriate authorities, as required

In addition, records shall be maintained for each reagent and consumable that contributes to the performance of examinations. These records shall include but not be limited to the following:

- identity of the reagent or consumable;
- manufacturer's name and batch code or lot number;
- contact information for the supplier or the manufacturer;
- date of receiving, the expiry date, date of entering into service and, where applicable, the date the material was taken out of service;
- condition when received (e.g. acceptable or damaged);
- manufacturer's instructions;
- records that confirmed the reagent's or consumable's initial acceptance for use;
- performance records that confirm the reagent's or consumable's ongoing acceptance for use.

The right procedures and records should ensure:	Equipment and reagents are kept in the right conditions
	Equipment and reagents are checked (verified / validated) before being put into clinical use
	There are methods of separating checked from unchecked
	There are records of when equipment / reagents went into use and when they came out of use
	There are instructions at hand for staff (SOPs, Kit Inserts, User Manuals)
	Incidents are reported and managed effectively

Information Management

The laboratory shall have access to the data and information needed to provide a service which meets the needs and requirements of the user.

The laboratory shall define the authorities and responsibilities of all personnel who use the system, in particular those who:

- Access patient data and information
- Enter patient data and examination results
- Change patient data or examination results
- Authorise the release of examination results and reports

The system(s) used for the collection, processing, recording, reporting, storage or retrieval of examination data and information shall be:

- Validated by the supplier and verified for functioning by the laboratory before introduction, with any changes to the system authorised, documented and verified before implementation

- Documented, and the documentation, including that for day to day functioning of the system, readily available to authorised users
- Protected from unauthorised access
- Safeguarded against tampering or loss
- Operated in an environment that complies with supplier specifications or, in the case of non-computerized systems, provides conditions which safeguard the accuracy of manual recording and transcription
- Maintained in a manner that ensures the integrity of the data and information and includes the recording of system failures and the appropriate immediate and corrective actions
- In compliance with national or international requirements regarding data protection

In summary

There are many valuable aspects of Laboratory Quality Management that can be applied to Anticoagulation Services. All services are under more scrutiny and IT security and data management are hot topics. Remember to document everything - If it's not documented, it didn't happen – and finally, use the expertise and help of your suppliers.

Patient Self-Testing

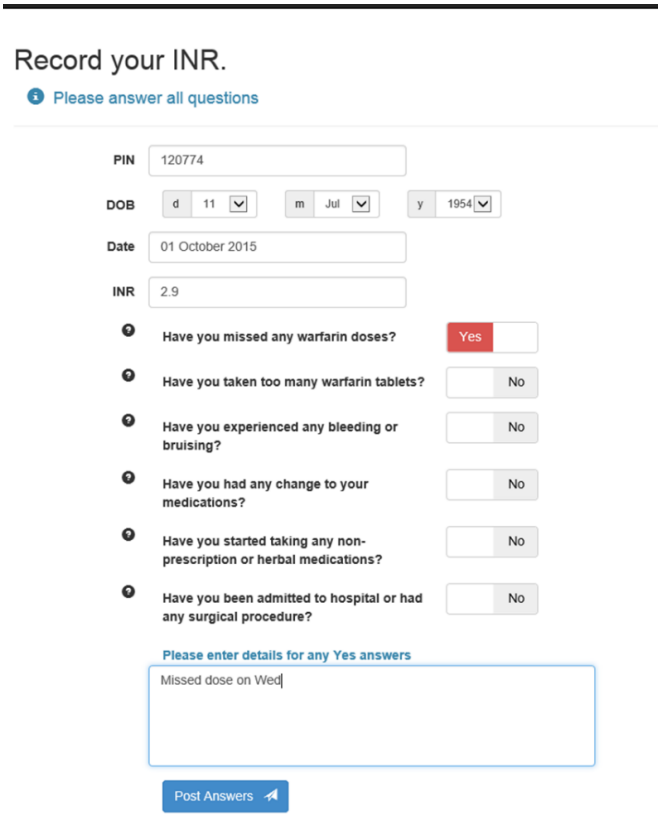
Alistair Stewart, 4S DAWN Clinical Software

There are a number of different approaches to managing patient self-testers using the DAWN system and the following cases outline 3 of these approaches.

Case 1 - DAWN INR Capture

DAWN INR Capture is a quick and easy, mobile/tablet friendly way for INR self-testers, domiciliary services and remote phlebotomy services to capture INR results and supporting information. It is also compatible for use with PCs, laptops, tablets, and mobile phones.

In-built checks and verification mean that the INR results can be imported straight into the DAWN AC patient record.



STEP 1
The patient is issued with a PIN number generated by, and recorded in, DAWN AC and issued via SMS, email or letter.

STEP 2
When the patient self-tests, they complete the DAWN INR Capture form (using the PIN and DOB to identify themselves - see image on the right) and clicks 'post answers'.

STEP 3
DAWN INR Capture sends the results to the DAWN AC patient record where dose and next test date are calculated.

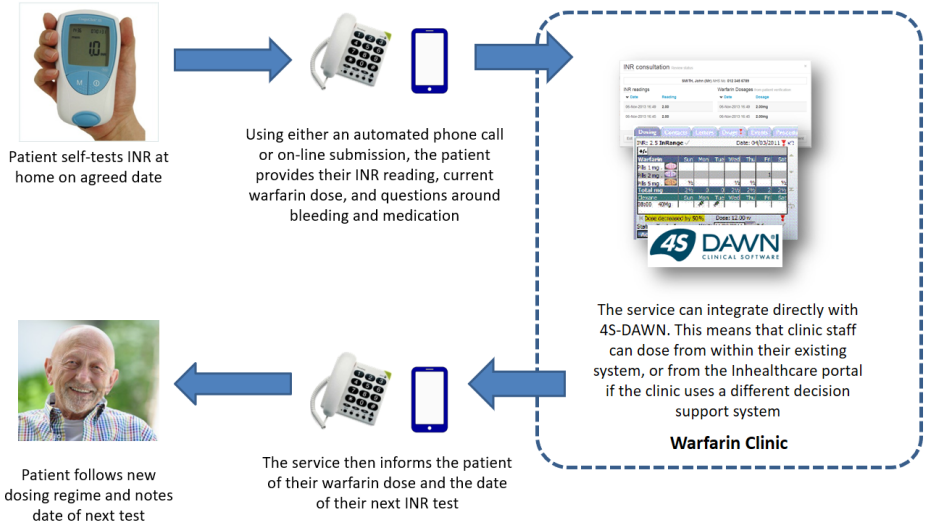
STEP 4
In range patients are sent dosing instructions via SMS, email or letter. Out of range patients are contacted by the healthcare professional.

Case 2 - Inhealthcare platform

The Inhealthcare platform enables patients to send their INR from home via a number of channels. The platform is integrated with DAWN AC to enable the patient's INR to be imported straight into the patient record. Once dosed, the patient's dosing information gets relayed back to the patient via the same channel.

There are currently five DAWN AC centres using the platform, monitoring over 800 self-testing patients per month with the following figures showing the benefits that this approach can bring:

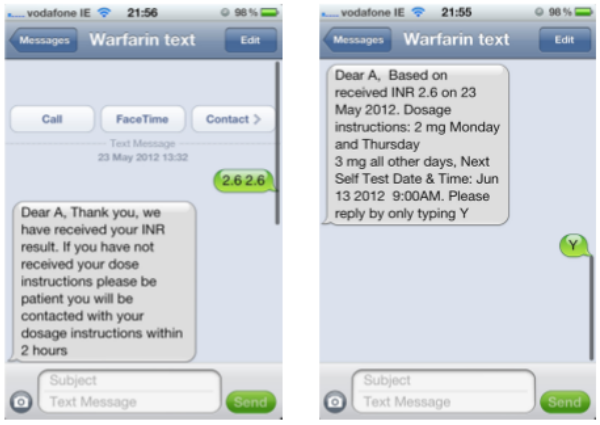
- Average TTR improvement for self-testers was 21%
- 21,000 clinic appointments saved in first 3 years
- As clinic capacity improved, non-self-testers improved TTR by 3%



Case 3 - Self-testing via Text Message

This approach monitors patient self-testers using text messages. Funded by the hospital, 300 CoaguChek XS devices were bought and loaned to patients.

A third-party software application for text messaging was already used within the hospital and this was utilised by the anticoagulation service for self-tester monitoring purposes. Communication with the patient is in the form of mobile phone text messages with the INR transmitted automatically into the DAWN system and a return text message sent to the patient with their dosing information.



