EDITH Ecosystem Meeting

Paris 18-19/1/2024

EDITH

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

Wellcome address

Irene Vignon-Clementel, Marie-Hélène Pautrat, Abdul Barakat, Jean Colombel (Inria & partners)

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Introduction

Liesbet Geris (VPHi, ULiège, KU Leuven)

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Agenda – Thursday

- *12-1: Lunch*
- 1-1.35: Welcome by hosts and European Commission
- 1.35-2: Introduction & organisation of the meeting
- 2-4: Parallel break-out sessions
- *4-4.30: Coffee break*
- 4.30-6: Break-out reports
- *6-7: Networking & drinks*
- *7-9: Dinner*

Agenda - Friday

- 8.30-9: The clinical perspective
- 9-11: Parallel break-out sessions
- *11-11.30: Coffee break*
- 11.30-1: Break-out reports (*breakout session chairs*)
- *1-2: Lunch*
- 2-3.30: Plenary presentations of existing platforms and initiatives + discussion
  - BBMRI-ERIC
  - EBRAINS
  - 12 Labours
- 3.30-4: Next steps & wrapping up

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Project & Results

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EDITH objectives

Ecosystem

Roadmap

Repository

Simulation Platform

Initial phase - approach

- Expedited start & early delivery of roadmap first draft
- Consortium internal activities to prepare public phase
  - On-site meetings in Leuven
  - Biweekly online meetings
- Targeted interactions with industry, clinicians & other experts
  - Industry Advisory Board
  - Advisory Group of Stakeholders

Initial phase - results

- Mapping of state of the art (technology, legal, standards, regulatory etc.)
  - LLM Web App for Knowlegde Discovery (website > Crowdsourcing)
  - FAIRsharing standards collection (website > Crowdsourcing)
- Mapping of the ecosystem
  - Identification of stakeholders (1st draft roadmap)
- Determined the vision & outline of the Roadmap (1st draft roadmap)

Roadmap - approach

- Creation of the first draft of the roadmap
  - Discussion of different sections in Vision meeting
- Deep Thinkers Meeting Rome
  - 100+ participants
  - Break-outs, plenaries, world café sessions
- Public feedback sessions online March 24, May 2 & June 1
- Public (conferences, workshops) & partner events (Siemens, Edwards etc)

Roadmap - results

- Preliminary version of first draft made available for public feedback
  - Mid June – Mid July
  - 400+ unique downloads of the Zenodo document
  - 60+ people requested access to editable google doc

- First draft of the VHT roadmap submitted on 31/7/2023
  - 1388 unique downloads
  - Increase in visibility and intrest from ecosystem

- Website / Zenodo community edith-csa

Published July 31, 2023 | Version v1
Project deliverable
Open

EDITH CSA Deliverable 3.2: first draft of the VHT roadmap

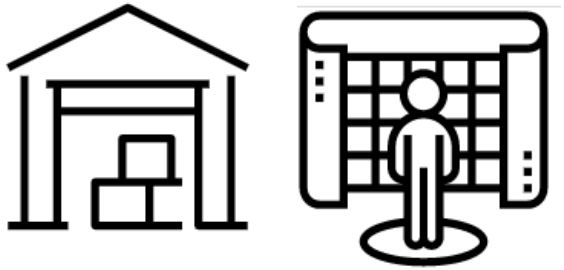
EDITH consortium

The VHT Roadmap is due – in its final version – by the end of the EDITH Coordination and Support Action (i.e., September 2024). The present document is the first draft of the Roadmap, This preliminary version of the Roadmap was planned in EDITH's Grant Agreement as an initial contribution to the internal decision-making process of the European Commission. It has the declared purpose of allowing the Commission to start specifying already at an early stage **by what steps the goal of pursuing the development of a VHT-based healthcare** will be likely **to trigger an effective engagement of Europe's researchers, clinicians, industries, and regulators**.

This interim version is therefore meant to highlight what is currently the **envisioned structure** of what will be in a year time the **final roadmap** and its main contents, leaving open the possibility that these contents can still be subject to both substantial and formal changes, in response to suggestions coming from both the European Commission and from different sectors of the broadening community of practice that the EDITH CSA is addressing.

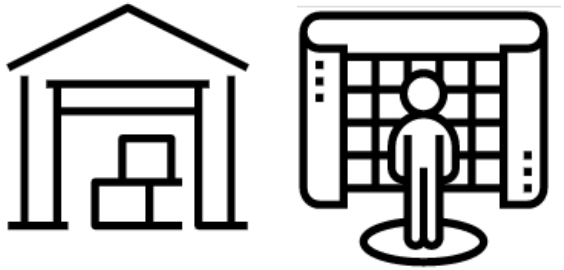
In consideration of these double-edge purposes, this preliminary draft aims to capture the **main concepts and the overall approach of the VHT Roadmap**, while also **identifying relevant challenges** (from the perspective of research, infrastructure, and other specific aspects) that need to be addressed in the remaining year of the EDITH CSA (and beyond) and which will require further analysis, with the support of the whole VHT Community. For the technology, standards, regulatory, and legal aspects, the draft provides an overview of the state of the art and an analysis of VHT-specific needs, without determining as yet any conclusive choice.

Repository & Platform - approach



- Pre-selected use cases studied
  - Workflows, Interoperability
  - Legal, Standards
  - Regulatory
  - Exploitation
- Internal meetings for use cases & global concepts
- User Experience sessions at Rome Deep Thinkers Meeting
- State of the Art initiatives, repositories & management tools

Repository & Platform - results



- Governance principles
  - Roles & reponsibilities, decision-making process, compliance & legal considerations
- Requirements
  - Catalogue, repository, single sign-on, interoperatbility, metadata
  - Legal considerations
- Architecture
  - Components, technologies, layers
- User interface, training, quality management
- Call for use cases (website > Get Involved)

Sustainability - approach

- Uptake
  - IAB, clinicians, other users
  - Analysis & implementation early prototype demonstrators
- Business model development
- VHT Market place
- Research infrastructure bench marks

Sustainability - results

- Analysis of use cases & structures
- Implementation in model execution environment

- VHT Value proposition for IAB & other stakeholders (1st draft roadmap)

- Evolutionary Ecosystem Approach (1st draft roadmap)

- Incentivization
- EU27 Member state strategy under development

VHT Manifesto

- Additional activity
- Driven by EC, facilitated by EDITH

- Why?
  - Way of demonstrating support from ecosystem
  - Increase visibility of VHT-related activities
  - High-level entry into the VHT

- www.virtualhumantwins.eu

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Paris meeting purpose

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Thursday break-outs

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Breakout sessions Thursday

- Integration of resources
- Ethical Manifesto
- Generation of data (OoC, sensing, …)
- Business models
- Envisioned platform processes and services
- User roles/identities
- Standards for digital twins and their implementability

Breakout 1: integration of resources

- Chair: Alfons Hoekstra (UvA)
- Note taker: Janaki Raman Rangarajan (VPHi)

- Aim:
  - How to compose workflows (leveraging the 6D DOT, leveraging knowledge graphs, exploiting LLMs)
  - how to execute them
  - can we identify standard DTH workflows
  - could there be standard components, e.g. for VVUQ automatically embedded, etc.
  - Could workflows automatically keep track of CoU, or infer and update credibility levels of workflows?

Breakout 2: ethical manifesto

- Chairs: Ine Van Hoyweghen, Elisabetta Biasin, and Elisa Leila Elhadj (KU Leuven)
- Note taker: Zita Van Horenbeeck (VPHi)

- Aim: foster collective reflection on the responsibilities of in silico modelers and the field itself
- Focus: the actual practices of in silico modelers & ethical and social responsibilities inherent in their work
- Format: interactive exercise offering space for reflection
- Final outcome: Ethical Manifesto, a compass for ethical decision-making and demonstrating the in silico community's commitment to RRI.

Breakout 3: generation of data

- Chair: Adrian Ionescu (EPFL)
- Note taker: Sanjay Pant (Lynkeus)

- Aim: identify the needed technologies capable to generate the (dynamic) data needed
  - vital sign sensors, biosensors, wearables, implantables and Organs On Chip hardware technologies with the challenges of their application and adoption in various medical use cases.
- Questions:
  - State of the art, human exposome, biofluids, Edge vs cloud, data security, involvement of MedTech ecosystem

Breakout 4: business models

- Chair: Enzo Fabiani (Pi School)
- Note taker: Roberta De Michele (VPHi)

- Questions:
  - How can we ensure fair collaborations (e.g., licensing, data access) through the VHT platform, fostering innovation?
  - What are the economic factors that have an impact on the ecosystem?
  - How to make the platform an accessible tool for doctors and patients (e.g., reimbursements)?

