Break-out: Clinical Engagement

Dr Caroline Roney, Dr Laura Bevis, Dr Elisa Rauseo

Digital Environment Research Institute - School of Engineering & Materials Science – William Harvey Research Institute
Queen Mary University of London

EDITH

EDITH project has received funding from the EU H2020 Research and Innovation Programme, under Grant Agreement n. 101083771

Introduction: Digital Twins in Healthcare

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Definition of Digital Twin

A Digital Twin is

a **virtual copy of the human organs, tissues, cells or micro-environment** that **constantly** adjusts to variations in online data and **can predict the future of the corresponding counterpart**

The Virtual human twin (VHT) is

an **integrated multi-scale, -time and -discipline digital representation of the whole body**, enabling a **comprehensive characterization** of the physiological and pathological state and allowing **patient-specific predictions** regarding disease and intervention options

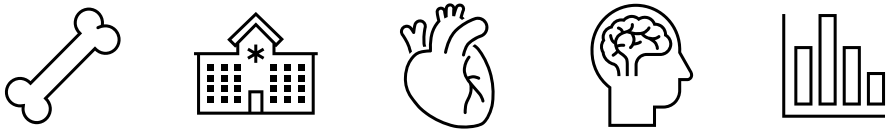
Their use/impact in healthcare

include **virtual trials, real-time monitoring, dynamic analysis, precise/patient-specific treatment**

Sun T, He X, Li Z. Digital twin in healthcare: Recent updates and challenges. Digit Health. 2023 Jan 3;9:20552076221149651. doi: 10.1177/20552076221149651. PMID: 36636729; PMCID: PMC9830576.

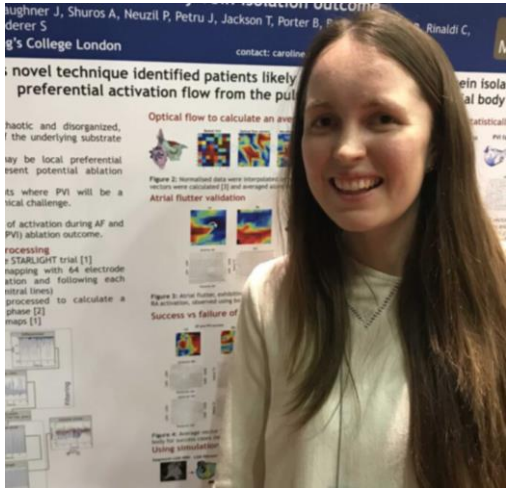
Introduction – EDITH

- Virtual Human Twin



- EDITH project
  - **Technology**
    - Individual resources: data, models, algorithms
    - Integration of resources
    - APIs
    - Infrastructure, networks
    - Connection EHDS, SIMPL
  - **ELSI**
    - Access, privacy
    - Ethics, code of conduct
    - Legal & policy aspects
    - Regulatory considerations
  - **Users**
    - Different profiles
    - Access & workflows
    - Interaction with other platforms & repositories
  - **Sustainability**
    - Clinical uptake
    - Large companies
    - Start-ups
    - Marketplace
    - business modelling
    - ERIC, EDIH

Introduction – Who we are…



Dr Caroline Roney

UKRI Future Leaders Fellow
Reader in Computational Medicine

Mathematics, Biomedical Engineering, Computational Modelling

Dr Elisa Rauseo

Cardiologist with special interest in Cardiovascular imaging and AI

Queen Mary University of London, Barts Health NHS Trust

Dr Laura Bevis

Postdoctoral Research Associate in Cardiac Digital Twins

Mathematician - Fluid Dynamics, Biological Modelling

All part of the Personalized Cardiac Modelling Lab, School of Engineering and Materials Science, Queen Mary University of London

