eHAction

Joint Action supporting the eHealth Network

# D5.2 Report on Identified Cross-Border Use Cases: Sharing and Learning from Best Practices on European Level

## WP5 - Innovative Use of Health data

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# Acronyms and Abbreviations

| Acronym | Description |
|---|---|
| AI | Artificial intelligence |
| eHAction | eHAction – 3rd Joint Action supporting the eHealth Network |
| eHN | eHealth Network |
| EHR | Electronic Health Record |
| EU | European Union |
| GDPR | General Data Protection Regulation (EU) 2016/679 - a regulation in EU law on data protection for all individuals within the European Union (EU) and the European Economic Area (EEA) |
| WP | Work Package or Work Plan |

# Executive Summary

One of the main goals of the eHAction is to integrate eHealth into health policy and align investments with health requirements. To facilitate the re-use of existing experiences and solutions, recommendations and practices available in the different Member States shall be transferred across countries. In this setting, Task 5.2 "Sharing and learning best practices on European level" plays a central role within the project by helping to develop a common knowledge base for the continuous exchange of best practices on the EU level.

On the European scale there already exist projects and initiatives, partially with support from public funds, that use or had used innovative ways to use and utilise health data in the cross-border context, and in accordance with EU regulatory framework(s). Some of them have already made significant progress, and it is essential to further exploit their findings, experiences and learnings for the use of innovative healthcare solutions in Europe.

We used approaches of an explorative literature review and in-depth interviews with partners from selected projects to derive practical use cases. The analyses confirmed that many of the stakeholders are facing similar challenges when it comes to developing and implementing eHealth solutions in the cross-border framework. In particular, issues of privacy protection, ethics, data security, health assessments, data quality, interoperability of health data systems, and demonstrating added value to the key actors (such as citizens, patients and professionals) were brought up in the literature and in the interviews.

Many Member States have introduced or are planning to introduce electronic health record systems locally, regionally or at nationwide levels. Thus, possibilities may open up to use and utilise health data from these increasingly wealthy sources of medical information for multiple purposes, such as significant advancement of medical research. These – likely cross-border and big data concepts – would further benefit societies, individuals and Member State health systems.

The scientific literature describes the results of the projects, which have utilised health data in a cross-border setting. The scientific literature is often at least two years behind the current knowledge of matters of fact or phenomena. However, in order to make rational policy actions at the European level, one should take these experiences and well documented findings into account. The peer-reviewed and tested nature of the scientific documentation gives strength to the findings and helps to understand the obstacles and policy needs for the cross-border exchange of health data.

# Introduction

One of the eHAction's main objectives is to improve the innovative use of health data. Tasks related to this eHAction objective are fulfilled by Work Package 5 (WP5): identified cross-border use cases, including assessment of pros & cons of stakeholders, and practical solutions with potential for European-scale benefits. WP5 has a vision to develop innovative usage of data across the healthcare sector to improve the knowledge base for health and healthcare policy. Deliverable 5.2 of WP5 has been established to target identified cross-border use cases for health data.

WP5 looks at data as a key driver of disruptive innovation in economic, societal and social systems. Therefore, WP5 as a whole is committed to make an impact on the use of health data as well as assisting data-driven innovation leading to patient-centred health systems, evidence-based health policies and decision-making.

We believe that understanding stakeholder needs and real-world use cases is essential in achieving our objectives. Therefore, WP5 has set out to collect, compile and share the experiences of Member States for developing a knowledge base and a framework for continuous exchange of best practices on the EU level.

Various publications have addressed the importance of further investigating the potential implications that the rapid development and increased prioritisation of various technological innovations in health have on society as a whole.

New and innovative ways to utilise health data can bring about a lot of added value for patients and healthcare organisations alike. Often it is important to enable sharing and processing of health data in the cross-border setting. The common perception is that cross-border use cases have become more common and there are more analytical tools available to utilise data, e.g. for the direct benefit of patients or research. At the same time new regulations, such as GDPR, and other affecting factors have to be taken into account in order to manage the risks of cross-border sharing of sensitive data.

**Big data** refers to complex and large amounts of information. Big data is massive in volume and collected from a variety of sources including mobile devices, medical databases, satellite images, genome sequences, video and social media feeds (Fuller et al. 2017). Analysis techniques for big data have been applied in the healthcare field and may provide insight for exposure and health outcome measurement. The five V's of big data characteristics make big data unique. Volume refers to the massive amounts of data that can be collected and stored. Velocity is the speed at which data are generated. Variety refers to the inclusion and use of multiple types of data in data analysis. Veracity is ensuring big data analysis and outcomes are accurate and credible. In addition, value refers to the types of insights that can be gained from big data collection and analysis.

Big data has been considered to be a breakthrough technological development over recent years. Notwithstanding, we have as yet limited understanding of how organisations translate its potential into actual social and economic value. In their in-depth systematic literature review on 67 papers on big data, Günther et al. (2017) found two socio-technical features of big data influencing the value realisation: portability and interconnectivity. In their conclusion for practice, organisations need to continuously realign work practices, organisational models, and stakeholder interests in order to reap the benefits of big data.

**Health analytics** has been defined as a process of delivering insights from health data to make informed healthcare decisions (Makhlysheva et al. 2018). While such aspects of health analytics such as the use of statistical models, data mining and clinical decision support have existed for decades, only recent availability of enormous volumes of data from various sources and increased processing power have made it readily available to support integrated decision-making.

In their scoping review of the literature on innovative technologies and social inequalities in health, Weiss et al. (2018) found 4139 studies, out of which 33 were included in their final analysis. The results highlighted the importance of variations in use that importantly shape social inequalities in health. In addition, focus on healthcare services technologies must be accompanied by investigating emerging technologies influencing healthy lifestyle, genomics, and personalised devices in health.

With its origins in the mid- to late-1900s, today **artificial intelligence** is used in a wide range of medical fields for various purposes. Overall, while artificial intelligence has come a long way since its infancy in terms of its incorporation into medicine, it still has a long way to go to reach a point at which it will be totally independent of a human professional (Becker 2019). However, its possible uses in diagnosis, treatment, and clinical research remain numerous, and the industry on some levels is beginning to prepare for the inevitable through the establishment of working groups, guidelines, frameworks, and the like.

**Precision health** relies on the ability to assess disease risk at an individual level, detect early preclinical conditions and initiate preventive strategies. Recent technological advances in omics and wearable monitoring enable deep molecular and physiological profiling and may provide important tools for precision health. In their prospective longitudinal cohort enriched for risk of type 2 diabetes mellitus and followed in median 2.8 years (sampled quarterly), Schüsser-Fiorenza Rose et al. (2019) explored the ability of deep longitudinal profiling to make health-related discoveries, identify clinically relevant molecular pathways and affect behaviour. They discovered more than 67 clinically actionable health discoveries and identified multiple molecular pathways associated with metabolic, cardiovascular and oncologic pathophysiology. They concluded that deep longitudinal profiling can provide relevant information for precision medicine.

The first paper indexed in Medline with the MeSH term “artificial intelligence” (AI) dates back to 1951, and today more than 16,000 peer-reviewed scientific papers are published in the AI field each year (Liu et al. 2019). Deep learning offers considerable promise for medical diagnostics. Liu et al. (2019) evaluated the diagnostic accuracy of deep learning algorithms versus health professionals in classifying diseases using medical imaging by using a systematic literature review of 31,587 studies published from 2012 to June 2019. A major finding of the review is that few studies, actually 14 out of 82 studies that met inclusion criteria, presented externally validated results or compared the performance of deep learning models and health professionals using the same sample. Reporting of deep learning studies was generally found poor. Most studies took the approach of assessing deep learning diagnostic accuracy in isolation that does not reflect clinical practice, and very few prospective studies were carried out in real clinical environments. A wide range of metrics were employed and there is inconsistency over key terminology used in the studies. Finally, most studies did not undertake an out-of-sample validation for both health professionals and deep learning algorithms.

# Background and scope

The overall objective of WP5 is to support the application of good practices in Member States and provide guidance at EU level on handling big data in health within the existing EU regulatory framework on secondary use of personal data (ref. EU General Data Protection Regulation 216/679), and consequently to ease the uptake of innovative usage of data across the healthcare sector for the benefit of society, individuals and Member State health systems.