Breakout 5: platform processes & services

- Chair: Amaryllis Raouzaiou (ATHENA), Sabato Mellone (UNIBO)
- Note taker: Artem Platonov (VPHi)

- Aim:
  - present processes, resources, and services related to the use and management of the VHT as an infrastructure and as an ecosystem;
  - a platform for meeting, growth and community development.
- Discussion: missing elements, required changes, …

Breakout 6: user roles/identities

- Chair: Gökhan Ertaylan (VITO)
- Note taker: Martina Contin (VPHi)

- Context
  - User roles are clusters of system privileges that are designed to achieve specific goals using the VHT infrastructure.
  - User profiles can consist of various user roles as a person can have different aims in using the VHT platform in her/his capacity.
- Aim
  - Look at roles & identities defined in roadmap (HC prof.; creator – acad/ind; public)
  - What is required, what is missing

Breakout 7: standards

- Chairs: Martin Golebiewski and Gerhard Mayer (HITS)
- Note taker: Martin & Gerhard

- Questions
  - Standardisation of VHT building blocks for interoperability and sharing?
  - Harmonisation of description by domain-specific metadata standards and terminologies/ontologies?
  - Quality standards?
  - Standardisation gaps?
  - Interaction with standard defining organisations

Thursday Break-out reports

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Breakout 1: integration of resources

Alfons Hoekstra (UvA)
notes: Janaki Raman Rangarajan (VPHi)

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Data objects

Annotation services

Model objects

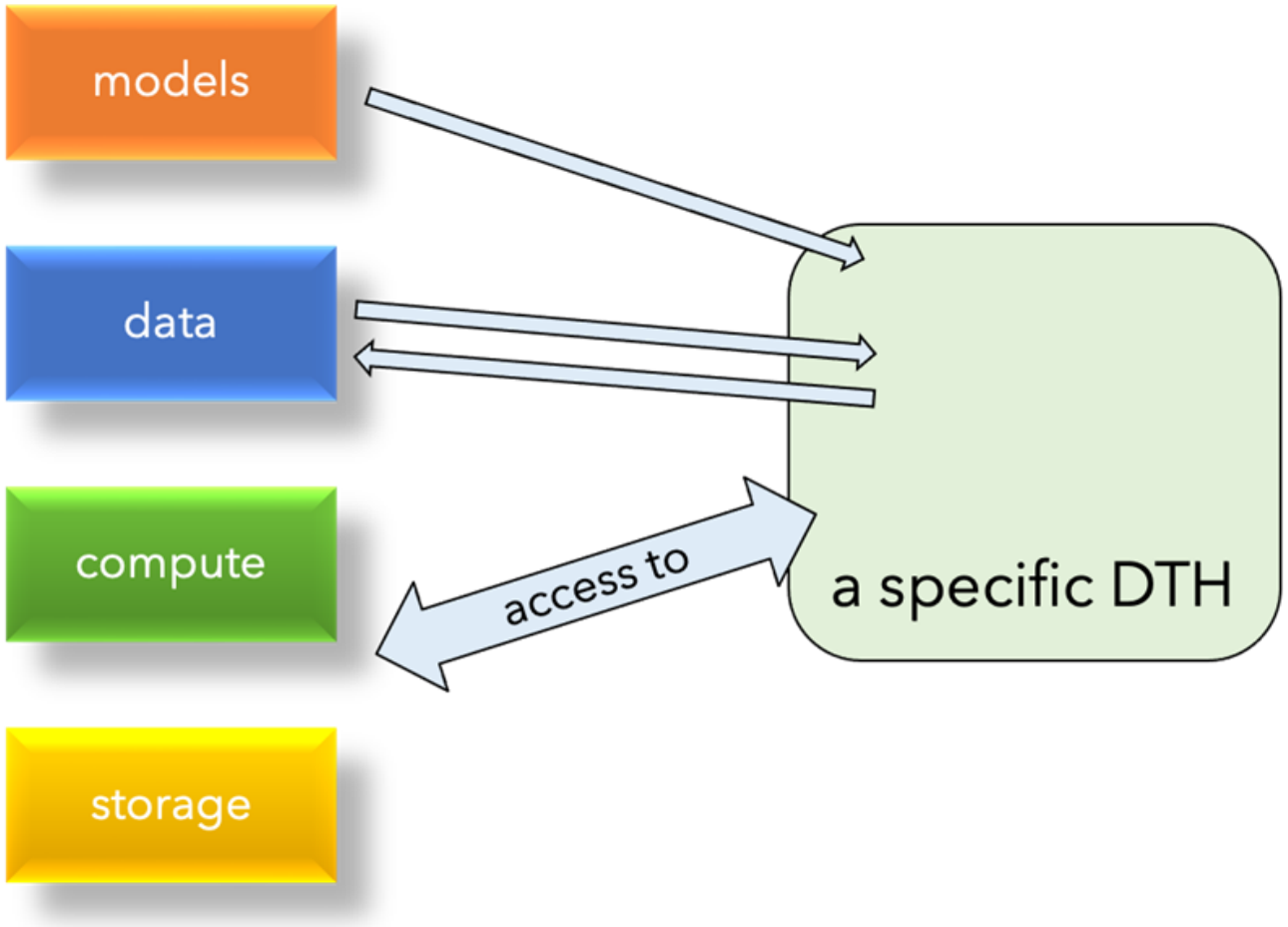
Workflow objects

Execution, storage, and networking services

Integration of resources on two levels

- *Inside* the models/data/compute/storage spaces
  - For *models*, e.g. integration of single scale models into multi-something models
  - For *data*, e.g. pooling of raw, synthetic, transformed, simulated data, including data transformation services, for (stratified) populations or individuals
  - For *compute* and *storage*, e.g. federating some local and remote resources
- *Between* models, data, compute, storage
  - This is actually needed to create a full blown DTH and to execute it.

Integration between models, data, compute, storage



Use workflows to achieve this.

Summary of questions

1. Do you agree that we define a workflow as the combination of models and input / output data, dynamically *requesting* access to compute / storage / networking resources?
2. Will we support a single workflow system, e.g. CWL and build on that, or support requested system?
3. Should we strive for a VHT-workflow standard, leveraging existing standards?
4. Are there prototypical DTH workflows, or standard components for DTH workflows?
5. Composing DTH workflows

Diverge … ?

Credibility and tracking it …

defintions of credibility

data credibility

Model credibility

Workflow credibility

and tracking it when doing greedy computations

some random notes

VHT standard, with constructs on credibility framed within a workflow

- we cannot enforce a standard (excludes), but we need to facilitate its realization

Community effort:

- whole range of CoU, put them into workflow one by one

Protype of WORKFLOWS - Workflow comes with UQ, by default

- Every DTH for personalized level need to have UQ is pre-requisite

Automate existing workflows

Workflow translation services

Breakout 2: Ethical Manifesto

Elisabetta Biasin, Elisa Leila Elhadj & Ine Van Hoyweghen (KU Leuven)

notes: Zita Van Horenbeeck (VPHi)

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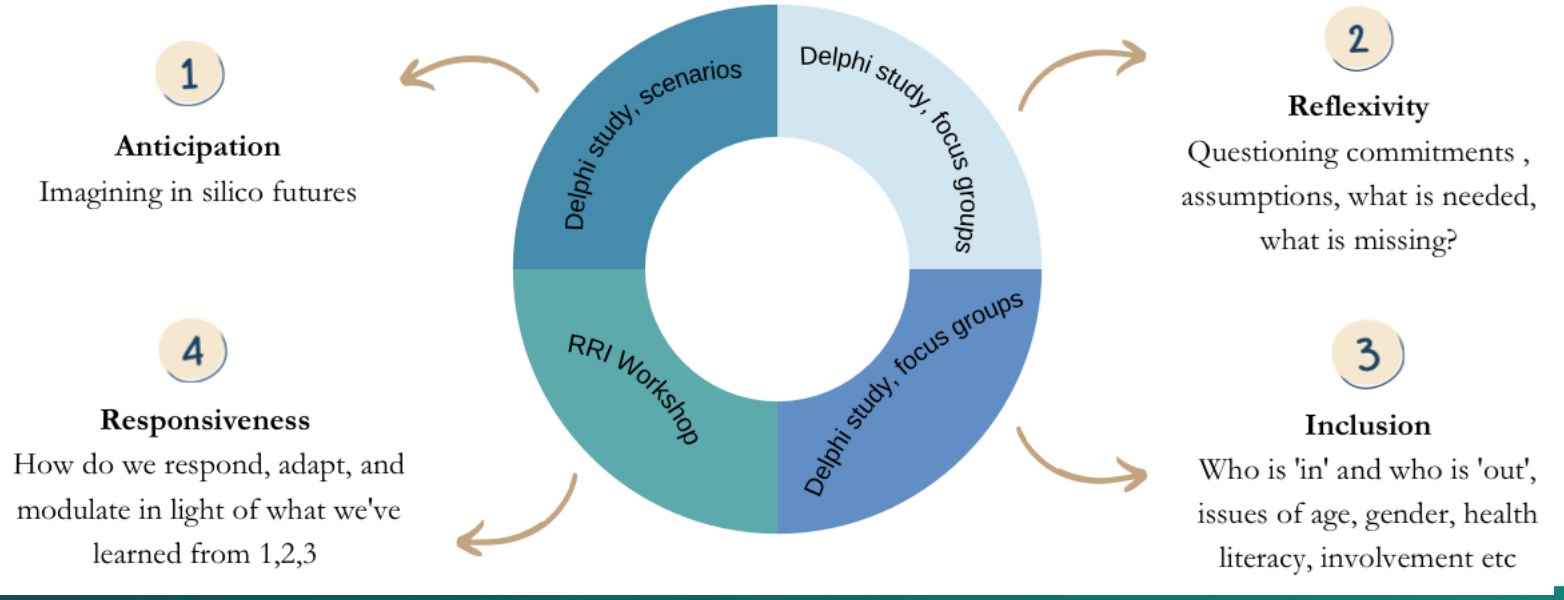
In Silico World & RRI

The **In Silico World** project aims at accelerating the uptake of modelling and simulation technologies used for the development and regulatory assessment of medicines and medical devices, by lowering seven identified barriers: development, validation, accreditation, optimisation, exploitation, information, and training.

