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Abstract (for dissemination)	The EurValve project will combine multiple complex modelling components developed in recent EC-funded research projects to develop a comprehensive, clinically-compliant decision-support system (DSS). The mathematical model at the heart of the DSS will be validated against the results of a multi-centre clinical trial. This document describes the training of personnel to upload data from this trial into the project's central trial data system.
Keywords	Decision Support, Valvular Heart Disease, Aortic Stenosis, Mitral Regurgitation

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EXECUTIVE SUMMARY

EurValve is developing a clinically-compliant Decision Support System to support healthcare professionals in the management of Valvular Heart Disease. The system will be designed also to assist the clinician in communication with the patient, enabling the easy description of the consequences of the disease, the prognosis, and the treatment options.

The Data Management infrastructure for EurValve encompasses Data Hosting and Data Collection. Data Hosting will use the technology stack developed as part of the VPH-Share project, and is discussed in Deliverables D2.1 and D2.2. This includes tools for extraction and transformation of clinical data from a wide variety of electronic systems and its hosting in a web based platform for access by the scientific researchers and their computational processes. These tools have been extensively tested on a large number of projects and, as partner Sheffield Teaching Hospitals (STHFT) played a key role in development, this will provide a reliable and extensible platform for researchers.

Data Collection involves the clinical trial centres using two systems within the hospital premises, one for medical images, the other for alphanumeric information.

- Imaging data is selected, anonymised and uploaded using a well-established clinical image management tool 'TrialConnect', authored by Deutsche Telekom.
- Alphanumeric data is entered and selected, anonymised and uploaded using a system authored by STHFT and in widespread use in Sheffield. A module has been specifically developed for use in the EurValve project.

Informal training has taken place across all centres during the development of the data collection platforms. A formal dedicated training session that explored the totality of the processes for both systems took place on Friday 23rd September 2016.

1 INTRODUCTION

The EurValve project includes a full clinical trial involving three clinical centres, Berlin, Eindhoven and Sheffield, each enrolling 40 patients requiring heart valve replacement. The clinical data obtained will inform several aspects of the project, including the machine learning processes and the construction of the central modelling mechanism.

Clinical data collection involves the clinical trial centres using two systems within the hospital premises, one for medical images, the other for alphanumeric information.

- Imaging data is selected, anonymised and uploaded using a well-established clinical image management tool 'TrialConnect', authored by Deutsche Telekom.
- Alphanumeric data is entered and selected, anonymised and uploaded using a system authored by STHFT and in widespread use in Sheffield. A module has been specifically developed for use in the EurValve project.

Informal training has taken place across all centres during the development of the data collection platforms, and a formal dedicated training session that explored the totality of the processes for both systems took place on Friday 23rd September 2016.

Development of the data collection mechanisms has involved close cooperation between DHZW and STHFT, to identify the requirements and construct systems tailored to the needs of the project. This has involved:

- System specification
- System construction
- System trial and evaluation
- Trial environment and eCRF establishment
- Introductory involvement of data personnel across all clinical partners
- Formal training session
- Continuing end-user support
- Mediation of support and update requests and project-specific adaptations

This Deliverable documents the information conveyed during the formal training session, and serves to confirm that each clinical centre is equipped to meet the data provision requirements of the project.

2 BACKGROUND TO DATA COLLECTION

EurValve brings together a set of technologies that are now well-established within the *in silico* medicine community, and which will be combined and uniquely configured into a tailored mechanism focused on heart valve treatment optimisation.

The EurValve project is a logical sequence of four overlapping product-related activities in which - against a backdrop of secure data storage (WP2) - a set of data processing and modelling tools is assembled (WP3), the digital patient definition is created and employed (WP4), the novel clinical decision support system is developed (WP5), and the resulting system is evaluated on a patient cohort (WP6). The project's parallel exploitation strand (WP7) ensures that the opportunities for the resulting integrated system are maximised.

The EurValve clinical trial follows the progress of patients receiving surgery for the replacement of one of their heart valves, aortic or mitral, and the data obtained from the study will be compared with the predictions obtained from the EurValve simulation. Collected data is in the form of medical images and a comprehensive set of alphanumerical information from the patient's clinical record. The EurValve data collection design process has ensured that all data items relevant to the project's intended maximal use of data are allowed for.

2.1 Clinical Data Systems - Imaging

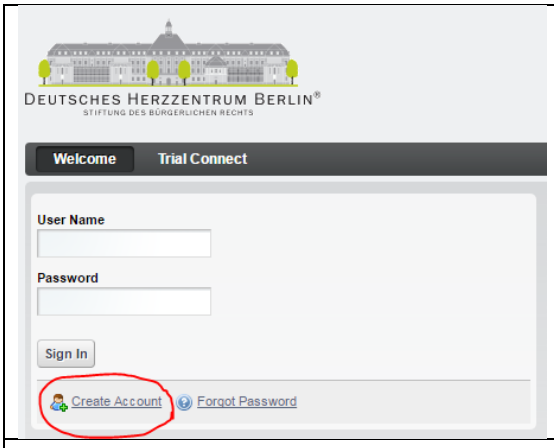

Figure 1 Trial Connect Home Page

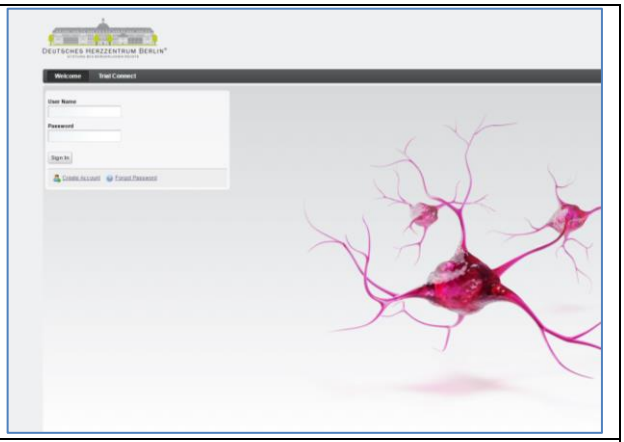

Figure 2 Trial Connect Log in page

An infrastructure technology (Trial Connect, Telekom Healthcare Solutions) has been developed and successfully integrated into former and current EU projects (e.g. Cardioproof; ESOPE). This technology allows the pseudonymisation, upload, and web based management of medical DICOM images in conjunction with relevant clinical information into a study database. It also includes a basic electronic Case Report Form (eCRF). For parametric data

necessary for the implementation of the models a second platform (ArQ) is used, hosted at the University of Sheffield.

Trial Connect is designed for research teams at universities, hospitals as well as contract research institutes and the pharmaceutical industry that need to manage scientific data cost- and time-efficiently, site-independently, and sustainably. What users get is an end-to-end tool environment in which they can work on studies across their entire life cycle and with a wide range of interfaces.

