

ITEA 3 PARTNER Project

D1.4: PARTNER clinical-technological collaboration Roadmap

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Executive Summary

This deliverable touches the clinical and technological considerations of the project as well as a focus towards all collaboration aspects already known and delivered, but also what to come in the remaining project time.

A collaborative roadmap is described by the two main partners taking the lead on this: Barco and Calgary Scientific, of course with a lot of input and use of deliverables of the other partners. From initial proof of concept demonstrators and interviews, some feedback on the clinical requirements are also included as well as the assessment of clinical standards. We also tackle technological issues related to protecting data storage, sharing, transmission and analysis. Besides that, policy regulations are discussed, and we do see a need for change for healthcare professionals may also raise some concerns. Finally, there are also changes for the self-management aspects of the patients themselves.

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List of abbreviations and acronyms

AMC	Academic Medical Center (Dutch Hospital)
Amsterdam UMC	Amsterdam University Medical Centers
GP	General Practitioner (Family Doctor)
TAVI	Transcatheter Aortic Valve Implantation (synonym of TAVR)
UBC	University of British Columbia
VGH	Vancouver General Hospital
CBNU	Chungbuk National University
TAVR	Transcatheter Aortic Valve Replacement (synonym of TAVI)
AoS	Aortic Valve Stenosis
MI	Myocardial Infarction
EMR	Electronic Medical Record
MDT	Multidisciplinary Team Meeting
AI	Artificial Intelligence
ML	Machine Learning

1. Collaborative Roadmap (covering all use cases)

1.1. Introduction

Collaborative sessions amongst healthcare providers can be seen broad. Clinicians still meet a lot internally by going to the physical meeting room or by just calling / 'skyping' each other. More remote people will be part of group discussions about patient care and even specialists from other countries can be consulted.

1.2. Overview

Barco is building a solution for discussing a number of patients in a group meeting where these patient lists get prepared well, and where all relevant clinical data is gathered and retrieved from the Electronic Medical Record through FHIR. History data can be manually added/copied and a kind of 'readiness' indicator shows how well prepared the patient is for the discussion. During the group meeting, any imaging data is brought into the meeting through 'smart sharing' technology matching the hanging protocol of the viewer application. Also, other relevant data (e.g. a last minute report) can be easily brought in into the live meeting so the full team can visualize and discuss this. As every type of group highlights different aspects, the solution is based on templates. TAVI specific templates have been drafted, this is applicable for the input of the clinical data, as well as the patient introduction dashboard (how a patient is introduced in the meeting) and also for the outcome format (what are the decisions taken), being translated into a report sent back to the Electronic Medical Record.

Barco will integrate with this EMR through SmartOnFHIR of other partners. Also, information and harmonized views will be integrated and shared into these group discussions so remote participants can always see exactly what is shown on multiple screens of the main meeting room. Results of analytics from other partners can also easily be brought in to the live meeting through participant sharing. Imaging data being shared into the meeting will be analysed in real time so context data can be automatically retrieved and used to validate this source and build intelligence around that. Multiple sources can be controlled to be shown on the live stage and more technology will be built to combine these with different layouts.

Calgary Scientific (CSI) has recently launched PureWeb Spaces for Healthcare which covers a variety of different collaboration use cases which are designed to improve enterprise workflows and enable real-time interactive collaboration for healthcare workers.

This can include:

- Multidisciplinary team conferences
- Healthcare team collaboration with other team members
- Medical Imaging & Reporting collaboration between clinicians
- Ad-hoc patient consultations

PureWeb Spaces is a secure, browser-based workspace where users can share and discuss content from multiple applications simultaneously with rich interactive capabilities and built-in audio/video conferencing. This can include medical imaging data from all departments and other clinical applications. ResolutionMD can be brought into Spaces to provide a more immersed

collaboration session where data from the EMR, ResolutionMD and other clinically relevant data are shared.

For the ITEA Project, the plan is to integrate Spaces with the Dapasoft portal to add collaboration capabilities to this portal.

2. Clinical requirements for the use cases

2.1. TAVI

From the first interviews and proof of concept demo's there is room for improvement in bringing data together faster and more efficient (still a lot of manual input). A connection through open standards like FHIR could be supported since it is supported by EPIC but obviously this requires an investment to setup. Information from wearables can also help in preparing patients for the TAVI procedure as well as during the group discussions. Data aggregation will be necessary to realize this. As of today, the outcome of a group discussion is already reported into the EMR.

