# Implementing innovative technology in the NHS – a Case Study

# Implementation of genotype-guided dosing of warfarin for atrial fibrillation and/or venous thromboembolism (VTE) to improve anticoagulation control.

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*John Hugh Wardle,*

*Associate Project manager, Innovation Agency.*

**Version 1.**

**Project Outline:**

Parallel cohort design with 6 sites, 3 of which provide DNA testing (GGD Implementation group) and 3 sites, similar in terms of patient demographics and clinic organisation (primary, secondary, community etc. operating as usual care (Comparator group) sites. The Royal Liverpool and Broadgreen University Hospital Trust is the host Trust. The comparator sites provide non-identifiable patient information relating to key outcome measures. In addition to either pilot testing or treatment as routine, patients in both the implementation and control sites complete short quality of life self-assessment questionnaires at first appointment and after 12 weeks. Patients and staff from the implementation sites will be asked to complete a questionnaire regarding their experience and perceptions of the test. A sample of staff and patients will be invited to expand on the questionnaire in either telephone interviews or focus groups. Staff also ensure that the DNA testing data is included in patient electronic records. Patients will be informed that we are using a new dosing system which involves looking at their genes and are requested to provide verbal agreement.

Evaluation in use/practice of the GGD technology in hospital based anticoagulation clinic settings Evaluation of application across the wider NHS. Enrolment of 300 participants per arm (implementation/comparator arms = 600 participants)

**Sites Engaged:**

**Implementation sites**

* Countess of Chester – Countess of Chester NHS Trust
* Warrington Hospital – Warrington and Halton NHS Trust
* Royal Liverpool and Broadgreen University Hospitals NHS Trust

**Comparator sites**

* Whiston Hospital – St Helens and Knowsley NHS Trust
* Aintree Hospital – Aintree Hospitals NHS Trust
* Preston Hospital – Lancashire Teaching Hospitals NHS Trust

**Key Partners**

* Innovation Agency North West Coast (formerly North West Coast Academic Health Science Network)
* Liverpool University Dept of Personalised Medicine
* NIHR North West Coast CLAHRC
* LGC Group

**Funding Sources**

Project funded by the NIHR CLAHRC and supported by the Innovation Agency, Academic Health Science Network for the North West Coast, the University of Liverpool and LGC Technology

**Project Manager Role and Engagement**

The project had been subject to significant delays. Originally scheduled to commence in the spring of 2015, the project had not initiated any sites by March 2016. There were a number of reasons for the delay primarily concerning reliability and updates to the technology and of the testing kits.

Sites began to open to enrolment from April 2016 commencing with the host site. As of the date of this report all sites are open to recruitment however the RL&BUHT has withdrawn from the project

JH LS (Consulting) Ltd was engaged to act as Project Manager in March 2016 and is a registered associate of the NWC IA. Specifically, the role involves supporting the initiation, start-up and delivery of the project by the clinical teams at participating sites.

The original contract arrangement was for 25 days over a seven-month period from beginning of March to end of September 2016. Note this arrangement has now been extended to the end of March 2017.

**Governance Issues**

Organisational agreement/permissions: The first issue to resolve with the sites concerned the pathway for organisational approval of a technology/service evaluation project. Past experience has shown that the differences between research project permission and evaluation project site approvals/permissions are not always clearly understood. Consequently, some sites treat all externally initiated evaluation projects as if they were a type of research project. However, technology innovation projects have more in common with audit/service evaluation than research and consequently should be managed as such. Delays, sometimes significant, were encountered as managers at some sites worked through this process.

On the other hand, at some sites, R&D Offices were clear that they did not deal with projects of this type but were not always clear as to who else would lead locally. On occasions a referral went to an audit department or lead or sometimes to the clinical lead for a specific directorate. Again, understanding of the process was variable and approaches were inconsistent. It would be accurate to say that at six sites there were six different approaches and as a consequence a great variety of pathways to work through.

The greatest consistency and easiest set-ups were at sites where innovation was allocated along-side R&D, essentially where organisations had established RD&I offices. In such circumstances, the general principles of innovation governance and site agreement tended to be better understood. Across the project generally however, optimal governance arrangements for innovation project management of this type were not always particularly well understood however in mitigation, most sites reported that projects of this type were relatively few in number and consequently local experience is limited.

**Protocol and Protocol Amendments**: The protocol as initially agreed was subject to a number of amendments, several of which occurred after initial local agreement was in place. This meant that additional work was required to ensure agreement remained in place and that agreements covered the amended documentation. This was a particular problem at one site.

