Professional MBA
Entrepreneurship & Innovation

Clinical and economic assessment of digital health innovations in Austria - an ecosystem view

A Master's Thesis submitted for the degree of
"Master of Business Administration"

supervised by
Deepa Mani, PhD

Valéria Szijártó, MD, PhD

11831500

Vienna, 20.06.2020

Affidavit

I, **VALÉRIA SZIJÁRTÓ, MD, PHD**, hereby declare

1. that I am the sole author of the present Master's Thesis, "CLINICAL AND ECONOMIC ASSESSMENT OF DIGITAL HEALTH INNOVATIONS IN AUSTRIA - AN ECOSYSTEM VIEW", 104 pages, bound, and that I have not used any source or tool other than those referenced or any other illicit aid or tool, and
2. that I have not prior to this date submitted the topic of this Master's Thesis or parts of it in any form for assessment as an examination paper, either in Austria or abroad.

Vienna, 20.06.2020

_____
Signature

Preface

Adaptation and flexibility; two terms, that are often associated with entrepreneurship and were emphasized during the master program several times. I did not expect, that these terms will determine the work leading to this master thesis. But COVID-19 came and changed everything in the personal and professional life of billions, including my nicely planned route towards completing this thesis.

Extraordinary support becomes apparent in extraordinary times. I have no words to express my gratitude towards all those helping me completing this work. The two experts, who – even in times, like this - found the time and energy to share their knowledge and experience. Employees at FFG and FWF, for showing remarkable patience and attitude towards "theoretical" questions. My supervisor, Deepa Mani, for providing inspiring comments on the work. Fellow students and the program managers sending formatting guidelines, recommending good thesis examples or just keeping me motivated. My friends, for understanding, that social distancing was not only on the physical, but on every possible level. And my family, for their never-failing love and support. This thesis is dedicated to all of them.

Abstract

Digital health products are expected to disrupt healthcare by improving quality of care, efficiency and accessibility. The number of digital health products has grown rapidly, however there are just scarce examples of proven benefits of digital health solutions regarding their clinical outcome and cost effectiveness. Therefore, clinicians, regulatory bodies and insurance agencies often remain sceptical about new digital health innovations.

In this thesis I explore the possibility to validate digital health solutions in Austria and compare these possibilities to international practices.

First, a model of a digital health validation ecosystem was established based on the literature. To identify the elements of this model in Austria, literature search was performed, expert interviews were conducted and the publications on Austrian digital health clinical trials were reviewed. The challenges and barriers in the ecosystem were identified by expert interviews.

The Austrian digital health validation ecosystem is strengthened by the national digitalization strategy, the presence of an electronic health record system, numerous public funding opportunities, an accelerator program for digital health and the high digital literacy of the citizens. However, there are gaps in the infrastructure and in private financing opportunities supporting digital health validation. Furthermore, resistance of clinicians towards digital health creates a barrier for developers.

Based on international examples, the Austrian ecosystem could benefit from the development of real-world testbeds and from a national framework describing the necessary evidence for reimbursement. These elements could support the development of validated digital health solutions and position the country as a leader in digital health.

Contents

Table of figures

List of tables

List of abbreviations

ABM – Agent-based modelling

ADHA - Australian Digital Health Agency

AI – Artificial Intelligence

AIT – Austrian Institute of Technology GmbH

BVSHOE - Bundesverband Selbsthilfe Österreich (Federal Association of Self-Help Austria)

CBA - Cost benefit analysis

CCA - Cost consequence analysis

CEA - Cost effectiveness analysis

CMA - Cost minimization analysis

CMS - Centres for Medicare & Medicaid Services

CRO – Contact Research Organization

CUA - Cost utility analysis

DHI – digital health intervention

DVG - Digitale-Versorgung-Gesetz (Digital Health Service Act)

eHSG - eHealth Stakeholder Group

EIT – European Institute for Innovation & Technology

ELGA - elektronische Gesundheitsakte (Electronic Health Record)

EMA – European Medicines Agency

FDA – Food and Drug Administration

FFG – Österreichische Forschungsförderungsgesellschaft (Austrian Research Promotion Agency)