2.2. Non-Acute Heart Failure

Stabilized or non-acute Heart Failure diagnosis and urgency of care is determined by clinical symptoms assessment and confirmation from additional diagnostic investigations. To address these clinical requirements for the non-acute Heart Failure use case, the following areas were targeted for improvement:

- Comprehensive clinical data capturing.
- Integration with external reporting systems (laboratory results, diagnostics, reporting).
- Data aggregation.
- Collaborative care.

(XCO)

A comprehensive clinical assessment is an essential component to patient evaluation, as it provides meaningful information with respect to diagnosis, prognosis, and management of heart failure. The clinical requirements for stable heart failure should be as per European Society of Cardiology (ESC) guidelines. For our use cases, a patient-centric approach should be geared towards providing early, real time, remote monitoring of biometric markers for early intervention, so patients receive timely care to mitigate hospital admissions and timely follow up. Key clinical requirements for evidence-based care would include initial assessment and follow-up monitoring, establishing a care plan and goals of care according to the patients' condition and needs, pharmacological optimization, self-care patient education and feedback, and advanced care planning. Additionally, administrative requirements such as optimize patient access, system integration and coordination of care should also be considered. To illustrate a potential use case with various remote monitoring stages, we have developed the following table.

Monitoring Stage	Motivation	Clinical requirements of healthcare professionals	Needs of patients/caregivers

Heart Failure Stable Status	Community/home based monitoring to maintain wellness and patient optimization of self-management	Routine, real time tracking of physiologic metrics, patient education	Awareness of physiologic metrics and self-monitoring for normality
Step-up monitoring and therapy adjustment	Community/home based, increased monitoring to prevent further deterioration, and adjustment of therapies to re-establish stability	More intense monitoring periods (e.g. daily, or even multiple times per day) of physiologic metrics, and adjustment of medications to ensure reversal of clinical course back towards stability or detection of deterioration requiring further stepping up of therapy or emergency admission	Partnership with health professionals to closely watch physiologic metrics, and adhere to increased therapies to watch of frequency of abnormalities and correlation of symptoms to try to re-establish stabilization or if patient worsens, seek further help or present self to the emergency department if a dangerous level is reached

2.3. Cardiac rehabilitation

(CBNU)

Cardiac rehabilitation use case is to provide patients who need cardiac rehabilitation with a solution for monitored exercises at homes by using wearable devices and collaborative workflow so that patient's condition in forms of lifelog data can be constantly monitored at their residency. In order to carry out Cardiac rehabilitation use case, the following requirement should be considered at least:

1. Lifelog data from various health IoT (sensor, mobile device, etc.) should be stored in real-time.
2. Patients should be able to enter information about their condition (rating of perceived exertion during exercise, abnormal symptom or pain during exercise, medications, activity, diet, etc.) directly into patient health record.
3. Patients and medical staff should be able to search the patient's lifelog data as well as EMR data in original or summary form (e.g., charts, graphs) according to various conditions such as device and period (hourly, daily, and weekly).
4. Alarms should be provided to patients and medical institutions and should be recorded in the patient's medical information when target values (e.g., target heart rate) are met or exceeds thresholds, or abnormal symptoms occur.
5. Patients should be provided with reminders after lifelog data of patients are monitored (e.g., when no lifelog data are collected more than 1 week).

(XCO)

Treating and managing cardiovascular disease has a significant financial impact on healthcare systems. For patients who have had a cardiac event, rehabilitation empowers them to make the necessary lifestyle changes, and can also reduce hospital unplanned readmission. Unfortunately, fewer than half of cardiac patients are enrolled in such programs, and an even lower percentage complete cardiac rehabilitation secondary to service availability and prolonged wait times.

Alternative models of cardiac rehabilitation models are needed to provide accessible and cost-effective services. Remote monitoring strategies would serve to support patients having greater access to cardiac rehabilitation programs not available within their community and also a viable option for low to medium risk patients which decreases wait times and increases capacity for higher risk patients requiring onsite supervised exercise and monitoring in a hospital setting.

Our cardiac rehabilitation use case would enable remote patient assessments, health behaviour interventions and risk factor modification, adaptations of program models to improve accessibility especially for the under-served populations, development of self-management techniques based around individualized assessment, problem-solving, goal setting and follow-up, exercise training, outcomes assessment and performance measurement.

3. Assessment of clinical standards

3.1. Guidelines

(AMC)

A proposal to optimize care for TAVI patients has been published by Dr. Nishimura as a guideline for these patients: <https://www.ncbi.nlm.nih.gov/pubmed/31002751>.

