

An Interoperable eHealth Reference Architecture for Primary Care

Wendy Oude Nijeweme – d’Hollosy
EEMCS/BSS Telemedicine
University of Twente
Enschede, the Netherlands
w.dhollosy@utwente.nl

Lex van Velsen
EEMCS/BSS Telemedicine
University of Twente
Enschede, The Netherlands
Roessingh Research and Development
Enschede, the Netherlands
l.vanVelsen@rrd.nl

Alexander Henket
Nictiz, Centre of expertise for
standardization and eHealth,
The Hague, the Netherlands
henket@nictiz.nl

Hermie Hermens
EEMCS/BSS Telemedicine
University of Twente
Enschede, The Netherlands
Roessingh Research and Development
Enschede, the Netherlands
h.hermens@rrd.nl

Abstract— eHealth is still not widely used in primary care, because barriers still exist around integrated and interoperable technological infrastructures for eHealth. This paper describes the design of an interoperable eHealth reference architecture for primary care and its evaluation with experts. This reference architecture aims to facilitate IT specialists in setting up interoperable eHealth infrastructures within primary healthcare organizations. The design of the reference architecture was based on the results of 14 working sessions with 10 eHealth Small and Medium sized Enterprises (SMEs) and the theory behind the Refined eHealth European Interoperability Framework (ReEIF). The evaluation with experts revealed additional conditions that – next to the reference architecture – are needed before interoperable eHealth in primary care can actually be achieved.

Keywords— eHealth - Health information exchange (HIE) - Interoperability - IT health standards - Primary care - Reference architecture - Refined eHealth European Interoperability Framework (ReEIF)

I. INTRODUCTION

eHealth technologies are health services delivered or enhanced through the Internet and related technologies [1]. Although eHealth is seen as a promising means to improve the quality of care, it is still not widely used in primary care [2]. One significant reason is that barriers exist around integrated and interoperable technological infrastructures for eHealth [3]. Interoperability is defined as the ability for two (or more) systems or components to exchange information and to use the information that has been exchanged [4]. Medical interoperability is termed health information exchange (HIE). HIE is focused on reliable and interoperable electronic sharing of clinical information among physicians, nurses, pharmacists, other health care providers, and patients across the boundaries of health care institutions, health data repositories, laboratories, public health agencies, and other entities that are not within a distinct organization or among affiliated providers [5]. Unfortunately, current available health information systems and digital devices in primary care do not facilitate smooth HIE. One important cause is the usage of standalone systems that store data in different formats and without means for data exchange. To enhance interoperability among IT applications in primary care, primary organizations should be able to set up interoperable infrastructures that allow for easy integration of existing IT systems and new eHealth technologies. Issues that have been found to hinder the development of interoperable infrastructures in healthcare include the complexity of the healthcare domain due to its many stakeholders, the large amount of possible IT health standards that can be chosen from, and problems affecting privacy and security [6-9].

This work is partly funded by a grant from the Netherlands Organization for Health Research and Development (ZonMw), grant 10-10400-98-009. The authors would kindly like to thank the participants in the evaluation study for their time, effort, and willingness to cooperation in our research.

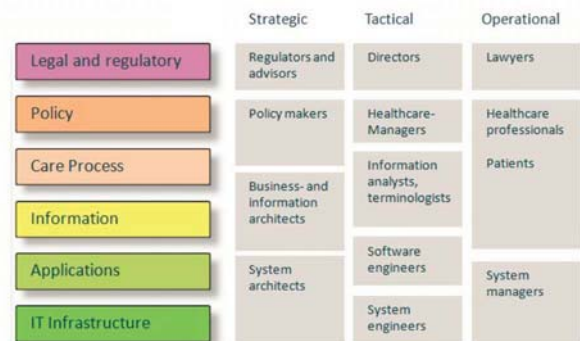


Fig. 1. Overview of different stakeholders at different levels in the ReEIF. Image source: eHealth Network - Refined eHealth European Interoperability Framework ([12] page 11) used with permission of Nictiz.

Interoperability in healthcare is subject of extensive research, because efficient HIE will improve quality of care [5]. For example, the Health Information Management Systems Society (HIMSS) started the Integrating the Healthcare Enterprise (IHE) initiative. The IHE addresses the implementation of standards-based interoperability solutions to improve information sharing, workflow and patient care [10]. IHE Europe is also involved in the project “eStandards: eHealth Standards and Profiles in Action for Europe and Beyond” [11] that has delivered input to the Refined eHealth European Interoperability Framework (ReEIF) [9,12]. The idea behind the ReEIF is: “Interoperability between two independently operating organizations (e.g. hospital, GP, patient) can only be established when the internal architecture is well appointed by making agreements with all stakeholders at all levels in the organization” [12].