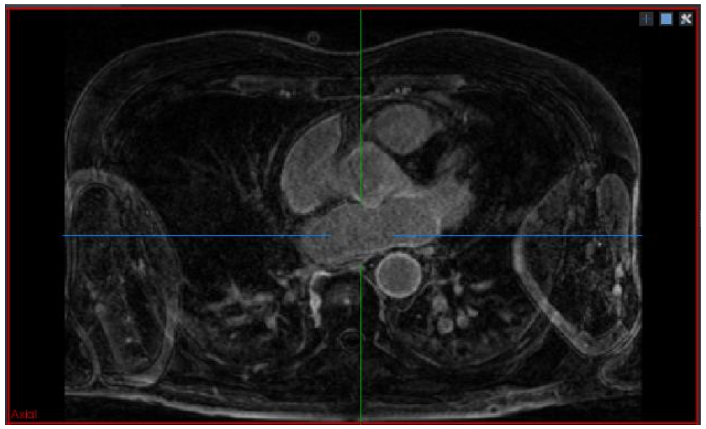
Task 2.9 of EDITH: Connecting Technology and Clinical Practice

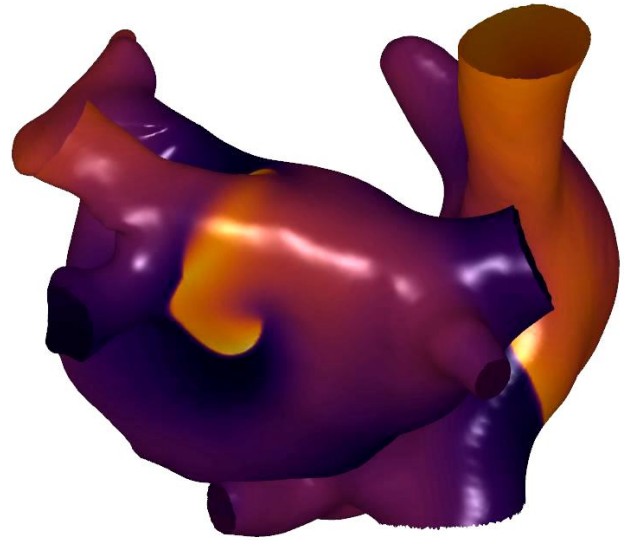
- **Aim**: Facilitate the interaction between VHT tool developers and clinical end-users, including patients.

- **Coordination**: Led by Queen Mary University of London (QMUL) and Barts Health NHS Trust, with collaborative contributions from partner institutions.