Our Responsible Research and Innovation approach:



Ethical Manifesto

Speaker 5: "I say that we make beautiful models, and we give them to clinicians and they could get X numbers of variables usable for the patients and they decide which one to give. I mean, it's not us."

Speaker 3: "I understand. It's a shared responsibility, but you have to imagine the worst-case scenario and you have to warn the policymakers that we're giving you a new technology. It can do all these beautiful things, but be aware it can also do all this bad things. No, you disagree?"

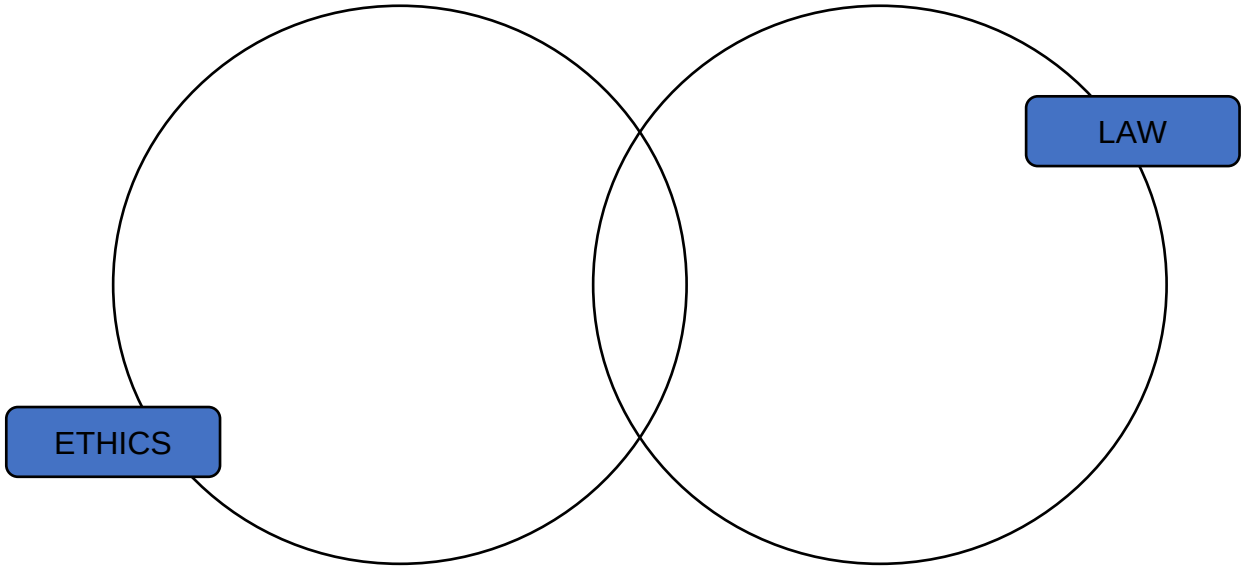
Speaker 5: "No, no, I don't disagree. But I mean, they should also know that it depends on the human and it's at human level, you know, clinicians have their own principles they should be following. They should judge."

Speaker 3: " [...]. You are responsible for your own. Of course, others have their own share of responsibility, but you have your own."

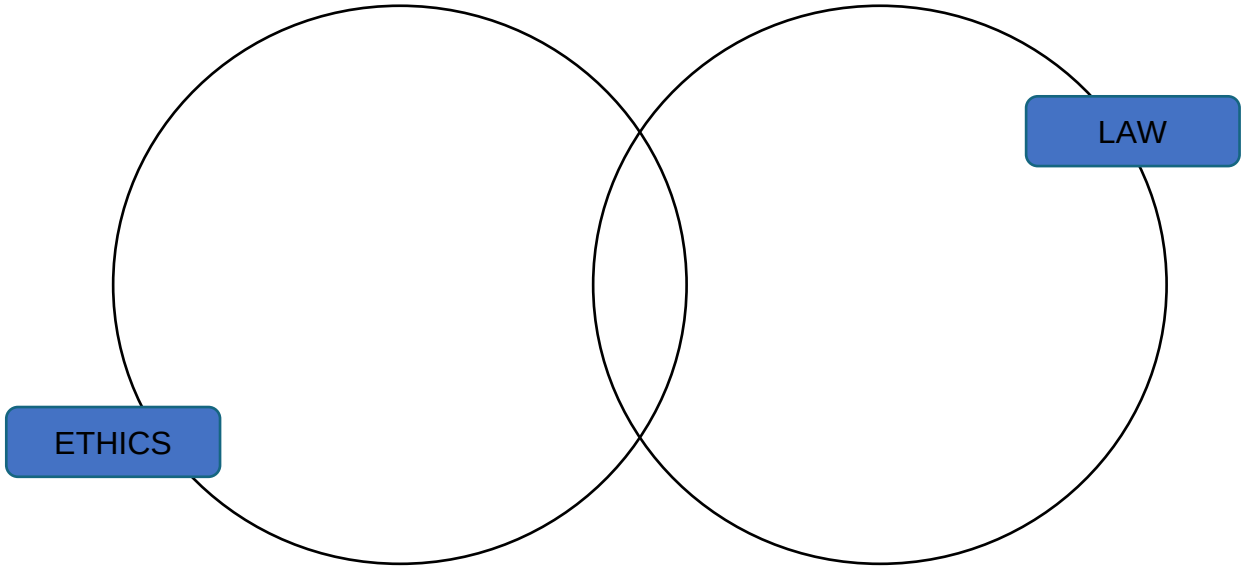
(Quotes stem from Group 2 of the RRI ISW workshop)

We need an Ethical Manifesto on ethical and social responsibilities, which can serve as a sort of compass for in silico modelers and the in silico community as a whole!

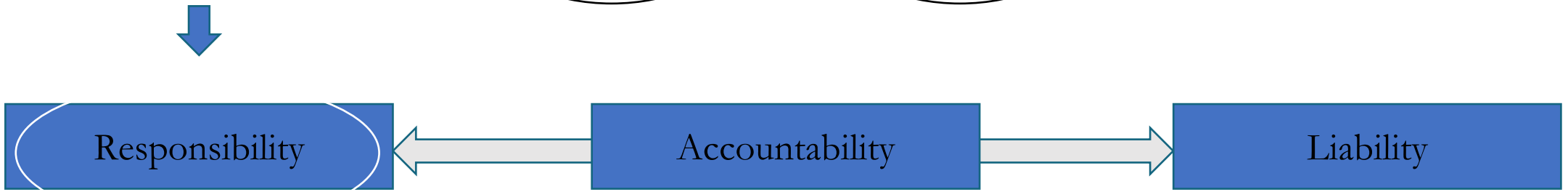
On Responsibility



Ethics and Law are not the same.
They may have overlaps, but they are different



Our focus today



Session Layout

- Moderated Group Conversations of 5 participants per group
- Card-based method inspired by the IMAGINE RRI tool developed by Felt et al., (2018)

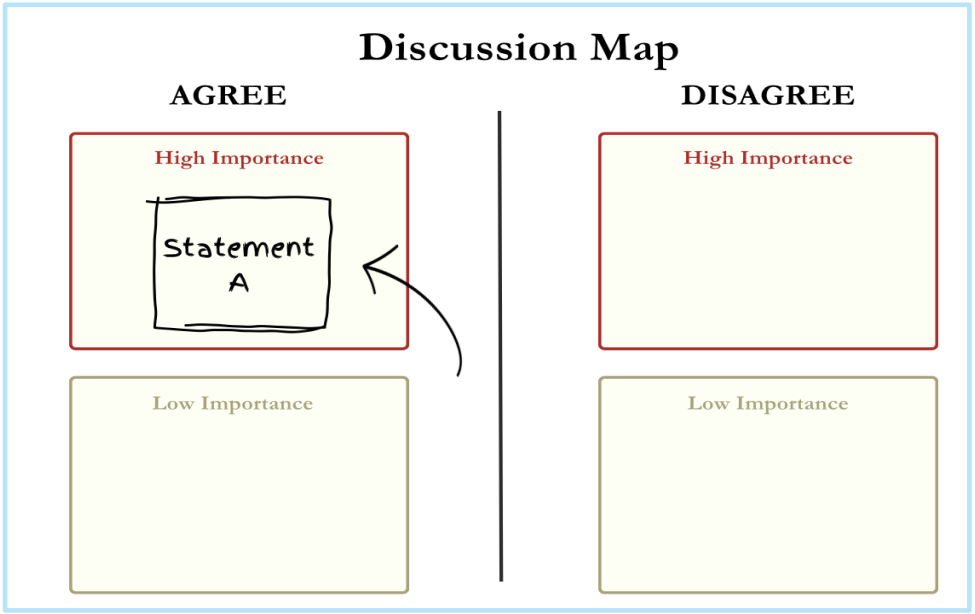
Schedule

14:20 – 15:00 Group Conversations (1st part)

15:00 – 15:05 Short break

15:05 – 15:45 : Group Conversations (2nd part)

15:45 – 16:00 : Summary & Conclusion



Breakout 3: generation of data

Adrian Ionescu (EPFL)
notes: Sanjay Pant (Lynkeus)

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Breakout 4: business models

Enzo Fabiani (Pi School)
notes: Roberta De Michele (VPHi)