How to deal with bouncers

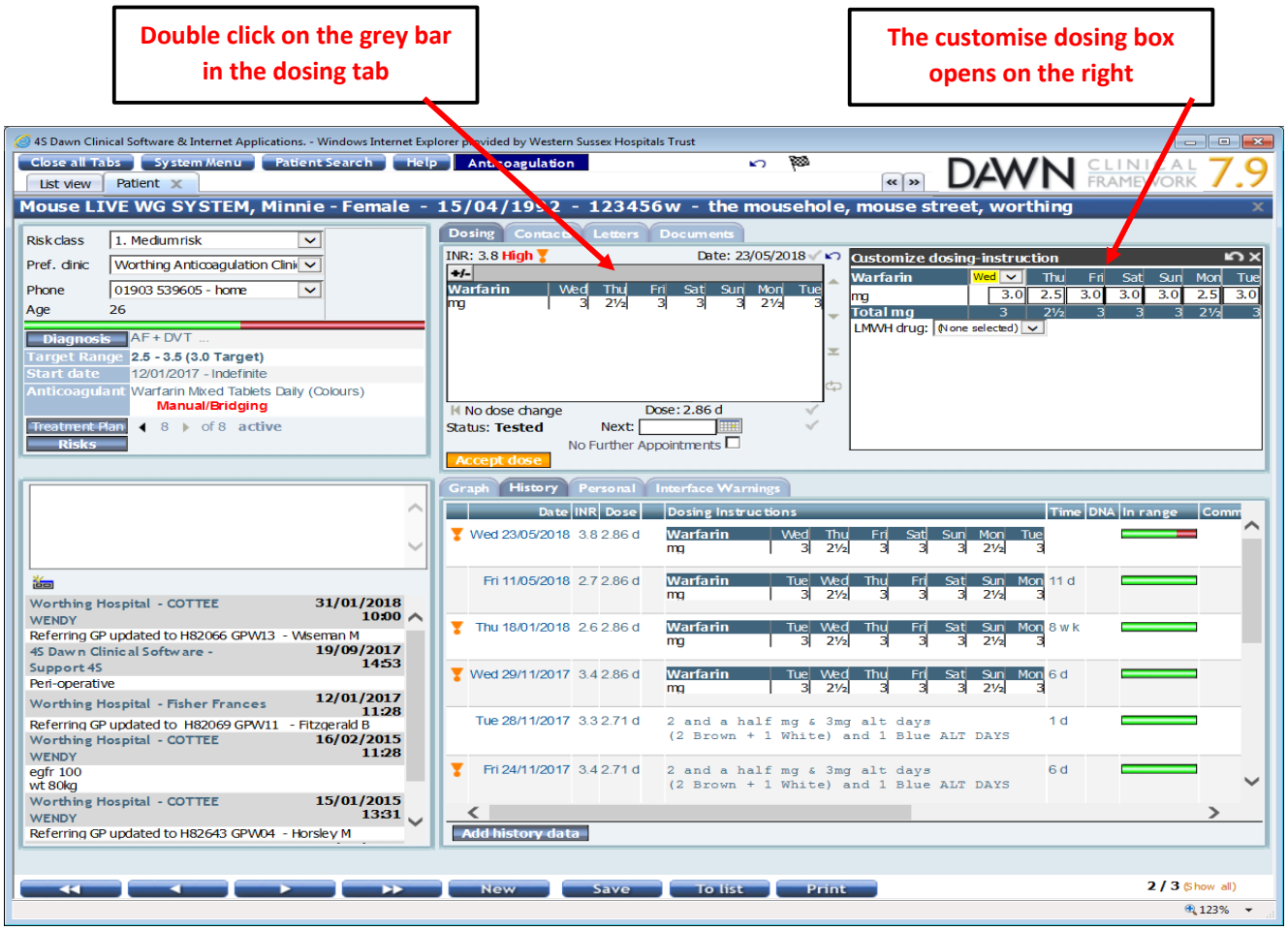
Wendy Cottee, 4S DAWN System Manager, Western Sussex Hospitals NHS Foundation Trust

All anticoagulation services dosing warfarin have patients for whom a particular dose is not quite enough, but the next increment of dose is too much and so the INRs bounce up and down. As a result, the patient is often just above or just below their target range.

The DAWN algorithm tends to apply 5%, 10%, 15% and 20% dose changes and these options work for the majority of patients but these are savage dose changes for dose sensitive patients who are on small doses. For example, a 5% dose change can have an extreme effect on a patient who is only on ¾ of a milligram.

For the last few years, DAWN has offered customisation of dose patterns as an option in the system and it is used at Worthing and St Richards where Time in Range statistics have improved as a result.

On the DAWN patient record, the grey bar in the dosing tab can be double-clicked to open the customisation box:



Advantages of dose customisation

- Allows daily itemisation of dose, which many services use anyway, particularly for the elderly – patients find this useful and often use the dosing letter as a tick list
- Allows tiny dose changes which allow sensitive patients to achieve an in-Range INR and stay in range
- Once customised, further tiny dose changes are easy – just change one dose within the pattern – and cause minimal disruption to the patient.
- As long as 0.5mg doses are allowed it also works for Sinthrome
- Allows for dose changes to be spread over the week rather than a bolus increase which may skew the INR

Disadvantages of dose customisation

- Dosing becomes more complex for the patient or their carer to understand – but it can often be simplified
- Some patients ignore the customisation if they think it looks complicated and as a result their INR stays down, or up. Often just some additional explanation is needed to provide the patient with clarification and talking them through the dose change works well

How tiny can the dose changes get?

Worthing and St Richards have a <2mg dose 'small increment warfarin' regime which is particularly useful for those patients who are elderly and more sensitive to warfarin and require tiny dose changes. This regime, including 0.25 and 0.75mg doses allows, without customisation, the following dose changes:

0.25	**0.38**	**0.48**	**0.5**	**0.63**	**0.75**	**0.88**	**1**	**1.13**	**1.25**	**1.38**	**1.5**	**1.63**	**1.75**	**1.88**	**2.0**

By customising within DAWN, the service is able to achieve the following dose changes:

0.04	**0.07**	**0.10**	**0.14**	**0.17**	**0.21**	**0.25**	**0.29**	**0.32**	**0.36**	**0.40**	**0.44**	**0.48**	**0.54**	**0.57**	**0.61**
0.67	**0.71**	**0.75**	**0.78**	**0.82**	**0.86**	**0.92**	**1.0**	**1.04**	**1.07**	**1.10**	**1.14**	**1.17**	**1.21**	**1.25**	**1.29**
1.32	**1.36**	**1.40**	**1.44**	**1.48**	**1.54**	**1.57**	**1.61**	**1.67**	**1.71**	**1.75**	**1.78**	**1.82**	**1.86**	**1.86**	**1.92**
1.96															

If the anticoagulation service thinks that a patient requires these tiny dose changes, the first job is to check whether the patient, carer or family member can cut a 0.5mg tablet in half and the majority of people are able to.

The more the anticoagulation service uses the customised dosing functionality in DAWN, the more evidence there is that it works for the patients who need it.

The patients like having a pattern that they can follow or tick off as taken and they certainly like coming into and staying in range as this involves less blood tests. For some patients, a weekend or consecutive day dose change is preferable, and the service is strict about putting the differing doses on days that are midway through the dosing week to avoid skewing the INR on test day. Using customised dosing has enabled some patients to go from weekly tests to 12 weekly.

The table below is an example of a patient for which customised dosing was used in DAWN. The patient, with AF, had a target of 2.5. Starting from the bottom it shows that the patient had been stable on 4.71mg for 6 months when the INR came back low. The dose was put up to 5 mg and the INR started to increase so the patient was left on 5mg. The next test came back with an INR of 3.4. In case this was a blip, the anticoagulation team put the patient back onto 4.71 but this once again dropped the INR to 1.7.

The patient was seen as a classic 'bouncer' and after one more attempt at 5mg, their INR went straight back over target again to 3.3. The team then decided to use customised dosing to try and bring the patient back in range and stable. A dose of 4.86mg was given and the patient began to respond, staying in range briefly before dropping back down to an INR of 1.8.

Another tiny increment was made to 4.93 and whilst this is such a tiny change, for the patient, it worked and as a result they responded well and stayed within range whilst also increasing their testing interval.

date	**INR**	**Dose**	**Instruction**	**MON**	**TUES**	**WEDS**	**THURS**	**FRI**	**SAT**	**SUN**	**Interval**
06/11/2017	2.4	4.93		4.5	4.5	4.5	4.5	4.5	5	4.5	84
14/08/2017	2.8	4.93		4.5	4.5	4.5	4.5	4.5	5	4.5	70
19/06/2017	2.5	4.93		4.5	4.5	4.5	4.5	4.5	5	4.5	56
08/05/2017	2.4	4.93		4.5	4.5	4.5	4.5	4.5	5	4.5	42
10/04/2017	2.6	4.93		4.5	4.5	4.5	4.5	4.5	5	4.5	28
27/03/2017	2.5	4.93		4.5	4.5	4.5	4.5	4.5	5	4.5	21
13/03/2017	1.8	4.93		4.5	4.5	4.5	4.5	4.5	5	4.5	14
27/02/2017	2.1	4.86		4.5	5	4.5	4.5	4.5	5	4.5	14
20/02/2017	2.5	4.86		4.5	5	4.5	4.5	4.5	5	4.5	14
13/02/2017	1.7	4.86		4.5	5	4.5	4.5	4.5	5	4.5	7
06/02/2017	3.3	4.71	4.5 / 5 alternate days								7
30/01/2017	1.7	5	5 daily								7
23/01/2017	3.4	4.71	4.5 / 5 alternate days								7
16/01/2017	1.8	5	5 daily								7
09/01/2017	1.6	5	5 daily								7
10/10/2016	2.2	4.71	4.5 / 5 alternate days								84
Previously	stable on 4.71mg for 6 months										

Worthing's customised dosing handout is available online with the presentation slides from this talk: http://www.4s-dawn.com/products/anticoagulation/user-group-meeting/

DOACS: The evolution of the anticoagulation clinic

Terry Dowling, Principal Pharmacist, Haemostasis & Thrombosis, Guy's & St Thomas NHS Foundation Trust (GSTH)

Anticoagulation clinics are traditionally responsible for monitoring treatment with VKAs with monitoring that is structured[1], evidence-based[2,3] and with shared care that is easy to define. With DOACs it is a grey area with no INRs or regular follow-ups, shared care responsibility is less clear[4] and monitoring is based more on a consensus guide[5]. This is reflected in practice around the country with no standardised approach towards initiation and follow-up of DOACs or who is responsible for these (Anticoagulation Clinics, Consultants, GPs).