Main summary of these recommendation follows the ESC and ACC guidelines and reflect the multi-disciplinary consensus of partnering clinical organizations within the field of cardiology. The main aim is a proposal for an integrated model of care for patients with valvular heart disease. This proposed integrated care model does well fit the PARTNER project as the goals of PARTNER are constructive for to allow integrative care by defragmenting health records and test results and integrate innovative technologies as wearables and telemonitoring.

(CBNU)

Cardiac rehabilitation use case requires patient's access to their health records to view and input their various lifelog data including cardiac rehabilitation data, medication, and their physical conditions. However, current medical regulations in many countries do not allow patients' access to their health records that can be presented to their physicians, which makes aggregation of patients' lifelog data very limited. Access to patient's health records should be allowed to patients in order to collect their lifelog data and make the best out of it regarding monitoring and treatment of patients with chronic diseases.

(XCO)

Digital health is a rapidly advancing field and current clinical standards do not incorporate remote patient monitoring in diagnostic or treatment guidelines due to limited clinical evidence to substantiate claims to improve outcomes, reduce costs or increase efficiencies. A recent meta-analysis by Benjamin Noah found substantial gaps in the evidence base that must be considered before implementation of remote monitoring technologies in the clinical setting. Moreover, regulatory authorities have been struggling to keep pace with the changes and have recently

started to implement methods for evaluating new digital health technologies that have emerged which do not fit into current drug or medical device categories.

4. Technological issues in protecting data storage, sharing, transmission and analysis

4.1. Security aspects

Patient data analysis must be performed for creating a clinical decision support system for outcome prediction in TAVI. This is achieved by applying state-of-the-art machine learning algorithms which are trained with the data provided by the hospital to being able to generalize on new data. This results in a prediction obtained within a certain accuracy that can be measured by a validation process on retrospective data or on a prospective study. The data is encrypted in the model and most of the time cannot be recovered since the model holds a summarized representation of all data collections.

The entire data resides in the PACS of the hospital and the model can reside in the hospital in the form of a software, or on a host with two different approaches to query the model for the predictions:

1. The model is sent to the browser of the medical doctor (in JavaScript) and the analysis is performed on the browser. In this way the data does not go out from the hospital (not always possible since sometimes the model requires computation power which is not available on the client side)
2. The anonymized patient data is sent in an encrypted and safe form to the channel to be analyzed and only the outcome is sent as response to the client side.

For the Dutch use cases, KPN Zorgcloud is fully separate from the 'regular' internet. Data stays in the Netherlands in 2 separate data centres managed by KPN-E-Zorg.

4.2. Patient privacy and security

Health data tends to be stored and distributed among a variety of disparate systems, which usually includes legacy databases. These databases are often standalone, each with their own set of security procedures. This makes updating data erroneous, and can lead to inconsistencies and inefficiencies which inhibits access, delays processing times and increases cost per transaction.

Therefore, a major challenge is achieving privacy and security which is vital for optimizing the benefits for patients and to achieving the objectives of the PARTNER collaboration. There are several issues which must be addressed:

- a) Scalability: Scalability refers to future expansion of a system to be efficiently handled by a growing number of diverse users. Success depends on a centralized administration as well as regular updates of security protocols.
- b) Interoperability of healthcare records and imaging: To create interoperable systems amongst the collaborators, efficient and secure data handling is needed for all levels of research, development, pre-commercial testing and the final on-the-market commercial solutions. The integration and interoperability of the respective technological capabilities of the partners to optimize healthcare delivery must include data acquisition, IOT, bioinformatics, machine learning, data analytics, and assessment applications.

- c) Access control: This refers to who can access the resources available on the network and can be achieved through authentication and authorization.
- d) Patient's understanding: This implies that patients have an exclusive right to know and understand how their sensitive and private health information is kept and utilized by any healthcare provider.
- e) Patient's control: This allows patients to be given permission to determine who can access his/her health data.
- f) Confidentiality: Health information should be kept away from people who should not access it. The sanctity of the information should be maintained.
- g) Data integrity: This ensures that manipulation and omission of health information is totally prohibited. Hence, health information being shared should be a true representation of original information without any form of amendment or alteration.
- h) Consent: This implies that patient's information could be accessed only with their consent unless there is an exception such as for use in emergency cases.
- i) Auditing: This is a requirement that health data should be well monitored frequently along with any form of activity to ensure that data is well secured and protected. This will assist user to know the confidential status of his data.