The process chain extends from setting up new studies, sequence control and project communication to evaluating and analysing image data by means of innovative web technologies. Trial Connect uses Telekom's data centres that fully comply with German data protection standards. So these certificated data centres provide a trustworthy and reasonably priced environment in which to archive data and facilitate a wide range of data reuse.

The platform will be used for all prospective clinical study data acquired in EurValve. It will allow to access and process images using in part web-based tools providing seamless data integration into a modelling workflow (combined web image and clinical data management system). We expect its adoption in EurValve to be of value as it provides an established technology at a key infrastructural level of the clinical trial.

The details of the interactions with the TrialConnect software that were featured in the formal training session are documented in Annex 1.

2.2 Clinical Data Systems - Alphanumeric

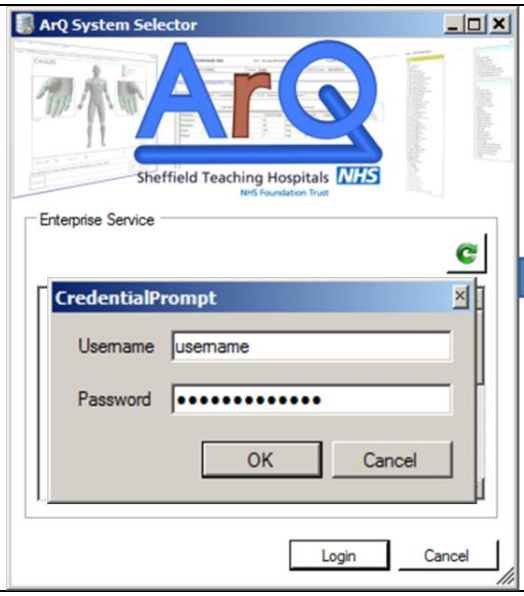

Figure 3 ArQ Login screen

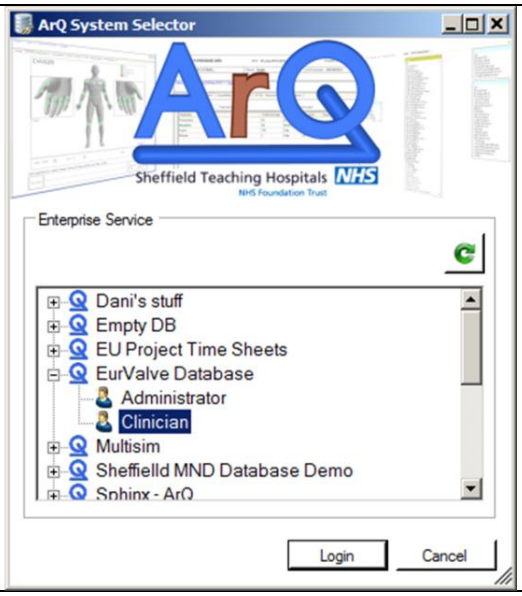

Figure 4 ArQ User Categorisation

Sheffield's ArQ clinical data collection system has been developed by a UK National Health Service team of IT experts to meet exactly the needs of clinical data capture in a hospital environment.

ArQ is a clinical database engine that supports both research activities and clinical service provision by allowing rapid deployment of bespoke data collection/management tools. The software is able to integrate with key existing systems, including laboratory results services and clinic lists and brings added value to routine clinical data with advanced information management. Search facilities are provided that lets users run complex queries and export results into numerous formats for further analysis.

The platform will be used for all prospective clinical study data acquired in EurValve. It will allow users to access and process alphanumeric data, providing seamless data integration into a modelling workflow (a combined web image and clinical data management system).

The details of the interactions with the ArQ software that were featured in the formal training session are documented in Annex 2.

3 FORMAL TRAINING

Training in the Trial Connect and ArQ systems was arranged for the relevant partners in September 2016. The training was hosted in an interactive online system called TeamViewer, (https://www.teamviewer.com/en/download/windows/).

Registration for Trial Connect was required at: https://dhzb.trialconnect.de/ before the teaching session. Activation of the accounts then took place. Each clinical site had prepared some exported DICOM data so that it could be ensured that the system was operating correctly at all sites. Anonymisation of the uploaded DICOM images is an in-built feature of the TrialConnect system.

Registration for ArQ was also required before the teaching session. Activation of the accounts then took place. Each clinical site had prepared some dummy clinical data so that hands-on experience of the platform was possible.

The full details of the training processes conducted during the EurValve formal training session are documented in Annex 1 and Annex 2, and the participants across the three clinical sites are identified in Annex 3.

The training process took place over a 120-minute session and users had the opportunity to examine each aspect of the processes in detail and to interact with the experts for each system to confirm aspects of the processes. Online data is also available for both systems, as a permanent resource for existing users to refresh their understanding and for new users to acquire the necessary skills. At each clinical site, live data provision will only be permitted after local determination of acceptability, and procedures for data audit are in place.

4 CONCLUSION

Representatives from all sites where clinical data is generated participated in the video conference. Patient imaging data (echocardiography, MRI and CT) were uploaded live from DHZB. All the data collection process and the respective tools needed in the data collection process were introduced and discussed.

All clinical sites will upload further sample imaging and alphanumeric data sets within the next weeks to ensure the platform will be capable of handling all types of data sources needed within the project.

After the test phase is complete the TrialConnect environment will be switched to a 'production' mode that meets all the criteria for the clinical study, including pseudonymisation, audit trails and digital signatures.

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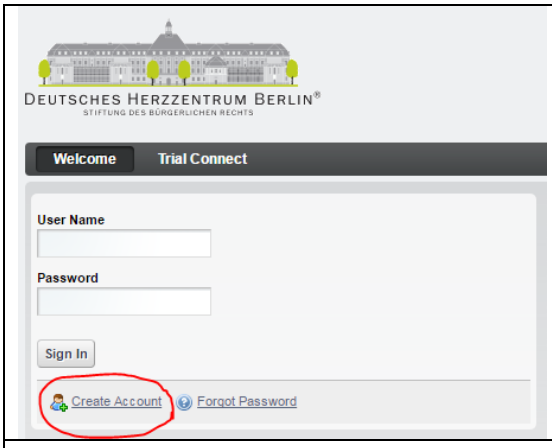
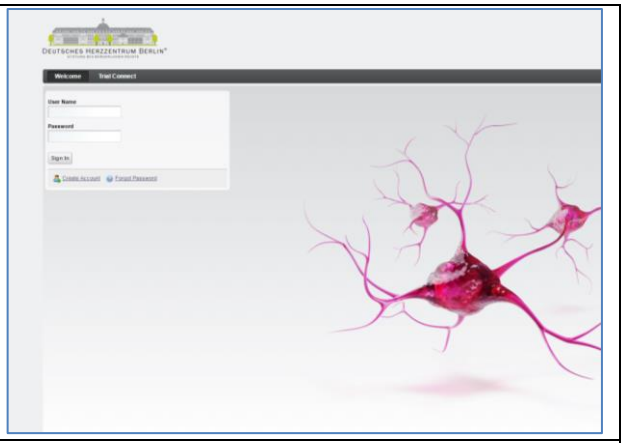
ANNEX 1: TRIALCONNECT TRAINING INSTRUCTIONS