The ReEIF identifies 6 different interoperability levels at which different stakeholders have to collaborate to make the corresponding level operational. These six levels involve the following topics 1. Legal and regulatory, 2. Policy, 3. Care process, 4. Information, 5. Applications, and 6. IT infrastructure (Fig.1). Interoperability issues can be addressed efficiently and in the right sequence by successively go top down through these different interoperability levels with the right stakeholders.

The IHE and the ReEIF provide guidelines on eHealth interoperability, mainly focused on large organizations, like hospitals. However, additional steps are needed towards the design of actual interoperable eHealth infrastructures for primary care, because organizations in primary care are smaller and usually do not have an IT department with knowledge on eHealth interoperability. Therefore, this paper presents the design of an interoperable eHealth reference architecture that illustrates how to translate a primary healthcare process into an interoperable eHealth infrastructure that can technically support the HIE within this healthcare process. This

design was based on results of working sessions with eHealth providers and the theory behind the ReEIF.

The reference architecture and its application within a theoretical case – i.e. interoperability of a web-based decision support system on the referral of low back pain (LBP) [13,14] with other relevant IT systems - were assessed during an evaluation study with IT health information experts. This evaluation has resulted into additional relevant insights that – next to the reference architecture - need to be known before interoperable eHealth in primary care actually can be achieved.

II. METHODS

Fig.2 shows a quick overview of the applied methods in the design and evaluation of the interoperable eHealth reference architecture with the following three main steps:

1. *Design of an interoperable eHealth reference architecture for primary care (Step1, Fig.2):* In the autumn of 2014 and the spring of 2015, 14 working sessions were held with 10 Small and Medium sized Enterprises (SMEs). These SMEs offered eHealth functionalities, like video consultations, activity monitoring via on-body sensors, training programs for rehabilitation, and coaching programs for patients with COPD and Asthma. The SMEs discussed how their existing eHealth applications could be integrated into one common interoperable infrastructure. The outcomes of these sessions together with the interoperability levels “care process”, “information” and “applications” of the refined eHealth European Interoperability Framework (ReEIF) [12] were used as input in the design of the interoperable eHealth reference architecture;
2. *Example application of the reference architecture in a theoretical case (Step2, Fig.2):* The reference architecture was applied to the case for optimizing the referral of patients with acute low back pain (LBP) in primary care. For this case, we designed an interoperable eHealth infrastructure on paper based on the reference architecture designed in step 1. This infrastructure integrated a web-based clinical decision support system (CDSS) on the referral of low back pain with other relevant IT systems in primary care.
3. *Evaluation study (Step3, Fig.2):* In 2017, eight health IT experts were interviewed to determine if the reference architecture can be used to accelerate the development of interoperable eHealth infrastructures in primary care. These experts had at least 5 years of experience in the health informatics domain and possessed theoretical knowledge of and experience with interoperability and

e-standards in healthcare. During these semi-structured interviews, the following topics were addressed:

- Demographics: educational background, knowledge of and experience in health information exchange and standardization of the interviewee;
- SME characteristics (when applicable): eHealth solutions provided by the SME the interviewee was working for, and applied interoperability approaches;
- Evaluation: evaluation of the reference architecture and its application in the theoretical case on readability, completeness, and financial and technical feasibility.

A document was sent to each interviewee prior to the phone interview. This document described the reference architecture and the theoretical case. All interviews were recorded and summarized in a report. This summary report was sent to the corresponding interviewee for feedback on completeness and interpretation of what was said. Then, these reports were analyzed based on the approach of Framework analysis [15]. This means that the analysis was guided by data retrieved from the reports, starting the analysis with the global topics from the interview scheme, and theme concepts emerged during the analysis.

III. RESULTS

A. SME working sessions

The SME working sessions resulted into an infrastructure with three layers: 1. a frontend layer, 2. a middleware layer, and 3. a data layer. The eHealth applications in the middleware supplied the different eHealth functionalities in this infrastructure. During these working sessions, the following technical issues appeared to be important, and were solved as follows:

1. *Service oriented architecture (SOA):* The infrastructure focused on the core functionalities of each eHealth application strengthened by adding the core functionalities of other eHealth applications. In this way, the infrastructure was oriented on bringing together and integrating the best functionalities represented as services.
2. *Single sign-on:* All different eHealth functionalities had to be accessible at once by means of single sign-on to save the user time; extra login actions were no longer needed.
3. *Shared core dataset:* Data exchanged among different eHealth applications had to be part of a shared core data set with data items agreed upon by all involved SMEs. Other data, used by a single eHealth application, were stored locally for the benefit of speed of data accessibility.
4. *Communication bus:* The usage of a communication bus kept the integration of the eHealth services manageable. General services that were needed by multiple applications – e.g. single sign-on, authorization, logging, data import, data export - were located in the bus. An application could connect to the bus through an application programming interface (API) to be able to use these general services, to deliver its functionalities to the infrastructure, and to exchange data with other applications.