**Medical Engineering** – Organisational Indemnity: When using new equipment NHS organisations have a register to complete which ensures NHS indemnity is in place to cover the use of the product within its area of responsibility. Similarly, all electrical equipment must be safety tested prior to delivery to the clinical area, both need to be in place even for training purposes. With regard to the former, once again, different organisations had different requirements which meant it was difficult to put together a suite of documents that would enable the registration to proceed quickly. Again, the delay in the delivery of the equipment from the supplier meant that arrangements had to be put in place at very short notice.

**Material Transfer Agreements**: One of the significant successes of this project was securing agreement from the second and third sites to go live to adopt the Material Transfer Letter of Agreement developed by Liverpool University and initially agreed with the Royal Liverpool Hospital. This represents a very good example of pragmatic and proportionate local project review.

**Data Confidentiality**: The Patient Information Form (PIF) was initially reviewed, including patient representative review, at the RL&BUHT and three of the remaining four sites were happy to accept this review for their own internal purposes – another good example of proportionate and pragmatic shared working across multiple sites. One of the sites had internal systems managed through their own RD&I office and no delays were experienced. However, at one site, a query was raised relating to confidentiality and post-codes. This was quickly resolved by a software upgrade but unfortunately the person raising the query was then absent for an extended period of time without a nominated alternative contact. Consequently, significant work and time was required to resolve this barrier.

**Management issues**

This section has been divided into two main elements. The first concerns activities relating generally to site set-up and the second to on-going project management activities; it should be noted however that there is often overlap and certain areas of activity will be re-initiated during the course of the project. Ultimately, as with any other project, the goal is to achieve completion of the project safely, within budget and to agreed timeline and to enrolment/recruitment target.

**Site selection**

The current PM was not involved in any of the initial site selection so is unable to comment on the approach taken and selection criteria, if any, that were applied. However, with the benefit of hindsight, it is now clear that various factors, mostly concerning service configuration, workload and staff deployment issues have meant that several sites, particularly the RL&BUHT have struggled to meet their recruitment targets. It would be useful to know whether other sites were considered and if so, what did the selection process involve and on what basis were sites included i.e. was the selection essentially geographical or were other factors such as previous performance, previous clinical partnerships and joint working, personal knowledge and professional relationships considered? Similarly, were additional concrete factors such as similarity of service configuration, as suggested in the protocol introduction, actually key criteria?

**Feasibility - Level 1 and level 2 Feasibility Assessment**

**Level 1** feasibility involves, in this case, consideration of whether the technology, in its current form, is generally compatible with clinical service arrangements in the NHS i.e. is it in principle possible to deliver the project successfully in the UK?

**Level 2** feasibility involves an assessment at each site to ensure that a project can be delivered there. It will involve a review of the site at both an organisational level i.e. does the site host the relevant services with sufficient capacity and does the clinical team have sufficient expertise (capability) in the area of practice; has the site and team delivered before or are they a new/up and coming centre with little or no established track record of delivery in this field? Also, does the organisation treat sufficient numbers of the target patient population, have sufficient availability of appropriately trained staff, and possess an adequate clinical environment including space and accommodation as well as factors such as location, availability and timing of accessible clinics. All these factors will need to be taken into account. Other factors of interest will concern training needs, logistical support requirements, population dispersion and geographical dispersion of clinics and an assessment of the clinical team in terms of knowledge, known performance factors and motivation

Again the current PM was not involved in site feasibility assessment so again it is not possible to comment on these factors directly. What would appear to be clear from subsequent performance across the project at all sites is that there are rather less patients being referred to commence warfarin therapy than was initially expected. This is quite likely due to the fact that there was a considerable time delay between any initial work of this type and initiation of the project and it seems that many more patients are now being commenced on DOACs than the protocol envisaged. It is also possible that earlier audits if carried out at sites and completed significantly prior to initiation might have missed this trend and that at Spring 2015 this trend was less evident.

**Recruitment planning (RP)**

This element links partly to Level 2 feasibility but expands to cover additional on-going factors. For example, RP needs to consider and account for issues such as staff withdrawal, staff absence, reconfiguration of service provision etc. In other words, what is the plan B? It is clear that the somewhat startling anecdotal evidence of widespread prescribing of DOACs was not really anticipated or at least was somewhat underestimated also, possibly, the difficulty and complexity of accessing potential participants, even in the comparator arm, commenced on warfarin in the community by GPs. A further issue here is that the DVT patient group, not initially included in the protocol, has proved an extremely difficult to access as they are generally managed under different directorates and follow different referral pathways. Consequently, overall, recruitment has remained sub-optimal.

