Model Driven Paediatric European Digital Repository

Call identifier: FP7-ICT-2011-9 - **Grant agreement no**: 600932

Thematic Priority: ICT - ICT-2011.5.2: Virtual Physiological Human

Deliverable D2.2

Revised Requirements Analysis Document

Due date of delivery: 28th February 2015

Actual submission date: 24th March 2015

Partner responsible for this deliverable: OPBG

Version: 2.2.3

Start of the project: 1st March 2013
Ending Date: 28th February 2017

Dissemination Level: Public

Document Classification

Title	User Requirements
Deliverable	2.2
Reporting Period	2
Authors	OPBG
Work Package	WP2
Security	PU
Nature	R

Document History

Name	Remark	Version	Date
Marcello Chinali		V1.0	29-01-2015
Marcello Chinali	Clinical workflows added for each disease	V2.1	20-02-2015
Marcello Chinali	Revised version after the discussion during the Internal Review in Amsterdam	V2.2.1	25-02-2015
Marcello Chinali	Integration of the contribution by the technical partners	V2.2.2	12-03-2015
Marcello Chinali	Final version including the feedback by the internal reviewer	V2.2.3	23-03-2015

List of Contributors

Name	Affiliation
Marcello Chinali	OPBG
Giacomo Pongiglione	OPBG
Henning Mueller	HES-SO
Ranveer Raaj Joyseeree	HES-SO
Patrick Ruch	HES-SO
Gabriele Rinelli	OPBG
Silvia Magni Manzoni	OPBG
Melania Manco	OPBG
Blegina Shashaj	OPBG
Gessica Vasco	OPBG
Pieter van Dijkhuizen	IGG
Andrew Taylor	UCL
Alex Jones	UCL
Jakob Hauser	DHZ
Tobias Heimann	SAG
Olivier Ecabert	SAG
Jaap Harlaar	VUA

List of reviewers

Name	Affiliation
Giacomo Pongiglione	OPBG
Bruno Dallapiccola	OPBG
Edwin Morley-Fletcher	LYNKEUS

Abbreviations

CUR	Clinical User Requirements
PM	Project Management
DoW	Description of Work
WP	Work Package
CVD	Cardiovascular Disease
JIA	Juvenile Idiopathic Arthritis
NNMD	Neurological and Neuromuscular Diseases

Table of Contents

1. Introduction

Being the MD-Paedigree a clinically driven project, the main objective of WP-2 is to guarantee that the features and capabilities of the disease models merge the clinical needs and provide a significant impact on current clinical practice workflows, improving patient care and supporting medical practice in the everyday activity.

In the D2.1 document delivered at month 12 "Initial requirements analysis document including priorities for the implementation", we have defined the most pressing requests of the clinical partners for the MD-PAEDIGREE derived models. In addition, specific lists of variables for each clinical area have been defined.

2. Purpose

This document is designed to update the clinical requirements for the disease modelling for each area of the MD-Paedigree clinical project – these being cardiomyopathies, obesity related cardiovascular risk, juvenile idiopathic arthritis and neurological and neuromuscular diseases.

In order to achieve this aim, the D2.2 contributes to ensure that the models incorporates the user requirements of the clinicians and that the resulting models can have a significant and innovative impact on the existing clinical workflow on patient care. The ultimate goal is to assure that the computational models obtained from the project can improve the current knowledge and understanding of the disease by simulating different aspects on the evolution of a disease, including the effect of a specific therapeutic intervention (being this either pharmacological, behavioral or surgical). Based on the targeted clinical need definition of the user requirements will play an active and interdisciplinary role in enhancing the integration process of computer models into clinical practice.

In the current document, we have gathered feedback from the technical partners, updated changes in the clinical areas derived by the evolution of the study, and started the process of defining the prospected clinical impact of the use of disease modelling in clinical practice for each of the studied disease areas. As detailed in the D2.1, the requirements analysis is a continuing process throughout the years of the project and thus the deliverables of the WP2 represent living documents that are updated with requirements coming up throughout the whole data acquisition process, in parallel with the clinical workflows gaining experience process.

2.1 Scope

This document is applicable to the MD-Paedigree project until the next programmed document release (D2.3: "Update on the Clinical Requirements Document").

2.2 Project Overview

MD – PAEDIGREE *Model-Driven European Paediatric Repository* is a research project funded by the European Commission under the Virtual Physiological and Human Area (VPH) of the ICT Theme of the Seventh Framework Programme (contract no. 600932).

MD-Paedigree validates and brings to maturity patient-specific computer-based predictive models of various paediatric diseases, to increase their potential acceptance in the clinical and biomedical

research environment as newly-defined workflows for personalized predictive medicine at the point of care.

MD-Paedigree aims to advance the state-of-the-art of patient-specific computational modelling of different paediatric diseases and translate the latest advances into clinics to improve disease understanding, therapy outcome, and provide an infostructure platform for assessing new therapies at the point of care.

MD-Paedigree's goals therefore are to integrate and share highly heterogeneous biomedical information, data and knowledge, using best, jointly develop reusable, adaptable and composable multi-scale VPH workflow models and to support evidence-based translational medicine at the point of care practices from the biomedical semantic Web.

MD-Paedigree represents a major step towards personalized paediatric e-Health, based on data-driven models, patient-specific simulations and a sustainable data and model repository. It fosters the state-of-the-art of patient-specific computational modelling of the selected diseases and translates the latest advances into clinics to improve disease understanding and provide a platform for testing new therapies at the point of care. In fact, MD-Paedigree demonstrates how a dedicated VPH repository can provide full accessibility to existing and further developing knowledge in paediatrics to all interested bio-medical researchers precisely through linking data with models, thus proving the large-scale benefits of having both the data and models readily available at the point of care.