These decisions on technical issues were also input in the design of the interoperable eHealth reference architecture.

B. Theory of the ReEIF

Next to the conclusions of the working sessions, three levels of ReEIF [9,12] were used in the design of the interoperable eHealth reference architecture, i.e. 1. Care process, 2. Information, and 3. Applications (Fig.1). Only these 3 levels were involved, as the design of the reference architecture was zoomed in on the translation of a primary healthcare process into an interoperable eHealth infrastructure to technically support this process. An important part of this translation is choosing the right IT health standards.

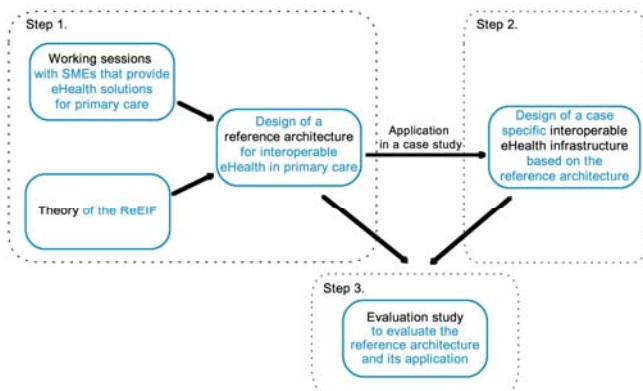


Fig.2. Quick overview of the applied research methods in the design and evaluation of the interoperable eHealth reference architecture and how these are related to each other. “SME” in this figure stands for “Small and Medium sized Enterprises”.

To keep the reference architecture readable, the interoperability level “IT infrastructure” was not involved as for the IT infrastructure it is often enough to align already existing general web-based open standards and protocols [12].

a) Care process level

In general, a healthcare process (Fig.3) starts with a *healthcare problem* that can be treated in primary care. During the *consult* with the healthcare professional, a decision is made on the *care plan*, based on anamnesis and physical examination. The care plan can be actual treatment, or a self-care advice to the patient, or further referral to another healthcare professional with a specialization that better suits the healthcare problem. When the patient stays in this healthcare process, the effects of the care plan will be *monitored*.

When the general healthcare process is worked out into further detail for a specific healthcare problem, this will result into a specific *care path*. For example, the care path for a patient with acute low back pain differs from the care path for a patient with COPD. In primary care, stakeholders that should analyze and agree on the details of care paths are primary healthcare professionals, and preferably also patients (Fig.1). Information analysts should also be involved for the technical analysis of information that should be exchanged.

b) Information level

Throughout a healthcare process, (health) information is gained and used during different actions at different moments. eHealth functionalities can support the retrieval and usage of this information. Fig.3 shows examples of possible eHealth functionalities at different moments in a healthcare process. In order to exchange data among patients, healthcare professionals, and IT systems, data should be standardized and represented in a data model (Fig.4). Healthcare professionals, information analysts, and terminologists should agree upon this data model (Fig.1). Health terminology and code systems are used to enable interoperability of data elements [3,12]. International terminology and code systems relevant for primary care are the International Classification of Primary Care (ICPC) [16], the International Classification of Diseases (ICD) [17] and SNOMED CT [18].

c) Applications level

The eHealth functionalities as shown in Fig.3 represent services delivered by eHealth applications (Fig.4). One application can deliver one or more eHealth functionalities. Agreements have to be made about which applications have to be involved in the infrastructure, how these applications will handle import and export of health information, and how information is integrated and processed in a user-friendly way [12]. Here, software engineers should be involved (Fig.1). For the import and export of health information, health communications standards should be deployed. International health communication standards used in primary care are versions of HL7 [19] and EDIFACT [20].

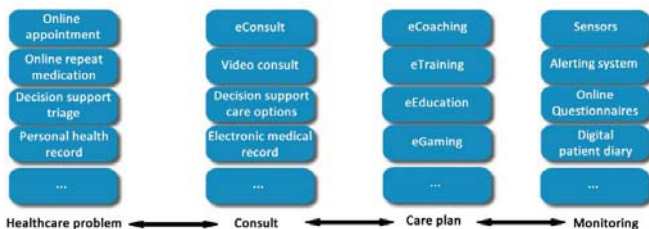


Fig.3. Overview of possible eHealth functionalities at certain points in the healthcare process that provide information.