5. Policy regulations on devices or patient information that enable or impede progress

5.1. GDPR aspects

Since May the 25th 2018 the General Data Protection Regulation (EU) 679/2016 (GDPR) is in place for all EU member states. It replaced the Data Protection Directive 95/46/EC.

Because of these regulations special attention has been paid inside the PARTNER project to:

- Implementing retention effectively in the cloud.
- Breaching response and coordination.
- Processing of personal data outside the EU.
- Data portability for the controller.
- Data ownership.
- Risk management.
- Cloud architecture and privacy by design.
- Visibility regarding metadata and Data Minimization.
- Security of Privacy.

For the Dutch use case the MedVision platform (MEDrecord) is certified according to ISO27001, NEN7510 and MedMij (HI7 FHIR). Therefore, the Dutch use-case is in line with all GDPR implications mentioned in the list above.

For the Dutch use cases, KPN is certified according to Goed beheerd Zorgnetwerk (GZN), NEN7510, ISO27001 and is fully operation in accordance with the Dutch Telecommunications law. The GDPR is fully integrated in all Dutch law.

Calgary Scientific (CSI) has recently provided a GDPR statement to its partners who integrate the ResolutionMD product into their platforms and sell in the EU. This GDPR statement is primarily focused on the security considerations for all integrators to provide secure remote access from personal devices and desktop computers to diagnostic-quality medical images and other patient data. The Institution that uses the product is responsible for granting appropriate authorization to specific users to access patient data stored in an institution's repositories. A site can implement additional access controls where data can have additional access rules for VIP patients, restricted

studies, sensitive studies and study that can only be viewed by specific users. All connections are secure and audited. No data is ever transmitted outside the institutions when the system is setup on-premise or beyond the cloud instance which can be deployed in the specific EU country.

5.2. Sensor data

Discussions on this study are in starting phase. Consent is typically requested to share data with 3rd parties (sometimes the parties are explicitly mentioned, sometimes also the purpose of sharing). We follow the (Dutch) CCMO guidelines, and often add a table where we specify which data will be collected, with whom it will be shared, and how long it will be stored.

In a previous study with wearables executed at the AMC the use of a patient informed consent form according to the latest GDPR rules was sufficient to a) collect data from consented subjects, b) share data pseudonymously with vendors and 3rd parties for data analytics, c) share and store data anonymously for product development. For data analytics it is often not possible to use completely anonymous data as the results of a certain analytic need to be translated back to a specific patient or vice versa. However, to ensure privacy, a pseudonym can be used and the translation to identifiable patient data should be done on a need-to-know basis.

In this study the sensor data was also encrypted and transmitted securely, in order to make sure only the receiver with sufficient rights to access the data had access and could read-out vital signs information from the wearable.

Based on user experiences in this patient group we know that special attention should be given to user friendliness of the entire system and not solely the wearable. A relay, such as a data collection device connected to the wearable should be avoided and if necessary easy to operate.

5.3. EHR sample data

AMC provided anonymized data for 5 TAVI patients so specific templates and clinical data can be validated. These are being stored into a sample EMR and accessed through SmartOnFHIR (sandbox).

CBNU has generated a set of dummy patient data for development of prognosis prediction model of patients in Cardiac Rehabilitation use case. This dummy data set has medical history, lab test, and lifelog data (Table 1).

Table 1. Dummy patient data of patients in Cardiac Rehabilitation use case

patient ID	age	gender	ACS event number	Family history on ACS before 55 years of age	has type 2 diabetes	has hypertension	smoking status	exercise frequency per week	BMI	blood pressure	serum cholesterol	low-density lipoprotein cholesterol(mg/dL)	Frequency of target heart rate range during exercise (last 2 weeks)	Minute of target heart rate range during exercise(m) (last 2 weeks)	Frequency of abnormal ECG during exercise (last 2 weeks)	Walk count (last 2 weeks)
ACSP-0010	61	M	2	Y	N	N	N	4	23	110/70	175	80	180	68.8	0	95336
ACSP-0011	62	M	2	N	N	N	N	5	24	115/75	178	83	57	110	5	41000
ACSP-0012	63	M	2	N	N	N	N	4	25	105/65	172	82	175	71	0	95346
ACSP-0022	55	M	1	Y	N	N	Y	0	25	110/80	210	147	175	105	5	95366
ACSP-0023	57	M	1	Y	N	N	Y	0	25	100/70	200	143	180	100	3	95377

Inside the MedVision platform (MEDrecord) the data from various devices is saved based on FHIR defined profiles. For this reason, an ECG observation has been developed and based on this definition the ECG data will be captured and stored.