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Main foreseen business models and revenues

- **1st — Specific tech tools (STT):** provide a specific tech tool in a Virtual Twin solution workflow
- **2nd — Tech transfer or spinoff businesses:** Virtual Twin spinoff emerging from the labs
- **3rd — Intermediary businesses (IB):** that brings assistance at each step of the VHT process

Some revenues could be generated from:

- **Taking part in the VHT Marketplace** through licensing or subscription fees (e.g., pay-per-use or annual subscription access) — healthcare industries
- **Consultancy services** for customising virtual twin solutions to specific healthcare use cases
- **Bringing expertise** (e.g., data processing services, AI tools)
- **Multi-skill integration** (e.g., hardware and software)
- **Collaboration** (e.g., royalties, licensing) between healthcare companies

Major costs & Risks

- Data processing costs
- Certification (Risk-management + Technical Documentation + Clinical trials)
- Computing costs
- Personel and experts

- Market risks: lack of interest or trust by the users, market overload and chaotic competition
- Complex and long approval processes
- Malicious or improper use of accessible open model

but some risks can be seen as opportunities

Incentives and needs

- Stakeholders want:
  - available data
  - adequate computing infrastructure

- There is a need to:
  - define cost-effectiveness from HTA (on the long-term)
  - make sure the VHT platform is robust enough
  - facilitate the production of proprietary licenses

VHT could make the difference

- VHT should **make the go-to-market process for a model easier, faster** and **cheaper** providing an ecosystem of different stakeholders helping through the various steps
- In **increasing the uptake in precision medicine**
- **Enabling synergies across Europe** (skills, data access, etc)
- **Facilitating early access** and **adoption**
- Accessing the **data** (challenging)
- A **macro-economic analysis** should be performed. Europe should be the first to provide this!

Breakout 5: platform processes & services

Amaryllis Raouzaiou (ATHENA), Sabato Mellone (UNIBO)

notes: Artem Platonov (VPHi)

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Discussed aspects

1. Platform
   - Preparatory phase: predefined UCs – scope/objectivities + technical aspects
   - Trinity of software: catalogue, repository, platform
   - Cross-cutting directions: open source, distribution & federation, distributed platform
   - Main functionalities: loosely coupled soft and services, workflow, Jupiter notebook

2. Governance
   - Populating VHT: resource acceptance, role of community, resources not accepted can go to edith-catalog

   One has to register to be a part of the platform and being able to upload

   Legal aspect, copywriting (authorization) - compliance

   Standardization

Sustainability

1. We should make a decision about the accessibility of the data for users (free access, in return for sharing data, etc). partial solution would be without sharing the data, users will have to share outcomes
2. Principle of reciprocity: more you get more you give back

Credibility and Standardization

Pro:

1. Software standardization is important for clinical solutions. The software can come from outside EDITH, but then must comply with the standards
2. The researchers can be assessing the credibility of their own models
3. Going to the community for the answers to the untested questions
4. The criteria for standardization may become the key feature of EDITH, championing the standardization work is what nowadays a must. Standardization standards provided by EDITH may potentially become an extension of MDR
5. This improvement can go gradually step by step through the platform

Contra:

1. Standardization kills unique features inherent to biosystems. If we want VT to be a success it needs to work with individual cases
2. We need to be looking for specific points where VT will be better than traditional approaches and that is in the domain of unique characteristics

Miscellaneous

1. Efficacy of the workflow. A user must be aware of the step that should be taken to get to the desired outcome
2. To become efficient, the platform must be able to help identifying key parameters and flaws in the model
3. There should be alternatives to the most efficient model in case the accuracy is not the only requirement (e.g. using less parameters): a list of models (hierarchy) describing an organ/process
4. The data must be very user friendly otherwise no one will use it. So it must be very understandable and easy to use for clinicians (not developers)
5. The only way to promote VT is to make something to be mandatory, not just nice to have. Nice to have is not enough: what policymakers should do to force this process

Breakout 6: user roles/identities

Gökhan Ertaylan, Elfi Goesaert, Fredric Jung (VITO)

notes: Martina Contin (VPHi)

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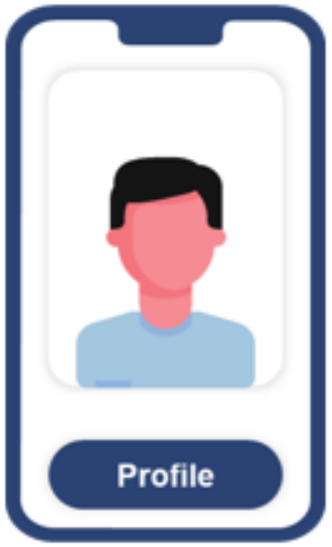
User Profile vs. Roles

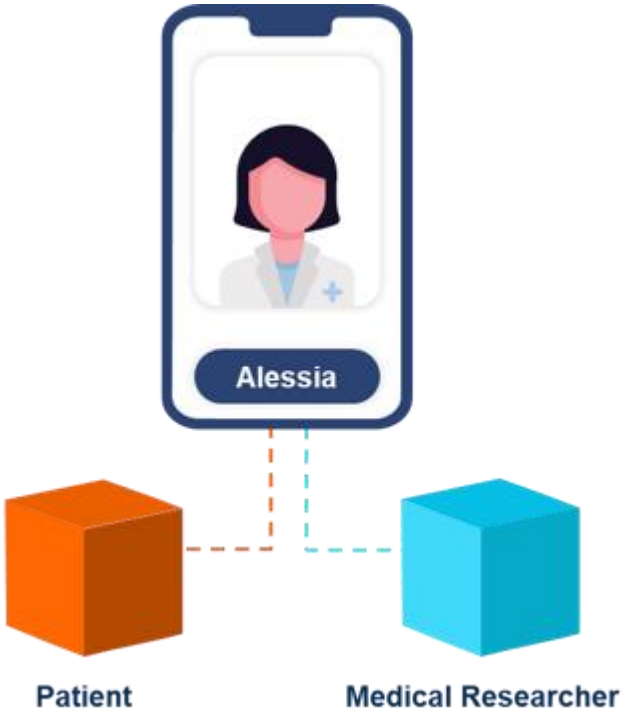


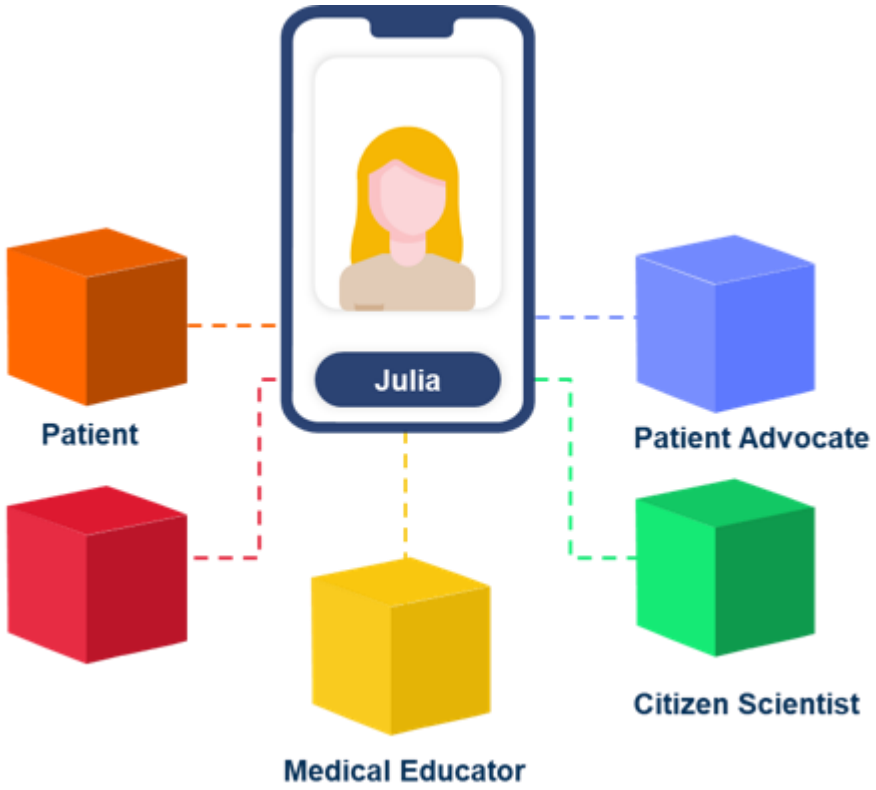
A user **profile** is a **collection of settings** and **information** associated with a user. It contains critical information that is used to **identify an individual**, such as their name, age and individual characteristics such as knowledge or expertise. The profile can be linked to external IDP (Identity provider) and thus authentication mechanism can be extracted to third party service.

The **profile does NOT distinguish the role** of the user in the system.

User **roles** is a collection of capabilities that can be used to give access to concrete part of the system.