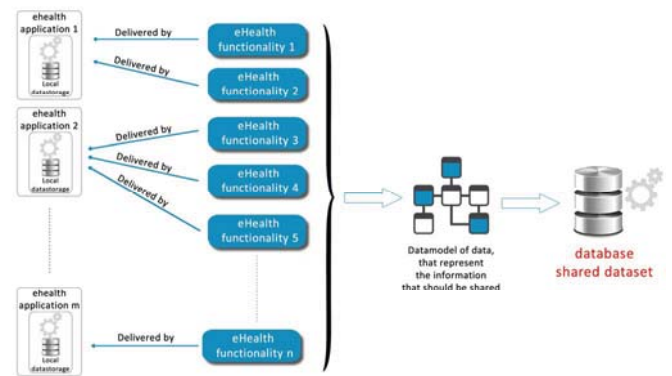


Fig.4. eHealth functionalities lead to information that is represented by data.

C. Interoperable eHealth reference architecture

Fig.5 shows the interoperable eHealth reference architecture for primary care that was designed based on the described SME working sessions and the theory of the ReEIF. It has been set up as a service-oriented architecture (SOA) and uses a communication bus that connects distributed applications. This reference architecture contains four layers: 1. Presentation services, 2. Functional services, 3. Middleware services, and 4. Data services. The Middleware services and Data services are part of the communication bus. These two layers contain generic services that are needed to manage smooth communication and data management among the distributed applications and data sources taking into account standardization, privacy, and security issues. For each single primary healthcare organization, it should be possible to customize services in the bus to the specific situation and wishes of the organization. Fig. 5 also shows data adapters. These data adapters take care of the necessary data transformations to enable data exchange among different applications connected to the communication bus.

The functional services layer contains services that support a healthcare path, i.e. a specific eHealth functionality, like eCoaching or eTraining. The functional services layer can also entail communication functionalities, such as eConsult or online repeat medication prescriptions (Fig.3). The functionalities of electronic medical record systems (EMR) are located in this layer as well, as these systems support health information management during the healthcare process and healthcare professionals prefer working from these systems [21].

The interoperable eHealth reference architecture shows three different kinds of health records: 1. Patient Health Record (PHR), 2. Electronic Medical Record (EMR), and 3. Electronic Health Record (EHR). In a PHR, a patient can access, manage and share health information in a private, secure, and confidential environment [22]. An EMR is a longitudinal electronic record of patient health information generated by one or more encounters in a care delivery setting [23]. An EHR, finally, is a repository of patient data in digital form, stored and exchanged securely, and accessible by multiple authorized users. It contains retrospective, concurrent, and prospective information and its primary purpose is to support continuing, efficient and quality integrated health care [24]. As the goal of the shared dataset in Fig.5 is to support data exchange among different parties, the shared dataset can be seen as an EHR.

The services in the Presentation services level are user interfaces. These interfaces allow end-users to interact with the connected eHealth functionalities. User interfaces in the Presentation services level can be user interface services delivered by applications, e.g. the user interface of the EMR system to interact with connected eHealth functionalities.

Connections with systems outside the primary care organization take place through external connections. In case of other healthcare organizations, secured national, regional or local networks are available. If possible, these networks should be used to connect with the primary healthcare organization for privacy and security reasons. Here, it is preferable to apply HL7 as communication standard for health data exchange, as this is the most commonly used international communication standard in healthcare [19]. Several HL7 versions exist, and the most applicable HL7 version for a given situation will depend on existing agreements between the primary care center and the external organization. Furthermore, it should be possible to connect with external web-based eHealth applications, like quantified-self applications used by the patient [25]. In case of external web-based eHealth applications, HL7 FHIR is the preferred standard for data exchange as this HL7 Standard uses a RESTful approach [26]. In all cases of external connections, it is preferable to use SNOMED CT and ICD in the mapping of a legacy terminology into a standard terminology and as health terminologies to ensure meaningful data exchange [3,27].

D. Application of the reference architecture in a case

The reference architecture was applied in a theoretical case. In this case, the care path to optimize the referral of low back pain (LBP) was translated into an interoperable eHealth infrastructure that could technically support the HIE during this process. At first, we described the total process of the (self-) referral and healthcare process of patients with LBP as seen by its stakeholders. In our case, relevant stakeholders were general practitioners (GPs), physiotherapists, medical assistants, and patients. Secondly, we identified the functionalities that had to be delivered by (web-based) eHealth applications. These functionalities were:

1. *Clinical decision support (CDS) on triage:* To select relevant

healthcare at a specific moment, which will be GP, physiotherapist, or self-care when the LBP exists less than 2 weeks.

2. *Training:* To provide information on how to cope with LBP and on how to perform training exercises that could help to reduce the LBP.
3. *Informing:* To provide the next healthcare professional with relevant information about the patient with low back pain in case of further referral within primary care (GP-> Physio or Physio ->GP) or outside primary care (GP -> 2nd or 3th care).