The purpose of D5.2 "*Report on identified cross-border use cases: Sharing and learning best practices on European level*" is to identify implementable and scalable real-life eHealth and big data applications of big data in public health in the EU. This is achieved by collecting, reviewing, analysing and synthesising cases from academia, businesses and service providers.

D5.2 investigates already implemented cross-border use cases of big data within the frameworks of existing actions such as European Reference Networks for rare diseases as well as in R&D including analytics. The deliverable further assesses the pros & cons of such data sharing experienced by stakeholders, and finally presents practical use cases with potential for European-scale benefits.

The scope of the deliverable is based on the definitions of innovation, big data (especially in health), interoperability and cross-border use cases. The scope of the deliverable is broadened by reviewing relevant big data applications in fields other than health, where innovative use of data has been demonstrated with the aim to explore the possibilities of employing similar ideas in the field of health.

Finally, the deliverable addresses the question of how already existing data sharing ecosystems across the EU can be utilised, and what the long-term perspectives can offer to Member States.

D5.2 is mainly built upon information from case studies on innovative use of data in the field of public health. It reports on the current status of data sharing in cross-border settings, specifically relying on literature review. It also attempts to provide a model for the wider WP5 on data processing and synchronisation needed for pooling data from various registers, studies, cohorts and countries for analysis.

In the case studies, certain information has been extracted and analysed, e.g. on diseases and population groups addressed, on types of technology, innovations and big data analytics algorithms used, on the data producers (undertaken by academia, industries, joint ventures) and on the scope of scalability to other countries in Europe and globally.

In addition, the acceptability of innovations or technologies to citizens, challenges in combining data from diverse sources and related database management, opportunities in the field of health, and interpretation and sharing of the results, especially by an individual, has been described and discussed. Perceived needs and barriers of users have been analysed as part of the case studies.

# Methods

Working definitions for health data, big data in health, big data analytics in health, innovative use of health data and artificial intelligence are presented as Appendix A.

An explorative literature review with the main focus on applications of innovations in health and big data from 2016 onwards was performed to cover recent developments. This was performed in the databases Medline, Web of Science and EBSCO Discovery Services. The search strategies are presented as Appendix B.

# Results

## Literature search results

Originally, a total of 1,878 references were derived. After removing duplicated references and concentrating to the most relevant references as stated in the D5.2 objectives (the first selection), 231 articles remained. Among the 231 selected articles, there were 107 (107/231; 46%) cross-border studies, 30 (13%) systematic reviews and 15 (6%) articles that were classified as both cross-border studies and systematic reviews.

## The 2-step article screening

The abstracts of these 231 articles were further screened and included into the review in case they referred to cross-border or multi-country studies or projects. In addition, to be included into the review, they had to express in writing an applied innovative approach of using big data or health data. This second selection step led to the inclusion of 90 articles for further in-depth analysis. Among the further screened 90 articles, there were 65 (65/90; 72%) cross-border studies, 11 (12%) systematic reviews and 10 (11%) articles that were classified as both cross-border studies and systematic reviews. Descriptive data on the 90 articles are presented in Appendix C.

## Further data collection

After this 2-step selection process of the articles, further descriptive data was gathered on each of the 90 selected articles on application type (big data, eHealth, telemedicine, mHealth, artificial intelligence), disease name(s) or target area(s), number of countries involved, and additional notes. The application type was big data in 24 (27%) articles, whereas it was eHealth in 45 (50%), telehealth in 12 (13%), mHealth in 17 (19%) and artificial intelligence in 4 (4%) articles. There were 9 (10%) articles, which included two application types. The number of countries involved was not available in many of the articles (51 articles; 57%). In articles where it was available, the number of countries involved varied from 1 to 31 (39 articles; 43%; mean 7.7 countries). Qualitative data on disease name(s) or target area(s), and additional notes are presented in Appendix C.

## Preparing for the final selection of the articles and projects

In order to further select the most relevant articles, a discussion took place. Both the Austrian and Finnish teams working on the literature review agreed that the articles should be read once again to gather information on whether the project was already finished or still running, to divide them into their different application field(s) (e.g., eHealth, mHealth, Telemedicine, big data), target area(s) or diseases (e.g., children, mental health, etc.) – placing more focus on long-term diseases –, to find out whether the projects were funded by the EU, and whether they were preventive or curative projects. This additional preparatory stage produced 30 candidate projects for further review. Qualitative data on these 30 candidate projects are presented as Appendix D.

We reasoned that EU funding was of utmost value in the sense that it indicated the project's larger relevance for European Union Member States. Altogether 25 of the candidate projects were EU funded, and 13 of these 25 EU funded projects were already finished.

## Additional documentation on cross-border use cases

In addition, four reports mentioned below were reviewed. A systematic review of the *Study on Big Data in Public Health, Telemedicine and Healthcare* covers topics of big data applications in health and innovations before 2016. Two other relevant reports are *From Innovation to Implementation - eHealth in the WHO European Region* and *eHealth innovations in Western Europe*, dealing with programmes and initiatives by countries which have more advanced healthcare ICT infrastructure. Yet another closely-related report is the *Report on main eHealth activities outside of the EU* (Joint Action to support of the eHealth Network, JAseHN, Deliverable 8.1.4 in WP8).

## The selected projects for in-depth interviews

Furthermore, taking into consideration other additional qualitative data gathered, we produced a short listing of the projects for further analyses utilising interviews. Interviews with the partners and stakeholders were conducted in order to collect information, which is not available in published form. The nine projects selected were: eHDSI, EHR4CR, epSOS, ICARE4EU, mPivas/Psylog, m-RESIST, PERSSILAA, RENEWING HEALTH and ROADMAP. Due to its relevance, an interview with the international flagship collaboration with Canada, as well as an interview with the ERN, were also performed. The underlying qualitative data used for the selection of these eight projects selected for in-depth interviews are presented as Appendix E. In addition, the eHAction Steering Council guided interview selection.

## Interviews

In order to conduct more in-depth interviews in a structured manner with selected projects, as discovered in the literature review, an 11-question questionnaire was produced. The purpose of the interview questionnaire is to collect information about multi-country or cross-border eHealth projects, in which the country in question has been involved. The questionnaire was sent for comments to the Joint Action WP5 members on 12 February 2019. Comments were received only from Greece. The questionnaire is presented as Appendix F.

On 26 June 2019, an invitation with attached data was sent to the WP5 participants in order to arrange a telephone meeting to discuss and organise the project interviews screened by the D5.2. This telephone meeting was scheduled to take place and was undertaken on 3 July 2019.

Each interview's duration was expected to be one hour or less. It could be done by phone or teleconference. In the meeting, the organisers asked the participants to provide the interview results in writing/written answers. The deadline for the interviews was set for 15 August 2019. Whatever the reasons, only four interviews were completed by the deadline. After reminders, the following project interview reports were available as of 29 October 2019.

- ERN “European Reference Networks”
- m-resist “Mobile Therapeutic Attention for Patients with Treatment Resistant”
- ICARE4EU “Innovating care for people with multiple chronic conditions in Europe”
- EHR4CR “Electronic Health Records for Clinical Research”
- eHDSI “The eHealth Digital Service Infrastructure”
- epSOS “The european patient Smart Open Services project”
- “International flagship collaboration with Canada for human data storage, integration and sharing to enable personalised medicine approaches”

The interview with the “International flagship collaboration with Canada for human data storage, integration and sharing to enable personalised medicine approaches” is available as recording only.

# Findings

## Use Cases

The following use cases were identified while conducting the literature review:

- Internet of medical things, medical devices and application for data gathering for diagnosis, care and prevention;
- Policy development toolkit for aging, sedentary lifestyle;
- Networks for cancer (or other competence) centres;
- Remote consultation, monitoring, care and self-management for aging people and/or people who have long-term illness;
- Sharing harmonised datasets between primary Sjögren's syndrome (or other) centres
- Use of data from electronic health records for secondary purposes;
- Citizens' or patients' nationwide access to their health data;
- Enhancing fair data principles (findable, accessible, interoperable, reusable);
- Interoperability between electronic health record systems and clinical (or other) research systems;
- Supporting the model for assessment of telemedicine applications;
- Setting up centres of excellence or competence centres; and
- Business modelling along the project time.