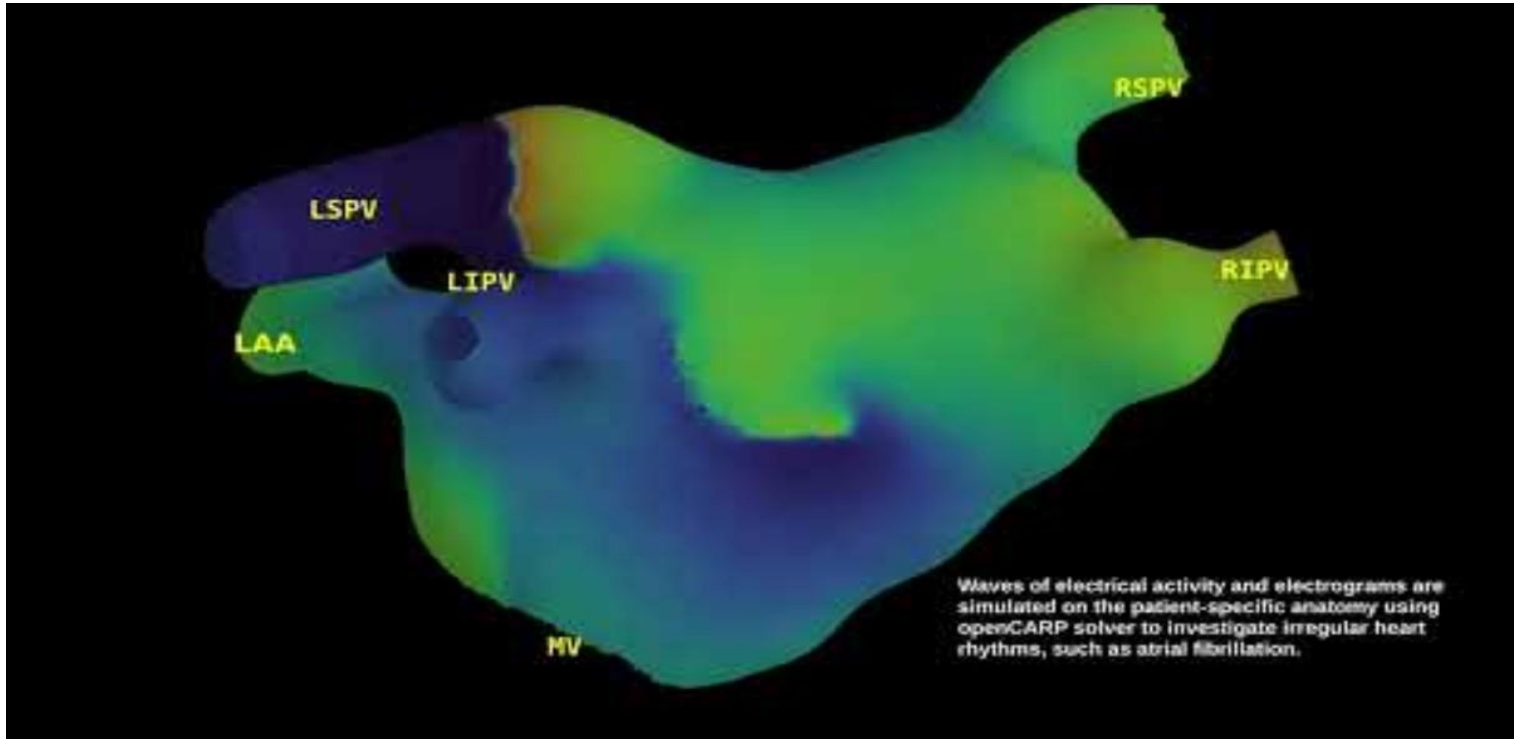
EDITH Cardiovascular use case

- Personalised simulations for atrial fibrilation
  - **Inputs:** Patient anatomy (CT or MRI), electroanatomical mapping (EAM) data
  - **Outputs:** Patterns of electrical activity that indicate targets for ablation treatment
- Clinical collaboration to ensure relevance





Introduction – Cardiovascular Example



Silico model for assessing individual responses to irregular heart rhythm treatments

Carlos Edgar Lopez Barrera, Winning Early Career entry Archer2 Image and Video Competition 2023

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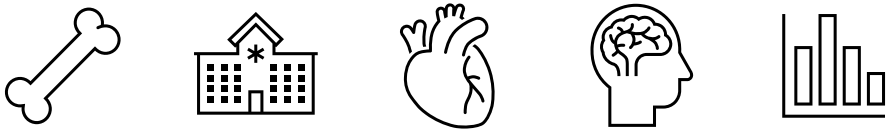
- Virtual Human Twin



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Introduction – Clinical Engagement & Uptake

First

- Introductions & split into groups
- Questions for discussion
  - **7 mins** in smaller groups
  - **3 mins** as larger group (1-2 groups feed back)

Then

- Short time for additional points
- Opportunity to submit thoughts/contribute following the meeting
- Discussion points added to EDITH roadmap and used to guide/improve the project

Group Introductions

EDITH

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Group introductions

Introduce yourself!

- Clinical/non-clinical?
- Interest in EDITH?

Group introductions

In your groups:

Add a post it on the virtual whiteboad telling us:

- (Optional) Name
- Background e.g. clinical/end-user or non-clinical
- Interest in EDITH

Virtual Post-its: https://jamboard.google.com/d/17RUCym9HBvY29X4K1XbEsRNSgegGK9DOwaQRCwzov8g/viewer?f=0

Group introductions

Name, background, interest in EDITH

~20 attendees, mix of backgrounds - around half clinical

Questions for Discussion:

Virtual Post-its: https://jamboard.google.com/d/17RUCym9HBvY29X4K1XbEsRNSgegGK9DOwaQRCwzov8g/viewer?f=0

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Question 1: Current clinical perspectives

What are clinician's current opinions on digital twins, and how do they perceive their impact in healthcare?

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Clinical perspectives

Limit and reduce variability in human judgement. Noise in decisions. Could reduce noise and bias

Must be able to implement in/across different systems e.g. NHS vs NIH vs European systems

Type and quality of data - data flow for models

Why do we need DTs? E.g. EU horizon call for liver diseases (9 partners), specific need of the DT unclear due to language barriers between modellers and clinicians

Anatomical, chemistry, other aspects, biomarkers, not just anatomy

Different scales - organ, cell - how to integrate these? Difficult to imagine a multi-scale organ model is possible clinically

Depends on the use case, and maturity of the use case. Even early models that are not validated can be useful. Personalised information

Needs to overcome a problem. Start with an unmet need. Often models do not match up with unknowns and challenges. Need to match up with needs. Medicine is conservative

Only pay if required - reduces costs, improves safety. Not used unless mandatory

Modelling needs to start with the clinical problem

Prove the use. Has to be in the guidelines. Otherwise too risky to use.

