Regions4PerMed

INTERREGIONAL COORDINATION FOR A FAST AND DEEP UPTAKE OF PERSONALISED MEDICINE – REGIONS4PERMED

Best Practices Booklet

Key Area 1: Big Data Electronic Health Records and Health Governance

1/7/2020

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Best Practices booklet

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1.HAITOOL - A real-time Hospital Infections' surveillance and hospital-wide smart clinical decision-support system

Project | Initiative title		HAITOOL - A real-time Hospital Infections' surveillance and hospital-wide smart clinical decision-support system
Organisation name		Global Health and Tropical Medicine – Universidade Nova de Lisboa
Country		Portugal
Region		Lisbon and Tejo Valey
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Keywords:		Health Information Systems Integration, Clinical Decision-making, smart algorithms, Big Data, Patient Safety
Duration:		From 2016 onwards…
Area of application		
DESCRIPTION	Main challenges tackled (max 200 words)	HAITooL was built using a participatory approach and the Design-Science Research Methodology (DSRM). DSRM connects applied research and professional practice by creating and evaluating information technology artefacts and in this case, an information system to monitor antibiotic resistance and to support antibiotic prescription. In order to solve the problem of multiple sources of hospital/patient data, a web-based information system was developed to support an SQL Server that extracts and aggregates patient-data (e.g. vital signs), results from microbiology laboratory, and data from pharmacy (antibiotic consumption). Data are periodically (every 5 min) extracted, using smart automatic routines programed in Java programming language, from the existing information systems in hospitals by an ExtracteTransformationeLoad (ETL) module, and are then processed and aggregated in a single data warehouse HAITooL was implemented in the participant hospitals side by side with healthcare workers and with a special involvement of hospital information system departments that provided support in managing both databases and data links. The implementation process took some time, mainly because of healthcare workers' busy schedule. Healthcare workers were often overloaded with work and HAITooL was not immediately perceived as a helping tool, therefore was not initially prioritized; after the first trials, the attitude changed significantly.
	Objectives (max 200 words)	To support patient safety on Antibiotic Stewardship Programmes through the co-design and implementation, in collaboration with healthcare workers, of a surveillance and clinical decision-support system to monitor antibiotic resistance and improve antibiotic prescription.

	Main concept and methodologies involved (max 200 words)	DSRM connects applied research and professional practice by creating and evaluating information technology artefacts -An information system to monitor antibiotic resistance and to support antibiotic prescription: (i) Problem identification: observational time-and-motion studies and meetings were conducted in participating hospitals to characterize and understand healthcare workers' workload involved with antibiotic prescription practices. (ii) Definition of objectives for a solution: a set of functional objectives was defined to establish an easy and innovative information system that aggregates, in real-time, all antimicrobial resistance-related information, enabling real-time antibiotic-resistant infection control and monitoring. (iii) Design and development: HAITooL enables management of consumption of antibiotics and monitoring infections; it acts as a clinical decision-support system for antimicrobial prescription; and it is aligned with ASP implementation guidelines. (iv) Demonstration: controlled local events with contextualized implementation (hands-on sessions) of the information system in participating hospitals (wide-database). (v) Evaluation: HAITooL design and implementation process, and its effectiveness on ASP implementation, was assessed by Osterle's principles and semi-structured interviews, supported by a pre-elaborated questionnaire that included questions on usefulness of HAITooL's features. (vi) Communication: of the results to the participating hospitals and to national and international ASP experts.
	Impacts (health, scientific, industrial, socio-economic or others enabled by the project/initiative (max 200 words)	HAITooL was developed by a multi-disciplinary team including researchers and healthcare workers, promoting the creation of a system better adapted to the context where it is implemented. The continuous contact with healthcare workers have contributed to add-value to the system functionalities, fulfilling their specific requirements. HAITooL reduces significantly antimicrobial resistance levels, and is already helping healthcare workers in the management of antibiotic resistance. Data collection on impact on antibiotic-resistance, clinical outcomes, and reduction of hospital cost has just started, and a prolonged period of time is needed to enable statistically significant outcomes in such a multivariate process. One major strength is that HAITooL follows several recommendations and guidelines on antimicrobial use, on information system implementation, and includes several features that a clinical decision-support-system should have to increase healthcare workers' compliance; therefore, HAITooL will be useful to fight antibiotic resistance. HAITooL's implementation presents a proof-of-concept on its usefulness to support ASP implementation. For instance, HAITooL enables easy access to microbiology results and to local epidemiological data, by providing integration of real-time microbiology results. This type of feature is a common

		intervention ASPs since it is effective in increasing the percentage of patients with appropriate empiric therapy and to reduce broad-spectrum antibiotic prescription.
	Funding and Investments (please specify the source: public, private, Structural or other types of funds)	The HAITooL smart decision-supporting system was supported by project 'HAITooL e A Toolkit to Prevent, Manage and Control Healthcare-Associated Infections in Portugal' EEA Grants, 000182DT3; and by Fundação para a Ciência e a Tecnologia for funds to GHTM e UID/Multi/04413/2013. One important resource was the (time) dedication of healthcare workers that contributed for the design of the HAITooL system.
	Key stakeholders involved	All healthcare workers involved in antibiotic monitoring and prescription processes (infection control team, physicians, pharmacy and microbiology laboratory staff) were enrolled in DSRM activities.