**Staff changes and organisational memory**: Between the initial approaches to sites in 2015 and re-initiation of the project in spring 2016 there were a number of key changes to site personnel, more in the RD&I management side than the clinical side that impacted particularly on project approval timelines.

**Site Communications and Support**: On-going support to the implementation sites is provided by the research nurses based at Liverpool University and support to the comparator sites is provided by the PM.

Re the implementation delay already described above, several clinicians noted their concern that they had not received any update or contact between initial approach and re-initiation in the spring of 2016. This meant that on occasions, a full re-submission and repeat of meetings with clinical teams, research office staff, admin, finance and medical engineering staff had to be carried out (especially given key staff changes and protocol amendments noted above) almost as one would with a new project. This lack of update and on-going briefing was probably due to an oversight, perhaps due to the absence of a nominated PM at the time.

Generally, responses to communications can be slow at some sites. This is generally a result of workload and the fact that with some staff supporting widely dispersed clinics, office/admin time is limited. Direct contact by phone or face to face is still by far the best method of information transfer and this is particularly the case at the comparator sites where there is no direct contact with the research team at Liverpool University.

**On-going Management and Delivery to Time and Target**: This is proving to be extremely challenging with this project. The key issues, as described above are access and availability of the appropriate patient population as services gradually reconfigure towards community based provision and the number of patients available to approach given an apparent wider prescribing of DOACs. It is perhaps the most interesting finding of this project so far that new warfarin starters with AF are so much more difficult to identify than they were two years ago when the primary research study completed. This certainly suggests there may be wider concerns in terms of health policy, prescribing policy etc. across the NHS as a whole – the implications of which could be far reaching particularly in relation to patient safety and cost.

**Timelines and momentum**: The importance of seeking to maintain momentum in any project cannot be overstated. Anecdotally and from discussion with the research team, it seems clear that following completion of the primary research study there was significant momentum towards implementing and completing the evaluation in practice soon afterwards. It is difficult to be certain but it may have been the case that if that momentum had continued at that time and that there had not been the delays caused

**Clinic organisation and structure**: One of the issues raised more widely concerns the location of new patients commencing on warfarin. The point concerning the differing clinical pathways for AF and DVT patients has already been referred to but there is also the issue of whether patients are being commenced and managed at GP practices resourced to do so. Further work may be required to identify if these numbers are significant and if so, how the project can inform future development of the technology to access these patients. Additionally, if and when service provision reconfigures towards a more community based model focussing around for example GP led services and home monitoring, how will the technology in its current form apply and/or adapt?

**Clinic Space/Equipment Storage Space**: On a very practical level, the equipment needs to be stored between clinics and sample kits need to be maintained at -20 degrees C. To ensure minimal wastage, -20 freezers need 24/7 monitoring and kit transfer to clinic from the storage facility needs to be organised immediately prior to the clinic, the number of kits required determined by the number of new warfarin patients expected. This requires additional screening of clinic lists and liaison with storage facility staff. In terms of clinic rooms in use, the equipment needs to be stored safely in an accessible place.

**Perception of additional workload**: Several members of clinical teams at sites have indicated that the additional time needed to enrol participants has caused additional workload and timing issues in clinics - adding around an hour to the patient stay in the implementation arm and up to half an hour in the comparator arm. A small budget is available to each site but it should be noted that this also needs to cover data upload – at around half an hour per participant. Consequently, there are only limited funds available to support any additional staffing to clinics. Specific impacts in relation to this point are still working through and it will be interesting to note over the lifetime of the project whether the funding allocations were sufficient to cover the full costs and/or provide a small incentive in terms of a sum that could be invested locally.

**Information Management, Data Collection and Confidentiality**: An issue raised by one of the sites prior to the current PMs involvement meant that the plan to use simple excel datasheets for data collection needed to be revised and a data collection tool developed. The issue concerned to data collection form requiring both participant initials and post-code and whether this information would be transferred off site. Whether this point was a risk to confidentiality is an arguable point but this was certainly a legitimate concern. In order to resolve this, the post-code, needed for the deprivation/health economic element of the project, needed to be converted to a deprivation code at site and the code then uploaded to the database. At the implementation sites software was developed to do this automatically via the GGD machine but at comparator sites this is a manual process. The time require is not a major issue but once again this created a delay in the design of the data collection tool.