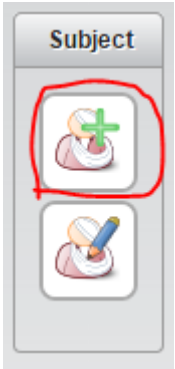
A tutorial video is available, and can be accessed at any time:
https://www.dropbox.com/s/8j9kpnuus46w1iy/TrialConnectImageUpload2.wmv?dl=0

Routine operation of the TrialConnect system is documented below, and begins with the user visiting the DHZB TrialConnect home page:

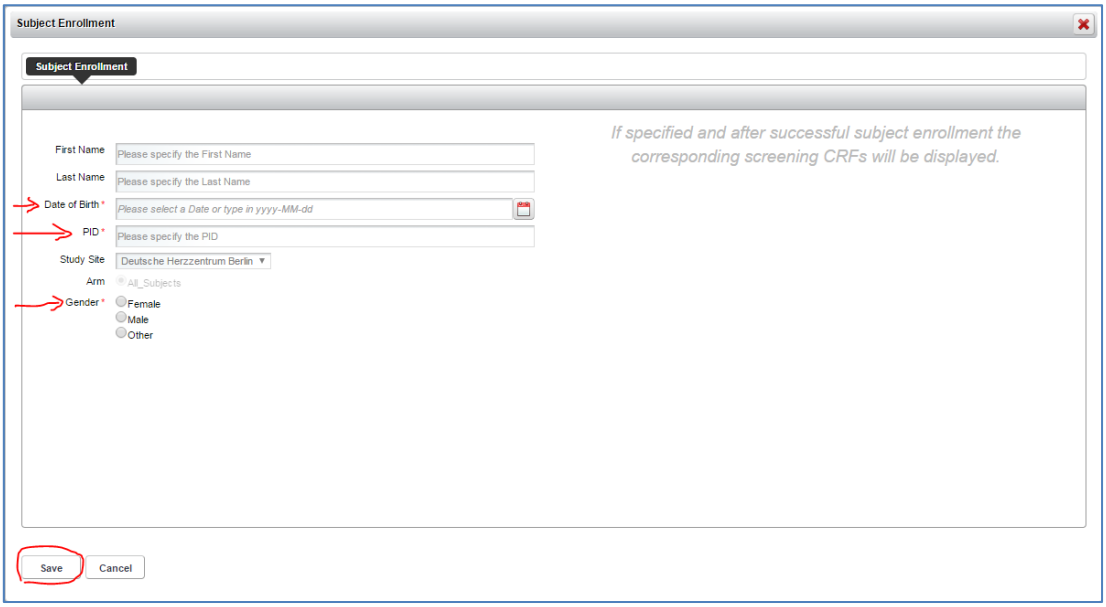
	
Trial Connect Home Page	Trial Connect Log in page

1. Once logged into the TrialConnect system, click on the "Documents" Button:

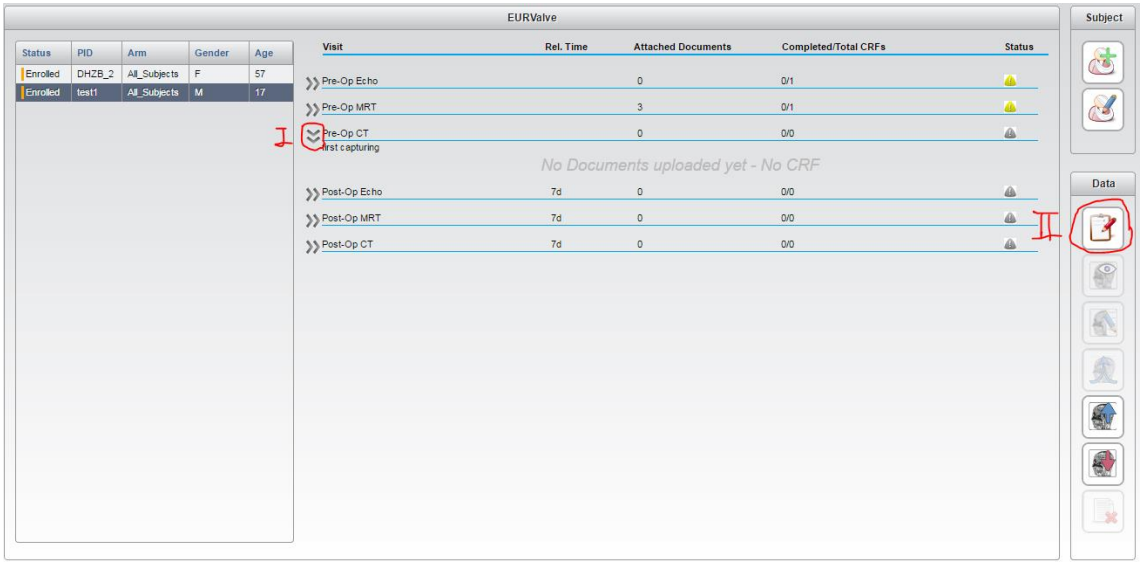
2. Click in "Enrol Subject" button in the upper left corner the browser window:



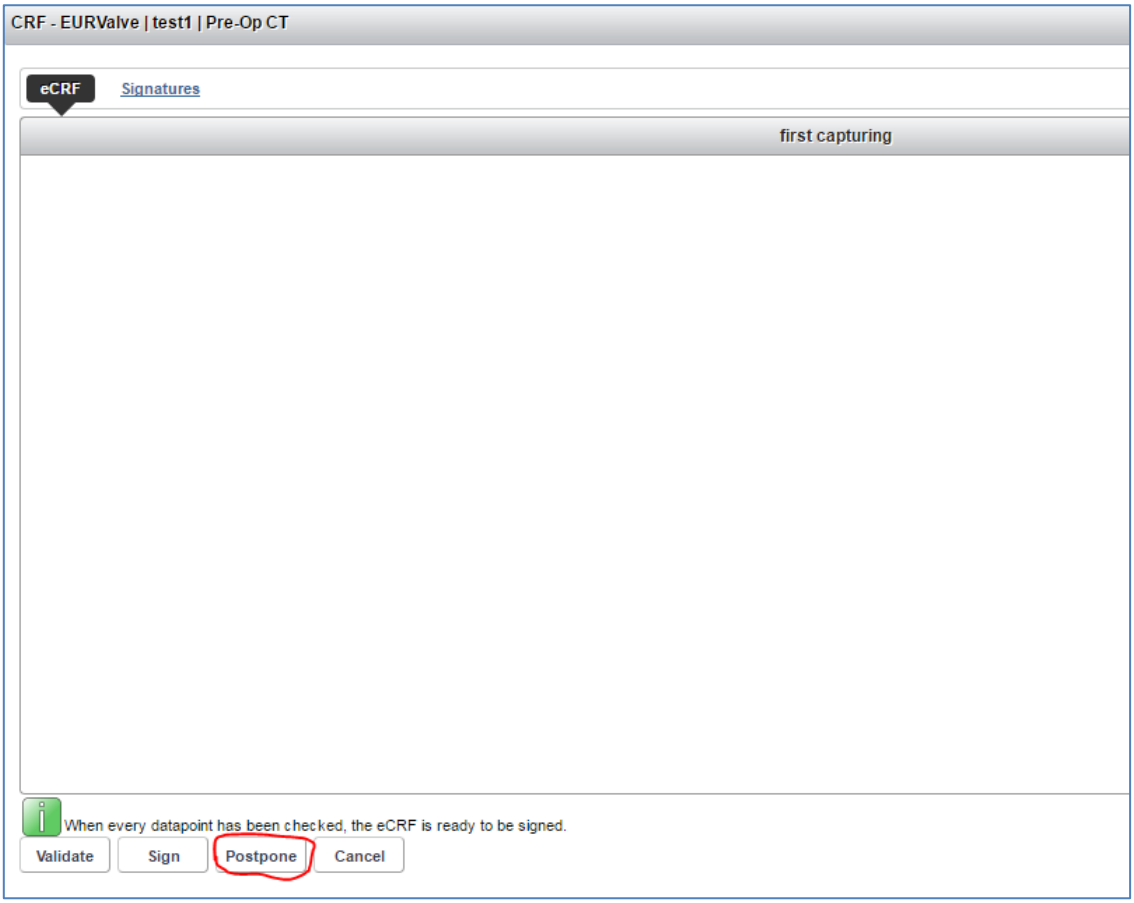
3. The “Subject Enrolment” Panel will appear and a basic set of information is accessible or can be entered, including the Identification number “PID”, and the Gender. Click the “Save” button after any changes:



4. To be able to upload images it is necessary to change the status of the visit for which the images need to be uploaded. To do so it is necessary to click on the visit then click the “Open CRF” button (and note that only one visit can be selected in order to edit the CRF, since the CRF is relative to each visit). Then continue to the next step:



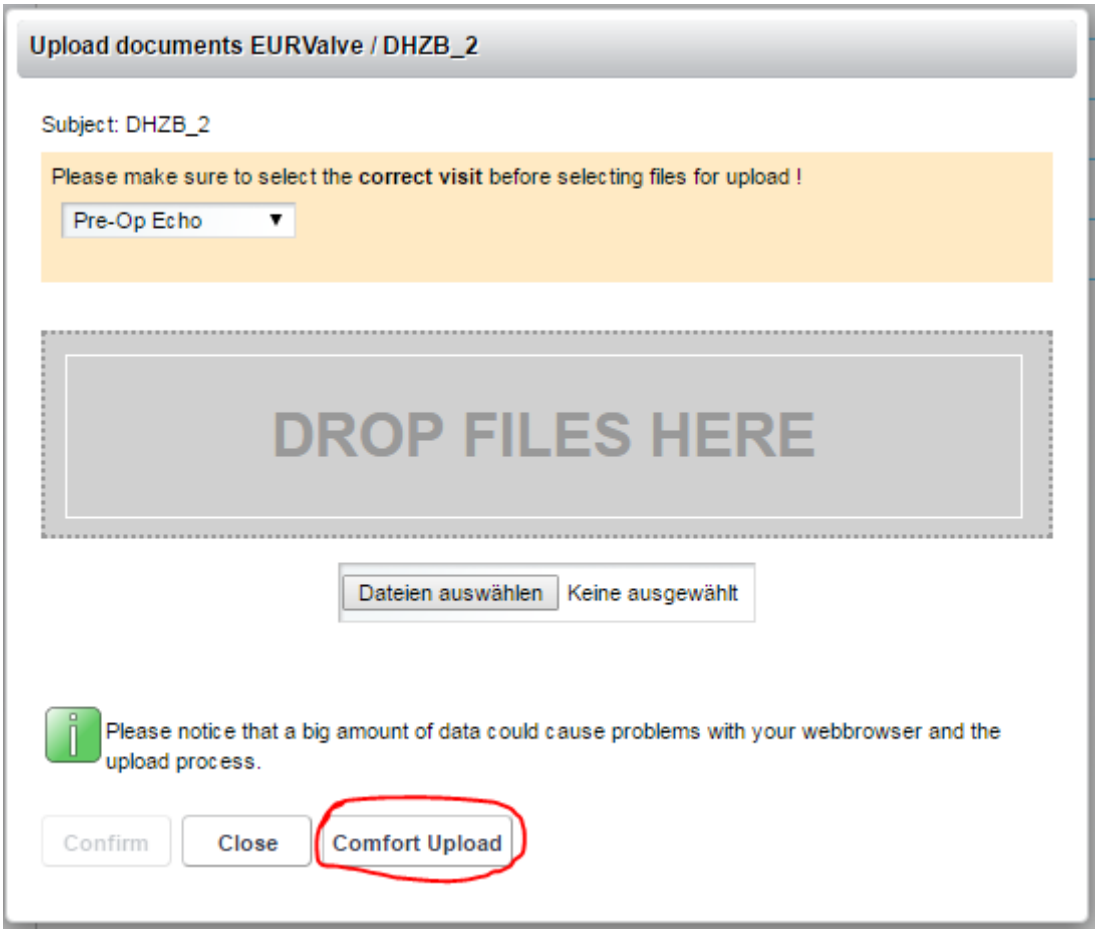
5. Since in EurValve the eCRFs are not embedded in TrialConnect, the CRF Panel is blank. However, to activate this patient visit it is still necessary to click on the "Postpone" button. Only then will it be possible to upload images:



It is only necessary to do this process once per patient (not for all the visits where images will be uploaded).