2. Data as a Service (DAAS)

Project | Initiative title		Data As A Service (DAAS)
Organisation name		ARIA spa
Country		Italy
Region		Lombardy Region
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Website:		NA
Keywords:		Healthcare governance, data innovation, data security, data curation
Duration:		From 2016. Ongoing project.
Area of application		Data Management
DESCRIPTION	Main challenges tackled (max 200 words)	To implement & improve a secured, scalable, privacy-by-design environment where accredited researchers can perform data driven analyses on the regional data information hub. To preserve data ownership while making it available for use. To increase data quality at the point of data collection. To enhance data value by making it FAIR (Findable, Accessible, Interoperable, Re-usable).
	Objectives (max 200 words)	To foster the regional healthcare system' change towards preventive, predictive, participated & sustainable healthcare.
	Main concept and methodologies involved (max 200 words)	Secured virtual desktop environment where researchers can perform data analyses by their working environment, but can download only aggregated data, when allowed, i.e. for scientific publication purposes. CDA2 Document Instances Validator for improving Inbound Data Quality.

		Data Catalogue to help finding the right data & assessing their quality.
	Impacts (health, scientific, industrial, socio-economic or others enabled by the project/initiative (max 200 words)	The main impacts are linked to the opportunity of supporting policy making decisions with better information & better knowledge of healthcare processes, with an in-depth analysis of care pathways & contextual factors that influence them, so that patients' perspective & care delivery issues can be better integrated into decision-making processes. The system is planned to be progressively expanded to research initiatives involving scientific & industrial sectors.
	Funding and Investments (please specify the source: public, private, Structural or other types of funds)	Public investments by Lombardy Region.
	Key stakeholders involved	Hospitals and Research Hospitals (i.e. Niguarda, Istituto Nazionale dei Tumori), Universities (Bicocca, Bocconi, …), Research Institutes (i.e. Mario Negri).

3. Return of genomic data to biobank participants, pilot projects of personalized medicine in Estonia

Project | Initiative title		Return of genomic data to biobank participants, pilot projects of personalized medicine in Estonia
Organisation name		Estonian Biobank, Institute of Genomics, University of Tartu
Country		Estonia
Region		Baltics, Scandinavia
Contact persons		Neeme Tõnisson, Lili Milani
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Website:		https://www.geenivaramu.ee/en/access-biobank
Keywords:		Large population biobank, genetics-first activities, data return to participants, research data in medicine, precision prevention, pharmacogenetics
Duration:		3 years
Area of application		Promoting of genetic awareness in population and among medical doctors. Genetics-first approach of hereditary diseases. Development of personalized medicine services, using population-based biobank data
DES	Main challenges tackled (max 200	Estonian biobank includes large numbers of currently healthy people. According to ethical principles, the broad consent

	words)	obtained from the participants and legal framework, one must respect the participants' right to know vs right not to know their genetic risk factors. Obviously, actionable disorders are the priority in data return, but with increasing genetic awareness, the less actionable genetic disorders might also be reported upon consent and phenotype. The right not to know demands a stepwise disclosure and stepwise counselling of participants. One of the key pillars of personalized healthcare is to encourage healthy living. Our counselling aim on complex diseases like type 2 diabetes and cardiovascular disease has been to encourage the subjects at higher risk to take early actions and minimize any possible harmful exposure. We try to positively promote a healthy lifestyle, not distress of being at risk. With research data being disseminated in healthcare, the biobank must comply to a strict quality control. Both QC and counselling activities demand funding that is currently limited to research projects. Contacting relatives in a family unaware of a genetic predisposition remains a challenge in both biobank and also clinical conditions, as it is largely the responsibility of index case.
	Objectives (max 200 words)	Our aim has been to test the genetics-first approach in a variety of conditions, from genetic actionable diseases – (familial hypercholesterolemia, hereditary breast cancer) to risk factors like hereditary thrombophilia and also complex diseases like coronary heart disease, type 2 diabetes, early menopause, polygenic breast cancer risk, etc. Among our long term and also the national priorities are the drug dosage recommendations based on participants' pharmacogenetic profiles.
	Main concept and methodologies involved (max 200 words)	The 20% of Estonian adult population already participating in our biobank offers a unique opportunity to develop, validate and introduce novel personalized healthcare services. In addition, using existing data in a biobank for the participant health purposes is a cost-efficient way in prevention of chronic diseases and their complications. We have returned data either directly from the biobank (broad profile, including high-risk findings, polygenic predictions, pharmacogenetics), or within different clinical collaborations. Depending on the severity of genetic findings, there are different options for data return. 1.In high-risk findings (e.g BRCA1, BRCA2, LDLR, APOB, etc.) - validation from a new sample is performed. The invite is