Observation	0..*	Observation
identifier	Σ 0..*	Identifier
basedOn	Σ 0..*	Reference(CarePlan DeviceRequest Immuni...
status	Σ ?! 1..1	code Binding
category	0..*	CodeableConcept Binding
code	Σ 1..1	CodeableConcept
subject	Σ 0..1	Reference(Patient Group Device Location)
context	0..1	Reference(Encounter EpisodeOfCare)
effective[x]	Σ 0..1	
issued	Σ 0..1	instant
performer	Σ 0..*	Reference(Practitioner Organization Patient ...
valueQuantity	Σ 0..1	Quantity
value	Σ 0..1	decimal
comparator	Σ ?! 0..1	code Binding
unit	Σ 0..1	string Fixed Value
system	Σ 0..1	uri Fixed Value
code	Σ 0..1	code Fixed Value
dataAbsentReason	0..1	CodeableConcept Binding
interpretation	0..1	CodeableConcept Binding
comment	0..1	string
bodySite	0..1	CodeableConcept
method	0..1	CodeableConcept
specimen	0..1	Reference(Specimen)
device	0..1	Reference(ECGDeviceMetric)
referenceRange	0..*	BackboneElement
related	Σ 0..*	BackboneElement
component	Σ 0..*	BackboneElement

5.4. Analysis

Analysis would still be based on theoretical use cases (no access to patient data) -> validation with clinicians will happen (Sopheon) – this could even result in a different workflow.

Data belongs to patients and is used to solve real clinical cases. Consequently, patient is the owner of his data (according to the new GDPR) and the hospital is responsible for taking care and for the protection of these data. The data is given, prior to agreement, to university or companies, for research purpose and this is possible only thanks to the prior consent that the patients expressed. As a preliminary step the data must be anonymized in such a way that it is not possible to recover the patient details.

If any device is used to collect data for the study, a document, where the risks for the patients are calculated, has to be presented to the medical research ethics committee of the hospital willing to host the clinical trial. Only after the approval of this committee the clinical trial can begin.

6. Entrenched practices of health systems and health professionals that need to change

6.1. Clinical decision support

Analysis of heterogeneous EHR data was traditionally done using statistical techniques such as logistic regression, decision trees, and multivariate regression. State of the Art computer power and AI techniques have resulted in new insight and possibilities for advanced CDS. This will have an important impact in the clinical scenario and on the clinical protocols without many changes in the current clinical workflows.

Once the patient data are collected the CDS can be used to obtain an AI (Artificial Intelligence) advice that can be used by clinicians to make the proper decision for the patient.

In the clinical workflow different (external) CDS systems can be used before the TAVI procedure, but also after the procedure (at home). The clinical workflow will have to be adapted consequently. No important changes in the clinical process are expected, since the current workflow already includes a decision which is carried on by the entire "Heart team". In this scenario the "Heart Team" will have also an additional information to consider given by the AI predictor.

Based on the input from TuE, both MedVision and Sopheon will implement operational CDS that can be used in practice with the patient. For the PARTNER setting there will be a webhook to the MedVision infrastructure for Sopheon to perform external CDS.

6.2. Challenges for Machine Learning in healthcare

Artificial Intelligence (AI), and more specifically Machine Learning (ML), have been gaining a lot of popularity over the last few years. If some are to be believed AI might usher in a new era for humanity, while, conversely, others would argue that it will lead to humanity's downfall. Utopian and dystopian views aside, machine learning has the potential for big improvements for a wide variety of problems, now and in the near future. Big strides have for example been made in the fields of speech recognition, game AI, and visual computing/image processing due to the use of machine learning.

In comparison, the use of ML in healthcare has seen a relative slow uptake. Although there is ample interest and there are many opportunities for ML to improve healthcare, its use also comes with a significant amount of challenges and raises an equal amount of questions. Many of these challenges and questions are covered in the *Artificial Intelligence in Healthcare* report by the UK's *Academy of Medical Royal Colleges* [1]. In this report the likely, near future, clinical impact of AI on doctors and patients in healthcare is discussed.