Emerging evidence or evidence gaps could potentially focus efforts for:

1. **Follow-up Dosing** (e.g. the detriment of inappropriate dose selection);
2. **Managing Uncertainties** (e.g. effectiveness in obesity);
3. **Managing Risk** (e.g. follow-up of combination antithrombotics)

Follow-up of Dose Selection

There are now more drugs, more indications and more criteria for dose reduction which all contribute to the potential for more errors.

For dosing in Nonvalvular Atrial Fibrillation (NVAF) the product characteristics (SmPCs) for Dabigatran, Apixaban, Edoxaban and Rivaroxaban contain guidance on standard dose, reduced dose, criteria for dose reduction, and CI/NR.

For dosing in VTE, guidance covers acute dose, standard dose, reduced dose, criteria for dose reduction, dose change after 6 months, any caution required e.g. CrCl, and CI/NR.

There are also other indications and related dosing specified so is the licensed dose the right dose? The advent and growth of DOACs has driven research into anticoagulation such that "we are now faced with […] a tyranny of choice"[6].

The Danish Registry

This study looked at reduced dose for DOAC versus standard VKA therapy[7]. The study showed a trend towards an increased risk of stroke, particularly with Apixaban although this was 'non-significant':

- **Stroke & systemic embolism**
  - NS increase with apixaban (HR 1.19: 95%CI 0.95–1.49)
  - NS decrease with rivaroxaban/dabigatran (HR 0.92 / 0.93)

The study was not able to confirm whether prescribers used off/on-label dose reduction and there was also a significant selection bias with the overall mean age at 73: lowest mean age = warfarin (71), highest mean age = apixaban (83) and higher CHADS-VASc & HAS-BLED scores and renal disease codes predicted apixaban use.

ORBIT II AF prospective registry (US)[8]

- 5,738 patients: 1 in 8 on wrong dose
- **3.4% overdosed** = ↑ risk all-cause mortality: HR 1.91 (95%CI 1.02–3.60)
- **9.4% underdosed** = ↑ risk of CV hospitalisation: HR 1.26 (95% CI 1.07–1.50) with no benefits seen in major bleeding (rates similar)

Predictors of "off-label" dosing

- High stroke (CHA2DS2-VASc) & bleed (ORBIT) risk
- Moderate renal impairment (CrCl = 30-50ml/min)

Yao et al (US insurance database)[9]:

- 14,865 patients: renal indication for DOAC dose reduction
- **Overdose** (4%) = ↑ risk of major bleeding (HR 2.19; 95% CI 1.07–4.46) + similar stroke risk
- **Underdose** (12%) = ↑ stroke risk with apixaban (HR 4.87; 95% CI 1.3–18.26) + similar bleeding rate
  - No statistical difference for dabigatran/rivaroxaban
- 50% of apixaban underdosing in age > 80 years old

The risks of underdosing are clear but is there a potential problem with underdosing in practice? A US hospital looked into this and carried out a single centre study[10] that found 13.3% of patients were on a reduced DOAC dose, but of those, only 43.3% met the criteria for dose reduction (54.7% on rivaroxaban, 32.2% on dabigatran, **10.7% on apixaban).** Therefore, only 10% of patients on 2.5mg bd of Apixaban met the criteria for dose reduction meaning 90% of patients on 2.5mg bd should have been on 5mg.

This also seems to be an issue in the UK. From the patients in the ARISTOTLE[11] study, 4.7% of those on apixaban were prescribed 2.5mg bd whilst crude dispensing data shows that Apixaban 2.5mg bd makes up 24% to 52% of all apixaban prescriptions in England[12]. This is a very high percentage and this data shows that there is still much work to be done to ensure that patients are on the right dose.

Managing Uncertainties

The following case study is used to illustrate uncertainties:

- Mr RG: 62yo male, truck driver, PAF, HTN, T2DM
- Switched from warfarin to rivaroxaban 20mg once daily

Assessments			
CHA_2DS_2-VASc	2		
HAS-BLED	0		
Wt	**143kg**	Height	180cm
BMI	**44.1kg/m²**		
Cr	100µmol/L	CrCl (adj)	98ml/min
Hb	146g/L	ALT	26

Medication
Atorvastatin
Metoprolol
Metformin
Candesartan
Omeprazole
Amlodipine
Humulin I
Beconase nasal

CHA_2DS_2-VASc components	Score
Heart failure / LVSD	1
Hypertension	1
Aged ≥75 years	2
Diabetes mellitus	1
Stroke/TIA/TE	2
Vascular disease (prior ACS, PAD, IHD)	1
Aged 65–74 years	1
Sex category (i.e. female)	1
Maximum score	9

Total score	Adj. stroke rate (%/year)
0	0
1	1.3
2	2.2
3	3.2
4	4.0
5	6.7
6	9.8
7	9.6
8	6.7
9	15.2

Letter	Clinical characteristic	Score
H	Hypertension	1
A	Abnormal renal / liver function (1 each)	1 or 2
S	Stroke	1
B	Bleeding	1
L	Labile INRs	1
E	Elderly (e.g. age >65 years)	1
D	Drugs or alcohol (1 point each)	1 or 2
	Maximum score	9

Total score	Major bleeds /100 PY
0	1.13
1	1.02
2	1.88
3	3.74
4	8.70
5	12.50
6	ND
7	ND
8	ND
9	ND

Validated in DOACs with similar intervention threshold of 2%/yr[13]

Can we use a DOAC for Mr RG? <u>According to the SPC, YES</u>.
However, the ISTH SSC[14] in 2016, made the statement that warfarin should be used in preference to a DOAC if someone's BMI is greater than 40 or their weight is greater than 120kg. Available evidence suggests peaks may be reduced & clearance may be increased leading to risk of underdosing. If using DOACs in the above, check drug-specific plasma peak & trough with validated methods:

- by anti-Xa (a/r/e) or dTT (d), or mass spec (any)
- If out of range, change to VKA rather than dose adjust

Why have the ISTH said this?
If we look at Phase II/III data from the DOAC trials there is a clear association between weight/BSA & volume distribution. So as weight increases it is expected that the concentration of the DOAC will be reduced. However, the effect on plasma levels is modest with less than 25% reduction in plasma concentrations [15]. Therefore, in the SPCs it states: "No dose adjustment necessary"

Other Studies

<table>
<tr>
<td>Pivotal Studies

• No exclusions based on weight / BMI
• < 15% subjects >100kg
• Efficacy & safety endpoints consistent in patients >100kg
– Also shown in meta-analysis[16]
• Limitations: paucity of outcome data beyond:
– Weight >120kg
– BMI >40kg/m^2</td>
<td>Kinetic studies

Specifically recruiting >120kg:
• Apixaban: 30% and 20% reduction in Cmax & AUC [17]
– Weight: mean 137kg SD +/- 18.3kg
• Rivaroxaban: No change in Cmax [18]
– Weight: Mean 132kg SD +/- 10kg

Local data (2017) – No troughs below expected range [19]
• 30 patients (26 SPAF)
– Rivaroxaban (19) & Apixaban (11)
– Weight: mean 137kg SD +/- 22kg</td>
</tr>
<tr>
<td colspan="2">"Real World Data"

Dresden registry (prospective) – AF [20]
• 9.8% patients with BMI >35kg/m^2
– Highest BMI 57.2kg/m^2
• No dose adjustments
• Cardiovascular outcomes, major bleeding and all-cause mortality consistent with general study population
• Beware the BMI paradox!</td>
</tr>
</table>

So the role of the Anticoagulation Clinic for the case study patient, Mr RG, was to continue rivaroxaban 20mg od (with main meal!) with a standard follow up and an additional follow up to assess the patients trough plasma level. The aim of this is to provide expert & individualised care and to build the evidence base & confidence.

Managing Risk

Referring back to Mr RG, our case study patient above, 2 months later he experiences chest pain and calls 999. He has an ECG in the ambulance: STEMI, and is transferred for PPCI.