## Findings from the Interviews

*General project information*

The first two questions from the interview questionnaire dealt with general information on the project and were dedicated to learn about the project goals, the players/stakeholder and partners involved.

All the projects selected for the in-depth interviews and analysis were EU co-funded projects. The players involved could be divided into the following categories:

- Public authorities (e.g. ministries)

- Research organisations (e.g. universities and like)
- Public health institutes
- Hospitals and clinics
- Private companies (e.g. pharmaceutical, IT), including SMEs
- Patient and health professional organisations
- Social welfare professionals
- Intergovernmental partnerships (European Observatory on Health Systems and Policies)
- Other

The objectives and goals of the projects analysed were very diverse and ranged from re-use of hospital EHR data for clinical research to development of a mobile ICT system addressing patient empowerment among those who present with treatment-resistant schizophrenia, or to innovative care approaches and dissemination of implemented ones for patients with multiple chronic conditions (MCC).

*Motivation of the players*

The main objective and goal among all the analysed projects was to invent and then implement innovative eHealth approaches and solutions for the prevention, diagnosis and treatment of a specific disease (e.g., schizophrenia, rare diseases, MCC).

Specific motivations from the stakeholder side to participate in the project could be found in the increase of efficiency, improvement of data quality and quality of patient care, cost reduction and enhancement of reputation.

*Obstacles in implementing the project*

- Interoperability of health data: guarantee access to combined health data from multiple sources.
- Business modelling: further use of project outcome is sometimes uncertain also due to unclear intellectual property rights. A deployment and/or implementation strategy for such products (like the m-RESIST case) needs to be elaborated.
- Sustainability of funding: projects like ERN might not (yet) have fully demonstrated their value, which in turn creates uncertainties around the decision-making and willingness of the Member States to adopt and invest on such innovations.
- Organisational problems: personnel changes and turnover especially in long-term projects, and the issue how to reach the right people, including the decision-makers.

  In the interview regarding eHDSI and epSOS the following obstacles were stated: semantic interoperability, the complexity of contents in healthcare, the difficulty to test and audit and low quality of testing data, different countries have different degrees of maturity in

how information moves within and outside the country, different information contents and the differences in the data structuration (patient summaries).

*Challenges related to using data in healthcare*

Challenges related to using data in healthcare repeteadly mentioned during the interviews can be categorised into the following groups:

- Regulative challenges concerned data protection and privacy, ethics and security. Data protection and GDPR framework limitations were also mentioned.
- On the technical level, low compatibility/interoperability and quality of health data were mentioned as challenges.
- From an economic perspective the high costs for eHealth solutions was addressed.
- In the interview regarding eHDSI and epSOS the main challenges mentioned were that different countries have different IT-systems for healthcare and electronic prescription contents vary as to their validity (from 2 weeks to 2 years).

*Smart project level tips emerging from the experience and learnings in the projects to avoid or overcome obstacles and challenges*

The seventh question of the interview asked for three smart tips on project level.

To ensure a sustainable project outcome, it is important to put focus also on business modelling. For example, EHR4CR project dedicated a whole Work Package to the topic of business modelling. As a successful result, two spin offs (InSIte, i~HD) and one follow-up project (EHR2EDC) resulted from the investment in focusing on business modelling. Potential financial and funding resources should be mapped in order to guarantee implementation and advancements of the project results and developed products.

Stakeholder involvement, especially patient organisations, during the whole project time, including the planning, was brought up as one of the most important lessons learned during the Orphanet and ERN projects. Cooperation between IT developers, health professionals and patients is an important key to make a data system easy to use and user friendly.

The interviewee from the m-RESIST projects recommended to lay down and communicate clear rules of data sharing and access, as well as intellectual property rights of the results of the innovative use of health and healthcare data. In addition, clear internal communication rules, external communication to promote confidence and value in trustworthy practices were important to the interviewees as well. The provision of results (including primary and preliminary findings) along the study was also highlighted. These results were important in order to keep the wide (scientific) public informed what is going on and what are the steps in the project (m-RESIST).

*Smart policy level tips*

Demonstrating value (and add-on value) was one of the topics addressed most often, when asking for tips on policy level emerging from the project. According to the interviewees, policy-makers in general need evidence and empirical information, especially regarding costs and benefits of the

new (e)health technologies. Gaining knowledge was also regarded as a benefit. However, value proposals often need to be quantifiable.

The m-RESIST and ICARE4EU representatives provided us with very specific tips emerging from their respective projects.

ICARE4EU smart policy tips:

- Policy-makers can improve care for people with multimorbidity by better integration and patient-centred care.
- Policy makers can foster both integrated and patient-centred care by developing multidisciplinary guidelines and new professional roles (e.g., care coordinator), by implementing individualised care planning, with support of eHealth, and also by promoting collaboration between healthcare and social welfare services, patient organisations and carers.

m-RESIST smart policy tips:

- Predictive analytics require big data: patient data, sensor data, GPS data or telephone usage to measure physical activity, communication, social relations. Efficient utilisation of available technical results, development of IT application(s) and digitally enabled innovative care services can be fostered and assisted by regulated and promoted access to health(care) data through institutional, inter-institutional, national and cross-border digital e-health infrastructure. These measures can be even more effective if involvement and empowerment of the key stakeholders in the co-creation activities are fostered too.
- The feeling of personal care and attention is important for patients. A positive approach should be communicated instead of privacy and data protection concerns (no “Big Brother” fears).
- National patient pathway coordination and self-help system would promote screening and individual stress management. Use of psychoeducation materials and psychoterapeutic apps.
- Health insurance funding measures: take into account the costs reduced by pre-screenings.

*Room for improvement*

One question in the interview addressed ideas from the projects that are useful and needed to improve public health in relation to eHealth.

For a positive adoption of eHealth tools, the following aspects seem crucial according to the ICARE4EU representative:

- Developing adequate and/or clear legal frameworks (e.g., patient accessible EHRs), with attention to ethical aspects such as privacy/security issues;
- To provide innovative and sustainable funding systems, incentives and reimbursement mechanisms for large-scale implementation of eHealth;
- To have adequate technical, institutional and organisational infrastructures facilitating communication between care providers;

- To assure interoperability and compatibility of technologies between different ICT tools/systems, and standardisation of processes.

A similar response was received from the EHR4CR representative. The m-RESIST interviewee added that mapping and understanding stakeholder needs and fears – as well as the use of big data – should be considered to improve public health.

*Issues regarding cross-border cooperation in eHealth*

Some of the topics already discussed were recurring in the context of the question on issues which should be solved or addressed on the EU level to improve cross-border cooperation in eHealth.

- Sustainability in the form of follow-up projects, funding for validation of efficiency, support of the scale-up for the proved results.
- Quality and interoperability of health data needs to improve.
- Legislative framework limitations.

The ICARE4EU study has identified the following barriers for using eHealth tools:

**Table 2. Barriers for using eHealth tools included in the programs from the ICARE4EU study (% of agree) [a].**

| Barriers | Programs with at least 1 eHealth tool, N = 58 | |
|---|---|---|
| | N | % |
| Inadequate funding | 35 | 60 |
| Compatibility between different eHealth tools | 32 | 55 |
| Inadequate technical ICT support | 32 | 55 |
| Inadequate ICT infrastructures | 31 | 53 |
| Lack of skills among patients | 30 | 52 |
| Inadequate legislative framework | 29 | 50 |
| Lack of skills among providers | 26 | 45 |
| Uncertainty of cost-efficiency | 23 | 40 |
| Privacy/security issues | 20 | 35 |
| Resistance by care providers | 19 | 33 |
| Cultural resistance | 15 | 26 |
| Resistance by patients | 13 | 22 |

[a] Multiple answers were allowed.