**Technical Issues and Equipment**: The main technical issues concern the equipment itself, the dosing algorithm and the data collection tool (database). The first two have impacted at the implementation sites and the third across the study generally. Technical issues included concerns and additional work around testing equipment reliability. In terms of the algorithm, post study start-up, issues were identified and concerns raised re the dose calculated for certain patients. This caused further delays at the first implementation site. With regard to the database, this is currently still in development mode as issues were raised by the statisticians re the current data collection forms and the associated elements on the data collection tool. This means that sites are unable to upload data and training will need to be repeated.

**Logistics**: the main issue is the transfer of kits, sored at -20 degrees C to similar storage at sites. In the last few weeks, the Research Team and PM have done this by car as a temporary measure. This occurred because the low usage at sites, compounded by a freezer failure at the university meant that available kits needed to be redistributed to sites with higher enrolment numbers. Of course logistical arrangements including sample kit transfer would need to be built in to any long term plan for wider use of the technology.

**Training**: Equipment, sampling and technical/data procedure training at the implementation sites has been conducted by the research team at Liverpool. This has been successful. Training at the comparator sites has been carried out by the PM. Training is on-going and, due to the database reconfiguration mid project will need to be carried out again. Clearly this incurs additional resource commitments and cost however, given the extension to the project recently agreed, such costs can be managed within available resourcing.

**Interim Review of Lessons Learned and Interim Recommendations**

One of the first question that needs to be asked is where are all the new warfarin patients? It seems unusual that all the sites are reporting reduced numbers of referrals and increased preference for DOACs among patients and referring clinicians if no such trend exists. For future projects it may be worth considering a Screening Log (this project utilises only an enrolment and refusal log) to formally screen clinic lists in order to identify whether the patients are really not being referred for warfarin or whether busy staff are simply unable to make the approach to potential participants in time. This is routine practice in many research projects and is a simple and useful management tool.

A further key point concerns the importance of momentum. This project was subject to a delay of fourteen months from development to initiation at the first site. The protocol was in development for a similar period of time. The ultimate result was a significant loss of momentum and it has proved a challenging task to build that back again. The main cause of the delay was issues with the dependability of the equipment. At one centre training was commenced and then cancelled with a nine-month delay before contact was re-established with the site and in the mean-time several staff had left post; these factors exacerbated the delay. It is possible that the lack of a specific project manager and subsequent communication lapses may have contributed to the impact of the delay.

Although some centres had well developed processes for and good understanding of innovation governance several did not and pathways to organisational approval were very varied. The IA may wish to consider commissioning a piece of work aimed at developing best practice guidelines that could facilitate a more standardised approach. It is important that any such guideline emphasises that the research pathway is different. Having said that, the question as to why the two processes are so different is a point of interesting debate and might be an interesting question to raise with the HRA.

A key question concerns the equipment itself and its **applicability across clinical areas** other than hospital based clinics and therefore relevant to the wider NHS. Also, can portability be improved? These issues may form an important element of the formal end of project evaluation.

As part of its funding, sponsorship or support the IA may wish to consider whether it wishes to adopt both a structured site selection process and/or a formal approach to project and site feasibility assessment. Tools for this purpose are readily available and can be adapted

The IA may wish to consider whether, in projects of this type, a more formal approach to recruitment planning should be adopted. This would involve an audit of potential participants, a review of staffing and physical resources available to support the project including contingency plans, geographical factors and deployment of clinical teams, and research/innovation support staff.

It seemed clear from the outset that a bespoke data collection tool would be required and that use of simple spreadsheets would not meet the performance requirements for a project of this scale (600 participants across 6 sites). The first indication of this problem dates to Summer 2015 when data protection issues were first raised by one of the sites. Consequently, the problems caused by trying to launch the database in parallel with study launch could have been avoided.

Again, due to the delays in study launch already noted funds to sites necessarily had to be paid ‘up front’ before the end of the financial year 2015/16 as they had been allocated from that financial year. In the case of this project it may not have been possible due to the time constraints but the IA should consider whether as a general principle a staged payment approach based on activity and performance might have been more suitable.

The number of amendments to the protocol prior to and subsequent to study launch suggests this piece of work may not have received sufficient priority. For example, the amendment to add VTE patients was to be expected and the only surprise was its exclusion from the original protocol – the EU-PACT study, from which this project is the evaluation stage, included that group.

The IA may wish to consider whether a logistics back-up service, possibly courier based, should be costed into projects such as this where -20 degree dry ice transfer is required. Currently the system relies on the availability of dry ice at the university laboratories and transfer in the care of one of the research nurses or the PM.

At the time of this report, the major technical issues concerning the technology equipment including the dosing algorithm and test kits appear to have resolved. So far a single incident/adverse event has been recorded concerning the algorithm.