User Profiles vs Roles





User Roles

User roles is a collection of capabilities that can be used to give access to concrete part of the system. In the EDITH environment we can have following roles:

Patients/Citizens Category:
Patient: Patient Advocate: *Citizen Scientist*:
Healthcare Professional Category (Doctors, Specialists, etc.):
General Practitioner; Medical Specialist; Medical Researcher; Medical Educator
Creator/Model Developer Category (can upload new model version, train the models):
Data Scientist: Simulation Engineer: Model Developer/Owner
Platform Administrator Category:
System Administrator; Data Curator; DevOps specialist: Software Developer

Grants & Affiliations as orthogonal to Roles

Summary

- The list of roles is not exhaustive, new roles might be taken in consideration in the future as the needs arise.
  - How much it costs to have one more role in the system?
  - We would need to set up committee to define roles
  - Should people explain why they want to have access to a specific role?
    - Email address part of an institution
    - Proof of affiliation? Who should check it?
    - What does it cost the system to give a certain role? (in terms of security risk) For specific roles the level of scrutiny should be different (communicate with the 12 labours project)

Summary

- How do we envision the assignment of roles?
  - Role curation
    - Same roles can have different permissions in different countries
    - If you use the affiliation, it is up to that organization to take internal decision on the access level
    - Single users can have multiple affiliations
- Non EU users?
  - If you can be authenticated you can have a profile
  - Prevent unauthorized access to the system
  - Record what the individual is actually doing to check unusual behaviors (provenance)

Questionnaire will follow-up.

Breakout 7: standards

Martin Golebiewski and Gerhard Mayer (HITS)
notes: Claudio Capelli (UCL, Lynkeus)

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Introduction into Standards

- Standardization requirements for the VHT: Focus on data integration into models and model validation
- Forest of standards: formats, terminologies, metadata guidelines
- Example for community standards: COMBINE
- Standard for data formatting and description: ISO 20691
- Standard for biological material and data provenance: ISO 23494 series
- Standard for modelling in personalised medicine: ISO TS 9491
- EDITH Standards document (as a complement to the roadmap)
- EDITH implementation guide as a practical guideline

Discussion

- How should that all work in practice with all those different subdomain- and technology specific data and metadata standards? How should they all interoperate?
  → Covid-19 disease maps community as a good example that only worked based on standards (but implementation needed in tools/platforms to support standards
  → Standardization of data and modelling is a cultural change and needs time. It starts where the data is gathered/recorded (already at the patient side)

  It is almost impossible to implement it all in hospitals, not to speak about data transfer between institutions
  → Interfacing supported by standards is the key (e.g. HL7 FHIR)
  → Sometimes already small recommendations have a great impact (e.g. the use of units for measurements/parameters
- How to connect the VHT standardization to the GDPR?
  → GDPR is base for everything, especially important for standardization/harmonization of data access for sensitive data
- How users can be supported in the standardization?
  → helpdesk

Gaps

- Specific standard for model validation and reference data/reference models for validation
- Process for standardized model approval as medical devices, if used for clinical decisions/treatments or for drug approval
- IMPLEMENTATION in tools/platforms - technical help needed to achieve interoperability

Plenary address

Kyriacos Hatzaras (European Commission)

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Friday introduction

Liesbet Geris (VPHi, ULiège, KU Leuven)

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Breakout sessions Friday

8. Clinical engagement
9. Large infrastructures & networks
10. New use cases – how to?
11. Role of AI in the VHT
12. Incentivization
13. Preconditions for a thriving ecosystem
14. Trust in VHT

Friday Break-outs

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Breakout 8: Clinical engagement

- Chair: Caroline Roney, Elisa Rauseo, Laura Bevis (QMUL)
- Note taker: Artem Platonov (VPHi)

- Aim: investigate several questions around the clinical engagement and uptake of the EDITH project/digital twins in practice.
- Questions
  - Current clinical perspective on DT?
  - How can we effectively communicate about benefits
  - Credibility?
  - …

Breakout 9: Large infrastructures & networks

- Amaryllis Raouzaiou (ATHENA)
- Note taker: Janaki Raman Rangarajan (VPHi)

- Aim: present what is already available, collect feedback regarding other solutions we are not familiar with and present/discuss the connection of EDITH to all of them.
- Questions:
  - Do you know a large infrastructure or a network that is not mentioned in the presentation?
  - What is the type of communities we "have" to be connected with?

Breakout 10: New use cases – how to?

- Chair: Sabato Mellone (UNIBO)
- Note taker: (Lynkeus)

- Aim: present the application process for new use cases to be integrated into the EDITH repository and/or catalogue
  - How the evaluation takes place?
  - What levels of integration are possible and what requirements need to be met?
  - Discussion on points of attention such as intellectual property and data protection.
- Question: What can I do for EDITH and what can EDITH do for me?

Breakout 11: Role of AI in the VHT

- Chair: Gökhan Ertaylan (VITO)
- Note taker: Goran Stanic (VPHi)

- Aim:
  - data and model integration: harmonize data formats, transform this data into formats that predictive models can understand and use effectively, ensure models can communicate with each other.
  - resource orchestration and continuous updating of digital twins. AI in our platform should be recommending the most effective workflows, keep the digital twins up-to-date.
  - Evaluating the credibility of the data and models : assessing the quality of data we're working with.
  - chatbot interface to the envisioned VHT platform designed to be both user-friendly and highly accurate. Navigate users through the system and providing them with the needed support.

Breakout 12: Incentivization

- Chair: Roel Meiburg, Anna Niarakis, Irene Vignon-Clementel (Inria)
- Note taker: Martina Contin (VPHi)

- Aim:
  - What are challenges to create the missing part of the VHT puzzle?
  - What are the barriers to couple existing VHTs?
  - What are challenges to adopt VHT in the clinics?
  - Are these challenges different in different communities (Biology, Medicine, Comp. Science)?
  - How creative can we be about rising to these challenges?

Breakout 13: Preconditions 4 thriving ecosystem

- Chair: Edwin Morley-Fletcher (Lynkeus)
- Note taker: (Lynkeus)

- Aim
  - Evolution of the ecosystem
  - Market services
  - Business models & related questions

Breakout 14: Trust in VHT

- Chairs: Ine Van Hoyweghen, Elisa Lievevrouw (KU Leuven), Zita Van Horenbeeck (VPHi)
- Note taker: Zita Van Horenbeeck (VPHi)

- Aim
  - shed light on the diverse social facets of virtual human twins (VHT)
  - what will it take for a VHT to be deemed trustworthy (non-technical).
  - seek insights into the dynamics of why different stakeholders are willing (or not) to engage with VHT?
  - what does it take for stakeholders to be able to trust the respective VHT within their medical environment (whether it be in a hospital setting, at home, in a medical regulatory setting, in a research centre, etc.?)

Friday Break-out reports

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Breakout 8: clinical engagement

Caroline Roney, Elisa Rauseo, Laura Bevis (QMUL)
notes: Artem Platonov (VPHi)