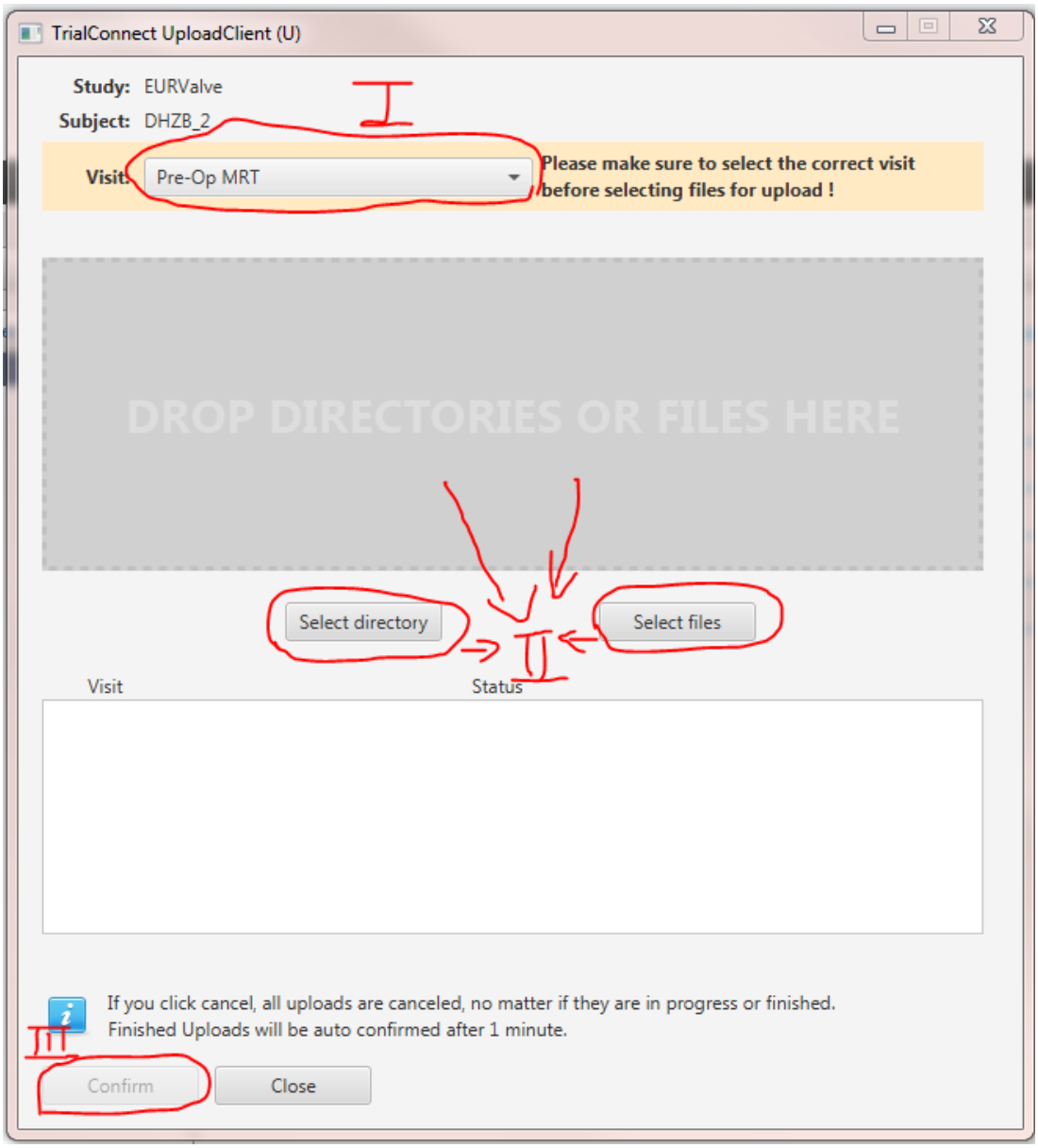
6. Click on the "Upload 'Document" button at the bottom-left of the window, which should be available:

7. The “Upload Documents” panel will open and the “Comfort Upload” button should now be clicked:



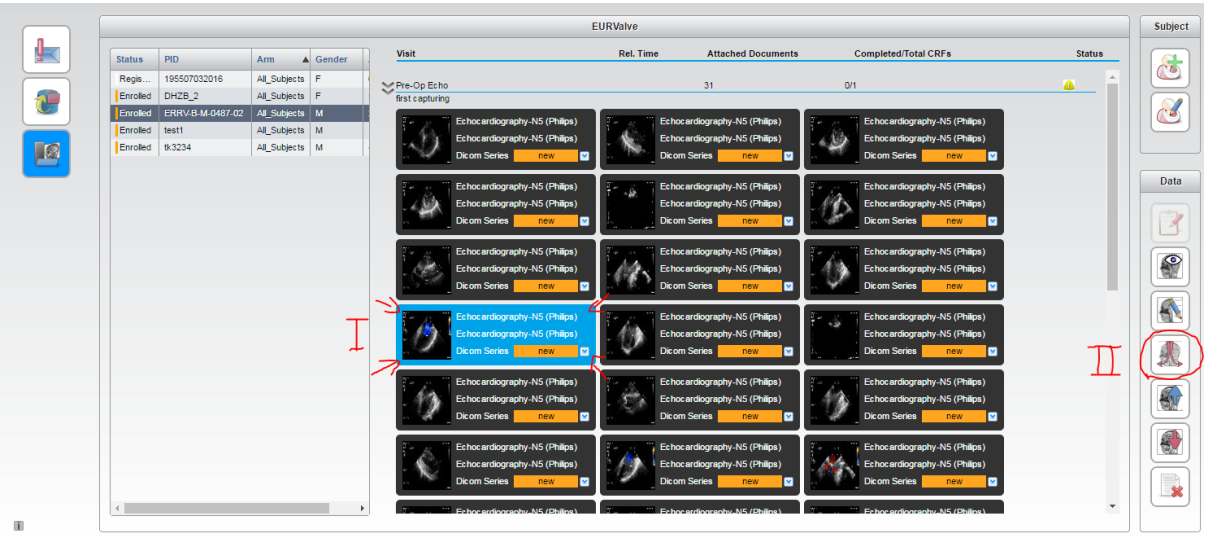
8. A Java file will be downloaded; save and open this:

9. Now on this screen choose the Visit to which the images should be allocated, and then the directory and files should also be selected. Alternatively, it is possible to drag-and-drop the folder/files to be uploaded onto the relevant location. When the upload is finished the "Confirm" button can be pressed (and if the button is not clicked within 1 minute, the upload will be auto-confirmed):