		neutral. Upon the first visit, a detailed consent is obtained. A full disclosure is performed only after the finding has been confirmed from a new sample. Our institute has both a genetic counsellor and a clinical geneticist available, thereby counselling can be performed directly in the biobank. 2.The disease risks, based on polygenic scores and total risk models, moderate risk monogenic findings (e.g.thrombophilia, lactose intolerance) have not been confirmed from a new sample, but the disclaimer states that the data from a biobank may need a clinical assessment if therapeutic actions are taken.
	Impacts (health, scientific, industrial, socio-economic or others enabled by the project/initiative (max 200 words)	Over 3,000 biobank participants have been counselled by November, 2019. We believe that existing genetic data in biobanks should be used for the good of participants as the best cost-efficient solution available. For high-risk monogenic findings, the clinical impact is also extended to their family members. In a vast majority of cases with high-risk monogenic findings (hereditary breast and ovarian cancer predisposition, familial hypercholesterolemia, etc.), the data returned has been the first time the genetic risk factor was ever revealed in the family. In case of breast cancer predisposition our evidence shows that clinical guidelines should be re-adjusted. The age limit of 45 to 50 years for testing is too strict. By more liberal access, much more individuals could be detected and properly managed. The same applies to familial hypercholesterolemia where we have seen that the genetic diagnoses have made a real impact. Nearly 2/3 of the participants had a lipid lowering treatment initiated. Genetic results have often been linked with distress and anxiety. From the filled questionnaires we can see that a vast majority of people, even with severe findings, are able to cope with their findings and consider participating in data return a right decision.
	Funding and Investments (please specify the source: public, private, Structural or other types of funds)	Estonian Biobank was established in 2001. It has been a long-term initiative funded from a variety of sources, from an initial private seed investment to a long-term strategic public and structural funding. The biobank has repeatedly received EU structural funding for collecting the multi-omics big data and creating the data handling capacity. We have received grants from the EU Regional Development Fund (Centre of Excellence for Genomics and Translational Medicine and Estonian Research Roadmap project) to fully develop the infrastructure of the biobank and to enable the development of new approaches

		supporting precision medicine. From 2019 to 2022, EU Regional Development Fund is investing additional 5 M Euros for the integration of Estonian biobank data and the national healthcare information system to promote the use of genetic information in healthcare. Our large scale research infrastructure has largely supported the success in publishing and obtaining research grants by our researchers. We are currently conducting government-funded clinical pilot projects of in the precision prevention of breast cancer and cardiovascular diseases and have received funding from EC (H2020, ERA-NET) for several research projects aiming to deliver personalized medicine with expected impact in Europe and globally.
	Key stakeholders involved	Our key stakeholders are biobank participants, researchers, collaborating healthcare professionals, health and research policy makers, governmental institutions, etc. Our biobank belongs to several consortia like BBMRI-ERIC, Global Alliance for Genomics and Health, EIT Health, Public Population Project in Genomics and Society, Connected Health, etc.

4.NAGEN 1000: An example of a Project for Regional Implementation of Personalised Genomic Medicine in Healthcare.

Project | Initiative title		**NAGEN 1000:** An example of a Project for Regional Implementation of Personalised Genomic Medicine in Healthcare.
Organisation name		Navarrabiomed, Universidad Pública de Navarra (UPNA), Complejo Hospitalario de Navarra (CHN), IdiSNA
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Region		Navarre
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Website:		www.nagen1000navarra.es
Keywords:		Genomics/Rare Diseases/eHealth/Bioinformatics/Big Data/PerMed
Duration:		01/2017-11/2019
Area of application		Personalised Medicine, Genomics, Public Health Services.
DESCRIPTIO	Main challenges tackled (max 200 words)	Local barriers and facilitators were identified using a scientific implementation approach: • Genomic technologies: In order to overcome the lack of local facilities, NAGEN externalizes sequencing services to CNAG, the Spanish world leader public centre for genomic analysis.

		Bioinformatic analysis also relies primarily on CNAG and the Bioinformatics Platform of the Rare Diseases Spanish Network (CIBERer), although this expertise is gradually been transferred to the local bioinformatics Unit along the course of the Project. • ICT: New ICT solutions have been adopted allowing the storage and high performance managing of massive genomic data, through an innovative partnership with NASERTIC, a public local company providing data analysis infrastructures such as the new IBM POWER 9 processor, which build on cross-disciplinary collaboration in research and development with the local industry. • ELSI: The local Health Research Authority has specifically resolved that the massive genomic information resulting from the Whole Genome sequence is also a part of the every patient's medical record and it is accordingly protected and stored under the standard Patient Protection Act. In order to enable the use of genomic data for research purposes, it has been proposed the foundation of a "Genomic Library", which would provide pooled anonymised genomic information upon request and pertinent EC approval.
	Objectives (max 200 words)	Main Objective: Implementation of the use of the information derived from the Whole Human Genome as a clinical tool for health provision services in the Public Health Service of Navarre. The project also aims to pilot this approach for research purposes and as a facilitator to introduce new technologies and explore development opportunities in the field of precision medicine in Navarre.
	Main concept and methodologies involved (max 200 words)	• Subjects and recruitment: NAGEN 1000 aims to recruit 1,000 patients and relatives, affected with one out of more than 200 rare diseases (RD). Albeit rare, joint RD's prevalence is high (2-5%), with a very high social impact, wide multidisciplinary medical coverage, and a high rate of identifiable genetic causes. These features point at RDs as a most adequate target to involve the medical community, raise the population awareness and offer good demonstration to support the evidence based medicine practice. The rate of 1 genome per 500 inhabitants facilitates an appropriate participation of patients and health professionals and a wide dissemination. • Clinical tests: Pertinent findings, explaining the referral condition, secondary findings on individual genetic predispositions and reproductive risks, and phamacogenomic variants, determining drug dosing and toxicity are reported based on patient's choice, providing the necessary evidence on the effectiveness of medical interventions based on genomic