FTC - Federal Trade Commission

FWF - Fonds zur Förderung der wissenschaftlichen Forschung (Austrian Science Fund)

GDPR – General Data Protection Regulation

GmbH – Gesellschaft mit beschränkten Haftung (Limited Liability Company)

GÖG - Gesundheit Österreich GmbH (Austrian National Public Health Institute)

GP – general practitioner

HSC – Health System Challenge

HTA – Health Technology Assessment

ICT – Information and Communication Technology

ICT – information communication technology

IMDRF – International Medical Device Regulators Forum

ITU - International Telecommunication Union

LBI – Ludwig Boltzmann Institute

ML – Machine Learning

NHS – National Health Service

NICE - National Institute for Health and Care Excellence

ONC - Office of the National Coordinator for Health Information Technology

PMA - premarket approval application

QUALY – Quality-adjusted life years

RCT - Randomized Controlled Trial

RPM - Remote Patient Monitoring

SaMD - Software as a Medical Device

SME – Small and Medium-sized Enterprises

UCPD - Unfair Commercial Practices Directive

USP – unique selling point

VC – venture capital

WHO – World Health Organization

1. Introduction

1.1 Problem formulation

Digital health innovations have the potential to improve all domains of healthcare from prevention, through diagnosis till management and follow-up. Patients could benefit from increased access to and higher quality of care, while the system could gain on the increased efficiency (and potentially lower costs). All of these are particularly important when considering the aging population globally, the increased burden of chronic diseases on the healthcare system and the unequal accessibility of people to the latest, often most expensive care options. These promises have led to large investments into the sector: VC investment into digital health grew 1000-fold over the last 10 years (Mercom Capital Group, 2019).

However, most of these economic and clinical promises have not been demonstrated yet. Although the RAND Health Information Technology Project team estimated that an electronic medical record system could save $81 billion annually in the USA (Hillestad et al., 2005) and similarly, large savings were projected by the European Commission from the introduction of eHealth services (European Commission, 2012), these estimations remained unproven (Kellermann & Jones, 2013).

Similar to the lack of economic validation, only a few products were clinically tested (Safavi et al., 2019). This is particularly problematic, since many digital health products can be used without the oversight by medical professionals and are out of the scope of regulatory control (e.g. health apps). The use of low quality, unsafe or even harmful technologies can lead to stress, dissatisfaction, delay in accessing proper care and worsening of health condition, just to name a few (van Velthoven et al., 2018).

Since digital health products are at the interception of different technologies, they should be validated from several perspectives (technical, privacy, clinical, usability and economic) (Mathews et al., 2019). However, there is a lack of comprehensive knowledge as well as guidance on how to develop this body of evidence (Goldsack et al., 2020). While data protection authorities focus on privacy and data protection, health authorities on safety and efficacy, and insurance companies on the costs, creating a complex validation ecosystem (Ferretti et al., 2019). Countries try to lower this complexity in different ways, and those, managing it well will become attractive for innovators(Arntzen et al., 2019).

The increase in high quality and validated digital health products is seen as key to exploit the full potential of digital health (European Commission, 2012) and guide the industry from the trough of disillusionment to the plateau of productivity.

1.2 Objective

There are international examples on how countries or even regions try to address the problem of non-validated digital health products. There is also a growing evidence on validation methods, frameworks specific to digital health. In this thesis, I will focus on the clinical and economic aspect of digital health validation. I will explore the Austrian ecosystem to identify supportive factors and potential barriers of conducting clinical and economic validation. Additionally, I will try to identify international good practices lacking in Austria, which finding can guide the further development of the Austrian digital health ecosystem.

Therefore, I will try to answer the following research questions:

- Are there any examples on the clinical and/or economic assessments done by digital health companies in Austria?
- Which support do digital health companies get for the validation of their products from different players in the Austrian healthcare and innovation ecosystem?
- Are there any gaps in the ecosystem or any challenges faced by digital health companies when conducting clinical or economic validation?
- Are there any examples for supportive ecosystem elements internationally that could supplement the Austrian scenery?