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*Scalable ideas*

For the m-RESIST project, one of their scalable idea was a clinical decision support system based on raw data collected by smart tools and computers (maybe even through a safe and secured remote connection). The project developed a mHealth-based intervention, designed for patients with treatment-resistant schizophrenia. The m-RESIST system offers a smartwatch app for patients, a smartphone app for patients and caregivers and a web-dashboard for clinicians.

The EHR4CR project has delivered scalable specific project outcomes: InSite is the commercial product resulting from the project and can be used by all interested hospitals; the European Institute for Innovation through Health Data (I~HD) has established in part the EHR4CR project to develop and promote best practices in the governance, quality, semantic operability and uses of health data, including reuse for research.

ICARE4EU has identified 8 highly potential programs that could further be scalable in the area of multimorbidity.

# Summary and Discussion

Our explorative literature search strategies yielded originally 1,878 references/articles, out of which 231 articles remained as the first selection. The abstracts of these 231 articles were further screened and included into the review, in case they referred to cross-border or multi-country studies or projects. In addition, to be included into the review, they had to express in writing an applied innovative approach of using big data or health data. After this second selection step, we were left with 90 articles for further in-depth analyses. Finally, after these further analyses we identified 30 candidate projects. The final selection, co-informed by the eHAction Steering Council, includes a total of nine projects to be interviewed. Seven projects were carried out until 29 October 2019.

To conduct a systematic or explorative literature review as in this case was a demanding multi-professional expert work compilation; not easily planned nor conducted.

An unfortunate feature that characterises these kinds of literature review is the time interval from an observation to published results. One may say that the literature is often at least two years behind the current knowledge of matters of fact or phenomena. This feature was also visible in our data. In particular, our original 231-article database included only a few published works on artificial intelligence. Many other works were available in other channels, such as news portals or the like. However, there was a plethora of those from eHealth or the big data area as expected.

However, in order to make rational policy actions at the European level, one should take these scientifically well-documented experiences into account. The peer-reviewed and tested nature of the scientific documentation gives strength to the findings and helps to understand the obstacles and policy needs for the cross-border exchange of health data. Regarding many recent “hypes” (regarding technologies or ideas such as artificial intelligence, big data, blockchain technology) it would be advisible to wait for more robust results in order to make informed policy decisions.

As presented in the Appendices, our systematic way of working produced more in-depth data, knowledge and observations step by step. The additional data gathering on qualitative aspects of the articles enriched the database. In particular, the disease(s) or target area(s) revealed the multi-faceted and rich phenomena in the database articles. These qualitative aspects proved to be crucial for understanding the article material at hand and for selecting the most relevant project cases for further data gathering in future in-depth interviews.

The in-depth interviews enlarged significantly the database and knowledge pool of this work package. Even though some time had already elapsed since the project end, we were provided with a wealth of good advice by the project interviewees. It may also be the case that these valuable pieces of lessons learned are the most important lessons in a very dense and sustainable form. By using both explorative literature review and in-depth interviews, we approach the concept of mixed methods analysis that has its place in evaluation and implementation science and research.

The analyses confirmed that many of the stakeholders are facing similar challenges when it comes to developing and implementing eHealth solutions in the cross-border framework. In particular, issues of privacy protection, ethics, data security, health assessments, data quality,

interoperability of health data systems, and demonstrating added value to the key actors (such as citizens, patients and professionals) were brought up in the literature and in the interviews.

Many Member States have introduced or are planning to introduce electronic health record systems locally, regionally or at nationwide levels. Thus, possibilities may open up to use and utilise health data from these increasingly wealthy sources of medical information for multiple purposes, such as significant advancement of medical research. These – like cross-border and big data concepts – would further benefit societies, individuals and Member State health systems.

The analysis of the conducted interview results show that there already exist a plethora of experiences and project results that are accessible and available from different projects. The projects could be consulted to develop a knowledge base and a framework for continuous exchange of best practices at the EU level.

Even though the selected projects for in-depth analysis had their foci on the intervention and implementation of innovative health technologies from very different disease areas (schizophrenia, rare diseases, MCC, etc.) most of them face(d) rather similar challenges when implementing their project.

## Recommendations on best practices on European level

The following recommendations can be given for consideration, taking into account the findings and use cases of the literature review and the interviews:

- Literature review, explorative literature review or systematic literature review may be considered in work packages, in which innovative or rather new substance areas are in focus;
- The challenge related to the literature reviews is the “age” of studies or the results obtained via the studies. These results date back – due to the process of scientific publishing – usually some years in retrospect, which one has to consider in advance in the planning stage of the work package;
- For the “burning” or “hot” topics, it is probable that some kind of information would instead be available via many news feeds or services, if one has capabilities to judge the relevance and trustworthiness of these data;
- Setting up multi-national, multi-professional and collaborative competence centres in the EU in selected cases would be highly beneficial for society as a whole;
- Enhancing FAIR data principles (findable, accessible, interoperable, reusable) and interoperability between data systems are already important infrastructure elements today and their value in an instrumental and strategic sense, is of utmost importance in the (near) future. These may be the cornerstones for big data and other applications, such as AI;
- Common requirements, definitions, data structures and classifications, such as those produced by the epSOS project, demonstrate that EU-wide interoperability,

standardisation and harmonisation efforts do not take place overnight. For these kinds of policies, one has to consider different intersections of the scale and pace of change: rapid enactment of large-scale change (a "big bang"), step-wise enactment of a large-scale change ("blueprint"), rapid enactment of multiple small-scale changes ("mosaic") or piecemeal enactment of small-scale changes over time ("incrementalism") (Tuohy 2018);

- Even though many healthcare systems in the EU Member States are national, they operate on regional or other area-based levels in practice. Thus, it may be considered that at least some cross-border innovations are more beneficial on the regional level as compared to the national level;
- The conducted interviews of EU-funded projects helped to find obstacles and experiences not documented in the literature. As a recommendation one should strengthen the publication of the results of the EU-funded projects in the scientific peer-reviewed journals. This can be seen as an essential step to strengthen the dissemination of the results and findings of these large projects;
- The peer-reviewed and tested nature of the scientific documentation gives strength to the findings and helps to understand the obstacles and policy needs for the cross-border exchange of health data. Regarding many recent "hypes" (regarding technologies or ideas such as artificial intelligence, big data, blockchain technology) it would be advisable to wait for more robust results in order to make informed policy decisions;
- The analyses of the conducted interview results show that there already exists a plethora of experiences and project results that are accessible and available from different EU funded projects. The EU funded projects could be consulted to develop a knowledge base and a framework for continuous exchange of best practices on the EU level. This pool of best practices could serve future projects and policy formation giving information on real-life obstacles and practical ways to overcome them.

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# Appendix A: Working definitions

- ***Health data***: patient data in health records (records kept by health professionals and care providers, as well as self-reported health data), data from apps and wearables, any background data that will give insights on the social determinants of health.
- ***Big data in health***: Consolidated data from existing fragmented data sources for the purpose of understanding, forecasting and improving health and health system status, needs and performance.[1]
- ***Big data analytics in health***: Statistical learning methods and algorithms applied to big data in health, which include descriptive analytics, mining/predictive analytics to support evidence-based decision making, analytical techniques that are ideal for analysing a large proportion of text-based health documents and other unstructured clinical data (e.g., physician's written notes and prescriptions and medical imaging).
- ***Innovative use of health data***: The process of translating an idea or invention into a good or service that creates value, or for which customers will pay. To be called an innovation, an idea must be replicable at an economical cost and must satisfy a specific need. Innovation involves deliberate application of information, imagination and initiative in deriving greater or different values from resources, and includes all processes by which new ideas are generated and converted into useful products[2]. The use of health data is considered "innovative" if this use results in better patient outcome and/or higher quality of healthcare delivery and/or higher productivity and performance.
- ***Artificial intelligence***: Artificial intelligence (AI) refers to systems that display intelligent behaviour by analysing their environment and taking actions – with some degree of autonomy – to achieve specific goals. AI-based systems can be purely software-based, acting in the virtual world (e.g. voice assistants, image analysis software, search engines, speech and face recognition systems) or AI can be embedded in hardware devices (e.g. advanced robots, autonomous cars, drones or Internet of Things applications). Many AI technologies require data to improve their performance. Once they perform well, they can help improve and automate decision making in the same domain.[3]

[1] This definition was derived from the following EU Study definition during the drafting process of this document "Big Data in Health refers to large routinely or automatically collected datasets, which are electronically captured and stored. It is reusable in the sense of multipurpose data and comprises the fusion and connection of existing databases for the purpose of improving health and health system performance. It does not refer to data collected for a specific study." (Source: EC. Study on Big Data in Public Health, Telemedicine and Healthcare available at https://ec.europa.eu/health/sites/health/files/ehealth/docs/bigdata_report_en.pdf )

We acknowledge that the definition will be further refined and continuously monitored during the life of the project, together with the authors of the study, taking into consideration the real-life evolution of the field.