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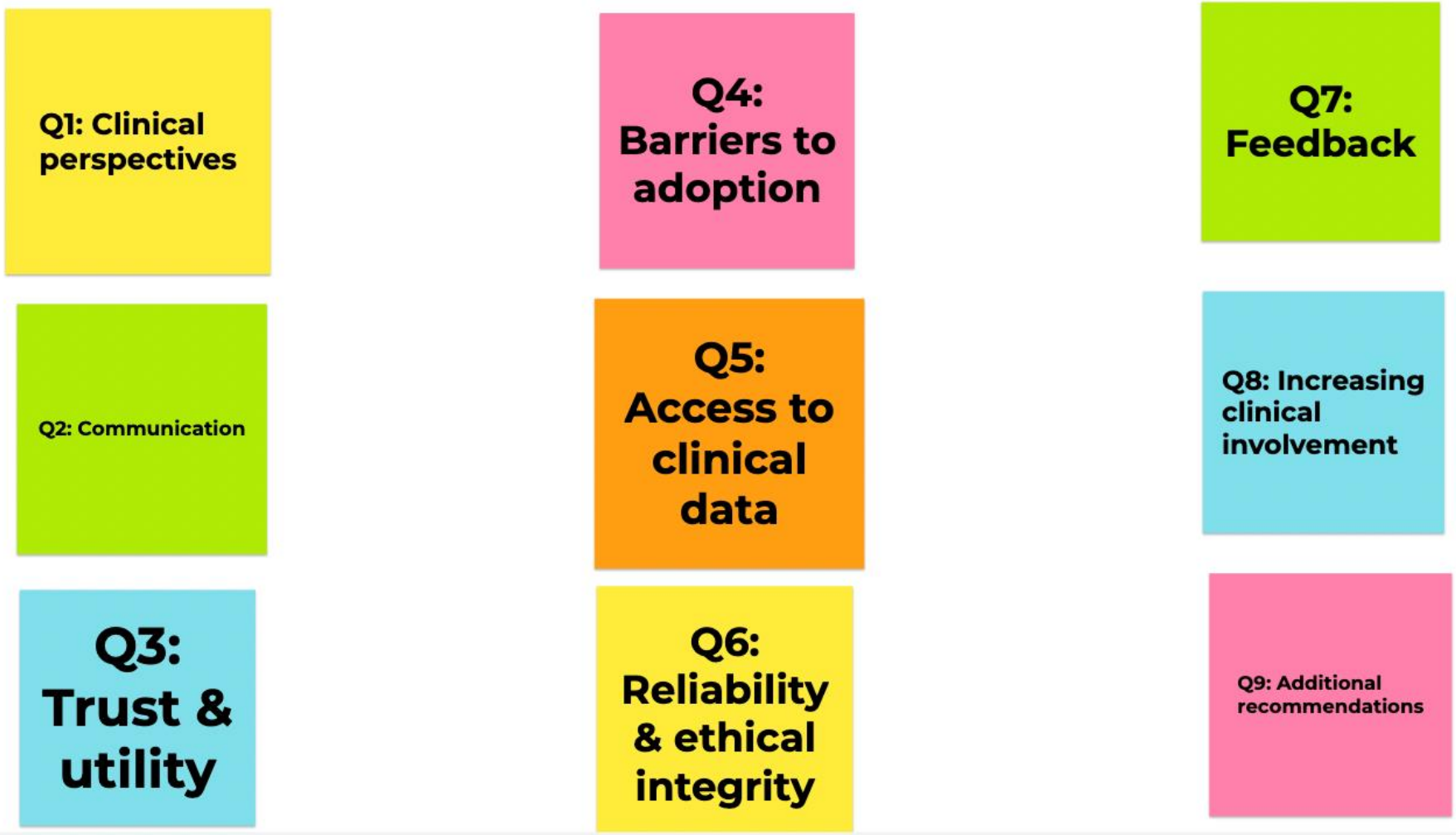
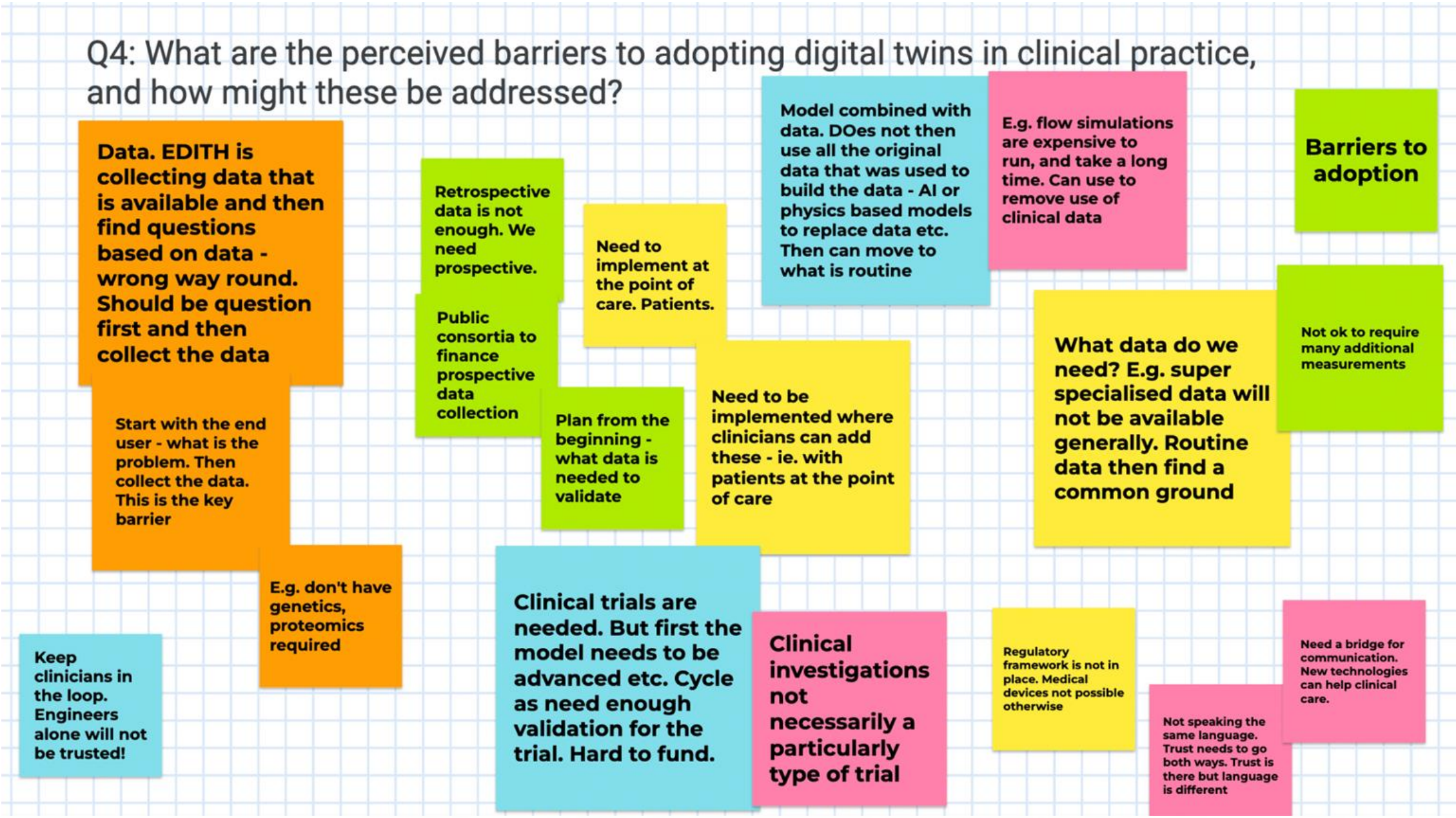
Questions


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
Q9: Additional recommendations

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



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

Vote on the most important question!

Q1: Clinical perspectives

Q2: Communication

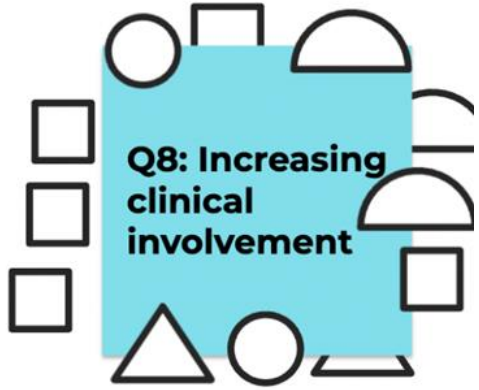
Q3: Trust & utility

Q4: Barriers to adoption

Q5: Access to clinical data

Q6: Reliability & ethical integrity

Q7: Feedback



Q9: Additional recommendations

Breakout 9: large infrastructures & networks

Amaryllis Raouzaiou (ATHENA), Evita Mailli (ATHENA)

notes: Janaki Raman Rangarajan (VPHi)

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Large infrastructures - overview

- Infrastructure
  - EHDS, EBRAINS, EOSC, ELIXIR, OpenAire
- Computing
  - EuroHPC, LUMI, PRACE, GEANT, National grids
- Other initiatives
  - Virtual Brain Twin

EDITH learning & alignment:
Technology, **Standards, workflows, federation, GOVERNANCE**

Related initiatives & needs …

- STRATIF-AI - digital twins for stroke
  - Multi-organ, across time
- DARWIN-EU
- SURF: Alzheimer Genetics Hub

Needs:

Accreditation for repository

- CoreTrustSeal

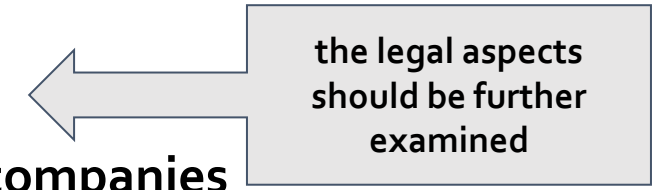
Standards to connect with large infra (e.g. OMAP)

Standard in data collection

Perceptions

- Computing resource is bottleneck **(No…)**:
  - Technical (feasible, available), legal (critical)
    - **BUT most crucial is financial part for resource utilization**

- Overcoming legal challenges in sharing data
  - Solution: Patient owns the data (GDPR)
    - P**atient has personal vault to collate data from hospital/companies**
  - Constraints:
    - Patients can opt out
    - Patients are conservative or hesitant to share
    - Patients are not informed



Challenges

"HEALTH is heavily dependent on lifestyle"

We DON'T have the correct data for improving the predictive capacity of models

- Longitudinal data
- life style and behavioral data (private tech companies)

NEED of public infrastructure for patients to SEEK lifestyle data from wearables/sensors

Breakout 10:
new use cases – how to?

Sabato Mellone (UNIBO)
notes: Lorenzo Cristofaro (Lynkeus)

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Breakout 11: role of AI in the VHT

Gökhan Ertaylan, Simon Denil (VITO)
notes: Goran Stanic (VPHi)

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AIM

Review together the *envisioned* role of Artifical Intelligence in the context of Virtual Human Twin (VHT) in healthcare and clinical practice.

"Draft" definition of Artificial Intelligence (AI)
in the context of VHT

AI can refer to the advanced computational technologies that will enable the simulation, prediction, and replication of human physiological and pathological processes.

This encompasses machine learning algorithms, data analytics, and neural networks that can process vast amounts of health data. AI in this domain should be **characterized by its ability to learn from and adapt to new information**, leading to better prediction of health outcomes, provide personalized medical insights, and support clinical decision-making.

Its role extends to the **continuous updating and refining** of the virtual twin as new data becomes available, ensuring an ever-evolving and accurate digital representation of the individual's health status. This form of AI will be pivotal in advancing precision medicine, enhancing patient care, and contributing to the broader understanding of human health and diseases.

AI utilisation in VHT platform

1) **AI as the Glue for VHT platform**: Data and model integration (linked data &/knowlegde graph)
   - data-data: harmonisation of formats
   - data-model: take given input data and convert to a suitable input for relevant model(s)
   - model-model: map outputs from one model suitable as input for another

2) **Resource orchestration & continuous updating of digital twins** (DTs) : recommender system for workflows

3) **Evaluation** (and credibility scoring) **of data and DT model quality for imported** within the platform (utilizing LLMs)

4) **Guide Chatbot interface to the VHT platform** with LLM tailored to the VHT platform as AI based Helpdesk and Education tool.