In case of further referral, the forwarding healthcare professional should provide the next healthcare professional with relevant health information about the patient. This information interchange had to be supported by HL7; HL7 CDA in case of further referral within primary care, and HL7 V2 in case of further referral outside primary care. The shared information was represented by data items described by SNOMED CT codes to provide the exact clinical meaning for an item to enable meaning-based retrieval of the data [18]. These codes were used to set up the data model for data storage in the shared data set.

Finally, we identified the eHealth applications that had to be part of the interoperable eHealth infrastructure. In this case, applications to be involved were:

- An online clinical decision support system (CDSS) for self-referral of patients with low back pain (Online CDSS triage);
- An online system for providing information on how to cope with the low back pain and to provide personalized exercises for training (Online training system);
- The EMR system of the general practitioner (EMR system);
- The EMR system of the physiotherapist (EMR system);
- The EMR system of the 2nd or 3rd care specialist, in case of further referral outside primary care (EMR system);

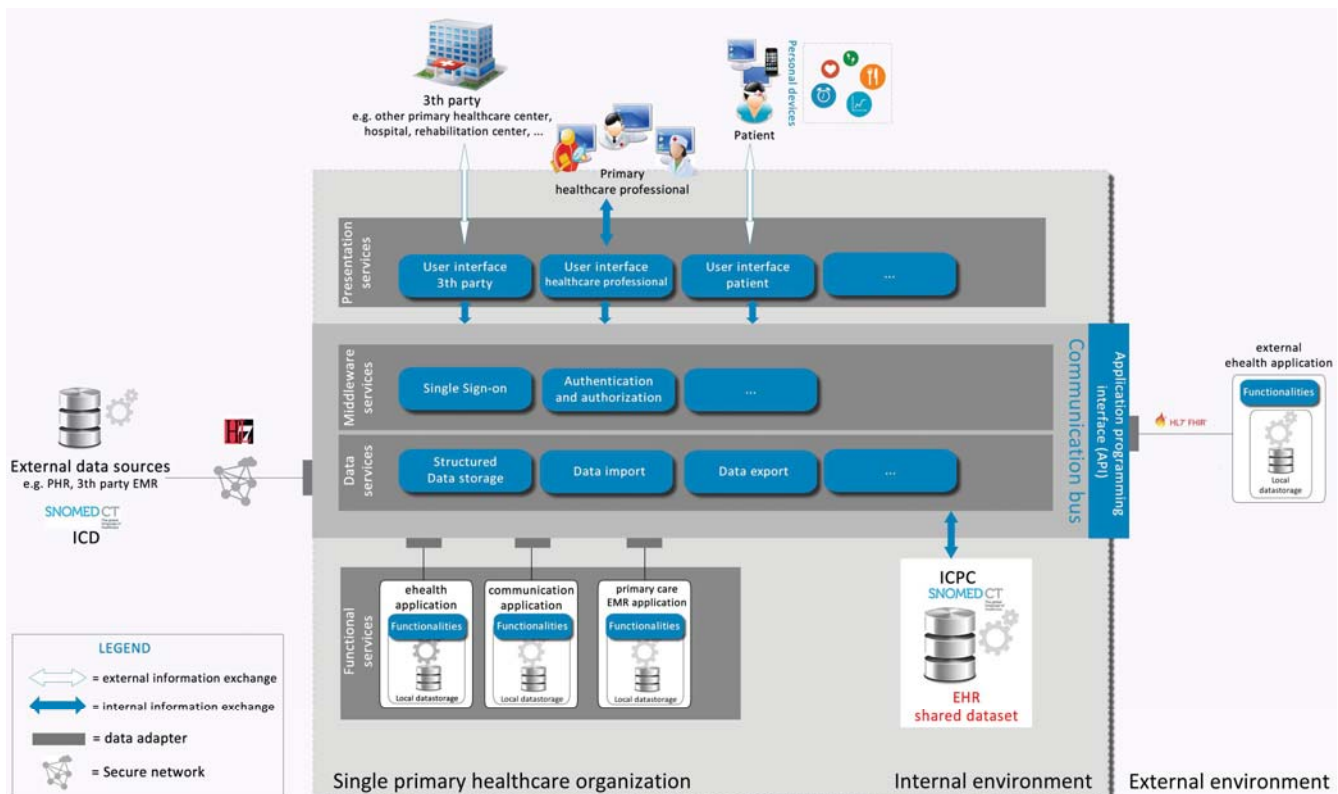


Fig. 5. Interoperable eHealth reference architecture for primary care. PHR stands for Patient Health Record, EMR for Electonical Medical Record, and EHR for Electronical Health Record.