[2] Source: http://www.businessdictionary.com/definition/innovation.html

[3] Source: https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:52018DC0237&from=EN

# Appendix B: Literature review search strategies

Data use or application for the benefit of health (with focus of innovative, new ways)

Database searches

| | |
|---|---|
| Web of Science | 617 |
| Medline (through Web of Science) | 637 |
| Ovid Medline | 9 |
| EBSCO Discovery Service | 615 |

Database searches yielded a total of 1878 references. After removal and initial screening of potentially relevant articles, we were left with 231 article abstracts (short-listing) for further enquiry.

**Inclusion criteria**

Inclusion criteria were not defined very tightly, since this preliminary searches idea was to give an idea of the scope and help to narrow it down. The focus was on real cases, projects and applications of eHealth.

**Exclusion criteria**

We excluded articles that presented us with discussions about potential applications, or papers on "what should be done", and technical papers (such as readability of health data, etc.)

**Search profiles**

**Web of science searches 9.10.2018**

TI=("big data" or "smart data" or "patient data" or "health data" or "health information" or "personal data" or "medical record*" or "health record*" or "health register*" or "PHR" or "e-health" or "m-health" or telehealth or telemedicine or informatics or bioinformatics or "machine data" or "real world data" or "real world evidence" or "swarm intelligence" or "health app*" or "predictive modelling") AND TS=(health* or illness or diseas* or medicine or medical or wellbeing or "physical activity" or lifestyle or safety or pharmacovigilance or "patient-cent*" or "cross border") AND TS=(europ* or EU or OECD or scandinavia* or nordic or canada* or australia*) (617)
Indexes=SCI-EXPANDED, SSCI, A&HCI, ESCI Timespan=2015-2018

**Medline (through Web of Science) 9.10**

TI=("big data" or "smart data" or "patient data" or "health data" or "health information" or "personal data" or "medical record*" or "health record*" or "health register*" or "PHR" or "e-health" or "m-health" or telehealth or telemedicine or informatics or bioinformatics or "machine data" or "real world data" or "real world evidence" or "swarm intelligence" or "health app*" or "predictive modelling") AND TS=(health* or illness or diseas* or medicine or medical or wellbeing or "physical activity" or lifestyle or safety or pharmacovigilance or "patient-cent*" or "cross border") AND TS=(europ* or EU or OECD or scandinavia* or nordic or canada* or australia*) (637)
Indexes=MEDLINE Timespan=2015-2018

**OVID Medline 9.10**

(pool* adj3 ("health data" or "medical data")).ti,ab (9)

**EBSCO DISCOVERY SERVICE searches 9.10**

TI ( ("big data" or "large data*" or "large sets of data" or "e-health" or e-science or escience or "m-health" or telemedicine or "real world data" or "real world evidence" or "smart data" or "swarm intelligence") ) AND (TI (health or medicine or medical or wellbeing or "physical activity" or illness or disease* or patient* or lifestyle or safety or pharmacovigilance or hospital) OR AB(health or medicine or medical or wellbeing or "physical illness or disease* or patient* or lifestyle or safety or pharmacovigilance or hospital)) AND (TI(europ* or EU or OECD or scandinavia* or nordic) OR AB(europ* or EU or OECD or scandinavia* or nordic)) (930) --> Limit to Academic journals, conference material, reports, dissertations/thesis, e-resources and ebooks (585)

"e-health innovations" or "ehealth innovations" (30)

**Search terms to consider if the search is conducted again**

electronic data capture
neuroinformatics
open data
Public data
Data mining/
pooled data
data pooling
data linkage
record linkage
precision medicine
patient generated data
patient-based evidence

# Appendix C: Descriptive data on the selected 90 articles

| Ref. no. | 1st Author | Cross-border | System. Review | Application type | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | Big data | eHealth | Telemed. | mHealth | AI |
| 8 | Rzokiewitz et al. | Yes | Yes | Yes | | | | |
| 9 | Joas et al. | Yes | No | Yes | | | | |
| 10 | Du et al. | Yes | Yes | Yes | | | | |
| 12 | Plueschke et al. | Yes | Yes | Yes | | | | |
| 14 | Anisetti et al. | Yes | No | Yes | | | | |
| 15 | Manogran et al. | No | No | Yes | | | | |
| 16 | Merchan Munillo et al. | Yes | No | | | Yes | Yes | |
| 17 | Alami et al. | No | No | | | Yes | | |
| 18 | Maissenhaelter et al. | Yes | No | Yes | | | | |
| 26 | Ronga et al. | Yes | No | | Yes | | | |
| 29 | Maglogiannis et al. | Yes | No | Yes | | | | |
| 30 | Harst et al. | No | No | | Yes | Yes | | |
| 35 | Melchiorre et al. | Yes | No | | Yes | | | |
| 45 | Schultz et al. | Yes | No | | | Yes | | |
| 47 | Deshpande et al. | Yes | No | | Yes | | | |
| 50 | Kemp et al. | Yes | Yes | | Yes | | Yes | |
| 51 | Luechtefeld et al. | No | No | | | | | Yes |
| 54 | Kuiper et al. | Yes | No | | | | Yes | |
| 56 | Donker et al. | No | No | | | | Yes | |
| 57 | Bidargaddi et al. | No | No | | Yes | | | |
| 59 | Duncan et al. | No | No | | Yes | | | |
| 66 | Fragidis et al. | Yes | No | | Yes | | | |
| 69 | Brito-Zeron et al. | Yes | No | Yes | | | | |
| 70 | Vaccarino et al. | No | No | Yes | | | | |
| 73 | Kühne et al. | Yes | No | | Yes | | | |
| 75 | Serhani et al. | No | No | Yes | | | Yes | |
| 78 | Gentil et al. | Yes | Yes | Yes | Yes | | | |
| 80 | Triantafillou | Yes | Yes | | Yes | | | |
| 83 | Nahum-Shani et al. | No | No | Yes | | | | |
| 86 | Leyh-Bannurah et al. | Yes | No | | | | | Yes |
| 87 | Hampel et al. | Yes | No | Yes | | | | |
| 93 | EMA | Yes | No | Yes | | | | |
| 94 | Steinhauser et al. | Yes | No | | | Yes | | |
| 96 | Corripio | Yes | No | | | | Yes | |
| 97 | Bulgheroni | Yes | No | | | | Yes | |
| 98 | Nohr et al. | Yes | No | | Yes | | | |
| 100 | Rigby et al. | Yes | No | | Yes | | | |
| 104 | Hemingway et al. | No | Yes | Yes | Yes | | | |
| 107 | Calvo-Lerma et al. | Yes | No | | | | Yes | |
| 109 | Szócska et al. | Yes | No | Yes | | | | |
| 119 | Kuzman et al. | Yes | No | | | | Yes | |
| 120 | SyndiGate Media | Yes | No | Yes | | | | |
| 124 | Huerta-Ramos et al. | Yes | No | | | | Yes | |
| 128 | Burgun et al. | Yes | No | Yes | | | | |
| 139 | Spanoudakis et al. | Yes | No | | | | | Yes |
| 140 | Corripio | Yes | No | | | | Yes | |