Going through some of the literature, it becomes clear that one of the core reasons for the reluctance of using ML in healthcare seems to stem from trust. I.e. ML models often operate as a "black box" where input values are provided, and the ML algorithm "magically" calculates a result without providing any insights into how it calculated that result. This raises a number of questions. As a (somewhat contrived) example, consider a doctor that is using a decision support system (DSS) that is based on a "black box" ML model, and that the model provides a correct (and expected) result most of the time. Then what if the model provides an unexpected result for a patient? Should the doctor just accept the unexpected result because the model was correct at other times (automation bias also comes into play here), although the result might actually be incorrect? Or should the potentially correct result be dismissed, because the doctor considers it unexpected? Because of the "black box" behaviour there is no way for the doctor to know why the

ML model provided the result, which makes it difficult to trust or rely on it. If on the other hand the ML/DSS was interpretable, i.e. provided some intelligible way to trace back how the model came to its result, then the doctor could have made an informed decision on whether to accept or dismiss the unexpected result.

As the above example indicates, it is often desirable to make sure the used ML models are interpretable. This allows predictions made by the model to be more clearly understood. The latter is not only beneficial for the clinician using the ML model, but also for the model's developers. It allows them to better understand why a model is making certain decisions, which in turn facilitates improving the model.

One way to achieve better interpretability is by only using ML algorithms that are interpretable. But this might limit the complexity of the techniques and models used, which in turn might reduce their performance. Another approach is to use techniques/frameworks such as *SHapley Additive exPlanations* [2], that try to provide a generic way to “explain” the predictions made by (complex) ML models.

Note though that the need for interpretability also depends on the application domain of the ML model. If for example the ML model is used to optimise a logistics task, then a non-optimal result will probably not cause a severe patient risk. In such situations the “black box” behaviour of a ML model probably won't form a roadblock for its adoption.

Relating to the example given previously, another challenge is accountability. I.e. who will be accountable if a clinician relies on a faulty prediction made by the ML model to decide to use a treatment that turns out to be fatal for a patient? Is the clinician responsible because he made the final decision? Or is it the company (or developer) that created the faulty ML model? Or maybe the hospital because it approved the use of the ML based DSS?

This issue might become even more prominent in the future when(/if) the use of AI/ML transitions from a support role to a more active one. Similar to the pharmaceutical sector, some form of (governmental) regulation and (standardized) certification processes might be part of the solution here. This could for example help in setting the boundaries for the applicability of a ML model, and the expectations about its accuracy.

Regarding certification, special attention is required for continuously learning ML models. Because such models might change significantly over time, they will also require regular re-certification to guarantee their quality over time.

Another major challenge for ML models is the data with which they are trained. A general rule in ML is that a model is only as good as the data it gets. I.e. for a ML model to perform properly, it needs to be trained with a large amount of high-quality input data. This is basically a twofold requirement.

On the one hand the input data should be correctly and consistently labelled. Data which includes samples that aren't correctly labelled or that are missing values for some properties, will make it more difficult for the model to learn the correct underlying relationships. So the generic data processing idiom “garbage in, garbage out” also applies to ML. The training data also needs to be representative for the real-world data. Otherwise problems such as distribution shift, might cause the model to make good predictions on the training data, but fail when used later with real-world data. For example, a ML model that is trained only with data from elderly women, will probably make wrong predictions when provided with input data from an adolescent man.

On the other hand, most ML models also need a significant, if not huge, amount of data for training. If the training data set is too small, it will be difficult for the ML model to learn the underlying relationships in a generic way. Gathering (and cleaning up) the data required for ML is an often underestimated and time-consuming task. In some situations, generating artificial input data or augmenting existing data can sooth a ML model's hunger for data. But these approaches are often not applicable when working with clinical data, as for example you can't just generate counterfactuals or go back and undo a treatment. Somewhat paradoxically, in many cases a large body of clinical data exists, but it is scattered across different hospitals or other medical institutions that each have their own private data silos. Combining this patient data is not a trivial task. As for example privacy regulations need to be taken into account, and there are often non-negligible costs involved in adapting existing EHR systems to facilitate data sharing.

A platform such as *Kara* [3] might provide a solution to this problem. Their envisioned solution is a cloud system where patients, with consent, can share their data anonymously (and get paid) for use in training ML models. An issue with this approach though, is that because the developer of the ML model has no direct access to the patient data, it will be hard to validate the quality of the data.

The efforts made in the PARTNER project could provide a steppingstone on the path to making more data available in a harmonized way, and thus facilitate and improve the adoption of ML in health care.