The question here: **What is the optimal post-PCI/ACS antithrombotic therapy?**

What do we know?
- DAPT is indicated post ACS & PCI
  - Superior to aspirin alone[21]
  - Optimal duration varies[22,23]
- DAPT is inferior to OAC for stroke prevention in AF[24]
- Triple therapy significantly increases bleeding risk
  - VKA + aspirin + clopidogrel = >3 fold ↑ in non-fatal+fatal bleeding[25]

Prospective studies

<table>
<tr>
<td>• WOEST
– OAC = VKA
– 65% RRR in all bleeding
– 19.4% and 44.4% respectively
– High rates driven by minor bleeds
– TIMI major 3% and 6% respectively (n.s.)
– Composite efficacy endpoint</td>
<td>• PIONEER AF-PCI
– Triple therapy: VKA (2-3) + DAPT
– 1, 3 or 12 months DAPT: 50% = 12mo
– Rivaroxaban
– 15mg od (2/3 AF dose) + P2Y$_{12}$
– 2.5mg bd (ACS dose) + DAPT
– 40% RRR bleeding with rivaroxaban arms</td>
</tr>
</table>

– Death, MI, revascularisation, stroke, stent thrombosis – HR 0.6 (95%CI 0.38-0.94) – Underpowered – Non-standard OAC: INR target 2.0	– Composite TIMI major + clinically significant bleeding – 12% STEMI – Bleeding: Riva15 = 14.6%, Triple therapy = 36% – $P2Y_{12}$ choice: 5% ticagrelor, <2% prasugrel
• RE-DUAL PCI – Triple therapy: VKA (2-3) + DAPT – 1 month BMS, 3 months DES – Dabigatran + $P2Y_{12}$ – 150mg bd – 30% RRR bleeding – 110mg bd – 50% RRR bleeding – Bleeding: ISTH Major bleed + CRNM bleed – $P2Y_{12}$ choice: 12% ticagrelor – Non-inferiority for composite secondary endpoint – MI, Stroke, SSE, death, unplanned revasacularisation – Combined analysis of both dabigatran arms vs warfarin	

A summary of the studies

- Non-guideline INR targets
  - WOEST INR target 2.0 (1.5 to 2.5)
  - PIONEER / RE-DUAL target 2.5 (2.0 to 3.0)
  - ECS: 2.25 (2-2.5) [1]
- Not powered for efficacy
  - But no signal for loss of efficacy
- Rivaroxaban doses not proven in SPAF
  - Both dabigatran doses effective for SPAF
- Clear reduction in clinically significant bleeding
- All the evidence is for clopidogrel as $P2Y_{12}$ inh of choice
- Registry data: increased bleeding with ticagrelor / prasugrel – avoid[26]

The guidelines in this area are constantly evolving to include new antithrombotic strategies, new generation DES with shorter DAPT requirements and significantly reduced duration of triple therapy. It is important to provide practical advice including PPI throughout combined antithrombotic therapy (COGENT[27]) and specify plan & duration prior to discharge[28].

Post 12 months

- Combination antithrombotics increased MB but no benefit on stroke or mortality
  - Post hoc analyses of pivotal DOAC studies in AF
  - Retrospective cohort study[29]:
  - VKA + single antiplatelet in ”stable” CAD (>12 mo event free)
  - No reduction in MI or TE events
  - 50% increase in major bleeding
  - Still a caveat in guidance for ***high risk*** patients for recurrent MI / stent thrombosis

Enter: Anticoagulation Clinic

- Co-ordinate concomitant antithrombotics
  - Gather history
  - Stop primary prophylaxis
  - Liaise with specialists as needed
  - Inform with guidance & evidence
  - Use structured follow up
  - Concomitant antiplatelet = ↑ HAS-BLED = ↑ review frequency[30]

The message is that there is plenty for anticoagulation clinics to do in terms of following up dose selection to ensure the right drug and the right dose at the right time. Clinics can also help to tackle uncertainty by generating evidence where there is a lack of it, and manage risk by facilitating appropriate antiplatelet planning and ensuring plans are implemented (HAS-BLED / follow up).

Ref:
1. Keeling D et al. BJH 2011; 154: 311-324, ***2. Schulman S et al. Ann Intern Med 2011; 155: 653-659****,*
3. Barnes G et al. J Thromb Haemost. 2018; 16: 1307-1312, ***4. SEL APC DOAC Initiation & Transfer of Care 2016 via www.lambethccg.nhs.uk****, 5. Steffel J et al. Eur Heart J 2018;39:1330-1393,* ***6. Czuprynska J et al. Br J Haematol 2017;178:838-851,*** *7. Nielson PB, Skjøth F, Søgaard M et al. BMJ 2017;256:j510,* ***8. Steinberg et al. J Am Coll Cardiol 2016;68:2597–2604****, 9. Yao X et al. J Am Coll Cardiol 2017;69(23):2779-2790****,* ***10. Barra M et al. Am J Med 2016;129:1198-1204,*** *11. Granger CB et al. NEJM 2011;365:981-992,* ***12. Data from Openprescribing.net Aug-18 (consistent from Jan-17 to Aug-18) accessed 14SEP2018****, 13. Lip GY et al. Am J Med 2018; 131(5): 574.e13 – 574.e27,* ***14. Martin K, Beyer-Westendorf J, Davidson BL et al. J Thromb Haemost 2016;14:1308-1313****, 15. De Caterina R, Lip GY. Clin Res Cardiol 2017;106(8):565-572,* ***16. Van Es N et al. Blood 2014;124(12):1968-1975****, 17. Upreti VV et al. Br J Clin Pharmacol 2013;76:908-916,* ***18. Kubitza D et al. J Clin Pharmacol. 2008;48(11):1366-1367****, 19. Mahir Z et al. unpublished data,* ***20. Titti L et al. Int J Cardiol 2018;262:85-91,*** *21. Roffi M et al. Eur Heart J 2016;37:267-315,* ***22. Kedhi E et al. BMJ 2018; 363; k3793****, 23. Valgimigli V et al. Eur Heart J 2018; 39; 213-260****,* ***24. Conolly S et al. Lancet 2006;367:1903-1912,*** *25. Hansen ML et al. Arch Int Med 2010;170:1433-1441****,* ***26. Steffel J et al. Eur Heart J 2018;39:1330-1393****, 27. 1 Bhatt D et al. NEJM 2010;363:1909-1917,* ***28. 2 Steffel J et al. Eur Heart J 2018;39:1330-1393****, 29. Lamberts M et al. Circulation 2014;129:1577-1585,* ***30. Lip GYH & Lane DA. J Thromb Haemost 2016; 14: 1711-1714***

Adherence and monitoring of DOACs

Dr Jignesh Patel, Reader & Honorary Consultant Pharmacist in Anticoagulation, King's Thrombosis Centre, King's College Hospital

Trends show that anticoagulation prescribing has increased over the last few years, prompted by an increase in patients being anticoagulated as people live longer, diagnoses of AF are increased, and DOACs gain popularity. In addition, there is a clear trend of increasing DOAC prescribing and decreasing warfarin prescribing as alternatives are available for poorly controlled warfarin patients, and the apparent lack of monitoring required with the DOACs.

Real world versus trial patients

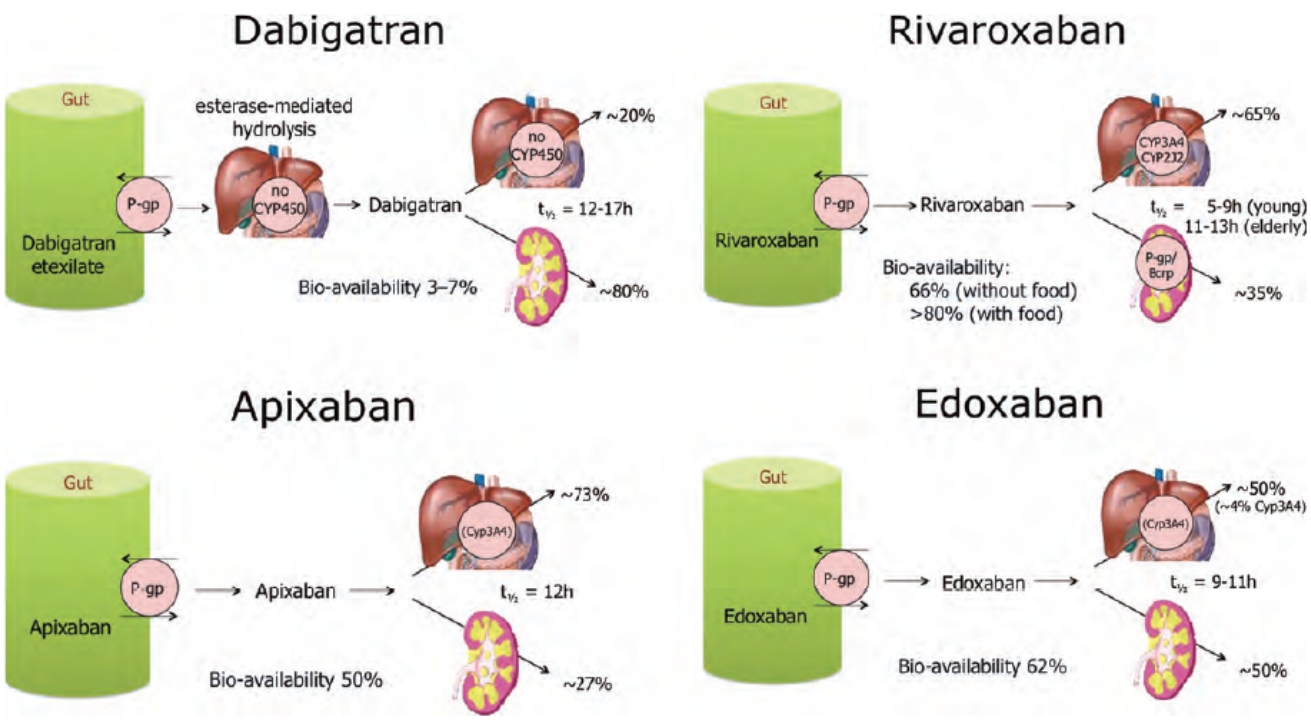
Clinical trials are often done with cohorts of 'healthy' patients who can request to join trials, rather than Mrs J, who is 92 years old with 5 comorbidities and dementia, so are we able to apply the results of the trials using these 'healthy' patients, to the patient we see in the real world on a daily basis?