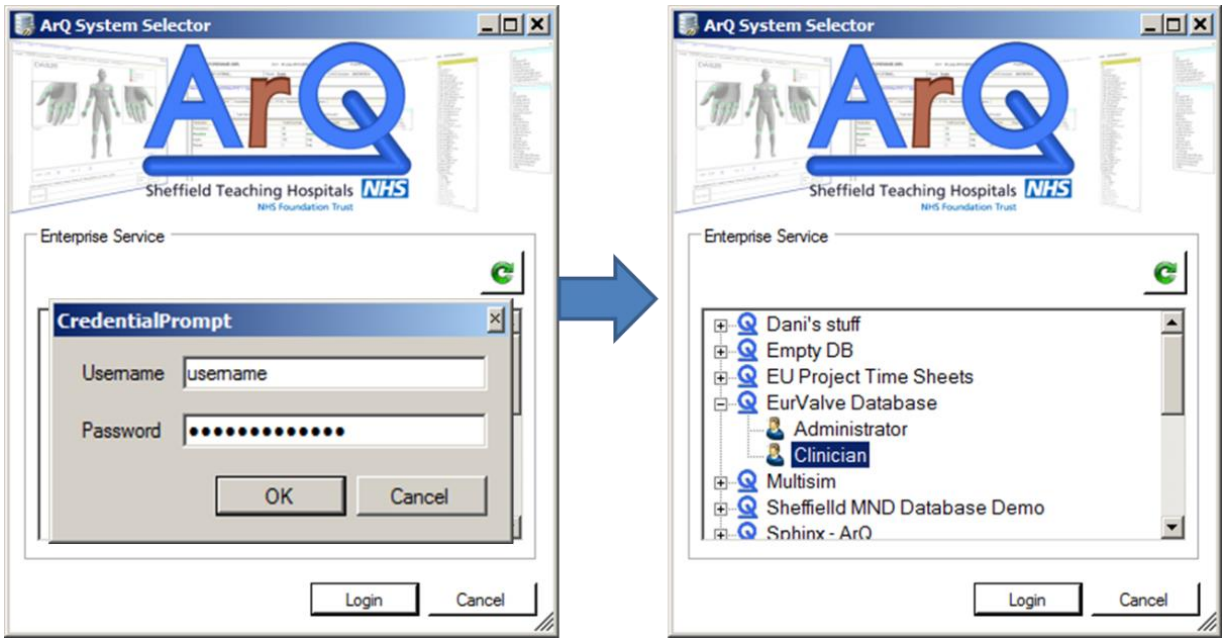


The images will be then uploaded.

10. In some cases, typically for echocardiography images, TrialConnect automatically aggregates several images or image-sequences into one set. If required, this can be corrected by selecting the aggregated image sequence and pressing the “Split selected document” button:



ANNEX 2: ARQ TRAINING INSTRUCTIONS AND CONFIGURATION



ArQ Login process

ArQ operates as a Windows executable, obtained by download from a location identified during the user registration process.

The executable connects to a remote server, and a login for the system must be obtained through the application process which was distributed through the Project Management Office.

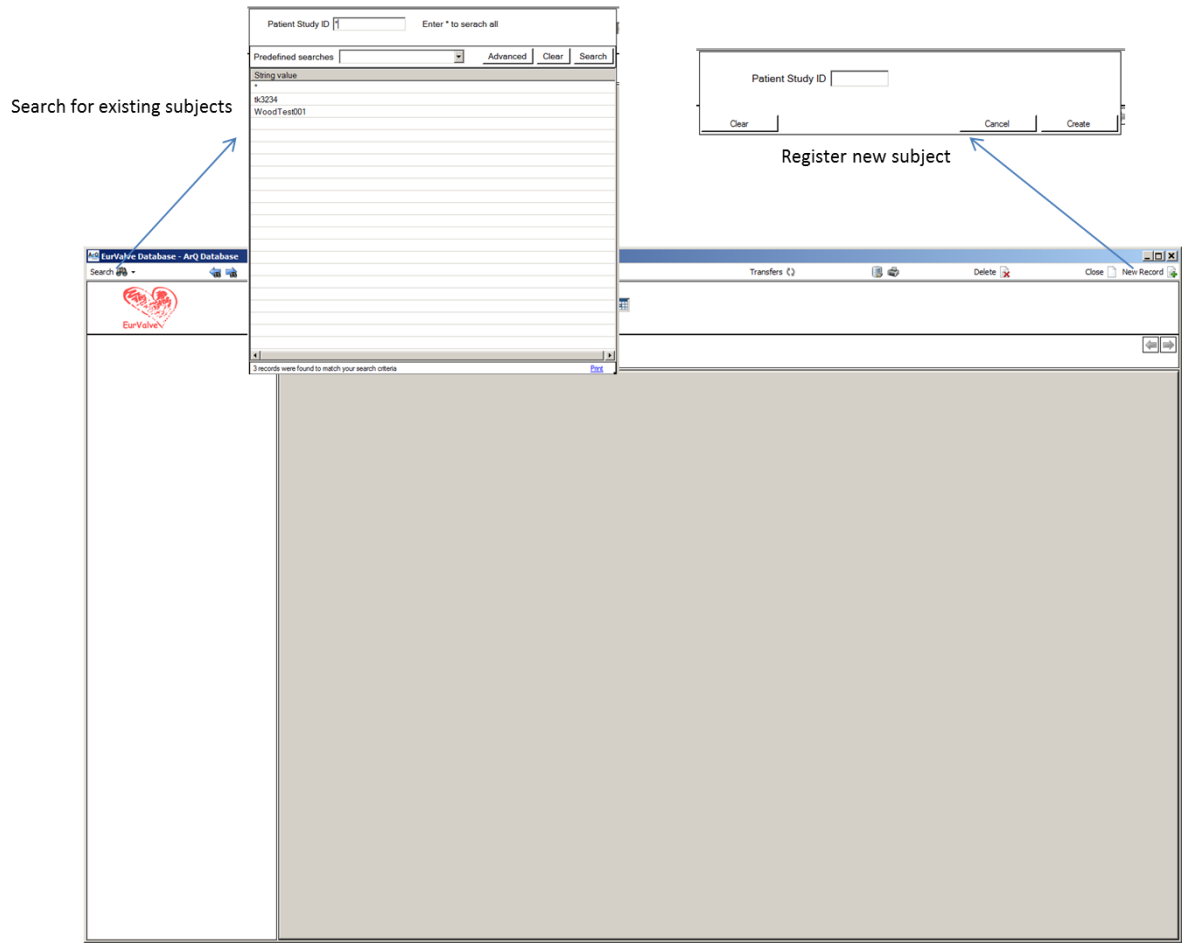
To obtain an account on the system the following information must be submitted:

- Forename
- Surname
- Partner/institution short name
- Preferred username
- Mobile phone number (Used to send your password via SMS)

User requests will be verified with the partner Principal Investigator.