1.3 Course of investigation

To answer these questions, I conducted literature search to explore requirements and good practices for clinical and economic validation. As a next step, I identified the elements of a digital health validation ecosystem based on the literature and placed them in an ecosystem model. For the analysis of the Austrian ecosystem, I identified the Austrian elements of this model from interviews with local experts, by conducting systematic review of published digital health clinical trials in Austria and finally by targeted literature search. Finally, international good-practices were selected from the literature overview to fill the gaps and

solve the challenges in the Austrian digital health validation ecosystem. The flowchart summarizing the course of investigation is in Figure 1.

Literature overview (Chapter 2)

• requirements on clinical and economic validation of digital health
• validation methods tailored to digital health, good practices

Model of the digital health validation ecosystem (Chapter 4)

• identification of the elements of a digital health validation ecosystem (literature analysis)

Elements of the Austrian digital health validation ecosystem (Chapter 5)

• Elements of digital health validation ecosystem in Austria (expert interviews, literature review, targeted literature search)
• Gaps and challenges in the Austrian ecosystem (expert interviews)

Good-practices to supplement the Austrian ecosystem (Chapter 6)

(expert interviews, literature analysis)

Figure 1 Course of investigation (own illustration)

2. Literature overview

2.1 Digital health: definitions and categories

There are several nomenclatures and definitions related to digital health technologies: eHealth, mHealth, digital health interventions to name a few.

According to the World Health Organization (WHO), eHealth is "the use of information and communications technology in support of health and health-related fields" and mHealth or mobile Health, (which is part of eHealth) is "the use of mobile wireless technologies for health" (World Health Organization, 2019b, p. ix). The same guideline provides the latest definition of digital health, as a "broad umbrella term encompassing eHealth (which includes mHealth), as well as emerging areas, such as the use of advanced computing sciences in 'big data', genomics and artificial intelligence"(World Health Organization, 2019b, p. ix). Additionally, the term "Information and Communication Technology" (ICT) represents eHealth, mHealth, telemedicine and telehealth. As summarized by Istepanian and AlAnzi, the relationship between the different terms may be depicted as shown in Figure 2 (Istepaniana & AlAnzi, 2020).
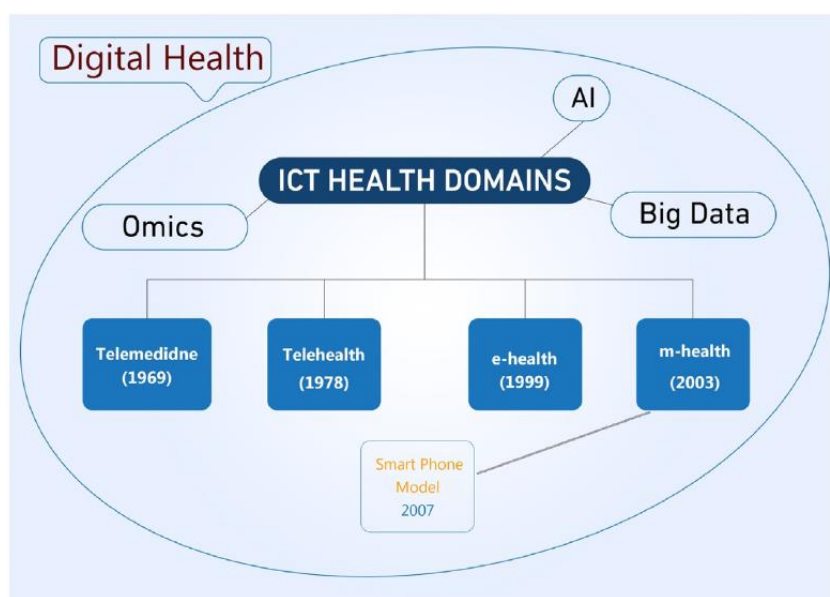
Figure 2 Relationship between the different domains and definitions related to digital health. Source: (Istepaniana & AlAnzi, 2020, p. 721)

A similar, but more informative definition was used by the Reimbursement Subgroup of the eHealth Stakeholder Group (eHSG) for digital health products and solutions: "Medical technologies and related services which utilise information and communication technologies (ICTs) across the whole range of functions that affect the health sector, that can improve

prevention, diagnosis, treatment, monitoring, prediction, prognosis and management of health" (eHSG SubGroup on Reimbursement, 2019, p. 6). In this thesis, the expressions eHealth and mHealth are used according to the latest definition of the WHO above, while for digital health, the comprehensive definition of the eHSG is followed.