Whilst the results of the trials are impressive, they vary in their inclusiveness due to underrepresentation e.g. ethnic minority groups; and the application of extracting inclusion/exclusion criteria. The study population becomes a small subset of the target population, which raises concerns as to whether it is valid to apply the results of the trial to the wider target population.

Also, should healthcare professionals be giving the same dose of Rivaroxaban (15mg twice a day) to a 40 year old patient with acute VTE **AND** an 86 year old patient who weighs 50 kilos? According to the guidelines yes, but this also then highlights the requirement for monitoring and particularly, monitoring concentration levels.

PK Summary of DOACs

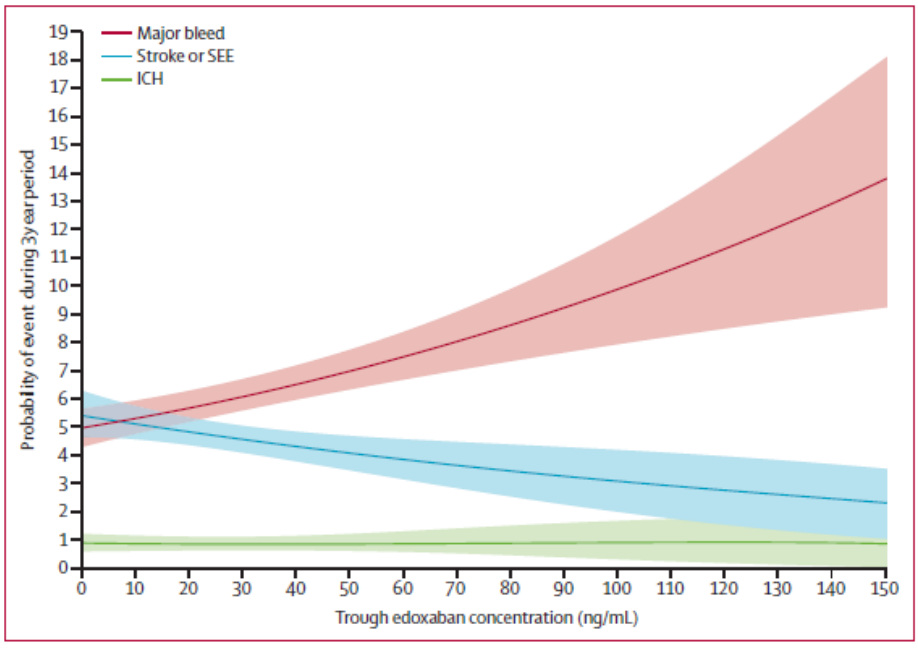
This image highlights that DOACs are counted together as a group of agents, which is correct, but they also have unique pharmacokinetic properties which enables the best type of DOAC to be chosen for a patient based on their circumstances.



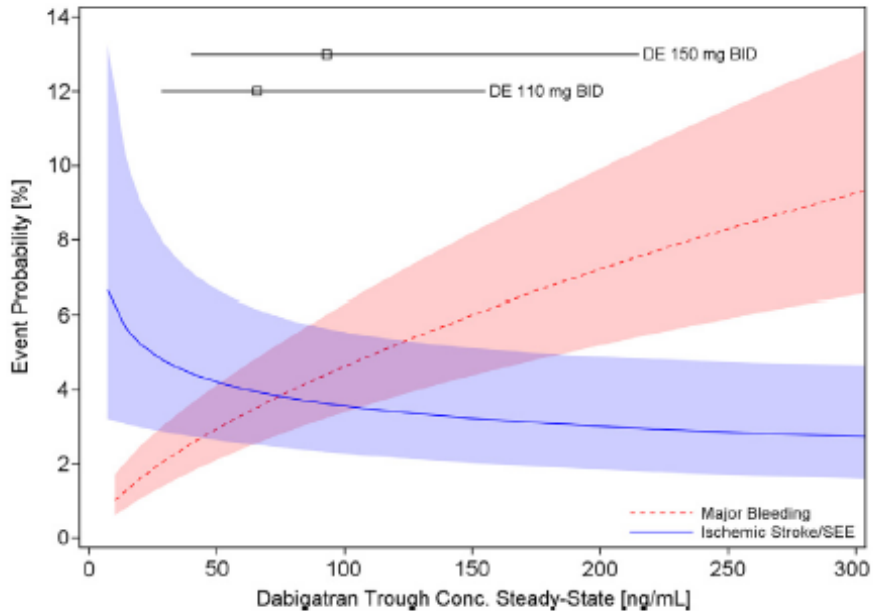
Why monitor?

Study data from the ENGAGE-AF and RE-LY trials has shown that as the trough concentration for the patient goes up, the risk of major bleed also goes up.

ENGAGE-AF



RE-LY



A real-world study published in JTH, found that if patients had a high CHA_2DS_2VASC score and a low concentration of DOAC then they are more likely to experience a stroke or systemic embolic event. However, this study is very limited and whilst it does hint that concentration does lead to effect, there is a lack of real-world data.

Within King's College, monitoring is done for patients that fall into the following areas:

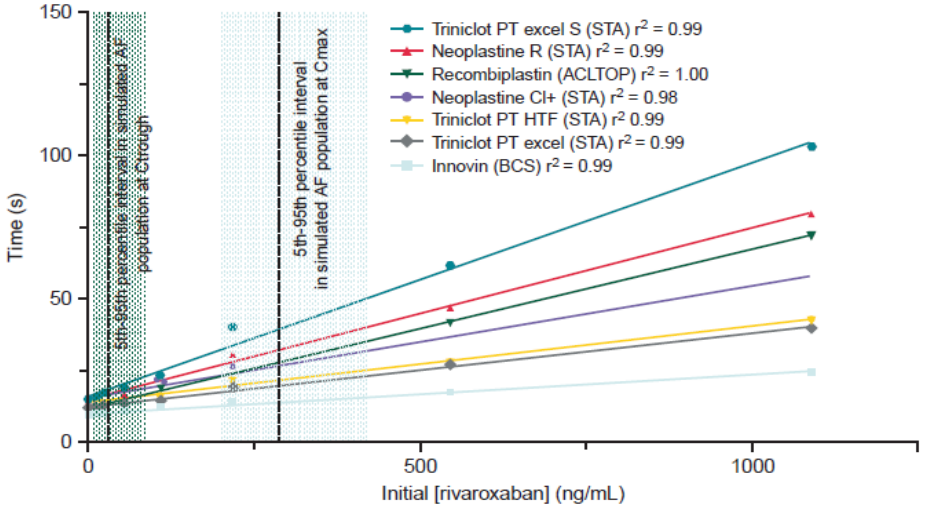
Scenario	Timing of drawing sample
Extremes of weight	Low body weight <50kg: trough activity High body weight >120kg: trough activity
Overdose or suspected overcoagulation	Anytime (time since last dose[s] should be recorded on request form)
Renal or liver dysfunction	Trough activity
Patient on concomitant interacting drugs	Trough activity
To confirm oral absorption	Peak activity

In terms of monitoring, there are two types of coagulation tests that can be done (general coagulation tests and concentration tests) and it is worth being familiar with the impact of these agents on the tests.

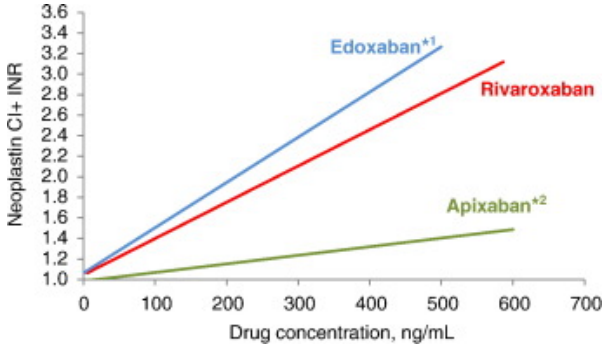
Dabigatran affect aPTT more than the Xa inhibitors, whilst the Xa inhibitors affect the prothrombin time more than Dabigatran. The Thrombin clotting time and the Ecarin clotting time are both increased specifically for Dabigatran but not affected by the Xa inhibitors.

	Apixaban	Rivaroxaban	Edoxaban	Dabigatran
aPTT	↑	↑	↑	↑↑
Prothrombin time	↑↑	↑↑	↑↑	↑
Thrombin clotting time	No effect	No effect	No effect	↑↑↑
Ecarin clotting time	No effect	No effect	No effect	↑↑
Drug-specific anti-Xa	↑↑	↑↑	↑↑	No effect

The effect of these DOACs is also dependent on the reagent that is used in the laboratory e.g. for Rivaroxaban:



At King's, Neoplastine CI+ reagent is used, and you can see the differences here when looking at the same reagent but with different DOACs. You can also see below that while the Xa inhibitors have an effect on prothrombin time, it is not consistent.



What sort of targets should anticoagulation clinics be aiming for?