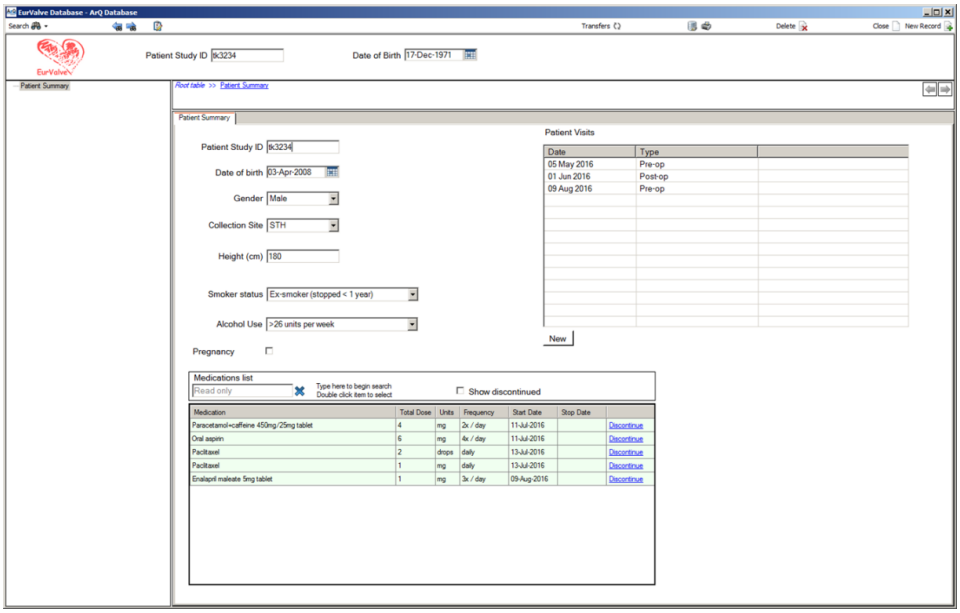
Users logging in to ArQ will see only the systems that their role allows and, for most users in EurValve, it is likely this will be only the EurValve system. Users with responsibilities in other research projects may see additional selections.

1. Once logged in, users need to either search for an existing subject, or register a new one with their primary identifier. It is not possible to register the same subject twice.



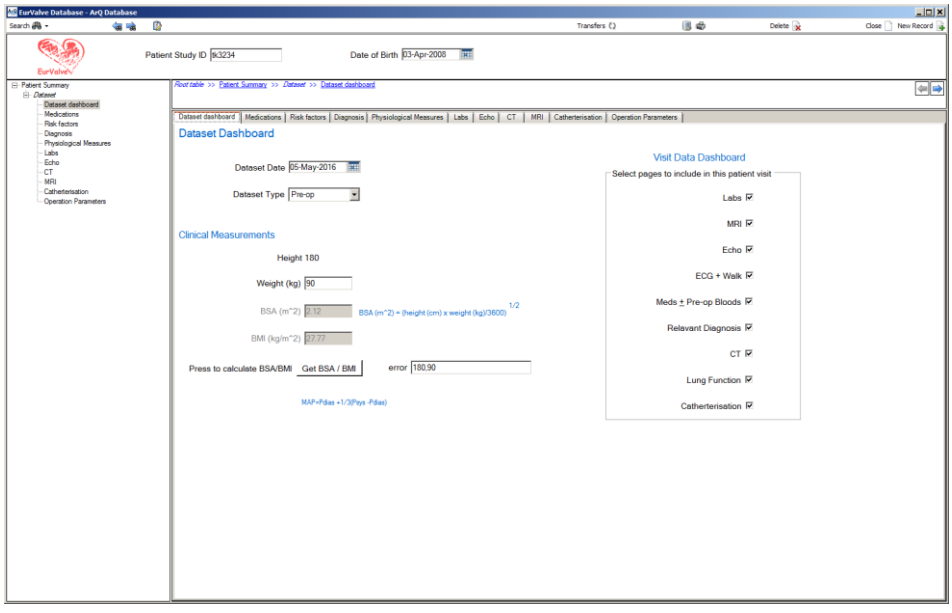
ArQ search or subject registration

2. The first page captures basic phenotypical information. It also displays, in a read only display, the medications the subject is currently receiving and a panel for the list of visits or events the subject has experienced. The "Patient visit" list is the entry point to the majority of the data collection and an existing visit can be accessed, or a new one created.



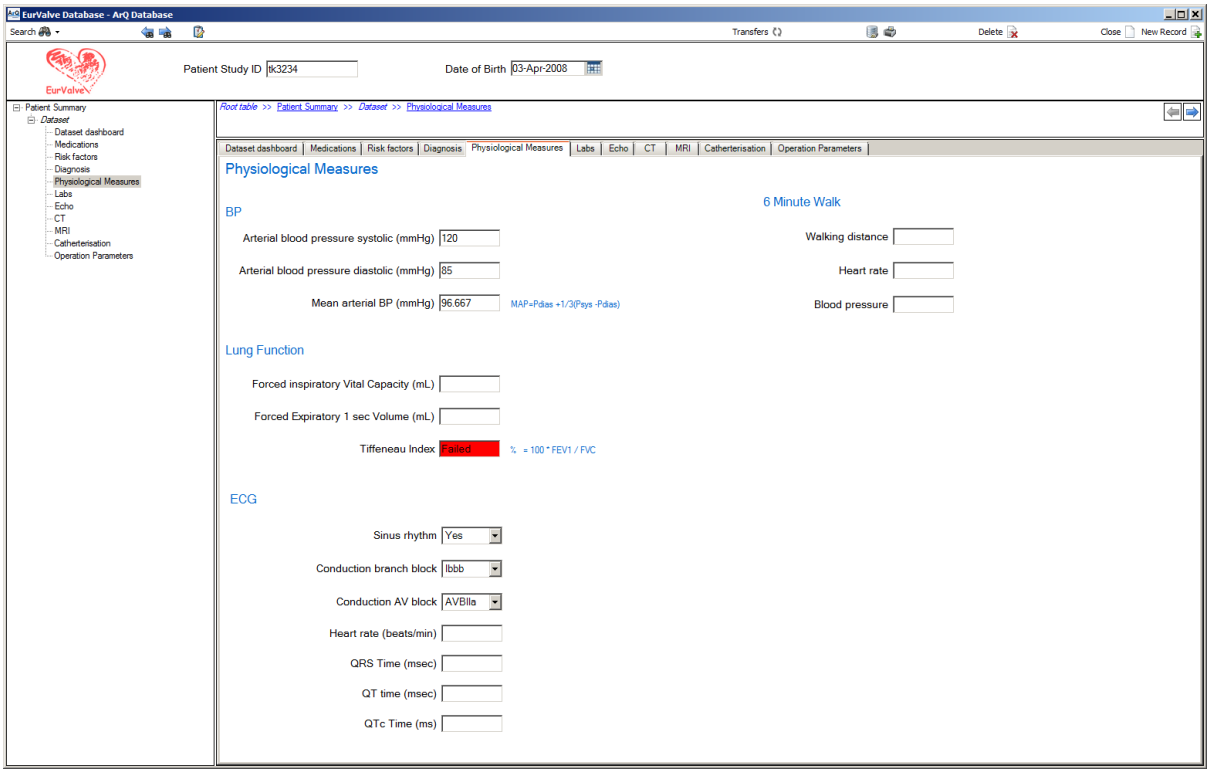
Patient level Screen

3. The tab shown below is the primary configuration screen for the subject visit. By selecting any of the check box options in the Dashboard group the classes of information to be collected during this event can be configured. As options are selected, so more of the data collection tabs across the top of the display become visible. This ensures that attention is focused on only those data relevant for this particular patient visit.