		medicine. • eHealth: The existing Electronic Health Record (EHR) has been modified to host a newly designed recruitment tool which enables and guides the identification and immediate referral of patients from any point in the Navarre health system network. An additional development makes it also possible that clinically actionable genomic results are available for participants with all other clinical information across the system.
	Impacts (health, scientific, industrial, socio-economic or others enabled by the project/initiative (max 200 words)	• Clinical and pre-clinical evidence: Up to date 700 individuals have been enrolled, and 33% of the participant families have now found the long-awaited genomic cause of their previously unexplained condition and are looking forward to an improvement of their medical care based on these findings. Additionally, 2% of participants carried personal risk, 4% reproductive risk, and 100% had on average 3.5 different pharmacogenomic actionable variants. Further, candidate genomic variants, potentially explaining patients' diseases, have been found in an additional 23% of the families, which provides an excellent base for new researches. • Healthcare workforce education and public empowerment: Monographic symposiums, briefing seminars, clinical sessions and face to face meetings, all opened to the participation of medical professionals in the region have been organized. Moreover, 18 specialities designated "physician champions", especially commissioned to spread the word, received a 50 category 1 and 2 CME credits tailored genomics education programme. Public involvement has also been possible through open conferences, a specific website www.nagen1000navarra.es , and launching press conferences. • Collaboration and networking: As a consequence of NAGEN 1000 formal contacts with other implementation international initiatives as the 100,000 Genome Project in England and Genome Quebec in Canada have been established while networking with key national organizations as the Spanish national node for rare diseases research (CIBERer). • PM optimised financing strategy alignment: NAGEN 1000 has now been mapped as a key milestone into the Navarra Government Personalized Medicine plan, which includes new PM and genomics €7Mio regional and ERA-PerMed calls now funding PharmaNAGEN and NAGENcol, spin-off projects named after NAGEN. Remarkably, NAGEN 1000 was recognized with the "Best Practice in Personalised Medicine" Award by ICPerMed in 2018.

	Funding and Investments (please specify the source: public, private, Structural or other types of funds)	Public funding: €2.9M Navarra Government. Departamento de Desarrollo Económico - Dirección General de Industria, Energía e Innovación, under the Regional Smart Specialization Strategy S3.
	Key stakeholders involved	•Navarra Government. •Navarrabiomed, Universidad Pública de Navarra (UPNA), IdiSNA. •Complejo Hospitalario de Navarra (CHN). •Navarra de Servicios y Tecnología NASERTIC. •AVANTIA 400+ Pyramide Asesores. •Centro Nacional de Análisis Genómicos CNAG (Barcelona). •Fundación Progreso y Salud (Andalucia Gov). •Rare Diseases Spanish Network (CIBERer).

5. Else Kröner Fresenius Center for Digital Health

Project | Initiative title		Else Kröner Fresenius Center for Digital Health
Organisation name		Technische Universität Dresden & University Hospital Carl Gustav Carus
Country		Germany
Region		Saxony, Dresden
Contact person		Project Office
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Website:		www.tu-dresden.de
Keywords:		eHealth, digital health, Living Lab, Hospital 4.0, Robotics, Implants and Sensors, Connected Care, Artificial Intelligence, Digitization
Duration:		2019-2029
Area of application		Medicine
DESCRIPTION	Main challenges tackled (max 200 words)	Digital technologies, sensors, wireless communication, robotics and machine learning offer substantial potential for better patient care and a smarter medical workplace. In contrast to established and well-funded molecular research structures, the interface between technology and medicine is scientifically and structurally under-developed. Thus, the digital revolution fails to fully deliver its benefits to clinical science and patients. Medical need needs to be matched by outstanding local

		capabilities. Dresden is Europe´s strongest microelectronics site, thus providing industrial players and SMEs in the field and harbors unique academic capabilities in electronics, sensor and communication technologies. Therefore, the Dresden campus has an exceptional profile and scientific excellence in the technologies for the digital patient interface. With this clear focus, we work on a highly competitive and in fact also synergistic agenda to "big data" approaches either in academia or industry because the patient interface is the weak link in many of other digital health projects and initiatives.
	Objectives (max 200 words)	Patient-focus is the core of the center mission and is taken into account and considered in all EKFZ activities. Especially here the digital revolution offers great chances for novel therapies, diagnostics and patient benefit allowing to get closer to personalized therapy (new sensors, personalized implants, 3D print) and disease processes (nanotechnology, smart implants). Additionally new technology may help to work more precisely and perform smarter, faster and less invasive interventions (assisting robotics, smart environments) and with better information at the point of care (augmented reality, context-sensitive information systems). To make digital health work and to strive for excellence, we overcome the traditional boundaries of medicine, engineering and computer science and establish a new structured research interdisciplinarity, physical proximity and joint training environment. By bringing together physicians and high tech specialists we use the great potential of the local technical expertise directly at the patient interface.
	Main concept and methodologies involved (max 200 words)	The center provides scientific infrastructure and advice in terms of data integration and security, implementation and regulatory affairs. Scientifically the center funds innovation projects that focus on digital interface agendas fitting in one of our three "Application rooms" (Sensors and Implants, Connected Care, Robotic coworking and Interventions),placing a strong focus on open and competitive interdisciplinary innovation packages to reduce the time from idea to prototype and patient. In order to explore digital innovation early in patient context, we utilize infrastructure in a direct patient care and research context and implement a 'Living Lab' enclosed in the University Hospital Dresden. The EKFZ creates a unique and physically tangible interdisciplinary environment between three faculties on the Dresden University campus and also includes selected high-profile investigators from other specialties. This