| Ref. no. | 1st Author | Cross-border | System. Review | Application type | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | Big data | eHealth | Telemed. | mHealth | AI |
| 142 | Ehrenstein et al. | No | No | Yes | | | | |
| 148 | Carrieri et al. | No | No | | Yes | | | |
| 149 | Ward et al. | No | No | | Yes | | | |
| 151 | Wang et al. | Yes | No | | Yes | | | |
| 152 | Ross et al. | Yes | Yes | | Yes | | | |
| 155 | Mano et al. | No | No | | Yes | | | |
| 157 | Baldacchino et al. | Yes | No | | Yes | | | |
| 158 | Tamblyn et al. | Yes | No | | Yes | | | |
| 162 | Kortüm et al. | No | No | | Yes | | | |
| 165 | Bradway et al. | No | No | | | | Yes | |
| 167 | Serhani et al. | No | No | Yes | | | Yes | |
| 168 | Beresniak et al. | Yes | No | | Yes | | | |
| 170 | Quaglio et al. | Yes | Yes | | Yes | | | |
| 171 | Bibault et al. | No | No | | | | | Yes |
| 172 | Kenter et al. | Yes | No | | Yes | Yes | | |
| 173 | Agius Muscat | Yes | No | | Yes | | Yes | |
| 174 | Sanchez | Yes | No | | Yes | | | |
| 176 | Villalonga et al. | Yes | No | | | | Yes | |
| 180 | Tyrrell et al. | No | No | | Yes | | | |
| 181 | Saganowski et al. | Yes | No | | Yes | | | |
| 183 | Mumford | Yes | No | | | Yes | | |
| 186 | Jackson et al. | Yes | Yes | | Yes | Yes | | |
| 199 | Corripio et al. | Yes | No | | | | Yes | |
| 201 | Holthe | No | No | | Yes | | | |
| 202 | Rubinstein | Yes | No | | | | Yes | |
| 204 | Moumtzoglou | Yes | No | | | | Yes | |
| 205 | Ming et al. | Yes | Yes | | | Yes | | |
| 206 | Hartung | Yes | No | Yes | | | | |
| 207 | Müller et al. | Yes | No | Yes | | | | |
| 208 | Zarkogianni et al. | Yes | No | | Yes | | | |
| 210 | Neuman et al. | Yes | No | | | Yes | | |
| 211 | Garmann-Johnsen | Yes | No | | Yes | | | |
| 212 | Genitsaridi et al. | Yes | Yes | | Yes | | | |
| 214 | Zhang et al. | No | No | | Yes | | | |
| 215 | De Moor et al. | Yes | No | | Yes | | | |
| 216 | Marano et al. | No | No | | Yes | | | |
| 217 | Brennan et al. | Yes | yes | | Yes | | | |
| 222 | Ekeland et al. | Yes | No | | | Yes | | |
| 223 | Hübner | Yes | No | | Yes | | | |
| 224 | Perez-Cebollada et al. | Yes | No | | Yes | Yes | | |
| 225 | Domenichiello | No | No | | Yes | | | |
| 228 | Hofmann-Apitius et al. | Yes | No | Yes | | | | |
| 229 | Schaller et al. | No | No | | Yes | | | |
| 230 | Carinci | Yes | No | | Yes | | | |
| 231 | Fonseca et al. | Yes | No | | Yes | | | |

| Ref. no. | Diseases, target areas | No. Countries |
|---|---|---|
| 8 | Physical activity, mental health, geriatrics, injury, smoking, alcohol | 10 |
| 9 | Birth cohorts, environmental health, chemical contaminants | 14 |
| 10 | Heart failure, RWD | ? |
| 12 | 14 different therapeutic areas to support EMA, pharmaceuticals | ? |
| 14 | Public health, privacy, GDPR | ? |
| 15 | Internet of medical things (IoMT), medical devices and applications | ? |
| 16 | epSOS project, interoperability | 25 |
| 17 | Telepathology network | 1 |
| 18 | Oncology, cancer | ? |
| 26 | Integrated satellite terrestrial network | 1 |
| 29 | Aging, sedentary lifestyle, dieat, obesity | 11 |
| 30 | 12 structural categories for telemedicine research projects | ? |
| 35 | Aging, long-term diseases, 101 integrated care programmes, EHR access | 24 |
| 45 | Blood pressure, telemonitoring system for hypertension | ? |
| 47 | Children, obesity, owerweight, apps, websites, helplines | 23 |
| 50 | HIV care cascade, eHealth | ? |
| 51 | Avoiding animal testing for hazards and toxicity of chemicals | ? |
| 54 | Cancer, cancer-related fatigue | ? |
| 56 | eHealth innovations for global mental health | ? |
| 57 | My Health Record (MyHR) national platform usability | 1 |
| 59 | Adults, physical activity promotion | 1 |
| 66 | Implementation process of a national EHR system | 13 |
| 69 | Primary Sjögren's syndrome, international multicentre registry (SJS) | 22 |
| 70 | Neuroscience, cerebral palsy, epilepsy, depression | 1 |
| 73 | Primary healthcare for children, use EHRs, public health monitoring | 13 |
| 75 | Epilepsy, seizure prevention, EEG monitoring, algorithms | ? |
| 78 | Primary care data gathering from EHRs | 12 |
| 80 | EHR implementation, usefulness critically reviewed | ? |
| 83 | Alcohol dependency, naltrexone, pharmaceuticals | ? |
| 86 | Cancer, prostate, pathology, prostatectomy | ? |
| 87 | Alzheimer's disease, precision medicine | ? |
| 93 | Medicines, pharmaceuticals, roadmap, recommendations, EMA | 10 |
| 94 | Telemedicine adoption in Europe | ? |
| 96 | Psychiatry, schizophrenia, treatment resistant, m-RESIST intervention | 3 |
| 97 | Psychiatry, assessment of psychotic symptoms, m-RESIST | ? |
| 98 | Nationwide citizen access to their health data | 3 |
| 100 | Children, eHealth strategies | 27 |
| 104 | EHR data for early and late translational CVD research | ? |
| 107 | Children, cystic fibrosis, joint and barrier-free CF treatment | 7 |
| 109 | Alzheimer's disease, hematologic malignancies, CVD, IMI2 | ? |
| 119 | Psychiatry, prevention of antipsychotic-induced side effects | 7 |
| 120 | Lung cancer, AD, precision medicine, genomics, EHR, bibliography, iASiS | 5 |
| 124 | Psychiatry, schizophrenia, treatment resistant, m-RESIST intervention | 1 |
| 128 | Re-use of health data in Europe for public health | 10 |
| 139 | Hearing impairments, supporting public health policies | ? |
| 140 | Psychiatry, schizophrenia, treatment resistant, m-RESIST intervention | 6 |