Independent of the actual definition, digital health uses a broad range of technologies and covers diverse products and services. The breadth of digital health solutions was demonstrated by the IQVIA Institute in 2017 (Fig. 3)

Figure 3 Digital health tools. Source: (IQVIA Institute for Human Data Science, 2017, p. 3)

In 2018, the WHO promoted a comprehensive classification of digital health interventions to ensure the use of shared language (World Health Organization, 2018). This classification is based on the targeted users, and it groups the digital health interventions into four main categories: i) targeting clients (and caregivers of clients), ii) targeting healthcare providers, iii) interventions for health system and resource managers and iv) interventions for data services. The categories are further divided into subcategories and the guideline provides examples of linking the interventions with a Health System Challenge (HSC) to demonstrate the potential benefits of digital health. The complete categorization is provided Appendix 1.

From a regulatory perspective, the digital health products can be classified as "medical devices" or products outside of the category of medical devices. In the EU,

> "'medical device' means any instrument, apparatus, appliance, software, implant, reagent, material or other article intended by the manufacturer to be used, alone or in

combination, for human beings for one or more of the following specific medical purposes:

- diagnosis, prevention, monitoring, prediction, prognosis, treatment or alleviation of disease,
- diagnosis, monitoring, treatment, alleviation of, or compensation for, an injury or disability,
- investigation, replacement or modification of the anatomy or of a physiological or pathological process or state,
- providing information by means of in vitro examination of specimens derived from the human body, including organ, blood and tissue donations,

and which does not achieve its principal intended action by pharmacological, immunological or metabolic means, in or on the human body, but which may be assisted in its function by such means" (The European Parlament and the Council of the European Union, 2017, p. 15).

In the USA, the Federal Food, Drug and Cosmetic Act defines medical device similar to the European regulations:

"an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part, or accessory which is:

- recognized in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them,
- intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or
- intended to affect the structure or any function of the body of man or other animals,

and which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of its primary intended purposes. The term "device" does not include software functions excluded pursuant to section 520(o)." (Title 21 - FOOD AND DRUGS CHAPTER 9 - FEDERAL FOOD, DRUG, AND COSMETIC ACT SUBCHAPTER II - DEFINITIONS Sec. 321 - Definitions; Generally, 2006, p. 32).

The category Software as a Medical Device (SaMD) was introduced by the International Medical Device Regulators Forum as "software intended to be used for one or more medical

purposes that perform these purposes without being part of a hardware medical device" (IMDRF SaMD Working Group, 2013, p. 6).

Medical devices are further classified based on their risk profile into class I (very low risk), IIa, IIb and III (high risk) subclasses. These risk categories determine how manufacturers must comply with regulations and the level of evidence needed to demonstrate their value. The rules determining the risk class of a medical device are constantly changing to adapt to the appearance of new technologies, e.g. the Medical Device Regulation (MDR) of the EU coming into effect on May 26, 2021 results in the "up-classification" of most Class I medical software to Class IIa or higher (Gathani & Cowlishaw, 2019).

Based on the broad definitions of medical device, only a few types of digital health products are exempt from regulations. A recent policy by the FDA defines software and app categories, where the FDA does not enforce requirements (exercises enforcement discretion) and brings several examples to aid developers (U.S. Department of Health and Human Services, Food and Drug Administration, Center for Devices and Radiological Health, 2019). As an example, such exceptions are software and medical apps that either help patients self-manage their disease (but does not suggest treatment), or automate simple tasks for healthcare providers (Gordon et al., 2020). Often, these non-regulated products are direct-to-consumer products (sold directly to consumer, i.e. patients) surpassing the insurance companies, clinicians and traditional pharmaceutical companies while providing patients with direct access to health-related services (Cohen et al., 2020).