		interdisciplinarity spans from joint teaching over joint professorships to joint projects. Our aim is to build flat hierarchies and a flexible and modern administration - while keeping an eye on the transparency of these structures at all times.
	Impacts (health, scientific, industrial, socio-economic or others enabled by the project/initiative (max 200 words)	A structured interdisciplinary directly on the Medical campus, facilitated patient access and a joint training environment for physicians, software engineers and medical technology engineers with a broad and open technological profile marks the highly innovative structure of the EKFZ. Because the center is based directly on the Medical campus, we can implement innovations faster at the patient interface than other initiatives. The EKFZ for digital health also serves as an academic and economic innovation nucleus for further digital health activities and investments from outside. Product development, clinical trials and specific implementation studies will attract additional funding from public research funding agencies, industry and health care providers. A strong expertise for regulatory, ethical and implementation issues is being built providing efficient support for novel ideas and products.
	Funding and Investments (please specify the source: public, private, Structural or other types of funds)	Initial funding comes from the private Else Kröner Fresenius Foundation, Bad Homburg, for which the TU Dresden University successfully applied. In a tough international review process, the center was selected for funding from initially 27 applications from all universities with well-known medical schools in Germany. The funding is supplemented by additional support from the Fraunhofer-Gesellschaft, the Helmholtz Association and the Free State of Saxony.
	Key stakeholders involved	Technische Universität Dresden, Faculties of Medicine, Computer Sciences and Electrical Engineering University Hospital Carl Gustav Carus Dresden

6.T2D: ML tools to learn from EHR

Project | Initiative title	T2D: ML tools to learn from EHR.
Organisation name	University of Miami, FL. USA
Country	Italy
Region	Lombardia
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Website:		https://www.frontiersin.org/articles/10.3389/fdata.2019.00030/full#B1
Keywords:		Type-2 Diabetes, Electronic Health Records, Machine Learning, Predictive Inference, Networks
Duration:		1 year
Area of application		
DESCRIPTION	Main challenges tackled (max 200 words)	Our work analyzes about 10000 US patient to assess whether EHR-embedded phenotypic features are potentially useful for T2D screening. Patients are candidate for screening based on a series of variables that appear relevant in predictive terms, ie, when applied to yet undiagnosed individuals, they allow accurate phenotypic detection. A challenge is to find what EHR components may contribute to outperform predictive learning algorithms applied over non-EHR studies. EHR collect large sample sizes for which sufficient statistics would be those containing all the sample information. A first challenge depends on the data structure. EHR patient heterogeneity cannot be categorized or reconciled under one distributional model. Aiming to mitigate the complexity inherent in EHR heterogeneity, an original approach is considered based on networks inferring EHR salient features and their interconnectivity. A second challenge is methodological and concerns the design of the network. This in tun involves choice of a suitable metric for the selected variables to communicate and build the needed prediction power. A third challenge is to interpret the results using multiple validations (literature, expert opinion, cross-reference with similar applications).
	Objectives (max 200 words)	The main objective is to establish significant associations and identify latent relationships between variables relevant to T2D possibly unseen by other methods. Other objectives are: a) to reduce redundancies that big data present as these are potentially harmful to predictive learning, and b) to exploit the interconnectivity of EHR features in order to achieve a coherent map.
	Main concept and methodologies involved (max 200 words)	Our methodological approach identifies specific T2D EHR drivers ensuring predictability, generalizability, and reproducibility of results. Building blocks are: (a) variables prioritized by ML algorithms; (b) network tools to conduct inference over interconnected variables; (c) significant interaction dynamics represented by the identified communities. The concept to keep is that communities absorb diversity among individuals who share major features underlying T2D and suggest an effective approach to patient stratification. Generalization of our approach to other disease contexts is possible. To leverage the prediction power of EHR features selected by two well-known ML methods, Random Forests and Lasso, we built a network map of associations between such features. A mutual information network represents the inference tool used

		to identify communities of risk factors and comorbidities that support the prioritization of the most significant T2D features and underlie the similarity/dissimilarity map of observed patient characteristics.
	Impacts (health, scientific, industrial, socio-economic or others enabled by the project/initiative (max 200 words)	EHR play an important role for the redefinition of phenotypes in view of the wealth and heterogeneity of information now available from disparate data sources. Our analyses indicated that EHR phenotypes significantly improved T2D detection. Because the communities that were detected appeared centered especially on T2D comorbidities and risk factors, our results are relevant to an assessment of T2D disease burden and prevention. Our analytical approach offers a solution for managing the EHR scale factor in a complex disease context. EHR are rich sources of phenotypic diversity through which novel stratifications of patients are expected. The specific significance assigned to the most relevant T2D communities can be inferred with accuracy from just a reduced number of EHR features. Both pre-screening of variables and calibration of predictive ML methods are necessary steps to optimize EHR-centered analyses.
	Funding and Investments (please specify the source: public, private, Structural or other types of funds)	The dataset is public (www.kaggle.com) and de-identified provided by the EHR company Practice Fusion and includes an unselected patient population who had a variety of lab tests, prescribed medications an diagnoses. The study included about 130000 EHR transcripts from about 1130 unique sites spanning all USA and collected between 2009 and 2012.
	Key stakeholders involved	Patients, Clinicians, Companies, Medical Laboratories, Scientists.