NEW! 5) **Discovery of missing components in the system**

Topic 1: AI as the glue for the VHT platform

Naming: data-> data set, measurements, models

Data-data: -> need more nuanced naming

- Not hierarchy but relationships and types
- Data transformation, linkage relationships, enrichment, transformation
- Provenance (synthetic data, measured, modelled …)

Data-model: -> need more nuanced naming

- Identifying missing data/links/… potentially generating missing

Model-model: -> need more nuanced naming

- Identifying links

New! Information retrieval: from literature/measurements to knowledge DB

Topic 2: Resource orchestrations

Resource orchestration & continuous updating of digital twins (DTs)

- Solving optimisation of cost or speed
- Both feasible and useful (high Utility)

Topic 3: Evaluation (and Credibility scoring)

Evaluation (and credibility scoring) **of data and DT model quality for imported** within the platform utilizing LLMs

- Naming is problematic ;evaluation ?, credibility ?

Model quality, quality assurance may be?

- Have different dimensions of credibility (bias, privacy, field of application …)
- e.g.: AI trained on **standards** to assess compliance
- Data provenance (raw data-> annotated data-> standardized data etc)

Utility of SYNTHETIC Data (Not only AI generated)

Topic 4: LLM chatbot tailored to VHT purposes

Chatbot interface to the VHT platform with LLM tailored to the VHT

- What types of knowledge to give AI access to
- Include data usage tags/ontology (can AI access this or is this too much power?)
- Cfr. SPARC for an example of data curation
- Pro-active stance suggested for platform and speeding adoption in field of healthcare (lagging
- Helpdesk functionality
- Educator Functionality
- Accessibility (language)
- Post-market monitoring for the platform?

Topic 5: Discovering missing functionality within the VHT platform

- How to reach from a repository and a simulation platform to the VHT we need to identify all missing components in the VHT platform..

Breakout 12: incentivization

Roel Meiburg, Anna Niarakis, Irene Vignon-Clementel (Inria)

notes: Martina Contin (VPHi)

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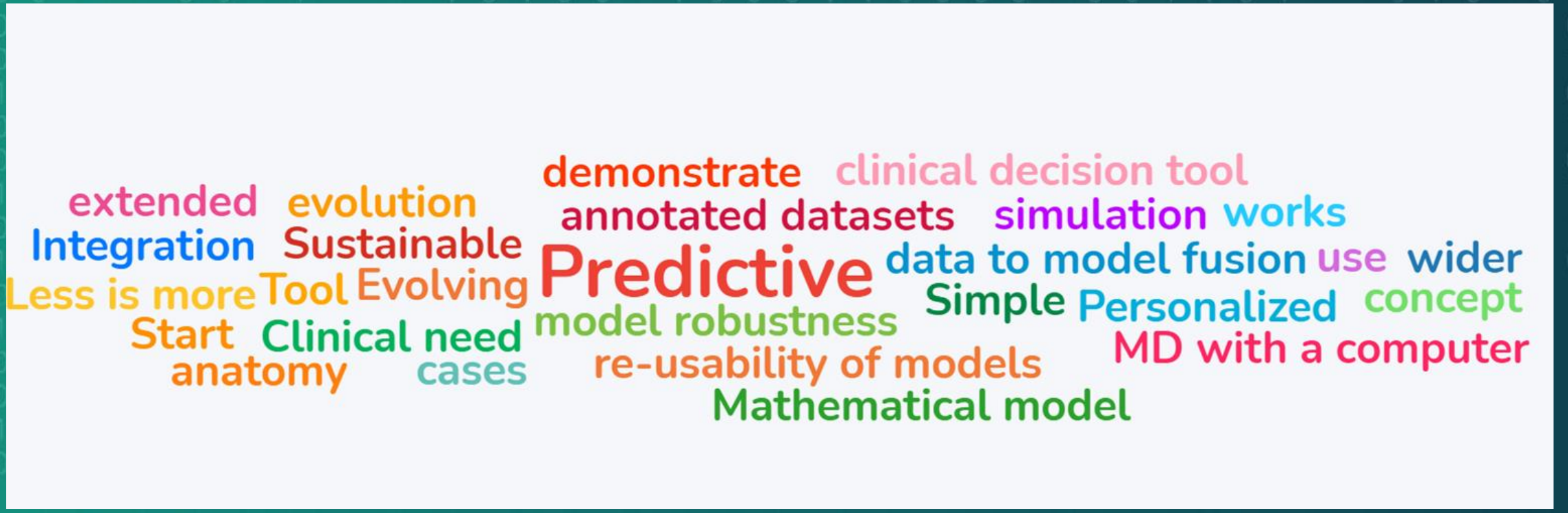
Brainstorming on VHT



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Brainstorming on incentivization

How to participate?

Copy participation link

1. Go to wooclap.com
2. Enter the event code in the top banner

Event code
OSZXUT

1. Send @OSZXUT to 06 44 60 96 62
2. You can participate

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Brainstorming on incentivization

Exercise on challenges

Dedicated Ressources	Trust	building trust and true spirit of collaboration	Regulation	Find a motivated doctor
Dedicated persons	Time	Stakeholder communication and understanding	not caring for most communities in the field	Clinical demand not well defined
Collaboration	overheads everywhere	Communication with user	not knowing the need of other fields	Reaching stakeholders
Misunderstanding	continuous financial support	Multi-stakeholder / Multi-perspective	community inertia	Proper clinical understanding
Resistance to change	Alignment			

Challenges

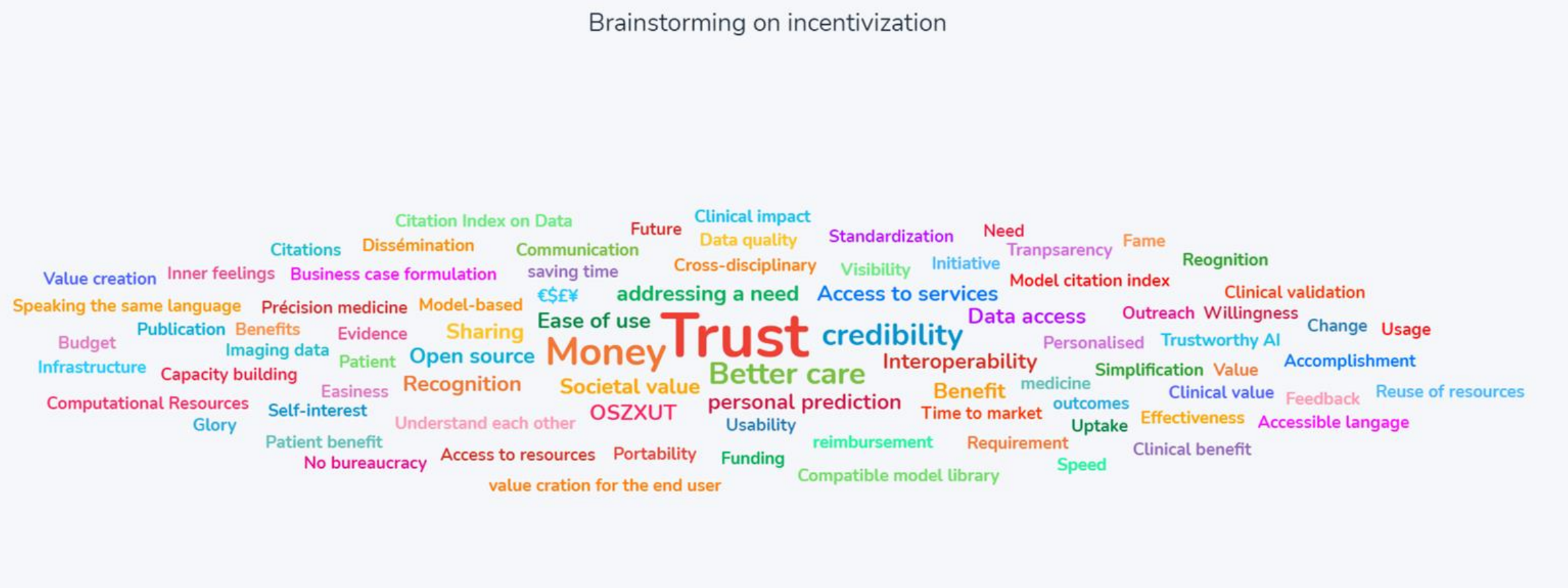
- Identify stakeholders (academia, industry, patient advocacies / orgs., governmental bodies, payers/med. insurancies, medical doctors + hospital management)
- Alignment on the goals for different stakeholders : clinicians, regulatory, patients, industries
- Resources (time & money)
- Start the virtuous circle (from clinicians decision to patient benefits and cascades their wishes of the VHT to be part of the clinical workflow)
- Common language & meaning among the different stakeholders
- Resistance to innovation/changes from clinicians
- Resistance to data sharing from patients (even a electronic Health record is not fully admitted yet)
- Heterogeneity of cultures within Europe (access/sharing of data; clinical registries)

how to meet the challenges

- start with the patients advocacy groups
- scientific proof (proof of concept) - successful examples
- collaboration between clinicians and modellers (and other stakeholders)
- approach it like a drug test (small scale proof, pilot study, in silico trial, small cohorts, scale up)
- meet the patients, think about application early on on designing a VHT project
- become aware of difficulties in clinical and modelling reality - build a common language (communication/ comprehension barriers)
- more interdisciplinary training, projects, conferences - opportunities to bring all stakeholders together