| Ref. no. | Diseases, target areas | No. Countries |
|---|---|---|
| 142 | Clinical epidemiology, EHR, record linkage | ? |
| 148 | Cancer, breast, screening programme, prevention, data linkage | ? |
| 149 | CVD, primary healthcare, smoking, diabetes, ethnicity, data linkage | 1 |
| 151 | Respiratory diseases, asthma COPD, EHR | ? |
| 152 | Implementing eHealth technologies, EMR, CDSS | 12 |
| 155 | Internet of things, health smart homes, aging | ? |
| 157 | Avoiding overdose risk by using an eHealth psycho-educational tool | ? |
| 158 | Diabetes, type 2, international pharmacosurveillance, EHR | 3 |
| 162 | Opthalmology, referral letters, clinical data from EHR, measurement data | 1 |
| 165 | Diabetes, insulin treatment, self-management, smartphone app | 1 |
| 167 | Epilepsy, mobile sensors, monitoring | ? |
| 168 | Cancer, EHR4CR platform, re-use of EHR data for clinical research | ? |
| 170 | Key trends, challenges for the deployment of eHealth in the EU | ? |
| 171 | Radiation oncology, learning health system, genomics, EHR | ? |
| 172 | Aging, frailty, functionality | 2 |
| 173 | epSOS project, interoperability, CEF, e-SENS, mHealth apps | ? |
| 174 | Innovation procurement,  EPP-eHealth project | ? |
| 176 | Patient monitoring | ? |
| 180 | Ankylosing spondylitis, an online AS Observer tool | 1 |
| 181 | Patient recorded outcome measures (PROM), GORD, reflux disease | 4 |
| 183 | Aging, elderly care | ? |
| 186 | Inflammatory bowel disease, Chrohn's disease, PROM, web-based management | ? |
| 199 | Psychiatry, schizophrenia, treatment resistant, m-RESIST intervention | 5 |
| 201 | Helsenorge.no, access, patient accessible EHR | 1 |
| 202 | Psychiatry, schizophrenia, treatment resistant, m-RESIST intervention | ? |
| 204 | Many therapeutic areas or diseases | ? |
| 205 | Diabetes, pregnancy, maternal and neonatal clinical outcomes | ? |
| 206 | Toxicology, REACH legislation and database, (Q)SAR use, read-across | ? |
| 207 | Radiology, medical imaging, CDSS | ? |
| 208 | Diabetes, sensors, glucose and lifestyle monitoring, CDSS | ? |
| 210 | Interventional decentralised telemonitoring (idTM 0), nephrology | ? |
| 211 | eHealth strategies, national context, regional implementation | 2 |
| 212 | Personal health record systems, requirement analysis | ? |
| 214 | Patient acceptance and use of consumer eHealth innovations, primary healthcare | 1 |
| 215 | Interoperability between EHR systems and clinical research systems | 7 |
| 216 | Remote medical assistance | 1 |
| 217 | National health models, eHealth adoption, national ePrescribing systems | 31 |
| 222 | Model for assessment of telemedicine applications | ? |
| 223 | eHealth technologies, innovation, advanced clinical practice | ? |
| 224 | Remote patient monitoring, secure patient-clinician messaging, use cases | ? |
| 225 | eHealth strategies, e-Government strategies | 1 |
| 228 | Bioinformatics, genetics, neurodegeneration, disease models (AD, PD, oncology) | 5 |
| 229 | Aging, dementia, caregiver, web portal, information and knowledge, experts | 1 |
| 230 | Pan-European health information system, cross-border data exchange | ? |
| 231 | epSOS, OpenNCP, patient summary, EHR, ePrescribing, semantics, standards, CEF | ? |

| Ref. no. | Notes |
|---|---|
| 8 | Many automated environmental assessments, e.g. neighborhoods, Google Street View |
| 9 | Human biomonitoring, exposure biomarkers, health indicators/information |
| 10 | OECD countries |
| 12 | Real-world data on 171 initiatives |
| 14 | Balancing quality of life and privacy protection in smart cities |
| 15 | Global infrastructure, data used for diagnosis, care and prevention |
| 16 | |
| 17 | Inherent issues of a complex telehealth network, implementation |
| 18 | Networks of cancer centers |
| 26 | Dynamic management of the bandwidth resources |
| 29 | Policy Development Toolkit (CrowdHEALTH) |
| 30 | Method to systematically evaluate and categorise finished projects |
| 35 | Remote consultation, monitoring, care; self-management, health data analytics, ICARE4EU |
| 45 | Under development using idTM and SciTIM software |
| 47 | MOCHA methodology, guidance for obesity/healthy lifestyle promotion |
| 50 | Most interventions in 17 studies used SMS messages to improve cascade outcomes |
| 51 | Read-across structure activity relationship (RASAR), natural language processing |
| 54 | Untire app |
| 56 | An editorial |
| 57 | Australia's national EHR system, Actionable Intime Insights (AI squared) software |
| 59 | 10 000 steps day target, smartphone app (iStepLog) |
| 66 | Pros and cons of EHR in different countries |
| 69 | Centers share a harmonised data infrastructure |
| 70 | Neuroninformatics platform (Brain-CODE), database architechture |
| 73 | MOCHA methodology |
| 75 | Three algorithms, MapReduce platform |
| 78 | 36 routine primary healthcare data collection projects, stakeholders, secondary use |
| 80 | |
| 83 | Q-learning applied to a SMART (ExTENd) naltrexone trial data |
| 86 | Natural language processing, extracting narrative written pathodological report data |
| 87 | From big data to smart data, biomarker-guided integrative disease modeling |
| 93 | Heads of Medicine Agencies and EMA joint big data task force |
| 94 | |
| 96 | Health professionals, sensor data, predictive modeling, CDSS, an app connected to a smartwatch |
| 97 | |
| 98 | HIS, PHR |
| 100 | MOCHA methodology |
| 104 | Many consortiums, academic, industry, IMI2, BigData@Heart |
| 107 | Nutritional goals and close nutritional follow-up, a new MyCyFAPP app |
| 109 | IMI2, BD4BO programme, ROADS/ROADMAP (AD), HARMONY, BigData@Heart (HF, AF, ACS) |
| 119 | Android smartphone, a new PsyLOG app, 8 functional categories |
| 120 | Precision medicine |
| 124 | Health professionals, sensor data, predictive modeling, CDSS, Barcelona case study |
| 128 | Many administrative databases, FAIR (findable, accessible, interoperable, reusable) data principles |
| 139 | EVOTION platform, big data analytics, maschine learning, data mining |
| 140 | Health professionals, sensor data, predictive modeling, CDSS, an app connected to a smartwatch |

| Ref. no. | Notes |
|---|---|
| 142 | Epidemiologic research is an exercise in measurement in an effort to mazimise signal-to-noise ratio |
| 148 | Home invitation increased mammography uptake by around 24% |
| 149 | Data linkage allowed use of information to examine ethnic health variations |
| 151 | |
| 152 | Recommendations for implementation based on data from reviews |
| 155 | Face recognition, emotion detection, a prototype |
| 157 | Risk estimation, design and feasibility of the ORION project |
| 158 | An international surveillance system based on EHRs may provide more timely information |
| 162 | Measuring devices connected to EHR (HL7 standard interface, PACS), OCT scans, IOLMaster, DW |
| 165 | Diabetes Diary (smartphone app), Diabetes Share Live (web portal) |
| 167 | A novel mobile-based architechture for monitoring life-long diseases, SME2EM |
| 168 | Cost-benefit assessment (CBA), acceleration of time to market |
| 170 | Healthcare needs to be seen as a truly collaborative process between all actors |
| 171 | EHR phenotypic profiles combined with advances in radiation oncology to be used for predictions |
| 172 | One-size-fits-all business model and implementation strategy failure, PERSSILAA eHealth solution |
| 173 | An update on eHealth developments in Europe, big project -> large number of countries |
| 174 | A network approach, potentially 15 000 hospitals in Europe |
| 176 | |
| 180 | AS Observer pilot study |
| 181 | |
| 183 | CHROMED |
| 186 | Telemedicine, mobile telephone, social media, IBD management |
| 199 | |
| 201 | |
| 202 | |
| 204 | A book |
| 205 | Insufficient evidence that telemedicine systems produce superior outcomes for DM women |
| 206 | A new web-based tool (REACH-across) in development |
| 207 | VISCERAL, Khresmoi |
| 208 | Optimal DM management requires redesigning the current healthcare delivery |
| 210 | |
| 211 | A case study in St. Gallen region in Switzerland and Agder region in Norway |
| 212 | |
| 214 | An e-appointment scheduling service, Rogers' Innovation Diffusion Theory |
| 215 | IMI, EHR4CR, proof-of-concept demonstrators, platform, various national legal frameworks |
| 216 | Method for system design for sustainability, hierarchical task analysis, Ovako work analysis system |
| 217 | Highest adoption proportions in NHS health model countries, especially in the Nordic countries |
| 222 | 21 pilots of the European project RENEWING HEALTH |
| 223 | eHealth innovation is more evolution than revolution, no innovation without sociocultural change |
| 224 | Machine-to-machine systems, M2M architecture in eHealth context, ETSI |
| 225 | Case study Italy |
| 228 | IMI, AETIONOMY Knowledge Base |
| 229 | eHealthMonitor, eHM Dementia Portal (eHM-DP) pilot, home-based care setting |
| 230 | Proposed information model, 4 action lines |
| 231 | OpenNCP interoperability architecture, IHE profiles, national gateways to foster an e-Health ecosystem |