E. Evaluation study

The interoperable eHealth reference architecture and its application were evaluated by IT health information experts to determine whether the reference architecture can be used in real practice to accelerate the development of interoperable infrastructures in primary care.

a) Participant and SME characteristics

Eight Dutch IT health information experts were interviewed. Most of were information analyst (75%), and had general knowledge on HL7 (63%) and SNOMED CT (50%). Seven interviewees (n=7) were employed by SMEs. None of them worked at the same SME. The number applications made by these SMEs varied from 1 to more than 10. Main functionalities of the developed applications were integrated care systems and online coaches - e.g. for COPD and Diabetes -, tele-rehabilitation, telemedicine, and clinical decision support. Most applications were focused to increase the self-management of patients. In case their technology was interoperable with other systems, custom-made solutions were used mostly (57%). In this, communication and terminology standards were only used when wished and agreed upon by the customer. During the interviews, an interesting quote on interoperability was:

“Interoperability with other systems is limited and not structured according to a standard yet. This is also because the other parties to connect to are not ready. So it is a chicken-egg problem. Nevertheless, we do offer a local solution through an API according to a REST methodology.”

It was also interesting to see that only one SME used SNOMED as terminology coding system. This participant mentioned the following: *“If the code is found in SNOMED, it will be the code used internally, but there is not always a SNOMED code possible because SNOMED is not complete. LOINC is used as code system in the data exchange with laboratories, because this was mutually agreed. NHG (=Dutch College of General Practitioners) codes are also used, especially when connecting with GP information systems, but also because these codes are received from the laboratories. In that respect SNOMED is still not very much in use in the exchange of health data.”* Another participant mentioned the following about SNOMED: *“The reference architecture mentions SNOMED, however the NHG prefers the usage of things they already have and do not see the need for new things.”*

b) Evaluation of the reference architecture

The analysis resulted into the following main themes: 1. Readability, 2. Completeness, 3. Financial feasibility, 4. Barriers to use the reference architecture, and 6. Positive points of the reference architecture. *Readability*: For most participants (63%), the interoperable eHealth reference architecture became clear after additional explanation. *Completeness*: Half of the participants missed some elements and standards. Missing elements were a service for user management and a service for customizing the communication bus settings. These services should be added in the Middleware layer. Missing standards were EDIFACT and XDS for document sharing, and NHG (lab) codes. *Financial feasibility*: Half of the participants mentioned that using the reference architecture is not financially feasible, because distinct primary healthcare organizations have limited financial options. Therefore, building a local interoperable eHealth infrastructure within a distinct primary care center is not interesting for business from the viewpoint of SMEs. *Barriers*: The lack of financial feasibility is one barrier to use the reference architecture (50%). Another barrier seen by participants was the gap between theory and practice, caused by reasons related to cost aspects, time pressure, and unwillingness of different parties to cooperate. Next to this, no consensus between stakeholders and a lack of vision of stakeholders were mentioned (63%) as obstacles in the achievement interoperable eHealth in primary care. *Positive points*: The participants indicated as positive that the reference architecture

forces structural thinking about the topic and it forces the usage of health communication and terminology standards. Another aspect seen as positive was the focus on specific roles of the applications, and the way data are shared across applications via the communication bus and the shared data set. Furthermore, participants see the reference architecture as a good base for further discussion on achieving interoperable eHealth in primary care.

IV. DISCUSSION

This paper describes a study that has resulted in an interoperable eHealth reference architecture for primary care (Fig.5). As such, this work makes a substantial contribution to the field, as, until now, research on interoperable eHealth was mainly focused on secondary care (hospitals). The reference architecture described in this paper aims to support IT specialists to set up interoperable eHealth infrastructures within a primary care organization in close cooperation with stakeholders. The aim is that this will result in a more sustainable IT infrastructure than the custom-made data exchange solutions that we found are omnipresent during the interviews during the evaluation study with IT health experts.

The reference architecture describes how a healthcare process can be translated into an interoperable eHealth infrastructure using a service-oriented approach and a communication bus that connects distributed applications. This approach is similar to service bus architectures that have been around in recent decades for hospital environments [28] but not in primary care. The results of the evaluation study show that the reference architecture can be used in theory, but that still additional conditions are needed before interoperable eHealth in primary care actually can be achieved. These conditions are:

1. consensus between different stakeholders is essential in setting up an interoperable eHealth infrastructure,
2. communication and terminology standards to be used should be available, complete, usable and up-to-date,
3. the profits for business should be clear when involving SMEs in setting up interoperable eHealth infrastructures,
4. most primary healthcare organizations have limited financial options and therefore, the possibility to access to an own customized environment within an (inter)national interoperable eHealth infrastructure would be beneficial to achieve interoperable eHealth within these organizations,
5. such a (inter)national interoperable eHealth infrastructure should be managed by a neutral party.