now the research style is too introspective—> change paradigm: more real world awareness (patient-centric)

auditorium


Brainstorming on incentivization
Citation Index on Data
Future
Clinical impact
Data quality
Standardization
Need
Tranpsarency
Fame
Citations
Dissémination
Communication
Cross-disciplinary
Visibility
Initiative
Reognition
Value creation
Inner feelings
Business case formulation
saving time
Model citation index
Speaking the same language
Précision medicine
Model-based
€$£¥
addressing a need
Access to services
Clinical validation
Data access
Outreach
Willingness
Publication
Benefits
Evidence
Sharing
Ease of use
Money
Trust
credibility
Change
Usage
Budget
Imaging data
Patient
Open source
Personalised
Trustworthy AI
Infrastructure
Capacity building
Interoperability
Simplification
Value
Accomplishment
Easiness
Recognition
Societal value
Better care
medicine
Clinical value
Feedback
Reuse of resources
Computational Resources
Self-interest
OSZXUT
personal prediction
Benefit
outcomes
Glory
Understand each other
Usability
Time to market
Effectiveness
Accessible langage
Patient benefit
reimbursement
Uptake
Requirement
Clinical benefit
No bureaucracy
Access to resources
Portability
Funding
Speed
Compatible model library
value cration for the end user

auditorium


Exercise 1: What are the challenges of incentivization? (X1)
Effective communication
Common agenda and priorities
Getting goals
Find a common ground
patients
Security on IP
Cultural change
Lack of vision
Selfishness
involved
what's
Communication
articulation
Fairness
Returns
Sharing
Heterogeneity
channel
Legal obstacles
Priorities
Buy in
Reward
Money
benefits
Interoperability
establishment
Non collaborative mindset
funding
Ethical aspects
HCP
Explaining
connecting to user groups
Time investment
engagement
Show vht outcome for patients
effective

auditorium


Exercise 1: What are the challenges of incentivization? (X2)
Motivate clinicians
Resources
demonstrating
working
Increasing
Distrust
Trust
Digital literacy
value
concrete
tech
Purpose
Uncertainty
Awareness
Legal
Clearly
ways
Market
Sustainability
Time investment
added
together
Cultural change
Motivation
Interoperability
familiarity
Legal certainty

auditorium


Exercise 2: How to meet these challenges? (X4)
Impact factor on Data/models
Access to knxokedge
More money
Accessibility
projects
Translate needs
Communication strategy
Cocration
Credit
Clinical/patient
Funding
Community drive
DT
Involvement
Awareness
Planning
Bribes
Communication
Give evidence of added value
Success stories
Open source
Obligation
Open access
Open Science
work
Reach out activities
MVP
Openness
groups
Demonstration of impact
Framework
Policy framework
Seeing big picture
low hanging fruit
Ambassador networks
Stakeholder engagement
concrete examples
Work load

Breakout 13: preconditions for a thriving ecosystem

Edwin Morley-Fletcher (Lynkeus)

notes: Claudio Capelli (UCL, Lynkeus)

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Breakout 14: trust in VHT

Ine Van Hoyweghen, Elisa Lievevrouw (KU Leuven), Zita Van Horenbeeck (VPHi)
notes: Zita Van Horenbeeck (VPHi)

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EDITH
Next steps & wrapping up

Paris 18-19/1/2024

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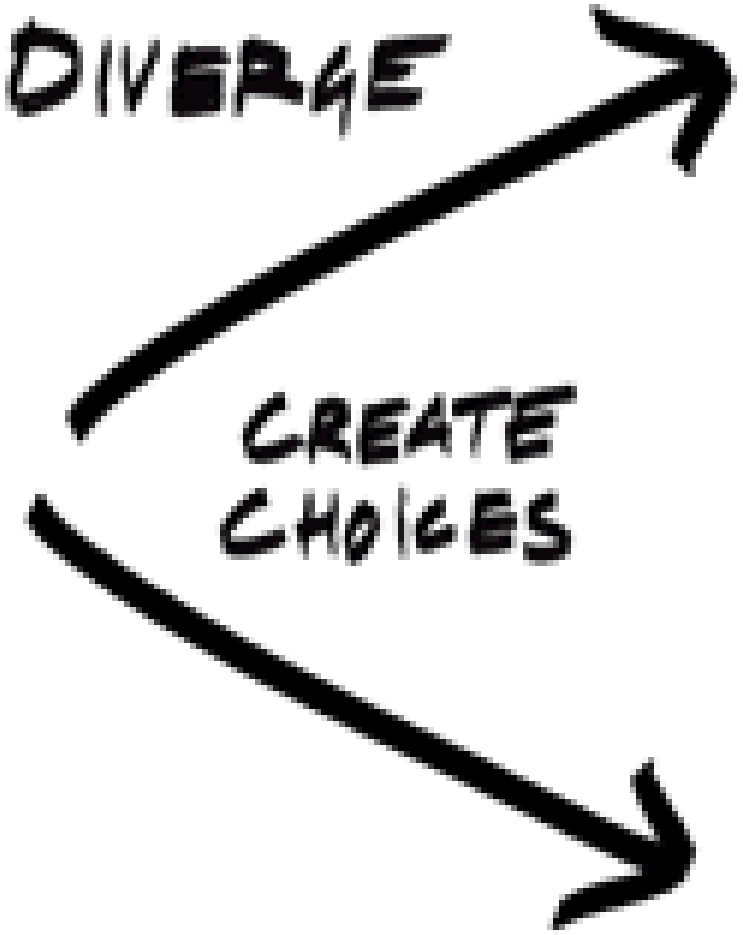
Follow-up

- Before the end of this meeting, you will receive an email with a summary of the wrap-up points
- If you do not receive this email, please check you spam folder
- If you do not find it in spam, please contact info@edith-csa.eu

- We will use this to send follow-up emails & report/slides from the meeting

18-19/1/2024



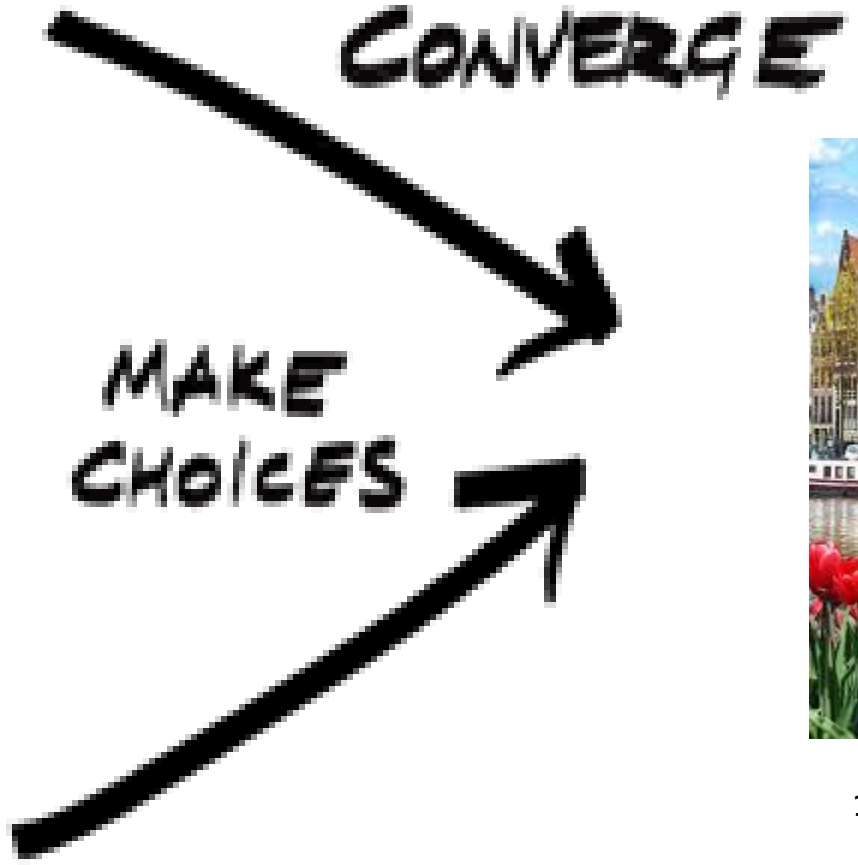
- Break-out sessions
- New use cases
- Many discussions

- Compiled into report
- Follow-up activities defined

Ongoing activities

- VHT manifesto - please help your organisation sign up: https://www.virtualhumantwins.eu/
- call for use cases: https://www.edith-csa.eu/call-for-use-cases/
- clinical community survey - please forward to your clinical collaborators: https://www.surveymonkey.com/r/vphcs2a

- Dedicated meetings on
  - Use cases
  - Platforms
  - Infrastructures
  - Clinical community
  - Patients
- Roadmap writing
  - Shared google doc
  - Slack channels



15-16/7/2024

Thank you to

- Inria team for hosting the event
- Lynkeus for logistical organisation
- VPHi team for all their support
- Breakout session chairs for their organising succesfull breakout sessions
- Speakers for accepting to share their experience
- You for coming here

Save the date

- KIT Amsterdam (Royal Institute for the Tropics)
- 15-16/7/2024

- And more
  - VPHi conference 2024
  - Digital Twin conference 2024