3. User Requirements

3.1 State-of-the-Art (starting point provided by the D2.1)

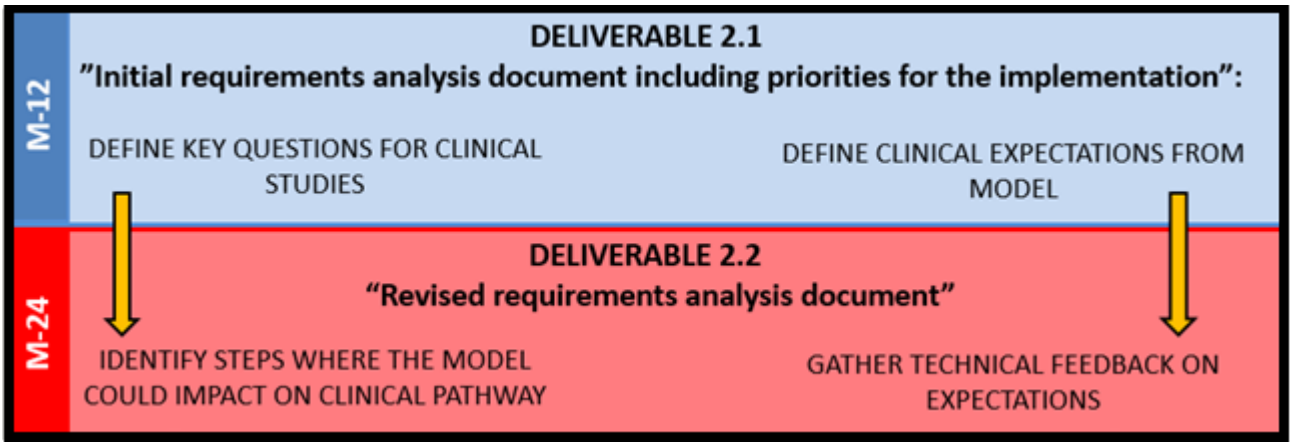
As defined by D2.1, an alternative approach using experience-evolving specifications as interpretations of user requirements has been chosen. This aspect is efficient for the MD-Paedigree project where the development and detailed definition of the specific clinical workflows has changed the original clinical protocols during the first study year. In fact, clinical user requirements have evolved, focusing on specific and more clinically relevant aspects of the four specific diseases addressed in project.

In brief, the D2.1 document have focused on the following aspects:

- **Clear identification of the main clinical questions raised in the different disease areas**:
    - Define the most critical and complex aspects of the different diseases.
    - Identify the aspects in which current medical knowledge is still limited due to a traditional research approach.
- **Specific level of priorities for each aspect of the clinical question of the clinical work-packages.**
    - Support in improving the understanding of complex pathological features of the disease
    - Support in predicting the evolution of the disease
    - Support in predicting the potential effect of treatment/intervention
- **Specific list of user requirements for each single clinical work package.**

Accordingly, D2.2 is focused on defining the current patient workflow for the four disease areas, in order to start identifying the potential effect of modelling in the change/improvement of the clinical pathway for the studied diseases and to gather feedback from technical partners on the D2.1. In addition, during the past year joined clinical and technical TCs to update clinical requirements have taken place, together with face-to-face clinical/technical tune-in meetings, held in Rome, London and other locations during the past months for the joined clinical and technical WPs for all the clinical areas.

Schematically the evolution of the work of the WP2 can be represented in a simplified fashion by the following scheme:



3.2 Synergy with other MD-Paedigree Requirements Work Package

During the second year of the project a number of steps have been undertaken to improve the integration among Work Packages. First, the present document has been prepared in cooperation with both WP12 and WP13, which have interactively shared information of clinical workflows, clinical validations and clinical expectations from the models. In addition, a number of specific teleconferences and dedicated face-to-face meetings have been organized to assure adequate clinical-technical understanding of the user requirements and the potentialities and limitations of the derived models.

The requirement gathering efforts have continued and reinforced those started in the first phase of the project and will continue throughout the clinical protocol data collection in order to assure that clinical requirements:

- Are clearly understood by the technical partners and conversely make sure that the technical and validation limitations are clearly understood by the clinicians.
- Support in providing models which can improve current clinical workflows (i.e. clinical prediction and prognosis tools, assure impact on clinical care).

4. Revised clinical requirements separated by clinical work-package

For each clinical area, a detailed clinical workflows were produced.

The aim of the workflow is to:

- Identify the steps of the **current patient's pathway**
- At which step the MD-PAEDIGREE models can potentially add value to the **prognosis prediction** and patient follow-up tasks.
- Define the **expected clinical impact** of the models provided by the MD-Paedigree on both:
  - *Quality of care (improving the outcome)*
  - *Healthcare workflows (reducing time loss)*

4.1 WP-3. CARDIOMYOPATHIES

Cardiomyopathy is a rare life-threatening disease leading to chronic cardio-active therapy, or even to mechanical support (artificial heart), heart transplantation or death. However, it is very difficult to predict which group any patient will end up in. Thus, the main user requirements for modelling in patients for cardiomyopathy regard the role of models in support patient management and prediction of outcome. The main issue for modelling in patients for cardiomyopathy regard both the understanding of the complex interactions between heart size, geometry and shape, cardiac workload, heart rate and heart pump function as well as the ability to provide better insight into prognosis and impact of treatment on cardiomyopathies, which will help in patient management.