The reference architecture advises the usage of a shared data set for health information exchange (HIE). Next to this, the connected distributed eHealth applications can also have their own local data storage. One could say that it would be more efficient to store all data centralized in the shared dataset, because than all data are available for all services in the infrastructure and data do not have redundantly be stored. However, applications provide quick access to data and are available independently of a working internet connection when using local storages [29]. Next to this, central data storage also has security issues [29] that will become much more complex when storing all collected data into the shared dataset. Furthermore, the data model of the central dataset will become much more complex and much more difficult to be agreed upon on by all stakeholders. Therefore, the interoperable eHealth reference architecture described in this paper contains centralized as well as local data storages. In all cases, data have to be managed on accuracy, completeness, granularity, timeliness, and interoperability [30].

The interoperable eHealth reference architecture advises the usage of terminology standards in data storage. This is, because a standardized health record serves as a bridge between different systems. Although the evaluation study brought forward that the usage of national standards instead of international standards can be forced by national

organizations – in the interviews the Dutch College of General Practitioners (NHG) – the recommendation of the reference architecture is to prefer international standards. In this way, designed infrastructures will become open to national as well as international parties when needed [19,31,32].

The design of the reference architecture was based on experiences on building interoperable eHealth infrastructures in real practice by using the input of the SME working sessions. In this way, issues that hinder the development of interoperable infrastructures in healthcare could be taken into account. Next to this, the reference architecture forces structured thinking on eHealth interoperability by its stakeholders and was identified as a good starting point for further discussion on the achievement of interoperable eHealth in primary care.

A. Study limitations

Consensus had to be made in the level of detail of the interoperable eHealth reference architecture. The reference architecture could be supplemented with more detail by also using the legal and regulatory, policy, and IT infrastructure levels of the refined eHealth European Interoperability Framework (ReEIF) [12]. However, this study was focused on how to translate a primary healthcare process into an interoperable eHealth infrastructure that can technically support the HIE within this healthcare process. Next to this, a balance was needed between the level of detail and complexity, as increased complexity would make the reference architecture unreadable. However, this does not mean that legal and regulatory and policy issues should not be taken into account when realizing an interoperable eHealth infrastructure.

B. Future work

This paper provides directions to setup interoperable infrastructures in primary care with the help of a reference architecture. The next step is to elaborate this reference architecture into further detail by the development and evaluation of real eHealth infrastructures based on this reference architecture.

V. CONCLUSIONS

This paper describes the design of an interoperable eHealth reference architecture for primary care to translate primary healthcare processes into interoperable eHealth infrastructures. However, additional conditions are still needed before interoperable eHealth in primary care can actually be achieved i.e. (1) consensus between different stakeholders, (2) usage of available, complete, usable and up-to-date standards, and (3) clear profits for business for SMEs when setting up interoperable eHealth infrastructures. Beneficial will be (4) the availability of an (inter)national interoperable eHealth infrastructure that is (5) managed by a neutral party.

REFERENCES

- [1] Eysenbach G. What is e-health? *Journal of medical Internet research*. 2001;3(2):p.e20.
- [2] van Velsen L, Oude Nijeweme - d'Hollosy W, Hermens H. eLabEL: living labs for implementation and evaluation of integrated technology in primary care. In *Proceedings of the 8th Int. Conference on Pervasive Computing Technologies for Healthcare. ICST; 2014, May. p. 256-7.*
- [3] Lewis J, Ray P, Liaw ST. Recent Worldwide Developments in eHealth and mHealth to more Effectively Manage Cancer and other Chronic Diseases–A Systematic Review. *IMIA Yearbook; 2016. p. 93-108.*
- [4] IEEE Std 610.12.-1990, IEEE Standard Glossary of Software Engineering Terminology.
- [5] Hersh WR, Totten AM, Eden KB, Devine B, Gorman P, Kassakian SZ, Woods SS, Daeges M, Pappas M, McDonagh MS. Outcomes from health information exchange: systematic review and future research needs. *JMIR medical informatics*. 2015;3(4).
- [6] Eden KB, Totten AM, Kassakian SZ, Gorman PN, McDonagh MS., Devine B, Pappas M, Daeges M, Woods S, Hersh WR. Barriers and