7. Telecardiology Pediatric Service reaches 21 years of continuous delivery

Project | Initiative title	**Telecardiology Pediatric Service reaches 21 years of continuous delivery**
Organisation name	Pediatric Cardiology Service – Coimbra University Hospital Centre
Country	Portugal
Region	Central Region
Contact person	Prof. Dr. Luís Velez Lapão
Contact email	luis.lapao@ihmt.unl.pt
Website:	
Keywords:	Telemedicine, Pediatric cardiology, Patient-centeredness, Clinical Decision-making, collaborative medicine, Big Data, Patient Safety
Duration:	From 1998 onwards…

Area of application		
DESCRIPTION	Main challenges tackled (max 200 words)	Pediatric Telecardiology Service enabled real-time clear communication and sharing of information, overcoming main barriers (e.g. geographical ones and shortage of healthcare professionals), improving access both in Portugal and Africa. The Pediatric Telecardiology Service enables real-time communication and the sharing of clinical information, overcoming many barriers (from geographical ones to shortage of healthcare professionals), improving access to specialized care both in Portugal and Africa Motivation and teamwork, and perseverance, were key for the Pediatric Telecardiology Service to tackle the window of opportunity which created conditions for sustainability.
	Objectives (max 200 words)	To provide Telemedicine services to promote more access to healthcare. Portugal was an early adopter of telemedicine to overcome both its geological barriers and the shortage of healthcare professionals. The Pediatric Cardiology Service (PCS) at Coimbra University Hospital Centre (CHUC) has been using telemedicine to increase access and coverage since 1998. Their Pediatric Telecardiology Service has been daily connecting CHUC with 13 other Portuguese national hospitals, and regularly connecting with Portuguese-speaking African countries, through a teleconsultation platform.
	Main concept and methodologies involved (max 200 words)	Potential of Technology: Telemedicine's original idea occurred during a visit to Mayo Clinic in the USA in 1995. This experience motivated the idea of using telemedicine to improve healthcare coverage in Portugal. Later, Dr. Eduardo Castela (the PCS service's Director; and a Mayo Clinic trainee), shared his experience with Lusitânia Fonseca, a Portugal Telecom Engineer and Head of the Innovation Department. She immediately saw an opportunity there, and in 1998 the first telemedicine consultation was a reality. Organization and Leadership A strong organizational culture, proved to be capable of overcoming the difficulties, often associated with the process implementation and growth. The PCS organization shows a dominant "Clan" culture, which reveals conditions for openness to innovation and creativity, based on the team work and leadership. According to Cameron and Quinn, when all of these characteristics are integrated in terms of quality management, the success rate increases significantly, benefiting people's empowerment strategies, team building and open communication.
	Impacts (health, scientific, industrial, socio-economic or others enabled by the	With more than 33 000 out-patient teleconsultations, growing steadily from 1998, the Pediatric Telecardiology Service has reached national and international recognition, being a pioneer and an active promotor of telemedicine in Portugal and Africa. This is among the unique case of telemedicine continuously working for more than 20 years. This telemedicine service has saved significant resources, about

	project/initiative (max 200 words)	1.1 million euros for the health system (e.g. in administrative and logistic costs) and approximately 419 euros per patient (considering an average of 1777 patients per year). PCS presents a dominant "Clan" culture. The Momentum's critical factors for telemedicine service implementation enabled us to understand how barriers were overcome (e.g. political forces).
	Funding and Investments (please specify the source: public, private, Structural or other types of funds)	The project was funded by both the Coimbra's Hospital and by the Ministry of Health. There was an initial investment in telemedicine infrastructure by the Ministry of Health. Now each consultation is paid as a fee for service by the Ministry of Health to the Hospital for funding the telemedicine services. These fees varied through time, due to negotiations between the Hospital and the Ministry of Health.
	Key stakeholders involved	Director of the Pediatric Cardiology service, the Coimbra's University Hospital Centre, the Ministry of Health.

8. Organizational and digital development in taking care of chronic disease.

Project | Initiative title		Organizational and digital development in taking care of chronic disease.
Organisation name		Azienda Socio Sanitaria Territoriale (ASST) di Vimercate
Country		Italy
Region		Lombardy
Contact person		
Contact email		
Website:		www.asst-vimercate.it
Keywords:		
Duration:		
Area of application		Healthcare Model Organization and Big Data Analytics practical application
	Main challenges tackled (max 200 words)	Healthcare organizational scenarios expected in the coming years require the re-design of the hospital processes through the adoption of new organizational models aimed at the proactive management of chronic and fragile patients. The introduction of new add value services for patients and the usage of Telemedicine and Artificial Intelligence technologies are considered key elements to support the expected change. ASST Vimercate has defined a new organizational process to enable the proactive "taking care" of chronic and frail patients. The definition of different professional roles, the introduction of an outsourced Service Center to manage healthcare activities and the introduction of the "Case Manager" role as a central point of reference to ensure the quality of the process and care are the main features of the new process. Moreover, ASST Vimercate, thanks to the application of the Electronic Medical Record in all its facilities, has started to use the "Big Data Analytics" technologies to develop predictive algorithms that support professionals in the early detection of patients suffering from specific chronic diseases and the onset of any complications. The actions carried out as well as the introduction of structured Telemedicine paths will allow a better planning of the healthcare and welfare activities.
	Objectives (max 200 words)	**Organizational and process objectives**: • Re-engineering of the process, with redefinition of the roles of the organizational Service Center (external) and of the Case Management function • Health Service demand analysis and stratification of chronic patients • Target and severity levels for proactive management