4.1.1 Updated Clinical Requirements

- **Unfold complex interactions.** Establishing the interaction between the different components of the heart and cardiac performance in dilated cardiomyopathy (mechanical modeling, hemodynamic modelling, fluid-structure interaction)
- **Predict the effect of time and intervention.** Predicting evolution of the disease and identifying possible predictors of outcome. Impact of changes in cardiac performance by changing heart rate and cardiac load using specific medications

4.1.2 Feedback from the technical partners on the D2.1 for WP3

A detailed list of parameters were provided to the technical partners through the D2.1 document. The technical partners have provided their feedback (as an *exemplia gratia* a full table reported in in Appendix 1 on WP-3) defining parameters which are potentially predictable by the developing model and parameters which most probably the models in development will not be able to predict:

Parameters that can be provided by the models:

- Changes in LV volumes, RV volumes, LV and RV ejection fraction, changes in LV mass, and mitral dilation.
- Changes in stroke volume and cardiac output caused by both time and medications.

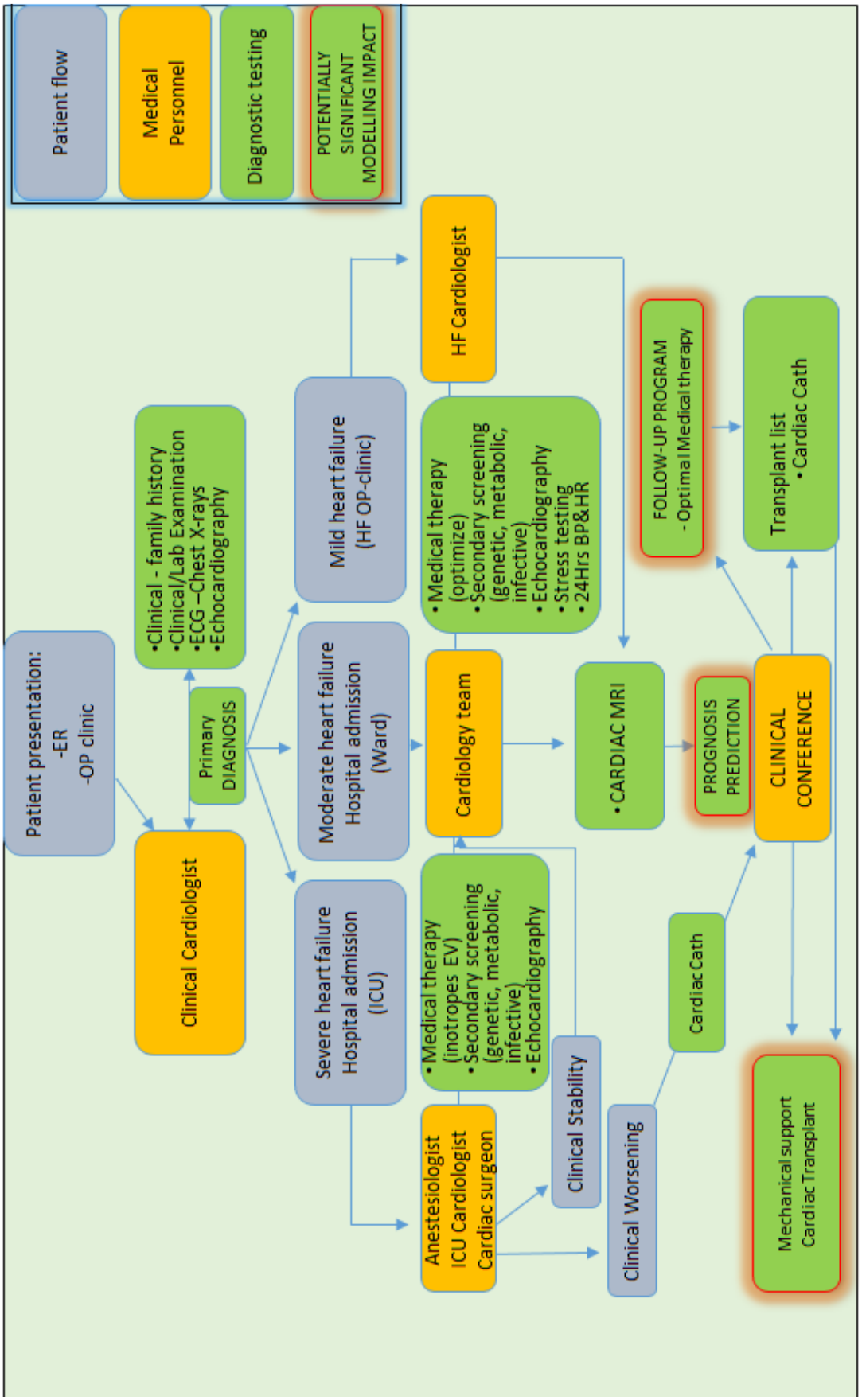
Parameters that cannot be provided by the models:

- Changes in left atrial dimensions and vena cava.

Parameter which might be provided but more interaction between clinical and technical partners is needed to correctly merge clinical request and the technical result:

- Changes on mechanical parameters, including systolic synchronicity

4.1.3 Detailed clinical workflow for WP3



4.1.4 Prospected Impact of Model on Clinical Pathway

From the detailed workflow we have derived that the models can significantly impact the care of the patients affected by cardiomyopathy by:

- **Identifying patients at higher risk** of outcome
- **Predicting of the timing from the onset of heart failure** to the need of transplant/mechanical support
- **Potentially guiding medical/therapeutic decision** on most efficient regimen for each specific patient (or 'patient type')

It should be noted that the WP3 represents the only WP in the study focused on a group of life-threatening and fast developing disease. Thus, it is probably the single clinical area in which the impact of the model will be tested to predict hard endpoints and patient outcome, including exitus. In this view, the ability of the model in predicting the effect of medications and to establish *a priori* the probable development of untreatable heart failure, will help the clinicians to identify in a timely fashion patients at higher risk of need of mechanical heart support and eventually of heart transplant. Needless to underline that this specific task could have relevant impact on both patient management and hospital related costs and burden.

4.2 WP4 - CARDIOVASCULAR DISEASE RISK IN OBESE CHILDREN

Obesity in childhood is the only non-clear-cut disease (but rather a risk factor) studied in the MD-Paedigree. As time of overt disease development from exposure varies between many years to decades, from the medical knowledge standpoint the development of a disease model for childhood obesity represents an unprecedented tool to answer important questions.