Another factor that hampers the use of the data scattered across hospitals' EHR systems, is the fact that the format used to store patient information in the EHR, and the details that are recorded therein, often varies between hospitals. As a result, in most cases clean up and reformatting of the data will be needed before it can be used to train a ML model. Also here, regulations from the government or public healthcare institutes might be part of a solution.

A final comment to make is that developing ML models in coordination with clinicians is commendable. This will make it more likely that the models will meet the relevant clinical standards, and that the goals of the ML model are practical in real-world usage. An added benefit is that the clinicians involved will have a better understanding of the ML models and their limitations.

For readers that want to take a deeper dive into the challenges (and opportunities) that machine learning (and AI) presents in health care, the following sources can be used as a starting point:

[1] Academy of Medical Royal Colleges. (2019, January). Artificial intelligence in Healthcare. Retrieved from http://www.aomrc.org.uk/wp-content/uploads/2019/01/Artificial_intelligence_in_healthcare_0119.pdf

[2] Lundberg, S. M., & Lee, S. (2017). A Unified Approach to Interpreting Model Predictions. *Advances in Neural Information Processing Systems*, 30, 4765-4774. Retrieved from <http://papers.nips.cc/paper/7062-a-unified-approach-to-interpreting-model-predictions>

[3] Dao, D. (2019, January 21). Kara: A privacy-preserving data cloud for health care. Retrieved from <https://www.notion.so/Kara-Primer-1b5290d3205e448384c6a365d2444f61>

van der Schaar, M., & Zame, W. (2018, December 21). Machine learning for individualised medicine. *Annual Report of the Chief Medical Officer 2018: Health 2040 - Better Health Within Reach*, 161-181. Retrieved from <https://www.gov.uk/government/publications/chief-medical-officer-annual-report-2018-better-health-within-reach>

Hibbert, A. (2018, November 27). Continuing to bridge the gap between medicine and data science. Retrieved from <https://www.amsterdameconomicboard.com/en/nieuws/continuing-to-bridge-the-gap-between-medicine-and-data-science>

Vayena, E., Blasimme, A., & Cohen, I.G., (2018, November 6). Machine learning in medicine: Addressing ethical challenges. *PLoS Med*, 15(11). Retrieved from <https://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1002689>

Sendak, M., Gao, M., Nichols, M., Lin, A., & Balu, S. (2019, January 24). Machine Learning in Health Care: A Critical Appraisal of Challenges and Opportunities. *EGEMS (Washington, DC)*, 7(1), 1. Retrieved from <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6354017/>

Challen, R., Denny, J., Pitt, M., Gompels, L., Edwards, T., & Tsaneva-Atanasova, K. (2019, February 19). Artificial intelligence, bias and clinical safety. *BMJ Quality & Safety*, 2019, 28(3), 231-237. Retrieved from <https://qualitysafety.bmj.com/content/28/3/231>

Ribeiro, M. T., Singh, S., & Guestrin, C. (2016, August 9). "Why Should I Trust You?": Explaining the Predictions of Any Classifier. *Proceedings of the 22Nd ACM SIGKDD International Conference on Knowledge Discovery and Data Mining*, 2016, 1135-1144. doi: 10.1145/2939672.2939778

Hughes, O. (2018, May 24). IBM's Watson Health about "augmented intelligence for clinicians". Retrieved from <https://www.digitalhealth.net/2018/05/ibms-watson-health-about-augmented-intelligence-for-clinicians/>

Downey, A. (2019, May 24). Google Deepmind's senior clinical scientist says AI will not "deskill" workers. Retrieved from <https://www.digitalhealth.net/2019/05/artificial-intelligence-deskill-clinicians/>

6.3. Different, improved workflow

(AMC)

By a better and more synchronized input for preparing TAVI patients, having access to dashboards of wearables, it will be easier to prepare patients faster and better for the TAVI group discussion. All necessary investigations will run smoother and more aligned. The group discussion itself, where the final approval for the TAVI procedure happens, will also run more efficient. As a result, the admission time for the patient will be shorter (KPI nr 2 – reduction of 1 day). Furthermore, there will be a reduction in double diagnostics and care is more aligned between care providers. Patient involvement and empowerment is supported by providing an overview of data that is collected and used and where patients are in the clinical pathway.