		pathologies definition (in coordination and collaboration with GPs) • Clinical offer reorganization, through the analysis of exam volumes by each supply point, saturation rates, diary opening • Collection of medical care demand from the Cooperatives with creation of dedicated slots • Bidirectional coordination and exchange of information in order to maximize efficiency in the booking process and in the relationship with patients • Introduction of digital collaboration tools and structured Telemedicine paths managed by the Service Center **Technological objectives** • Design and implement predictive algorithms, built on the basis of available clinical data to predict the development of the chronic disease, in terms of evolution of clinical parameters, prevention of clinical complications, patient re-hospitalization reduction, best practice adoption • Design and implement a predictive model to outline the evolutionary scenario of chronic diseases, based on the different treatment and innovative healthcare organization models (planning forecast) • Design and implement Telemedicine paths for efficient management of chronic patients with hospital access reduction and healthcare process optimization.
	Main concept and methodologies involved (max 200 words)	The implementation of innovative organizational models, can be supported by the use of innovative information technologies such as Telemedicine and Artificial Intelligence as well as with the reorganization of processes and better integration and collaboration between the various professionals. The information assets available at ASST Vimercate, due to over 10 years of Electronic Medical Record application, can be properly exploited with Big Data Analytics technologies to extract informative value and use it for a more intelligent and efficient management of health services. ASST Vimercate is implementing the following predictive models with Machine Learning algorithms: • Early detection of patients with chronic diabetes disease and prediction of the development of cardiovascular, renal and visual complications. • Early detection of patients with severe chronic kidney disease with prediction of the timing of possible entry into the dialysis treatment pathway. • 30 days re-hospitalization risk for all causes and 360 days for heart failure in case of hospital discharged patients with heart failure diagnosis.

		ASST Vimercate will apply Telemedicine to the following specific chronic paths: • Nephrology • Diabetes • BPCO • Hearth Failure
	Impacts (health, scientific, industrial, socio-economic or others enabled by the project/initiative (max 200 words)	The actions carried out by ASST Vimercate for social and health services reorganization and process efficiency, togheter with the support and use of innovative IT technologies, can effectively contribute to the development of new organizational models for the proactive management of chronic patients and fragile. **Organizational change** The management of the organizational and cultural change of the various professionals involved in healthcare process represents a key point to create a new model of health system that preserves the quality of services and ensures the economic sustainability. The introduction of a "Service Center" organized and equipped with advanced IT tools to enable inter-professional collaboration and bidirectional communication with patients as well as the central reference role of the "Case Manager" represent the efficiency and modernization elements of the "taking care" process. **Innovative Technology to support the change** The use of Big Data Analytics and Machine Learning technologies to develop predictive algorithms for early detection of particular evolutionary scenarios of chronic diseases as well as the introduction of structured and targeted Telemedicine pathways represent great opportunities for the improvement of healthcare organizations.
	Funding and Investments (please specify the source: public, private, Structural or other types of funds)	Public Investments
	Key stakeholders involved	

9. How Cluster Techforlife can sustain and improve Lombardy healthcare system

Project | Initiative title		How Cluster Techforlife can sustain and improve Lombardy healthcare system
Organisation name		Foundation Cluster Technology For Living Environments
Country		Italy
Region		Lombardy
Contact person		Cristina De Capitani
Contact email		Cluster@techforlife.it
Website:		http://cluster.techforlife.it/
Keywords:		personalized technologies for smart rehabilitation, frailty, chronicity; integrated approach to the cure of patients; business model for healthcare sector; Human Centered Design Approach
Duration:		From 2013 to now
Area of application		personalized technologies for smart rehabilitation, frailty, chronicity
DESCRIPTION	Main challenges tackled (max 200 words)	In Lombardy Region, people suffering from chronic disease are 3,5 million (30% of the Lombardy population). People with chronic disease need personalized cure pathways and needs to adapt their lifestyles to tackle the multiple requests of their diseases. The main challenge is to guarantee a high standard of care in the daily life of people with chronicity throughout technologies. Particularly, we aim at ensuring a **personalized motor and cognitive rehabilitation** process while promoting a better quality of life of patients. That's why we also focus on **monitoring and safety of patients at their homes.** Safety, High standard of care, which means personalized care, and monitoring are the main challenges we want to tackle with technology innovation. Introducing technology factor produces other challenges we cannot ignore: **cybersecurity and connectivity.** We also aim at producing technology innovation through **a high standard scientific approach** fostered by **multidisciplinarity**. We strongly believe in the **quadruple helix model** as a baseline for sustainable innovation. Applying the quadruple helix model constitutes itself a challenge due to the increasing complexity of processes, and the different languages and objectives of each stakeholder. Finally, we tackle the challenge of **technology transfer**, that includes also the realization of efficient business models.