Question 2: Enhancing communication

How can we effectively communicate the clinical benefits of digital twins across various medical specialties?

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How modellers can better understand clinical needs?

ESC - ML, AI, models in cardiovascular

Dissemination

Events: e.g. Royal society of medicine

Engineering side - engineers should go to clinical conferences. Problems and solutions need to be meaningful - check this with clinicians. More impact

Time and money limited in how many events can attend. How specific these should be?

Shift towards clinical solutions - dissemination

More likely to use if know about from conferences

Specific clinical conferences

Measure outcomes using clinical practice. Digital twins need to improve outcomes - not just mechanistic e.g. anatomy. Link to outcomes

Proof in the use

Outcomes for disease often clearly defined - modellers need to be aware of this

Clinical validation. Modellers and clinicians need to work with regulatory bodies to come up with standardised framework

Teaching - e.g. residents training. How to operate on a virtual patient

Specific courses - teaching, congresses

Patient associations - they need to assess if it is useful. How to include in the healthcare pathway.

These communities can disseminate to clinicians if they are useful

Question 3: Trust and utility

What outcomes and evidence are clinicians seeking to fully trust and integrate digital twins into their practice?

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Trust & utility

Increase collaboration by: clinical evidence, regulatory bodies, scientific focus not enough.

Show utility can gain trust

Clinicians involved in building the model - does this increase trust?

Impact and outcomes need to be shown - cost, superiority on relevant outcomes if cost is higher

Validation, verification (VVUQ) frameworks. Not widely communicated with clinicians - responsibility to not over sell. Think about the context of use

Need things they don't have or that can help with things that come up unexpectedly during surgery

Need to involve the end users. Unless we involve the patients, there will be no end use in any models!

Risk stratification/complexity quantification, earlier diagnosis, monitoring disease progression of patients

Motivation - not publishing papers, it is helping patients. Need to improve treatments.

E.g. 70% mortality, but low predictive ability, need to improve standard of care and decrease costs.

Openness to new technologies high in university hospitals. Harder outside of these environments

How to learn from modelling and clinical fields when we are all busy?

Target the right questions

Question 4: Barriers to adoption

What are the perceived barriers to adopting digital twins in clinical practice, and how might these be addressed?

Q4: What are the perceived barriers to adopting digital twins in clinical practice, and how might these be addressed?

Barriers to adoption

Data. EDITH is collecting data that is available and then find questions based on data - wrong way round. Should be clinical question first and then collect the data

Not speaking the same language. Needs to go both ways. Trust is there but language is different

Keep clinicians in the loop. Engineers alone will not be trusted!

Regulatory framework is not in place. Medical devices not possible otherwise

E.g. flow simulations are expensive to run, and take a long time. Can use to remove use of clinical data

Model combined with data. DOes not then use all the original data that was used to build the data - AI or physics based models to replace data etc. Then can move to what is routine

Not ok to require many additional measurements

Need a bridge for communication. New technologies can help clinical care.

Start with the end user - ask them what is the problem. Then collect the data. This is the key barrier

E.g. don't have genetics, proteomics required

Public consortia to finance prospective data collection

What data do we need? E.g. super specialised data will not be available generally. Routine data then find a common ground

Need to implement at the point of care. Patients.

Need to be implemented where clinicians can add these - ie. with patients at the point of care

Clinical investigations not necessarily a particularly type of trial

Clinical trials are needed. But first the model needs to be advanced etc. Cycle as need enough validation for the trial. Hard to fund.

Retrospective data is not enough. We need prospective.

Plan from the beginning - what data is needed to validate

Question 5: Enhancing model precision with patient-specific data

How can we overcome the challenges of privacy/security and data sparsity to access and integrate comprehensive patient-specific information into digital twins?

Q5: How can we overcome the challenges of privacy/security and data sparsity to access and integrate comprehensive patient-specific information into digital twins?

Once digital twin developed adding the patient specific data is ok. Data to train and validate the model is the problem.