4.2.1 Updated Clinical Requirements

The revised clinical requirements for the WP4 comprise both a statistical model and a mechanical model:

- **Statistical Model:**
  - Building a complete risk profile geno/phenotyping of the obese children (food intake habits, psychological profile, vascular reactivity under meal stress test, gut microbiome, inflammatory status, imaging testing, etc.), with the ultimate aim of the identification of different pathophysiological patterns in obesity, and thus identify individuals at higher risk of developing overt cardiovascular disease

- **Mechanical Model:**
  - Identifying possible cardiovascular predictors of the development of early markers of disease, especially in the context of vascular reaction to meal stress.
  - Establishing the interaction between the different components of fat (amount and distribution), and cardiovascular system (at both rest and under meal stress).

4.2.2 Feedback from the technical partners on the D2.1 for WP4

A detailed list of parameters were provided to the technical partners through the D2.1 document. The technical partners have provided their feedback (e.g. Appendix 1 for WP-3) defining parameters which are potentially predictable by the developing model and parameters which most probably the models in development will not be able to predict:

Parameters that can be provided by the models:

- Complete multi-scale statistical models for identifying patterns or clusters of obesity phenotyopes, including global and visceral fat distribution.

- Prediction of changes in heart rate, stroke volume, and vascular reactivity caused by weight change and meal stress in regards to body fat distribution.

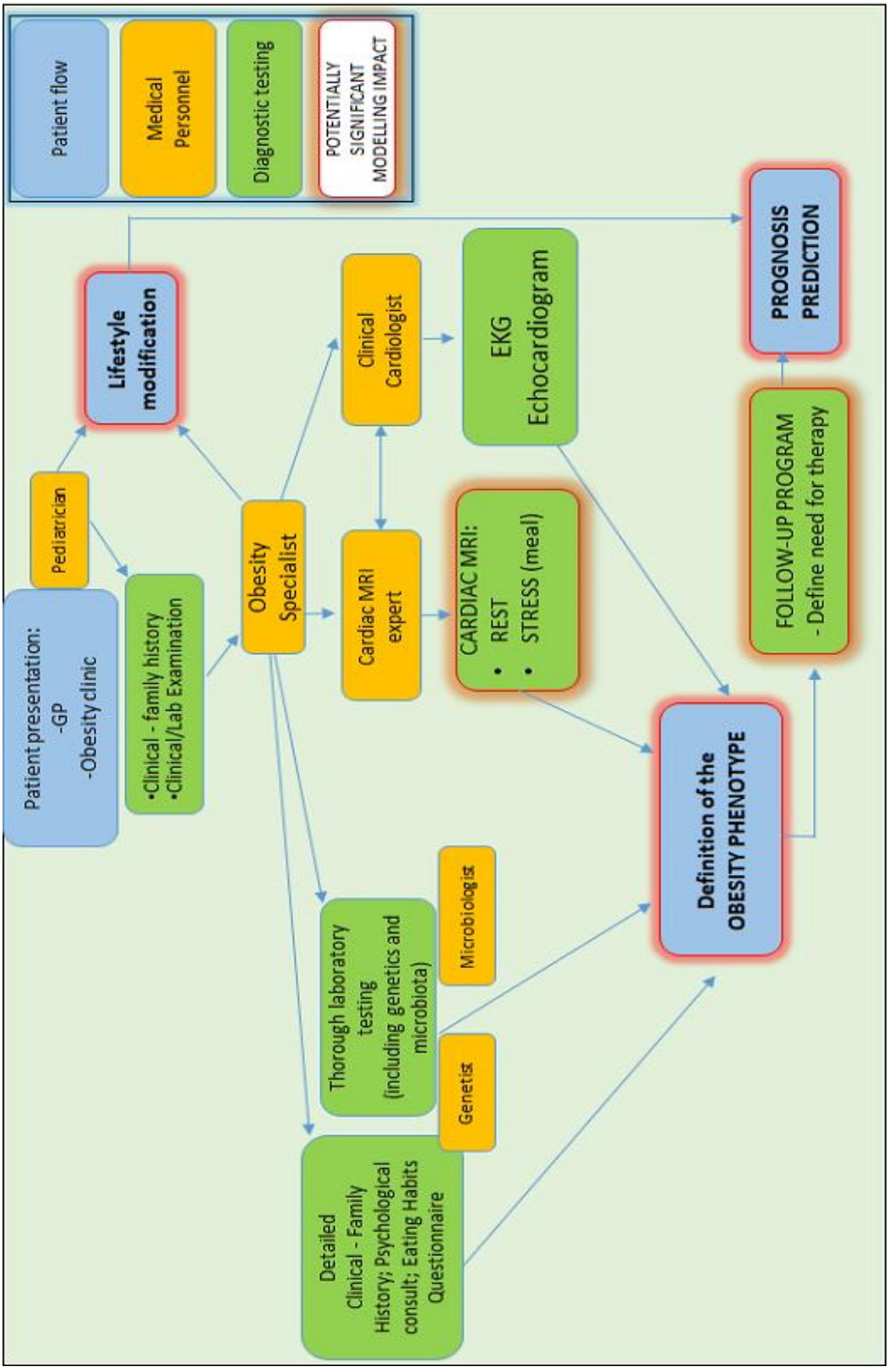
Parameters that cannot be provided by the models at current data acquisition status:

- Predict the effect on cardiovascular reactivity by lifestyle modifications (i.e. weight loss).

Parameter which might be provided but more interaction between clinical and technical partners is needed to correctly merge clinical request and the technical result:

- Specific role of genes and microbiota in defining the obesity phenotype.