	Objectives (max 200 words)	Foundation Techforlife is a technological Cluster aiming at improving the growth of the R&D&I field in the Lombardy region. The Foundation, according to the "Quadruple Helix Model", is composed by a multidisciplinary partnership of: Research Centers; Universities; Companies; Associations; Research Hospitals and their link to the local public authorities (thanks to that is a 3 stars Reference Site within the Lombardy Region prize). To reach the main goal of improving the growth of the R&D&I field, the Cluster has a set of sub-goals: - Promote the cooperation among its Partners, and its partnership and other national/international stakeholder, for research project, assignments, sharing of knowledge or technologies. - Identify funding (public or private; regional, national or international) to sustain their activities. - To be a link between the Public Authority and its Partners to translate the needs of our partnership to the PA. This is a strategic activity with which the Cluster aims to create the best playground for the growth of the Cluster's partnership.
	Main concept and methodologies involved (max 200 words)	The Cluster, to promote the cooperation among its partners, has developed 4 thematic Working Groups: - WG1 – "Technologies for the continuity of care" - WG 2 "Business model for healthcare sector" - WG3 "Living Environments of the future" - WG4 "Health Tourism & Sport" where the partnership cooperates to identify healthcare challenges and business models able to sustain the technological transferability to the market of the devices and services developed by the Partners. To promote its vision, moreover, the Cluster participates in research projects or endorse projects developed in its partnership. The Cluster also participates to working tables organized by the PA to share the needs and the works of the partnership. Finally, the Cluster organize and participates at fairs, event and congresses to promote the visibility of the projects and the partners activities.
	Impacts (health, scientific, industrial, socio-economic or others enabled by	From the establishment of the Cluster to now Techforlife supported the realization and dissemination of 9 funded projects. The Cluster create more than 10 business/research links per year within its partnership and between the partnership and local/international stakeholder.

	the project/initiative (max 200 words)	The Cluster
		also participates as Partner or subcontractor in 4 different research projects. In two of them it took the role of pivot to allow the participation up to three of its partners in the project. From the institutional and regulatory point of view the Cluster has contribute, with thematic of interest of the partnership, to the 2014 Lombardy S3 Programme and in its later updates. It has provided inputs to Fondazione Regionale per la Ricerca Biomedica (FRRB) to define the concept of Personalized Medicine. It is actively participating in three international networks to share the vision and interests of its partnership: Pilot Esther/Vanguard MEDTECH; EUSALP AG2 – Subgroup Health-Tourism; EIP on AHA Action Groups
	Funding and Investments (please specify the source: public, private, Structural or other types of funds)	The Cluster sustain its activities with different kind of economic resources: - Annual Fee payed by the partners - Participation as partner in funded projects - Participation as subcontractor of its Partners in funded projects
	Key stakeholders involved	The Cluster has a partnership composed by: - 21 Companies - 7 Research Centers - 4 Universities - 4 Hospitals - 4 Associations HERE the lists of Cluster's Partners. At Regional Level, the Cluster strictly cooperates with Lombardy General Directorate Research, Innovation, University, Export and Internationalization. The Cluster has also established connection with Italian healthcare main institutions like: Istituto Superiore di Sanità, Istituto Nazionale dei Tumori and Italian Association of Clinical Engineers.

10. Cohort Genomics: a framework to assist clinical research

Project | Initiative title		Cohort Genomics: a framework to assist clinical research
Organisation name		San Raffaele Hospital
Country		Italy
Region		Lombardy
Contact person		Daniela Toniolo
Contact email		toniolo.daniela@hsr.it
Website:		The Cohort Genomics Platform (CGP) has been implemented and it is running within the San Raffaele Hospital firewall as an intranet web-platform. The website is not available for now
Keywords:		Web-platform, biobank, genetic variants, mutations, framework, microservices, database, records, pedigree
Duration:		Not limited
Area of application		Clinical research
DESCRIPTION	Main challenges tackled (max 200 words)	A good collection of clinical and genetic data together with the corresponding biological samples properly stored would enhance the possibility to select cohorts of homogeneous patients, providing basic and applied research with new original projects and novel diagnostic tools. Cohort Genomics Platform would improve the information flow and contribute to the reduction of the organizational burden for clinicians by integrating all the steps that the clinician has to face before diagnosis and treatment. It is GDPR compliant, as DPIA certified in November 2019, since access to clinical data is possible through the anonymization service. This has a strong positive impact on data analysis fostering data exchange between clinicians and researchers without disclosure of patient identity.
	Objectives (max 200 words)	Development of an integrated system that will assist clinicians in the collection and storage of clinical information and biological samples from well characterized patients allowing a better use of fully-qualified data in clinical research projects. Different clinical and research areas can store data both from medical history and results linked to patient's specimens, like genetics, sequencing, histopathology results.
	Main concept and methodologies involved (max 200 words)	Cohort Genomics web-platform has been implemented adhering methodologies involved(max 200 to the micro-service architecture pattern. It is composed by a words)main web portal with several web services behind it. The modular nature of the micro-services architecture and the diversity of the involved kind of data has favored the adoption of different and suitable open web technologies. Among them, Ruby on Rails as

		backend engine, reactJS and SurveyJS for frontend, MongoDB and MySQL for the persistence layer and Docker for application containerization and orchestration.
	Impacts (health, scientific, industrial, socio-economic or others enabled by the project/initiative (max 200 words)	Cohort Genomics web-platform will improve collection and storage of clinical data for research and allow safe data handling for analysis. It will contribute to the success of clinical research and to a better definition of the diverse aspects of disease and therapy in the era of Big Data.
	Funding and Investments (please specify the source: public, private, Structural or other types of funds)	The Cohort Genomics web-platform was developed with structural funds
	Key stakeholders involved	Clinicians, researchers