From this page there are a possible 10 further data collection pages available. Below we show two further examples of pages with specific functionality that assists data entry for users.

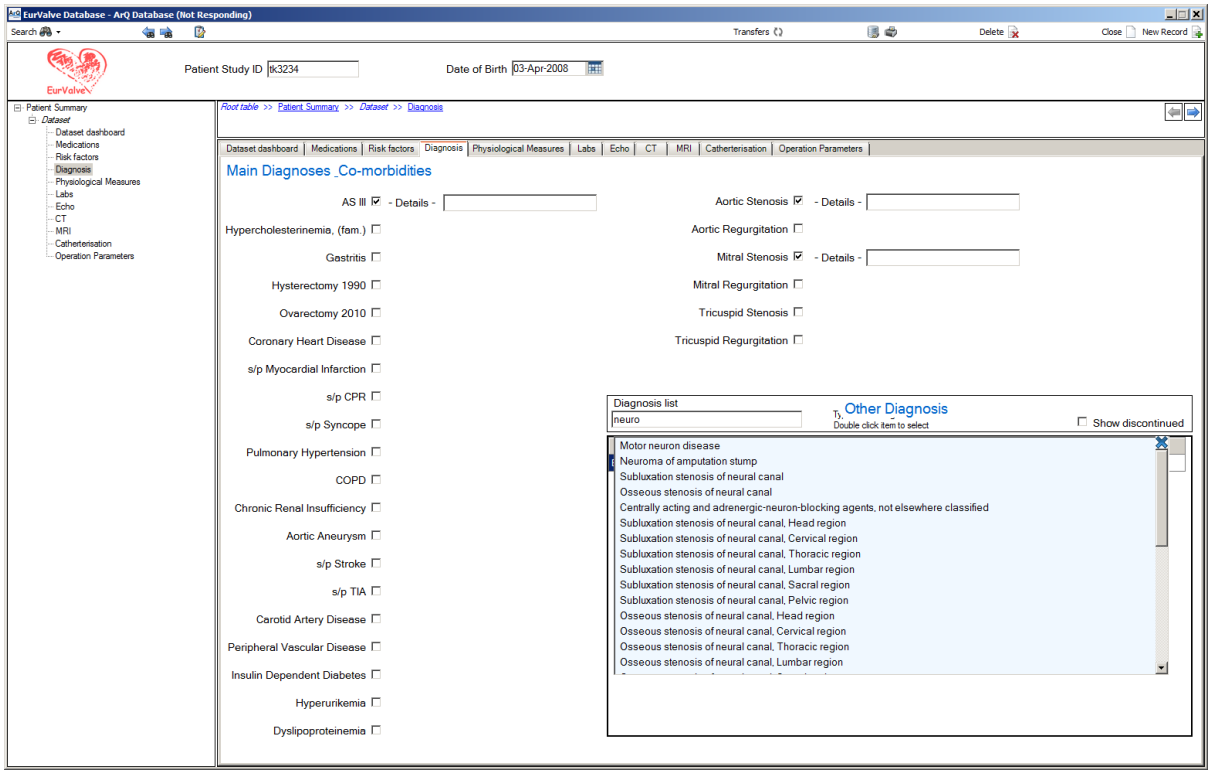
4. Below, the Physiology Measures screen shows examples of auto calculation controls. A good example is the "Tiffeneau Index" which currently has a 'failed' state because the two parameters above it contain no data. Not so obvious is the "Mean arterial BP" field which contains a value, but in fact this is an automatic calculation based on the two values above, and which has succeeded. Also to be noted is that these values are not simply evaluated on demand they are stored in the database and available for query by the research teams.



Auto calculation fields

5. The second feature of interest in the system is the live search facilities to add clinically coded information. This feature is used to capture both medications data and "Other diagnoses", shown below. Both use the SNOMED ontology services hosted in Sheffield to find and select the correct items from the list.

   Within the system, medications and diagnoses have very similar data models: items of known interest have specific database fields (true or false) plus a list of other items which are not known to be significant *a priori*. This gives the consumers of the data (researchers) a much easier mechanism for querying the data given that the majority of their interest will include the data items, but also allows new insights to be generated by the more complex machine-learning approaches by exposing high quality coded items for analysis.



Live search data entry for Diagnosis and Medication entry

ANNEX 3: TRAINING PARTICIPANTS

Those involved in the training are listed in the table below.

Catharina Hospital	Nelly Lumens
Catharina Hospital	Pim Tonino
Catharina Hospital	Jo Zelis
German Heart Institute Berlin	Joao Filipe Fernandes
German Heart Institute Berlin	Marcus Kelm
German Heart Institute Berlin	Titus Kühne
German Heart Institute Berlin	Alexander Meyer
Sheffield Teaching Hospitals NHS Foundation Trust	Steven Wood
University of Sheffield	Karen El-Arifi
University of Sheffield	Patricia Lawford
University of Sheffield	Keith McCormack
University of Sheffield	Paul Morris

Table 1: Training Participants

DEFINITIONS

List of Key Words/Abbreviations

AV	Aortic valve
BMI	Body Mass Index
BSA	Body Surface Area
CABG	Coronary artery bypass grafting
CCS	Canadian Cardiovascular Society grading of Angina
CFD	Computational fluid dynamics
COPD	Chronic obstructive pulmonary disease
CT	Computed Tomography
DICOM	Digital Imaging and Communications in Medicine Standard
dPmax	Max Pressure Drop
dPmean	Mean Pressure Drop
DSS	Decision Support System
eCRF	electronic case report forms
ED	End diastole
EF	Ejection fraction
ES	End systole
FS	Fractional shortening
ICD	International classification of disease
JSON	Javascript object notation
LA	Left atrium
LV	Left ventricle
LVEDD	Left ventricle end diastolic diameter
LVOT	Left ventricular outflow tract
LVPWD	Left ventricle posterior wall diameter
ML	Machine learning
MR	Magnetic resonance
MR(I)	Magnetic Resonance (Imaging)
MV	Mitral valve
NYHA	New York Heart Association Heart Failure Classification
PM	Project month
ROM	Reduced order modelling
RV	Right ventricle
s/p	status post
STL	Stereolithography
STS	Society of Thoracic Surgeons Risk Score
TAVI	Transcatheter aortic valve implantation
TEE	Trans-oesophageal echocardiography
TTE	Trans-thorax echocardiography
VHD	Valvular heart disease
WP	Workpackage