2.2 Industry overview and prospect

Digital technologies, particularly that of the mobile wireless technologies are gaining an increasing role and transforming many industries, including finance (banking), communication, music and movie industries. Due to the resistance of health care to fast changes, it is still lagging and there is still huge potential in the transformation by digitalization.

Mobile phones, smartphones represent large potential, due to their broad use even in low- and middle-income countries (World Health Organization Executive Board 142., 2017). The number of smartphone users worldwide were predicted to reach 3.2 billion by 2019, and further growth was projected with 3.8 billion users by 2021 (O'Dea, 2020), with the majority

of the users living in developing countries (World Bank, 2012). In healthcare, there is a continuous growth in the use of health mobile/tablet apps: while only 16% of healthcare consumers reported their use in 2014, nearly half of them did so in 2018 (48%) (Accenture, 2018).

Besides mobile phones, wearable devices represent large potential as well, during the period of 2014-2018, the number of patients using wearables more than tripled (2014: 9% vs 2018: 33%) (Accenture, 2018). According to the same report, healthcare consumers would be increasingly willing to use virtual care (through e.g. telemedicine) and see the benefit of artificial intelligence in healthcare (Accenture, 2018). These changes in healthcare consumers' perception pave the way for an even more digitalized healthcare system and open new possibilities for digital health companies.

Besides the increased appetite of consumers for digital health products and services, there are important advances in the regulations and reimbursement policies as well, promoting the digitalization of healthcare. For example, in the USA the Centres for Medicare & Medicaid Services (CMS.gov) introduced three new CPT codes for remote monitoring of physiologic parameters (remote patient monitoring or RPM) and for remote treatment management services (Validic, 2019). These codes establish the conditions for physicians and licensed medical professionals to get reimbursed for using digital health services. It is also seen as an important step toward value-based care initiatives and delivery.

Additionally, the U.S. Food and Drug Administration (FDA) established a certification process in its PreCert program for software as a medical device (FDA, 2019). This certification is different from the regular one, as it is based on the firm and the developers rather than their product. This way if the FDA finds a firm safe, the agency will not regulate each product of the firm individually but certify them all.

In Europe, the most recent example is the Digital Health Service Act (Digitale-Versorgung-Gesetz (DVG)) accepted in 2019 in Germany, which allows the reimbursement of low-risk digital health solutions for the diagnosis, monitoring or treatment of diseases or improvement of related healthcare provision by the statutory health insurance (Schickert, 2019).

Finally, the COVID-19 pandemic created a scene, where digital health technologies were implemented in an unprecedented pace and scale globally (Keesara et al., 2020; World Health Organization, 2020). Digital health was used as a response to the outbreak: to track people, aid risk assessment, help public health with surveillance methods. It was also used to mitigate

the effects of the pandemics by decreasing the need of in-person doctor visits with the help of telemedicine, remote monitoring and ePrescription (World Health Organization, 2020). Regulators responded with emergency authorisation of certain digital health services to aid the implementation (Keesara et al., 2020). Whether these responses to the crisis will lead to a broader strategic implementation of digital health and to the digital revolution of healthcare, it remains a question for now (Keesara et al., 2020).

Funding of digital health companies can be used as an indicator for the general interest in the sector. This investment has grown steadily for the last 10 years and digital health start-ups raised $10.6 billion in 2019 globally including VC funding, debt and public market funding: VCs covered the majority of the funding with $8.9 billion in2019 (Mercom Capital Group, 2019), from which $7.4 billion was invested in the USA (Sean, 2020). The numbers are the second largest – after 2018 - in the sector since 2010 (Fig. 4). According to RockHealth, the lower investment in 2019 vs 2018 shows moderations, rather than contraction (Sean, 2020).