GDPR and reuse of data issues

Laws in place for using retrospective data vary by country

How can we use secondary data? What should consent be?

UK biobank

Training a model requires specific datasets (needs anoynmisation)

UK/US definitions vs GDPR - can re-identify a patient, then not truly anonymised (can use AI to go back).

German system, re identify cases

Trust at different levels. E.g. pathology shows impact, but needs to be proved at integrated level

Special annotated datasets

Access to data strong in research hospitals

Data standardisation in place

Initiatives to harmonise datasets - share, label etc

More artificial / synthetic data. Can you trust this?

Privacy issues as it is still based on real data (AI reconstruction issues)

Depends on the model underlying the generated data, yes if based on validated model

Computational power so data need to go to a HPC and leave the hospital - issues?

Moving data: hospital -> HPC. Needs to be protected, anonymisation. Need to be able to identify and treat to go back to the patient data

Challenge of data linkage

True anonymisation not available, pseudo so can go back to patient

EU dataspace - enivisioned as hub of data, harmonisation, interoperability, computer models

Initiatives - federated platforms at the European level. EUCIAN. Likely to be a game changer

Patient consent

Question 6: Ensuring reliability and ethical integrity in digital twins

What measures can we take to ensure validation, continuous quality control, and security of digital twin models to maintain accountability and adhere to ethical guidelines in clinical use?

Q6: What measures can we take to ensure validation, continuous quality control, and security of digital twin models to maintain accountability and adhere to ethical guidelines in clinical use?

Reliability & ethical integrity

This Q was already covered by previous topics so moved onto Q7

Previous points: anonymisation, validation of models/artificial data, clinical/patient input for models/DTs, data standards, communication, etc.

Question 7: Feedback on EDITH

What is the current reception of the EDITH project among clinicians, and what are their expectations for its future?

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SEND OUT CLINICAL SURVEY FOLLOWING PARIS MEETING - attendees of this session can disseminate to colleagues

Useful to get opinions even if colleagues are not keen on EDITH/DT initiatives

Call for use cases

Call for clinical problems?

More EDITH sessions should be run be clinicians!

Attendees of workshop are already convinced. Need to reach general clinical audience - not sure how to use, trust etc.

Feedback

How do you sell to clinical community when a model is for a small use case?

Lots of modellers not clinicians

Need to target clinicians. At the moment, focus is on modellers and what they want (e.g website). Start with clinicians and what they need to increase collabs

Need more than one session - make clinicians more involved

Lacking strong opposition as we have a biased audience (already interested in DTs/EITH

Dissemination

Clinicians will be more involved when DTs/models meet a clinical need

Build together something that improves standard of care

How to communicate with patients EDITH

Clinicians do have time to attend meetings. Lots of clinical conferences. Use congresses etc for dissemination

EDITH/DT projects not well disseminated - present at medical conferences?

More clinical figures needed in EDITH

Send clinical survey to all colleagues

Collaboration early on

Do not forget patients!

Question 8: Increasing clinical involvement

How can we further enhance clinical involvement in the ongoing development and refinement of the EDITH project and other digital twin initiatives?

Q8: How can we further enhance clinical involvement in the ongoing development and refinement of the EDITH project and other digital twin initiatives?

Digital twins need to fill/ answer gaps in clinical recruitment. Patients who cannot be reached.

What are the clinical needs and demands? How should we focus our digital twin research.

Niches that need modelling.

Diseases without treatments - focus on real health need not just where current models are

How can a GP use a digital twin? Not just cardiology focus.

Crucial to reach clinicians

EDITH/DT intiatives to do some research into current clinical needs - check recent funding initiatives/calls in medicine, look for/build sources for this sort of info

Outcome focus - reduce complications etc.

Chronic disease focus

Needs are speciality specific

Note - many points addressed in previous questions for this topic

Incentives

Mentioned that incentives not necessarily needed - clinicians will be interested if cost effective and meets an unmet need

Recommend advertising the clinical involvement at future events - e.g. CARDIOLOGIST running session on ...

Question 9: Additional recommendations

What further recommendations do clinicians have to ensure that models are clinically relevant and developed in partnership with clinical expertise?

Q9: What further recommendations do clinicians have to ensure that models are clinically relevant and developed in partnership with clinical expertise?