4.2.3 Detailed clinical workflow for wp4



4.2.4 Prospected Impact of Model on Clinical Pathway

- From the detailed workflow we have derived that the models can significantly impact the care of the patients affected by obesity by:
  - **Identifying complex obesity phenotypes** associated with higher cardiovascular risk
  - **Predicting the effect of changes** in the amount and distribution of fat on of the cardiovascular system
  - **Predict the effect of lifestyle changes**.
  - **Supporting medical decision** from both the technical (i.e. defining the most appropriate and efficient clinical testing to stratify risk) and the clinical standpoint

It is important to underline that being obesity a not yet well-defined medical condition, in which a number of medical personnel is involved in the care and definition. As shown in the workflow, apart from the general pediatrician and the obesity specialist, a number of different medical specialists (including cardiac specialists, genetists and microbiologists) are involved in the definition of the state of the disease and in the management of care. Thus, the use of the model might significantly influence the definition of the disease in a number of steps of the current clinical workflow. The clinicians involved in the WP4, feel that a major scientific breakthrough, expected to be delivered by the mechanical modelling, would also be to establish whether the use of a meal-stress MRI as the only imaging test, might be sufficient in correctly identifying obese patients at higher risk (i.e. less favorable obesity phenotype). Thus reducing the role of time-consuming multidisciplinary imaging evaluation (including MRI fat distribution and cardiac ultrasound). In addition, it should not be underestimated the role of model prediction of the effect of weight loss, as it might represents a fundamental and crucial psychological reinforcement for the obese adolescents undergoing the needed lifestyle modifications (a process with well-known and established low compliance), which might significantly reduce the need of invasive bariatric surgery.

4.3 WP5 - JUVENILE IDIOPATHIC ARTHRITIS

The cause and pathogenesis of JIA are still poorly understood and disease heterogeneity implies that different factors probably contribute to its pathogenesis and development. Personalized joint biomechanical modeling allows critical evaluation of the forces within the joint under physiologic and pathological loading conditions, and evaluation of the impact of joint mechanical abnormalities on disease progression are needed for an accurate outcome prediction.

4.3.1 Updated clinical Requirements

The expected role of the multi-scale modeling is to make the exploration of complex systemic interactions and to improve early diagnosis and therapeutic intervention.

- **Unfold complex interactions**
  - Interaction between the different components the ankle region containing bone cartilage and ligaments- in defining functional impairment
  - Complex relationship between inflammation and movement ability
- **Identifying possible effect of time and intervention:**
  - Identify features of patients at higher risk of disease progression
  - Personalize risk stratification in order to start therapy more aggressively and or earlier.

4.3.2 Feedback from the technical partners on the D2.1 for WP5

A detailed list of parameters were provided to the technical partners through the D2.1 document. The technical partners have provided their feedback defining parameters which are potentially predictable by the developing model and parameters which most probably the models in development will not be able to predict:

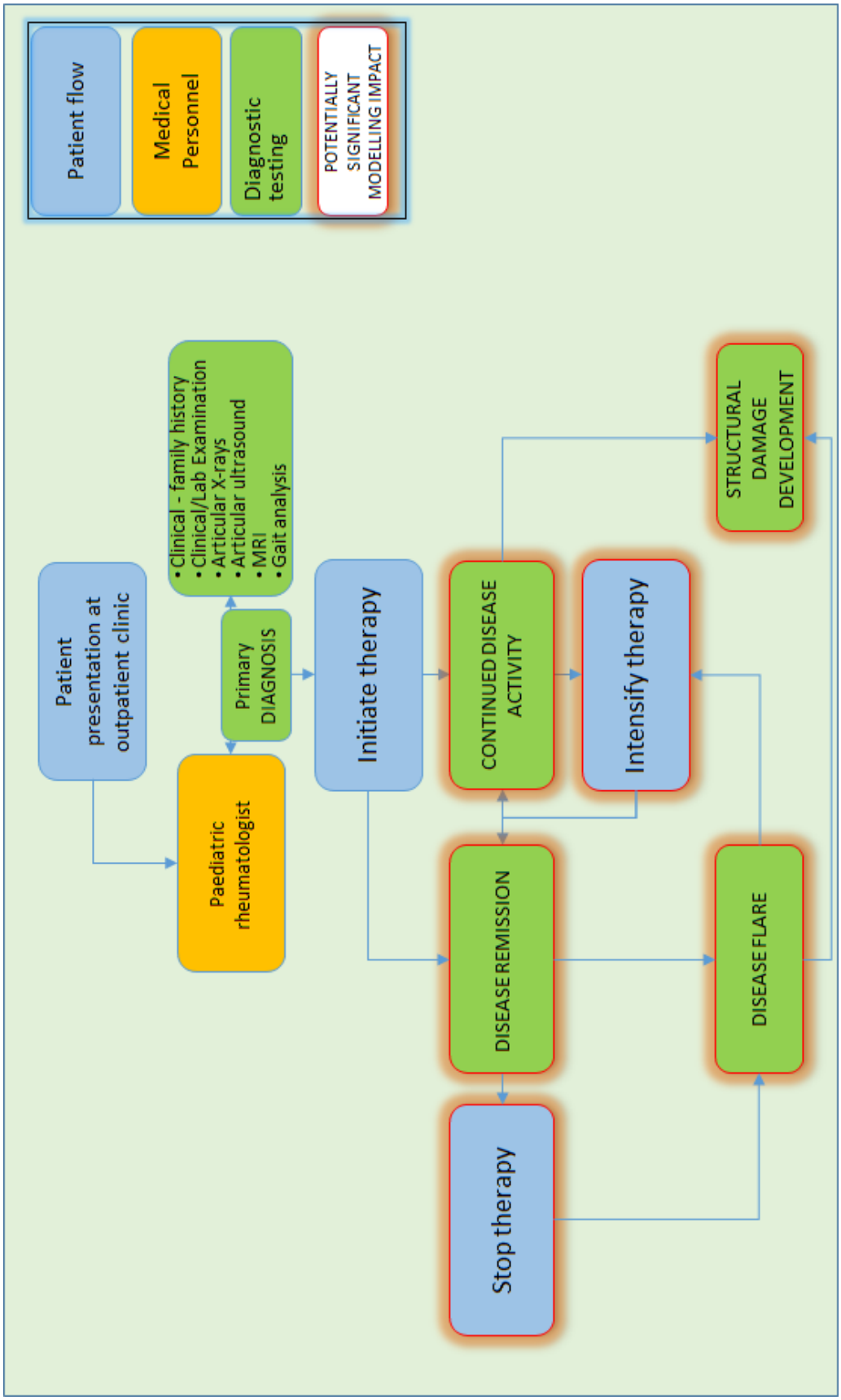
Parameters that can be provided by the models:

- Define the complex interaction between inflammatory parameters and functional parameters
- Predict the impact of different levels of inflammatory state on the functional parameters.
- Provide insights into the predict of disease development (flare, remission).

Parameters that cannot be provided by the models at current data acquisition status:

- Predict the incidence of structural damage development.

4.3.3 Detailed clinical workflow for WP5



4.3.4 Prospected Impact of Model on Clinical Pathway

- From the detailed workflow we have derived that the models can significantly impact the care of the patients affected by JIA by:
  - **Improve** definition of disease severity
  - **Predict** natural history of the disease and possible long-term disease-related structural damage.
  - **Target** therapy: the model is expected to provide useful information on the prediction of the effect of therapy administered at diagnosis in order to predict disease remission, continuation or flare.

It is important to underline that in the JIA work package the role of modelling might come into use in very early stage of the clinical workflow, thus significantly affecting patient care. Currently, medical therapy is started at the time of the diagnosis, however it is very difficult to predict whether the disease will flare or remit. Accordingly, the use of prediction models is expected to identify patient strata at the time of the diagnosis, proving very helpful in programming the medical course of the disease and correctly identify patients at higher risk of developing non-reversible joint structural damage.

4.4 WP6 - NEUROLOGICAL AND NEUROMUSCULAR DISEASES

In Neurological and Neuromuscular Diseases (NND) as well as in certain chronic diseases of the musculoskeletal system in children, treatments are strongly guided by maximizing the walking function of the human movement system, which is considered as highly valued by the patients. Although walking is a common task executed by a healthy individual in a seemingly effortless manner, it implies a complex involvement of inputs from several senses (visual, vestibular, proprioceptive, and somatosensory). The clinical study focuses on the walking ability of three different disease groups: Duchenne's muscular dystrophy, cerebral palsy and Charcot-Marie-Tooth disease. Its main clinical aim is to monitor disease course. However, in the CP group a specific interest on modelling relies on the possibility to predict the effect on walking of different therapeutic approaches, including surgical intervention.

4.4.1 Updated clinical Requirements

A number of specific clinical questions are expected to be answered by the models for each specific disease:

DMD & CMT:

- Obtain a detailed muscle/bone structural/functional interaction model (reproducing muscle length, weight, insertion points)
- Evaluate the impact of this interaction in defining walking functionality.
- Predict evolution of the disease (identify features of patients at higher risk of disease progression)
- Predict the effect of physical therapy

CP:

- In addition to what stated for DMD & CMT also obtain insight on treatment (virtual 'correction' of joint deformities and muscle lengthening)

4.4.2 Feedback from the technical partners on the D2.1 for WP6

A detailed list of parameters were provided to the technical partners through the D2.1 document. The technical partners have provided their feedback defining parameters which are potentially predictable by the developing model and parameters which most probably the models in development will not be able to predict:

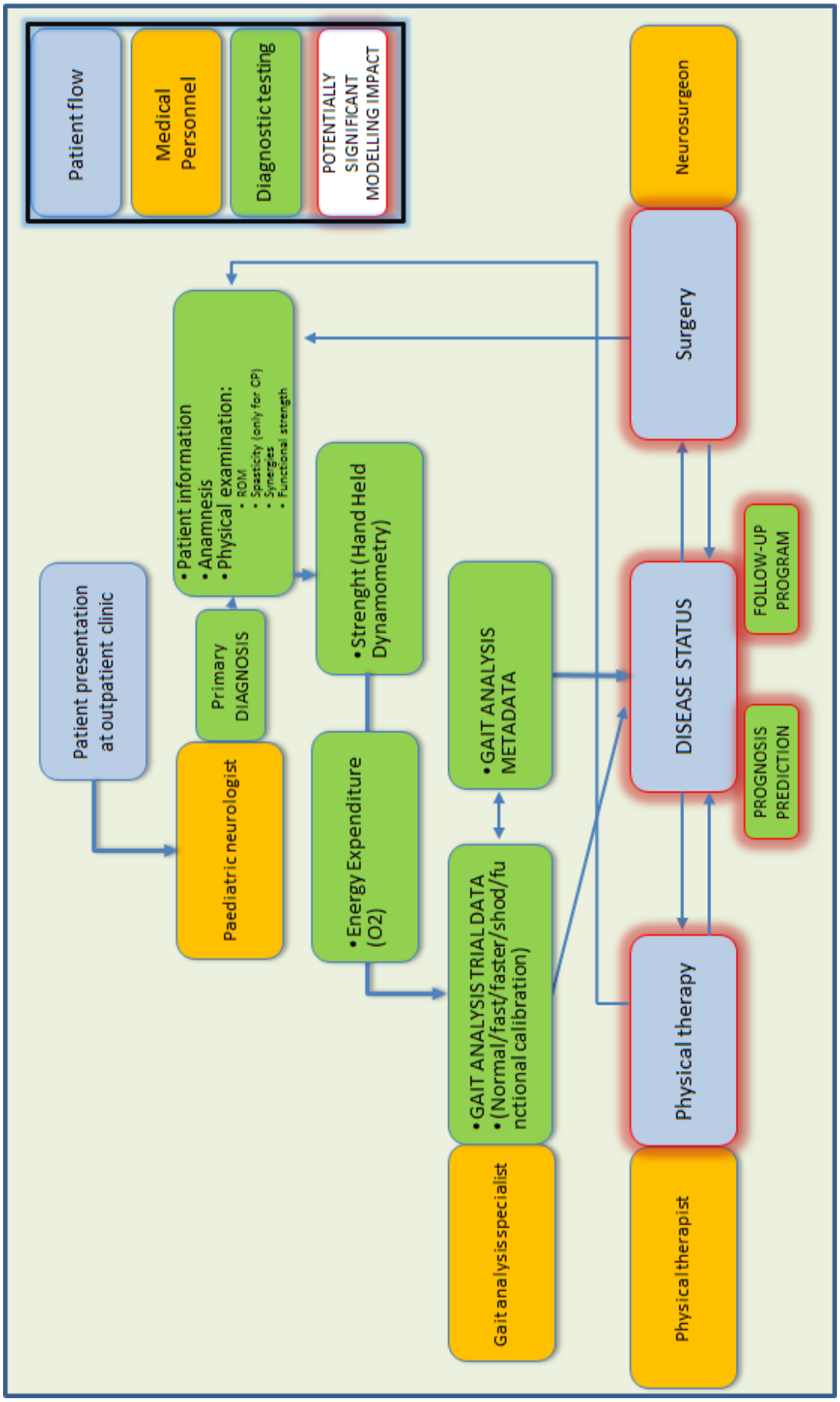
Parameters that can be provided by the models:

- Definition by combined gait analysis and MRI model of "patient specific" walking features and parameters.
- Prediction on the evolution of the disease over time in walking ability and strength.

Parameters that cannot be provided by the models at current state of data aquisition:

- Prediction on the effect of intervention on improvement in walking ability.

4.4.3 Detailed clinical workflow for WP6



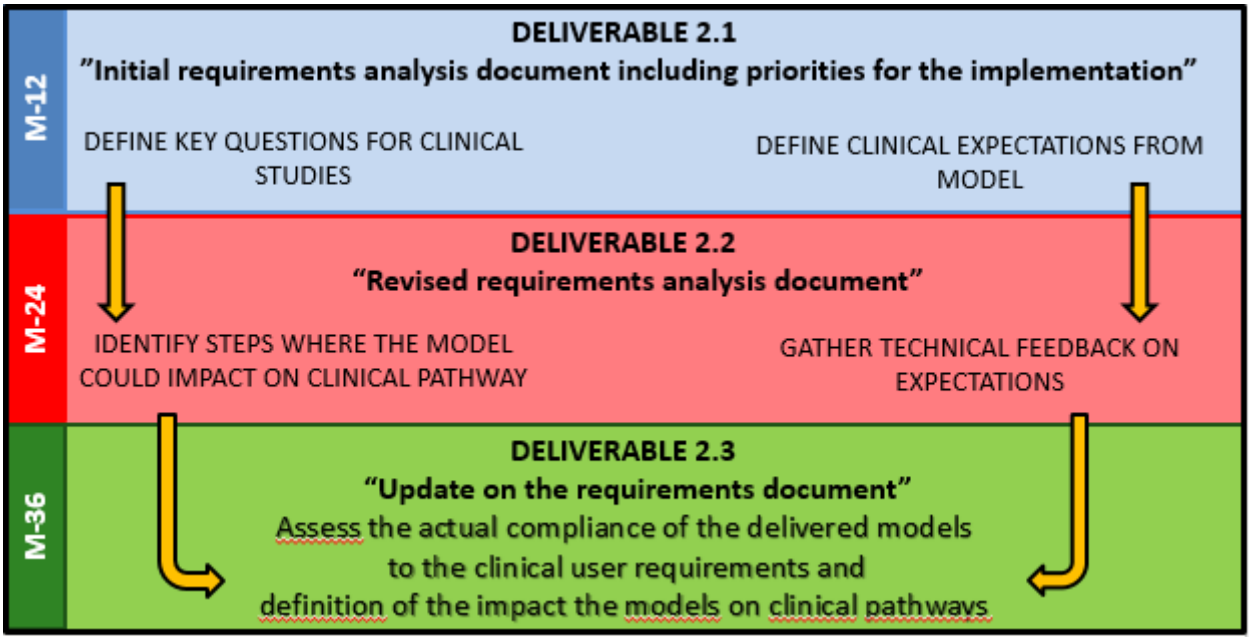
4.4.4 Prospected Impact of Model on Clinical Pathway

- From the detailed workflow we have derived that the models can significantly impact the care of the patients affected by NNMD by:
  - **Improve** definition of disease severity
  - **Predict** natural history of the disease.
  - **Target** therapy: the model is expected to provide useful information on the prediction of the effect of physical therapy and surgical intervention.

5. CONCLUSIONS

The revised user requirements contained in the present document, represent a step forward in defining clinical expectations from the models developed in the MD-Paedigree study. In brief, once defined the most relevant clinical questions for each of the disease areas, and define the clinical expectations for the prediction model, we have now gathered information from the current clinical workflows and updated the clinical expectations. In this view, the present Deliverable represents the first step in defining the expected role of MD-Paedigree models on clinical workflow and personalized patient care. As schematically represented in the table below, during the upcoming year, once the first predictive models will be available for testing and preliminary validation, we plan to foresee the potential impact of the use in clinical practice of personalized modelling. Furthermore, the D2.3 plans to evaluate the actual final compliance of the delivered models to both the clinical user requirements evaluated by the WP2, and the technical requirements analyzed by WP 13. Through this process, we also plan that the D2.3 will provide specific indications and insights to integrate the work of the D12.3 "Improved clinical workflows and outcome analysis", in order to clearly predict the potential role and impact of the MD-Paedigree models in routine clinical practice after the accomplishment of the validation process described in the D.12 workpackage documents.