'International Council for standardisation in haematology (ICSH) recommendations for laboratory measurement of direct oral anticoagulants'

Table 2 Expected peak and trough DOAC concentrations in patients treated for stroke prevention in NVAF or treatment of PE/VTE[1,4,14,15,19,26–28]

	Dabigatran		Rivaroxaban		Apixaban		Edoxaban	
Indication	Stroke prevention in NVAF	Treatment PE/VTE	Stroke prevention in NVAF	Treatment PE/VTE	Stroke prevention in NVAF	Treatment PE/VTE	Stroke prevention in NVAF	Treatment PE/VTE
Dose	150 mg bid	150 mg bid	20 mg qd	20 mg qd	5 mg bid	5 mg bid	60 mg qd	60 mg qd
Peak concentration, ng/mL	175[a] (117–275)	175[a] (117–275)	249[b] (184–343)	270[b] (189–419)	171[c] (91–321)	132[c] (59–302)	170[d] (125–245)	234[e] (149–317)
Trough concentration, ng/mL	91[a] (61–143)	60[a] (39–95)	44[b] (12–137)	26[b] (6–87)	103[c] (41–230)	63[c] (22–177)	36[e] (19–62)	19[e] (10–39)

What is adherence?

- …the extent to which patients take medications as prescribed by their health care providers

  Osterberg, 2005, NEJM
- …the extent to which a person's behaviour – taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider

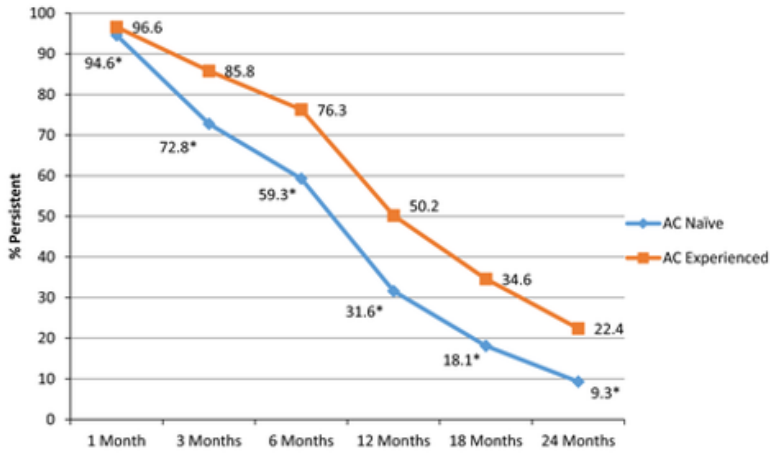
  World Health Organisation, 2003

The adherence problem

- In chronic diseases, estimates suggest average adherence rates of between 43% and 78 %
  (Osteberg, 2005)
- With vitamin- K antagonists: between 3% and 41% were found to be non- adherent
  (Schulman, 2009; Orensky & Holdford, 2005)
- DOACs according to BIG data:
  - 80- 100% adherence (Shore, 2014; Crivera, 2015)
  - 50% of patients non-adherent at 12 months (Zhou, 2015)
  - >25% of patients non- adherent (Gorst-Rasmussenet al, 2015)

- Non- adherence myths:
  - The patient doesn't care about their health and is misbehaving
  - There is nothing that health professionals can do to address it
  - Giving clear written and verbal information at the start is enough
  - There isn't enough time to talk about adherence with patients

Real-World Adherence and Persistence with Direct Oral Anticoagulants in Adults with Atrial Fibrillation



AC Naïve (N)	29,148	22,432	18,268	9,743	5,591	2,870
AC Experienced (N)	34,064	30,269	26,891	17,707	12,203	7,885

What can cause non-adherence?

- Intentional Non-Adherence
  - Patient makes a **conscious** decision not to take medication
- Unintentional Non-Adherence
  - Patient **unconsciously** fails to adhere

- Our beliefs influence our behaviour
- If medicines use/ adherence or non-adherence is a **behaviour**…
- … and beliefs influence behaviour…
- …then beliefs influence adherence
- Illness beliefs and beliefs about medicines can have a profound impact on adherence
- Beliefs are fluid and can be modified
- Modifying beliefs can lead to downstream behaviour changes

Simple tips to help patients be adherent

- Ask the patient about adherence
- Ask about the patient's routine with all their medication
- Consider reducing dosing complexity

- Contingency planning: If patient misses a dose have a plan in place about how this should be managed
- Address the purpose and benefits of treatment especially in asymptomatic patients
- Elicit negative health and medication beliefs of patients and address them in clinic
- Follow up treatment over longer periods during initiation

Adherence is important! Drugs don't work in people that don't take them. We all have a responsibility AND an opportunity.

Improvements to the anticoagulation service using DAWN

Terry Dowling, Principal Pharmacist, Haemostasis & Thrombosis, Guy's & St Thomas NHS Foundation Trust (GSTH)

The anticoagulation service at GSTH implemented DAWN AC in 2017 as part of ongoing improvements to the service spearheaded by the Service Development Lead. Senior nurses do the majority of the dosing with pharmacists also getting involved.

One of the areas for improvement is carrying out patient reviews and understanding how DAWN AC can be used for this, starting with patients who test their own INR. Previously the service had no way of keeping on top of these patients and wanted to use DAWN AC as more than just a basic record that these patients are self-testers.

For this cohort of patients, self-testing offers an alternative to venous phlebotomy; provides greater flexibility for those who work full time or travel frequently and has also been shown to give better INR control when the right patients take responsibility for their own testing.

A pan-London protocol was written as to how these cohorts of patients should interact with the anticoagulation service and outlined the responsibility of the service, the patient and also the commissioners and primary care providers.

As a result, the anticoagulation service has the following responsibilities in meeting local guidance for **initiating** patient self-testers:

- The service should inform GPs that the patient is self-testing their INR
- Full training is required on the Coaguchek and a record of this is required
- The patient's technique with the Coaguchek machine should be assessed and a record of this is required
- Patients should sign the Patient Agreement to confirm that they understand their responsibilities as self-testers and a record of this is required
-

In addition, meeting local guidance for **reviewing** patient self-testers includes:

- Performing a 6-monthly comparison between venous and POCT
- Assessment of the patient's technique
- Review of the patient's INR control and the frequency of testing
- Decision to be made by the practitioner as to whether the patient is still suitable to continue self-testing
-

The old process involved using a spreadsheet to manage patients and determine when they were due their venous comparison and this proved to be a challenge in terms of keeping track of the reviews that were due. In addition, very little else was recorded other than the patients name and the date they were due for review. Also, the patients were booked in quite haphazardly, some for a routine INR, some for a venous comparison and some for a thrombosis appointment. This made it very difficult to stay on top of this patient cohort. The outcome of the venous comparison was typed into the treatment notes on DAWN, but no further documentation was recorded.

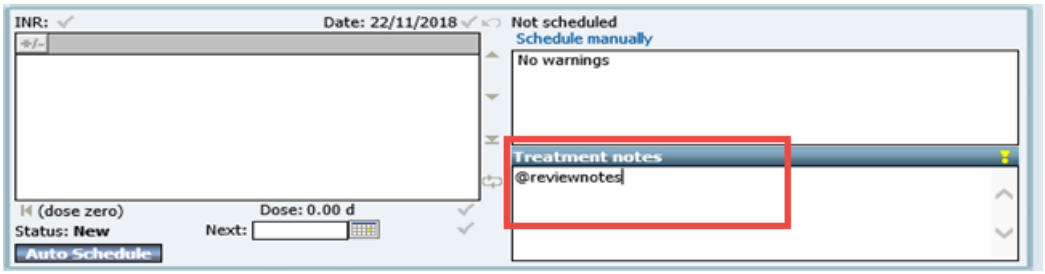
The question was asked 'How can the service utilise DAWN AC help to improve this process?' so that all of the information is in one place, easily accessible and auditable with a record of reviews and associated

information including training and calibration details. There were two main elements to this. Firstly the 'Review' function in DAWN to set the next review date and secondly, an easily generated record and letter of the outcome of the patient's review.

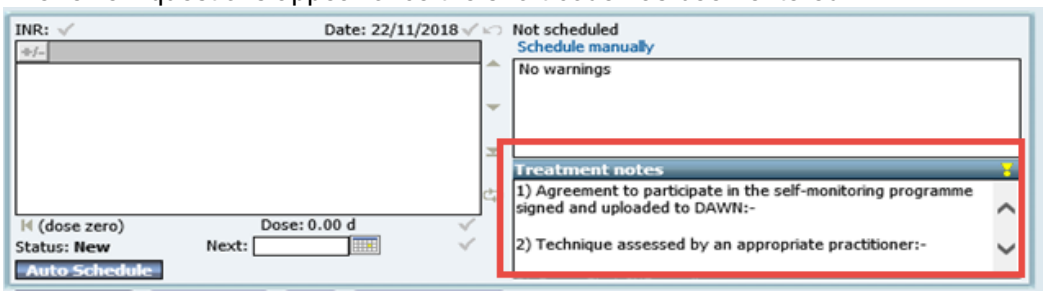
Although all clinicians use the EPR and the majority of outpatient letters are stored in the EPR, the limitations of the system prevented the anticoagulation service from using it for these reviews. As a result, it was decided that a copy of the patient's review letter from DAWN would also be stored in the EPR as well as DAWN so healthcare professionals outside of the anticoagulation service didn't have to log into another system to access the information whilst at the same time, all of the patient's relevant details pertaining to their anticoagulation therapy was available in a single place, the DAWN AC system.