(CBNU)

In the context of Cardiac rehabilitation use case, patients' lifelog data including sensor data and patient's subjective input on their conditions are to be stored in their health records with the help of the workflows in PARTNER Hub so that patient's lifelog data over a long period of time can be presented to their physicians and patients themselves. It will allow the physicians monitor and care patient's chronic diseases more efficiently.

7. Changes for patients to participate in optimal self-management

7.1. Other alarms

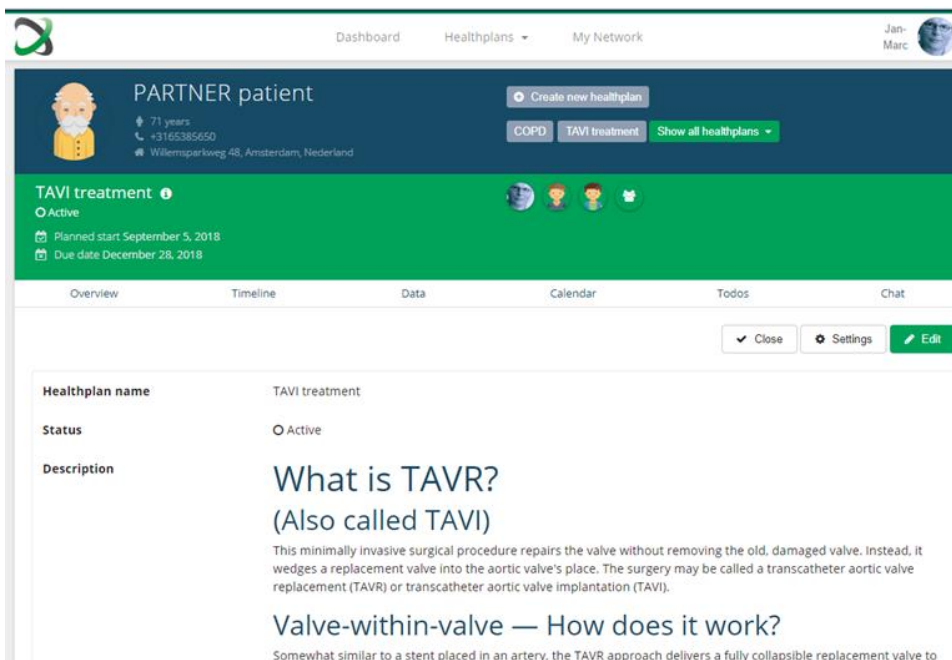
(CBNU)

In the context of Cardiac rehabilitation use case, patient's lifelog data (e.g., heart rate and ECG during exercise) are to be monitored in real-time by using mobile app and PARTNER Hub so that abnormal signals or signals that exceed threshold will lead to alarm the patient as well as caregivers. These alarms are to be recorded in their health records so that physicians can provide feedbacks to the patient.

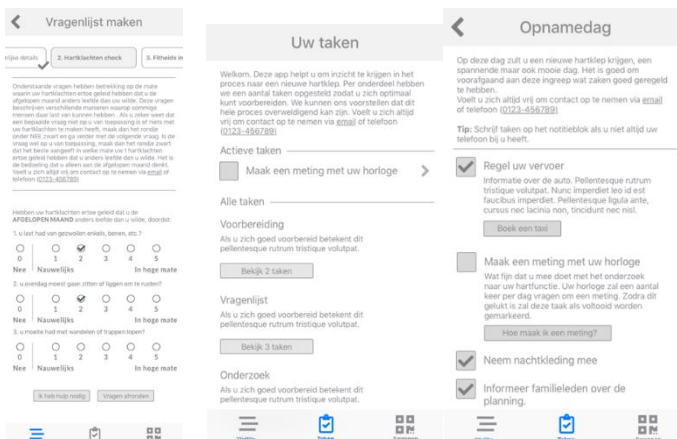
7.2. Better Self-Management

Because of the integration of Hospital data into a Personal Health Environment (PHE) from MedVision), enhanced self-management will improve quality of life for the patient and savings for the Hospital.

Pictures showing the MedVision PHE with TAVI workflow:



The new app that should help the patient guiding through the TAVI workflow (Careplan):



The iClinic Patient Portal will be able to exchange information with the iClinic Heart Failure EHR which will improve information availability to the patient as well as expand the opportunity to capture additional information on the patient that will provide benefit to the patient and the care providers. Patients will be able to better track their own symptoms and understand their disease condition through the use of a dashboard, medications list, medical reports, vitals tracking, questionnaires, education material and messaging. Included below are screenshots illustrating the aforementioned components that would improve patient self-management.