Schematic representation of the delivered and future work for the WP2



6. REFERENCES

1. Feng M, Zhang Z, Zhang F, Ge Y, Loy LY, Vellaisamy K, Guo W, Chin PL, King NK, Ang BT, Guan C. iSyNCC: an intelligent system for patient monitoring & clinical decision support in Neuro-Critical-Care. Conf Proc IEEE Eng Med Biol Soc. 2011;2011:6426-9.

2. Staemmler M. Service delivery for e-Health applications. Stud Health Technol Inform. 2011;169:537-41.

3. Torchio M, Molino F, Seidenari C, Molino G. Clinical database. Structure, development strategies and expected clinical applications. Minerva Med. 2003

4. Apr;94(2):111-22.Schout BM, Hendrikx AJ, Scheele F, Bemelmans BL, Scherpbier AJ. Validation and implementation of surgical simulators: a critical review of present, past, and future. Surg Endosc. 2010 Mar;24(3):536-46.

5. Ohmann C, Kuchinke W. Future developments of medical informatics from the viewpoint of networked clinical research. Interoperability and integration. Methods Inf Med. 2009;48(1):45-54.

6. Wong MC, Turner P, Yee KC. Involving clinicians in the development of an electronic clinical handover system - thinking systems not just technology. Stud Health Technol Inform. 2008;136:490-5.

7. Angelow A, Schmidt M, Weitmann K, Schwedler S, Vogt H, Havemann C, Hoffmann W; German Transregional Collaborative Research Centre on Molecular Pathogenesis and Therapy of Inflammatory Dilated Cardiomyopathy. Methods and implementation of a central biosample and data management in a three-centre clinical study. Comput Methods Programs Biomed. 2008 Jul;91(1):82-90.

8. Momtahan KL, Burns CM, Sherrard H, Mesana T, Labinaz M. Using personal digital assistants and patient care algorithms to improve access to cardiac care best practices. Stud Health Technol Inform. 2007

9. Park J, MacRae H, Musselman LJ, Rossos P, Hamstra SJ, Wolman S, Reznick RK. Randomized controlled trial of virtual reality simulator training: transfer to live patients. Am J Surg. 2007 Aug;194(2):205-11.

10. Lee NJ, Bakken S. Development of a prototype personal digital assistant-decision support system for the management of adult obesity. Int J Med Inform. 2007 Oct;76 Suppl 2:S281-92.

11. Eleveld DJ, Proost JH, Wierda JM. Evaluation of a closed-loop muscle relaxation control system. Anesth Analg. 2005 Sep;101(3):758-64.

12. Suryanarayanan S, Karellas A, Vedantham S, Waldrop SM, D'Orsi CJ. Detection of simulated lesions on data-compressed digital mammograms. Radiology. 2005 Jul;236(1):31-6. Epub 2005 Jun 27. PubMed PMID: 15983071.

13. Coble JM, Maffitt JS, Orland MJ, Kahn MG. Contextual inquiry: discovering physicians' true needs. Proc Annu Symp Comput Appl Med Care. 1995:469-73.

7. APPENDIX (example of feedback provided for WP3)

Below is provided, as an explanatory example, the modified variable list provided by the D2.1 for the WP3 (Cardiomyopathies). As shown, technical partners have identified within the specific list of variables provided by the D2.1, the list of variables for which computation models can be defined or cannot be defined. This feedback provides the clinical partners on what is to be expected from the models and understand the technical limitations, thus helping reducing the gap between technical and clinical partners on the expected role of modelling in clinical practice.

INPUT VARIABLE	EXPECTED MODELLED OUTCOME VARIABLE	
	CAN BE PROVIDED	CANNOT BE PROVIDED
Impact of Time	Left ventricular systolic/diastolic diameters Left ventricular mass Left ventricular volume Left ventricular sphericity index Left ventricular ejection fraction Left ventricular stroke volume Left ventricular mitral valve dimension Mitral inflow early and late velocities Mitral tissue Doppler velocities Right ventricular tricuspid plane excursion Right ventricular ejection fraction	Mitral valve regurgitant fraction Right ventricular systolic pressure Intra-ventricular systolic synchronicity Inter-ventricular systolic synchronicity Inter-ventricular interaction index Percent regional systolic myocardial deformation
Change caused by medications affecting heart rate	Left ventricular stroke volume Left ventricular cardiac output Left ventricular systolic/diastolic diameters Left ventricular sphericity index Left ventricular ejection fraction Left ventricular stroke volume Left ventricular mitral valve dimension Right ventricular ejection fraction Mitral inflow early and late velocities Mitral tissue Doppler velocities Right ventricular tricuspid plane excursion	Inferior vena cava dimensions Inferior vena cava respiratory variation Mitral valve regurgitant fraction Right ventricular systolic pressure Intraventricular systolic synchronicity Interventricular systolic synchronicity Interventricular interaction index Percent regional systolic myocardial deformation
Change caused by medications affecting pressure afterload	Heart rate Left ventricular systolic/diastolic diameters Left ventricular mass Left ventricular volume Left ventricular sphericity index Left ventricular ejection fraction Left ventricular stroke volume Left ventricular cardiac output Left ventricular mitral valve dimension Mitral tissue Doppler velocities Right ventricular tricuspid plane excursion Right ventricular ejection fraction	Inferior vena cava dimensions Inferior vena cava respiratory variation Left atrial diameter Left atrial volume Mitral valve regurgitant fraction Right ventricular systolic pressure