The team at 4S DAWN worked with GSTH to set up the export of letters from DAWN AC into the EPR system and also to set up the self-tester review within DAWN so that it could be completed easily.

A short code (.reviewnotes) was set up in DAWN and is used in the treatment notes to generate the review questionnaire.



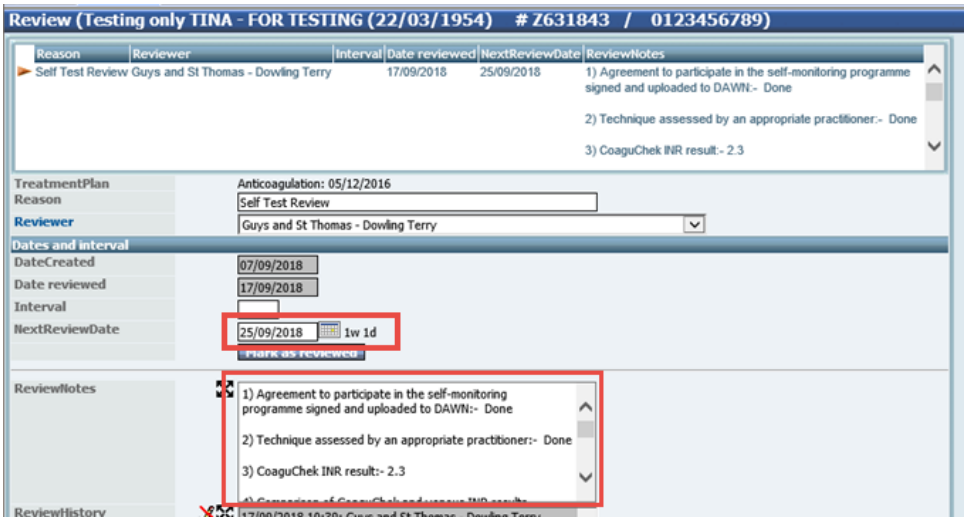
The review questions appear once the short code has been entered.



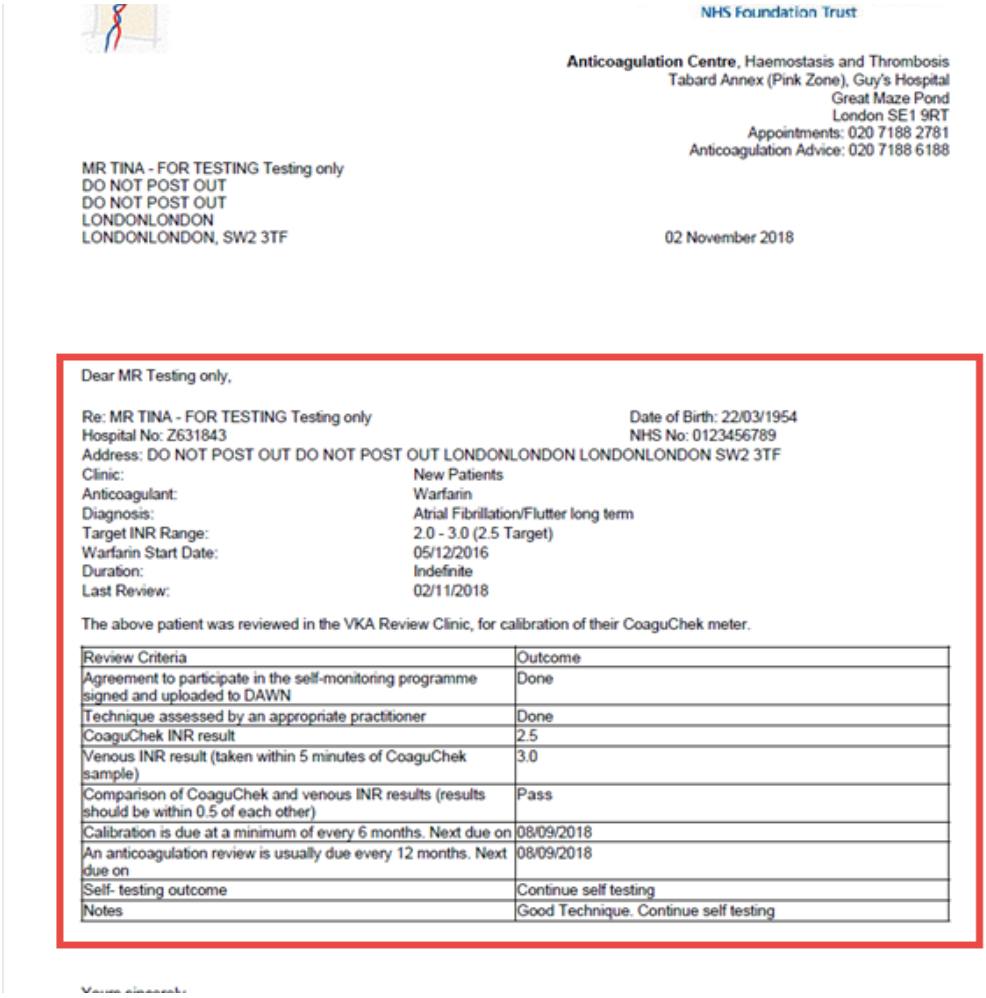
These questions are then copied and pasted into the review tab then deleted from the treatment notes. The questions in the review are designed to provide short answers so that the nurses can get through them quite quickly and you can see below, that the answers the nurses input are in red:

- 1) Agreement to participate in the self-monitoring programme signed and uploaded to DAWN:- **Done**
- 2) Technique assessed by an appropriate practitioner:- **Done**
- 3) CoaguChek INR result:- **2.3**
- 4) Comparison of CoaguChek and venous INR results (results should be within 0.5 of each other):- **Pass**
- 5) Calibration is due at a minimum of every 6 months. Next due on:- **08/09/2018**
- 6) An anticoagulation review is usually due every 12 months. Next due on:- **08/09/2018**
- 7) Self- testing outcome :- **Continue self testing**
- 8) Notes:- **Good Technique. Continue self testing**

These questions are completed in the review tab and the next review date is set.



A letter is generated using the custom drop-down list and the information from the questionnaire automatically populates the letter including patient information, treatment summary and INR to prevent the need to manually input key information.



NHS Foundation Trust

Anticoagulation Centre, Haemostasis and Thrombosis
Tabard Annex (Pink Zone), Guy's Hospital
Great Maze Pond
London SE1 9RT
Appointments: 020 7188 2781
Anticoagulation Advice: 020 7188 6188

MR TINA - FOR TESTING Testing only
DO NOT POST OUT
DO NOT POST OUT
LONDONLONDON
LONDONLONDON, SW2 3TF

02 November 2018

Dear MR Testing only,

Re: MR TINA - FOR TESTING Testing only — Date of Birth: 22/03/1954
Hospital No: Z631843 — NHS No: 0123456789
Address: DO NOT POST OUT DO NOT POST OUT LONDONLONDON LONDONLONDON SW2 3TF

Clinic:	New Patients
Anticoagulant:	Warfarin
Diagnosis:	Atrial Fibrillation/Flutter long term
Target INR Range:	2.0 - 3.0 (2.5 Target)
Warfarin Start Date:	05/12/2016
Duration:	Indefinite
Last Review:	02/11/2018

The above patient was reviewed in the VKA Review Clinic, for calibration of their CoaguChek meter.

Review Criteria	Outcome
Agreement to participate in the self-monitoring programme signed and uploaded to DAWN	Done
Technique assessed by an appropriate practitioner	Done
CoaguChek INR result	2.5
Venous INR result (taken within 5 minutes of CoaguChek sample)	3.0
Comparison of CoaguChek and venous INR results (results should be within 0.5 of each other)	Pass
Calibration is due at a minimum of every 6 months. Next due on	08/09/2018
An anticoagulation review is usually due every 12 months. Next due on	08/09/2018
Self- testing outcome	Continue self testing
Notes	Good Technique. Continue self testing

Yours sincerely:

The letter is sent out via email as a pdf and a record of this is stored in the letters tab on the patient record. DAWN also sends a copy to the anticoagulation service secretaries who send a copy to the patient's GP and also upload it on the EPR system which is a very quick and easy process.

The review list view in DAWN is used to see who is due their self-tester review and the administration team check this tab and book the patient in on the Trust appointment system 'PIMS'.

Finally, the signed training record and patient contract is uploaded to the documents tab on the patient record in DAWN AC so that there is a record of it alongside the other anticoagulation information relating to the patient.

Next Steps

- New clinic generated to book patients to increase income.
- Patients will be formally booked in for a review
- The income generated will be used to purchase the test strips
    - So patients aren't priced out from self-testing
    - Patients will still need to purchase their own Coaguchek
- The business case has shown that this approach will actually save the CCGs money

DAWN Version 8

George Kitching, 4S DAWN Clinical Software

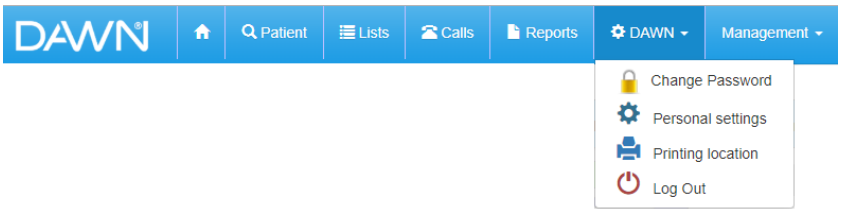
DAWN Version 8 has a new look and feel that modernises the look of the software, whilst bringing benefits such as use of the full screen, a larger font that is easier to read and the ability to customise the screen size with a zoom function.