# Appendix D: Qualitative data on 30 candidate projects for further review

| Project | Finished | Application type | | | | EU funded | Short listed |
|---|---|---|---|---|---|---|---|
| | | eHealth | mHealth | Telemedicine | Big Data | | |
| CrowdHealth | No | | | | Yes | Yes | |
| IMI2 BD4BO | No | | | | Yes | Yes | |
| ROADMAP | Yes | | | | Yes | Yes | Yes |
| HARMONY | No | | | | Yes | Yes | |
| BigData@Heart | No | | | | Yes | Yes | |
| PIONEER | No | | | | Yes | Yes | |
| BRIDGE Health | Yes | | | | Yes | Yes | Yes |
| InfAct | No | | | | Yes | Yes | |
| IASIS | No | | | | Yes | Yes | |
| MIDAS | No | | | | Yes | Yes | |
| Big Data Sjögren | No? | | | | Yes | No? | |
| BigO | No | | | | Yes | Yes | |
| EVOTION | No | | | | Yes | Yes | |
| Untire | No? | | Yes | | | Yes | |
| m-RESIST | Yes | | Yes | | | Yes | Yes |
| MyCyFApp | Yes | | Yes | | | Yes | |
| mPivas/Psylog | Yes? | | | | | Yes | Yes |
| epSOS | Yes | Yes | | | | Yes | Yes |
| MOCHA | Yes | Yes | | | | Yes | |
| ICARE4EU | Yes | | | Yes | | Yes | Yes |
| REACH-across | No? | | | | Yes | No | |
| AETIONOMY | Yes | | | | Yes | Yes? | |
| ORION | Yes | Yes | | | | No | |
| EHR4CR | Yes | Yes | | | | Yes | Yes |
| PERSSILAA | Yes | Yes | | Yes | | No | Yes |
| EPP-eHealth | Yes | Yes | | | | Yes | |
| TRANSFoRm eHealth | Yes | Yes | | | | Yes | |
| CHROMED | Yes | | | Yes | | Yes | |
| EUSTAR | No? | | | Yes | | No | |
| RENEWING HEALTH | Yes | | | Yes | | Yes | Yes |

| Project | Target/Disease Area |
|---|---|
| CrowdHealth | Aging, sedentary lifestyle, dieat, obesity (Policy Development Toolkit) |
| IMI2 BD4BO | Umbrella programme. Specific projects ROADMAP, HARMONY, BigData@Heart and PIONEER |
| ROADMAP | Alzheimer's Disease |
| HARMONY | Hematologic Malignancies |
| BigData@Heart | Heart |
| PIONEER | Prostate Cancer |
| BRIDGE Health | Birth cohorts, environmental health, chemical contaminants |
| InfAct | Health information (build on BRIDGE) |
| IASIS | Lung cancer, AD, precision medicine, genomics, EHR, bibliography, Precision medicine |
| MIDAS | Big Data platform |
| Big Data Sjögren | Sjögren, autoimmune diseases |
| BigO | Childhood Obesity |
| EVOTION | Hearing impairments, supporting public health policies |
| Untire | Cancer related fatigue |
| m-RESIST | Psychiatry, schizophrenia, treatment resistant |
| MyCyFApp | Children, cystic fibrosis, joint and barrier-free CF treatment |
| mPivas/Psylog | Psychiatry, prevention of antipsychotic-induced side effects |
| epSOS | eHealth pilot project: Patiet Summary, ePrescription |
| MOCHA | Children, eHealth strategies |
| ICARE4EU | Aging, long-term diseases |
| REACH-across | Toxicology, REACH legislation and database, (Q)SAR use, read-across |
| AETIONOMY | Bioinformatics, genetics, neurodegeneration, disease models (AD, PD, oncology) |
| ORION | Avoiding overdose risk by using an eHealth psycho-educational tool |
| EHR4CR | Cancer, EHR4CR platform, re-use of EHR data for clinical research |
| PERSSILAA | Aging, frailty, functionality |
| EPP-eHealth | Innovation procurement,  EPP-eHealth project |
| TRANSFoRm eHealth | Patient recorded outcome measures (PROM), GORD, reflux disease |
| CHROMED | Aging, elderly care, COPD, HF, sleep disordered breathing |
| EUSTAR | Interventional decentralised telemonitoring (idTM 0), nephrology |
| RENEWING HEALTH | Model for assessment of telemedicine applications (MAST) |

# Appendix E: Qualitative data on 8 projects selected for in-depth interview

| Project | Finished | Application type | | | | EU funded | Short listed |
|---|---|---|---|---|---|---|---|
| | | eHealth | mHealth | Telemedicine | Big Data | | |
| epSOS | Yes | Yes | | | | Yes | Yes |
| ICARE4EU | Yes | | | Yes | | Yes | Yes |
| m-RESIST | Yes | | Yes | | | Yes | Yes |
| ROADMAP | Yes | | | | Yes | Yes | Yes |
| mPivas/Psylog | Yes | | | | | Yes | Yes |
| EHR4CR | Yes | Yes | | | | Yes | Yes |
| PERSSILAA | Yes | Yes | | Yes | | Yes | Yes |
| RENEWING HEALTH | Yes | | | Yes | | Yes | Yes |

| Project | Target/Disease Area |
|---|---|
| epSOS | eHealth pilot project: Patiet Summary, ePrescription |
| ICARE4EU | Aging, long-term diseases |
| m-RESIST | Psychiatry, schizophrenia, treatment resistant |
| ROADMAP | Alzheimer's Disease |
| mPivas/Psylog | Psychiatry, prevention of antipsychotic-induced side effects |
| EHR4CR | Cancer, EHR4CR platform, re-use of EHR data for clinical research |
| PERSSILAA | Aging, frailty, functionality |
| RENEWING HEALTH | Model for assessment of telemedicine applications (MAST) |

# Appendix F: Questionnaire for in-depth interview

Introduction

The purpose of this interview is to collect information about multi-country or cross-border eHealth projects, in which your country has been involved. This interview information is gathered as a part of the eHAction project that is a Joint Action (JA) co-financed by the European Commission and the Member States.

For basic information about the eHAction, please visit http://ehaction.eu/

One of the eHAction's main objectives is to improve the innovative use of health data. Tasks related to this eHAction objective are fulfilled by Work Package Five (WP5). WP5 has a vision to develop innovative usage of data across the healthcare sector to improve the knowledge base for health and healthcare policy. WP5 looks at data as a key driver of disruptive innovation in the economic, societal and social systems. Therefore, WP5 is committed to make an impact on the use of health data as well as assisting data-driven innovation leading to patient-centred health systems, evidence-based health policies and decision-making.

We believe that close cooperation with stakeholders is essential in achieving our objectives. Therefore, the WP5 is going to collect, compile and share the experiences of Member States/Countries for developing a knowledge base and a framework for continuous exchange of best practices on the EU level.

The eleven questions are:

1. We would like to learn about your projects and their goals that involve more than one country and also use of health data. Could you, please, tell us?
2. Which players were involved in setting up the projects? By players we mean ministries, other authorities, patient organisations, professional organisations, researchers, service providers, other insurance organisations, and the like.
3. What were the motivations of these players targeted by the involvement?
4. What were or have been the obstacles in implementing the projects?
5. What were or have been the challenges related to using data in healthcare?
6. Do you have three (3) smart project level tips emerging from your experience or lessons learnt in the above mentioned project(s)? What can you recommend for projects to avoid or overcome obstacles, or challenges in project planning and implementation, or daily use of project results?
7. Do you have three (3) smart policy-level tips emerging from your experiences or lessons learnt in the above mentioned project(s)? What can you recommend for local, regional or national policy makers to help them to avoid or overcome obstacles or challenges in project planning and implementation, or daily use of project results?
8. In your opinion, which ideas from the above mentioned project(s) are useful and needed to improve public health in relation to eHealth?
9. Which issues should be solved or addressed (on the EU level) in order to improve cross-border cooperation in eHealth?
10. Which ideas are scalable to more countries?
11. Please, share papers or reports, or like project publications, or links to access these if possible.

(1) Additional information https://hbr.org/2017/03/how-to-get-ecosystem-buy-in
(2) Additional information https://healthitanalytics.com/news/top-10-challenges-of-big-data-analytics-in-healthcare