Associations such as Biomed Alliance(?) mentioned as suggestion to reach clinicians?

Do not target clinicians. Clinicians do have time. They actually attend more conferences than modellers. Need senior clinicians running EDITH to bring others

Additional recommendations

The whole process should include clinicians. From the data collection, to the model, to the predictions and to the clinic

Define the purpose should be the beginning of the process. WHY are you building the DT. Involve clinicians and patients to define the problem and the use case

Asked the clinicians what they needed from it, so they have some influence in its development

Other EU consortium. Prediction of sepsis focus guided by clinicians. Need influence in meetings

Car engineers run the industry sessions?

Needs to start from the top - have clinicians in the board

Vote for the most important question!

Q1: Clinical perspectives

Q2: Communication

Q3: Trust & utility

Q4: Barriers to adoption

Q5: Access to clinical data

Q6: Reliability & ethical integrity

Q7: Feedback

Q8: Increasing clinical involvement

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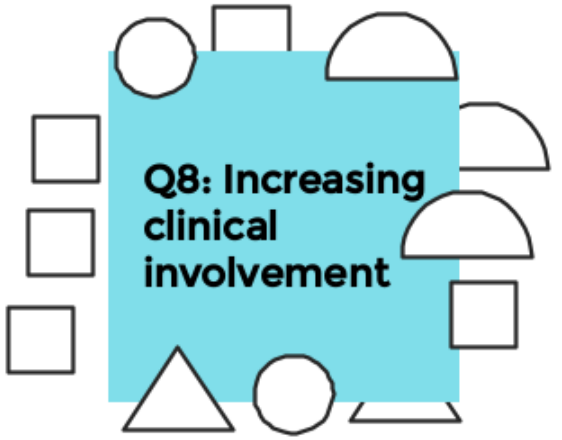

Q9: Additional recommendations

Any further thoughts?

Clinicians at the top of EDITH

More input on the use cases

More clinical input from the beginning - in defining the purpose of the DT

Association covering biomed alliance - grouping ESC, other fields - ask to go to participants to see possible applications

ESC and European grants - clinical viewpoint is strong

Closing remarks:

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Next Steps – This meeting

- Summarise points to present in the next session
  - **Add a few quick bullets here during the discussions of key points to present**
  - **Check that the group agrees with the key points from the discussion**
  - …
- Will also hear from the other break-out groups
- Points will be incorporated in the next version of the EDITH roadmap

Slides for reporting session:

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Key Points

- More clinical representatives in EDITH at every level
- Clinicians can then disseminate EDITH at other events - clinical ambadassors
- Models and EDITH should focus on unmet clinical needs
- Clinicians should be involved in defining the purpose of the model (model defined by the clinical need, not the available data or modellers' interests)
- Clinicians involved throughout the modelling process
- Consider patient needs, perspectives and views to define the purpose of the model (include patients through the whole DT process)
- Trust is not the main issue between engineers and clinicians – language and communication is
- Regulatory aspect should be mandatory and well defined (this will lead to adoption)
- For a model to be clinically useful, it needs to be cost effective and clearly improve outcomes
- We need more prospective data and clinical trials to build and validate models
- Data re-use issues
- **Send clinical survey link to attendees to disseminate to colleagues**

Vote for the most important question!

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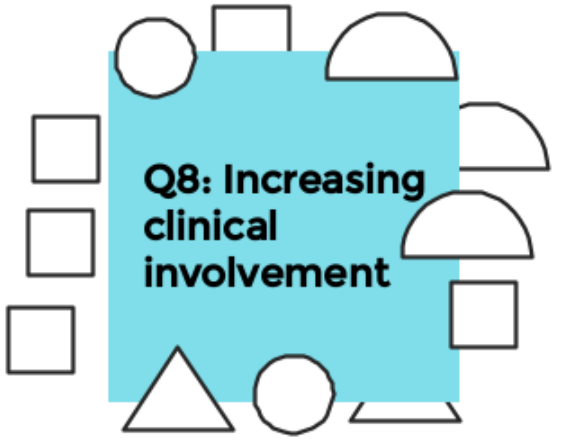

Q9: Additional recommendations

http://www.edith-csa.eu

Deliverables available under tab ‘dissemination/material’

Indication of interest via contact form on site

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