- facilitators to exchanging health information: a systematic review. *International journal of medical informatics*. 2016;88:44-51.
- [7] Iroju O, Soriyan A, Gambo I, Olaleke J. Interoperability in healthcare: benefits, challenges and resolutions. *International Journal of Innovation and Applied Studies*. 2013;3(1):262-70.
- [8] HIMMS. Interoperability & Standards. <http://www.himms.org/library/interoperability-standards>, Accessed 18 May 2018.
- [9] Antilope. Advancing eHealth Interoperability. <https://www.antilope-project.eu/front/index.html>, Accessed 18 May,2018
- [10] Siegel EL, Channin DS. Integrating the Healthcare Enterprise: a primer: part 1. Introduction. *Radiographics*. 2001 Sep;21(5):1339-41
- [11] eStandards: eHealth Standards and Profiles in Action for Europe and Beyond. <http://www.estandards-project.eu/index.cfm/about/>, Accessed 18 May,2018
- [12] eHealth Network. Refined eHealth European Interoperability Framework, Document,http://ec.europa.eu/health/ehealth/docs/ev_20151123_co03_en.pdf, Brussels, 23 November 2015.
- [13] Oude Nijeweme-d'Hollosy W, van Velsen LS, Soer R, Hermens HJ. Design of a web-based clinical decision support system for guiding patients with low back pain to the best next step in primary healthcare. In *Proceedings BIOSTEC 2016;5:229-39.*
- [14] Oude Nijeweme-d'Hollosy W, van Velsen L, roothuis-Oudshoorn KGM, Soer R, Hermens H. Should I see a healthcare professional or can I perform self-care: self-referral decision support for patients with low back pain. In *proceeding IEEE International Conference on Healthcare Informatics (ICHI)*. 2016:495-503.
- [15] Gale NK, Heath G, Cameron E, Rashid S, Redwood S. Using the framework method for the analysis of qualitative data in multi-disciplinary health research. *BMC medical research methodology*. 2013;13(1):117.
- [16] ICPC-2. International Classification of Primary Care. Second edition. Oxford: Oxford University Press, 1998.
- [17] World Health organization (WHO). Classification of Diseases (ICD). <http://www.who.int/classifications/icd/en/>. Accessed 10 December 2017.
- [18] SNOMED. <http://www.snomed.org/snomed-ct>. Accessed 18 May 2018.
- [19] Health Level Seven (HL7). <http://www.hl7.org/>. Accessed 2 April 2018.
- [20] Hestbech H, Hansen SW, Schmidt TA. The quality of EDIFACT referrals from primary care to the emergency department. In *Scandinavian Journal of Trauma, Resuscitation and Emergency Medicine*. BioMed Central. 2013;21(S2):A46.
- [21] Oude Nijeweme-d'Hollosy W, van Velsen L, Huygens M, Hermens H. Requirements for and barriers towards interoperable eHealth technology in primary care. *IEEE internet computing*. 2015;19(4):10-9.
- [22] Tang PC, Ash JS, Bates DW, Overhage JM, Sands DZ. Personal health records: definitions, benefits, and strategies for overcoming barriers to adoption. *J Am Med Inform Assoc*. 2006;13 (2): 121–6.
- [23] Heart T, Ben-Assuli O, Shabtai I. A review of PHR, EMR and EHR integration: A more personalized healthcare and public health policy. *Health Policy and Technology*. 2016.
- [24] Häyrynen K, Saranto K, Nykänen P. Definition, structure, content, use and impacts of electronic health records: a review of the research literature. *International journal of medical informatics*. 2008;77(5):291-304.
- [25] Appelboom G, LoPresti M, Reginster JY, Connolly ES, Dumont EPL. The quantified patient: a patient participatory culture. 2014:2585-87.
- [26] Bender D, Sartipi K. HL7 FHIR: An Agile and RESTful approach to healthcare information exchange. In *proceedings IEEE 26th International Symposium on Computer-Based Medical Systems (CBMS)*. 2013:326-33.
- [27] Wade GG, Rosenbloom ST. Experiences mapping a legacy interface terminology to SNOMED CT. *BMC medical informatics and decision making*. 2008;8(1):S3.
- [28] Loya SR, Kawamoto K, Chatwin C, Huser V. Service oriented architecture for clinical decision support: a systematic review and future directions. *Journal of medical systems*. 2014 Dec 1;38(12):140.
- [29] Löhr H, Ahmad-Reza Si, Winandy M. Securing the e-health cloud. In *Proceedings of the 1st ACM International Health Informatics Symposium*. ACM. 2010:220-229.
- [30] Cremer OL, Bollen CW. Clinical data management. *Quality Management in Intensive Care: A Practical Guide*. 2016:103.
- [31] FHIR Foundation. Enabling health interoperability through FHIR. <https://www.hl7.org/fhir/>. Accessed 18 May.
- [32] Benson T, Grieve G. Principles of health interoperability: SNOMED CT, HL7 and FHIR. Springer. 2016.