The underlying functionality of the DAWN system is the same, but the facelift has given it a feel that many will be familiar with through the use of social media, including common symbols and concepts such as homepage, search, settings etc alongside colours, making it easier for new users to learn how to use the DAWN system.

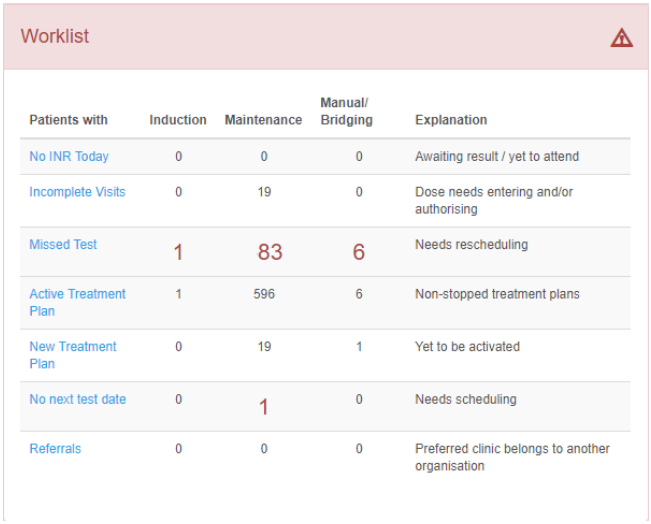
The new design is also responsive, so it automatically optimises itself to the device/screen resolution that you are using. If you have a large monitor for a desktop PC, DAWN will use the full screen width. If you are using an iPad or tablet with a much smaller screen area, it collapses items that are displayed side by side on larger screens so that they appear one below the other to make optimum use of the screen whilst still being easy to read and navigate.

DAWN Version 8 is supported across a range of browsers (Google Chrome, Microsoft Edge, Mozilla Firefox, Safari) and devices (PC, laptop, tablet, iPad) giving much more flexibility to customers.

The menu that had previously been on the front page of DAWN AC is now at the top of the screen and therefore accessible at all times regardless of the area of DAWN you are currently accessing.

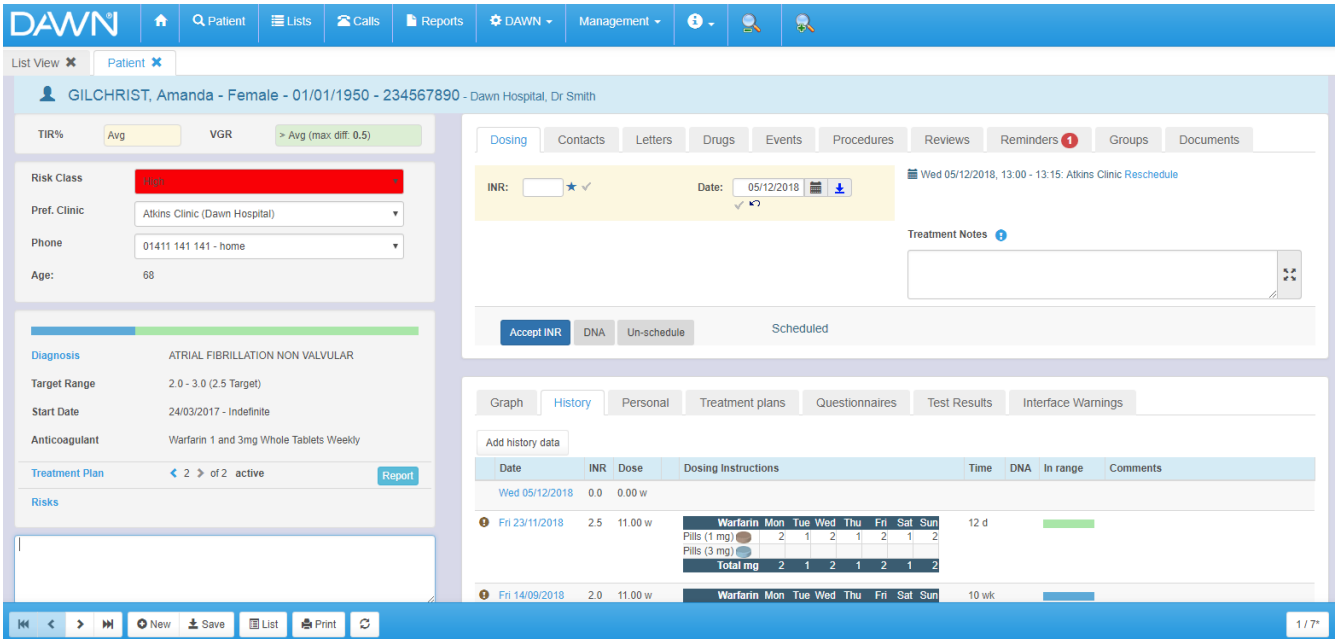


Upon logging in to the DAWN system, there is now a dashboard that is split into key dashboard panels (see worklist panel below) that cover key elements of the system and follow a traffic light warning system so that any information that requires attention is highlighted red and all elements that do not require attention will be green. This makes it easier to quickly see and address any patients and/or system issues that need to be dealt with.

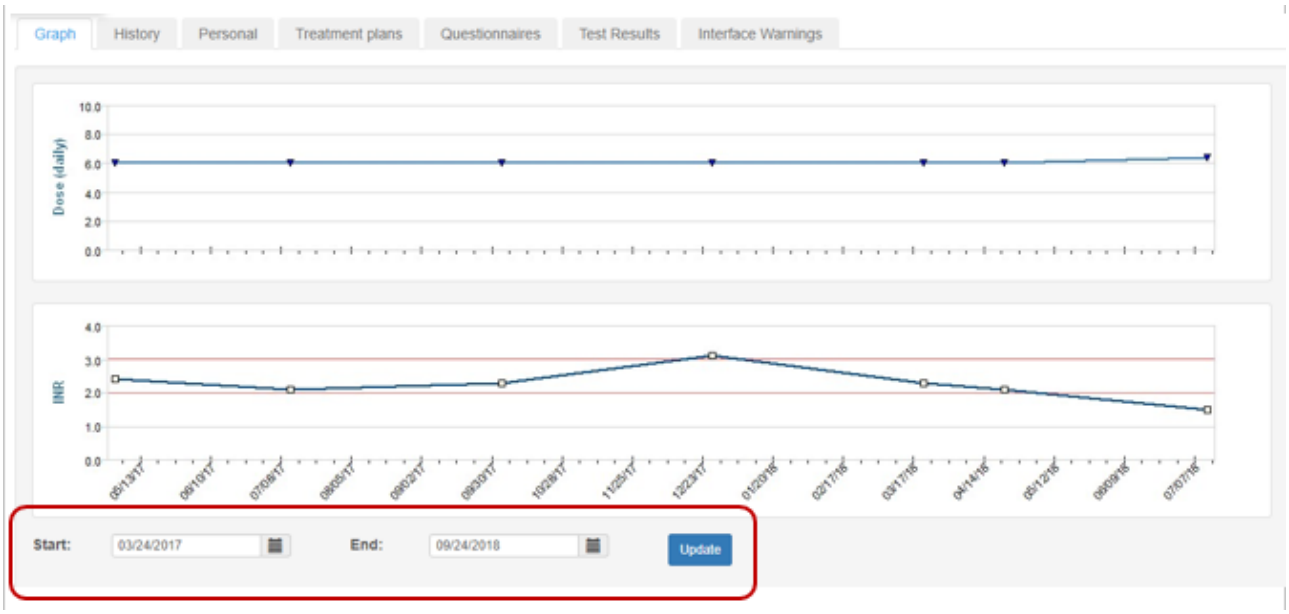


Patients with	Induction	Maintenance	Manual/ Bridging	Explanation
No INR Today	0	0	0	Awaiting result / yet to attend
Incomplete Visits	0	19	0	Dose needs entering and/or authorising
Missed Test	1	83	6	Needs rescheduling
Active Treatment Plan	1	596	6	Non-stopped treatment plans
New Treatment Plan	0	19	1	Yet to be activated
No next test date	0	1	0	Needs scheduling
Referrals	0	0	0	Preferred clinic belongs to another organisation

The patient record contains the same information as DAWN version 7 and in the same place, but this has also been updated to improve the look, feel and user experience.



Within the patient record, the Graph tab has also been improved, enabling users to specify start and end dates.



DAWN Version 8 is due to be tested by a number of customers to ensure that all of the message templates, list views and other functionality work as expected when run through various workflows.

The DOAC modules and other custom questionnaires are due to be converted to Version 8 early in 2019, but for customers without the DOACs who wish to upgrade now, please contact Mel, Melissa@4s-dawn.com to discuss moving to Version 8.

The upgrade to DAWN Version 8 is included as part of your annual support and maintenance costs so there is no charge, however please be aware that there are a number of pre-requisites that must be in place in order to upgrade, including having a test system.

For more information on DAWN AC Products and Services:
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