Similar to other emerging industries, the Asian digital health market is rising and expected to have further great potential (MobiHealthNews, 2020).
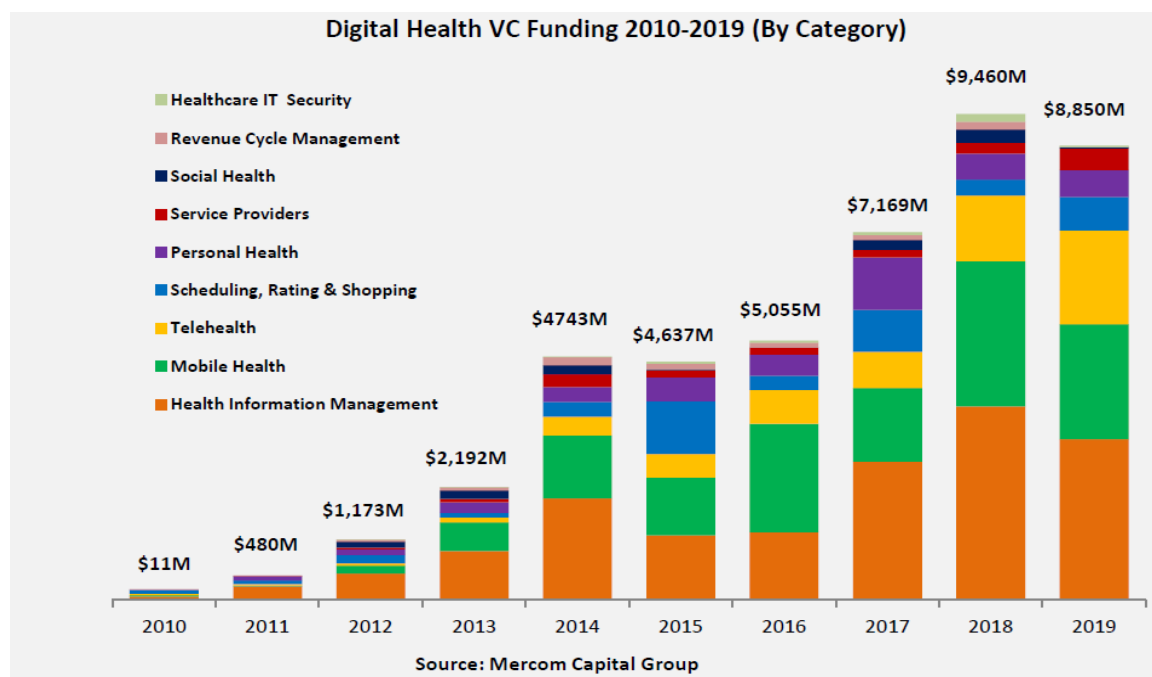
Figure 4 VC funding of digital health companies globally according to product categories. Source: (Sean, 2020)

Recently the most VC investment goes into products within the health information management category (mainly for data analytics and clinical decision support systems), mobile health technologies (including apps and wearable technologies) and telehealth (Mercom Capital Group, 2020).

Indicating the maturity of the industry, digital health investors are becoming specialized to the field, as 60% of the investors in 2019 were repeat investors (Sean, 2020).

2.3 Validation of digital health innovation

Definitions of verification and validation (analytical and clinical) as part of the quality management systems can be found in several standards and guidance documents (comprehensive summary is in Table 1 of (Goldsack et al., 2020)). In general, verification is the evaluation of performance during development in a test/model/simulation environment and it is typically done internally by developers (at the bench or in silico). In contrast, validation is the translation of verification results from bench to in vivo and is intended to ensure, that performance meets the user's (clinicians', patients', etc.) requirements.

Digital health is at the intersection of several distinct disciplines (life science, computer science, behavioural and engineering sciences), therefore the validation of the products and services are complex processes to cover all aspects. Additionally, they are often facing patients and clinicians/health care professionals simultaneously, while claiming benefits for even more stakeholders (e.g. insurance, public health, healthcare organizations). The value delivered by digital health to each stakeholder may be distinct, therefore dedicated studies might be needed to validate for the different stakeholders. To capture this complexity, Mathews et al. proposed that digital health innovations should be evaluated from four aspects (Fig. 5) (Mathews et al., 2019).
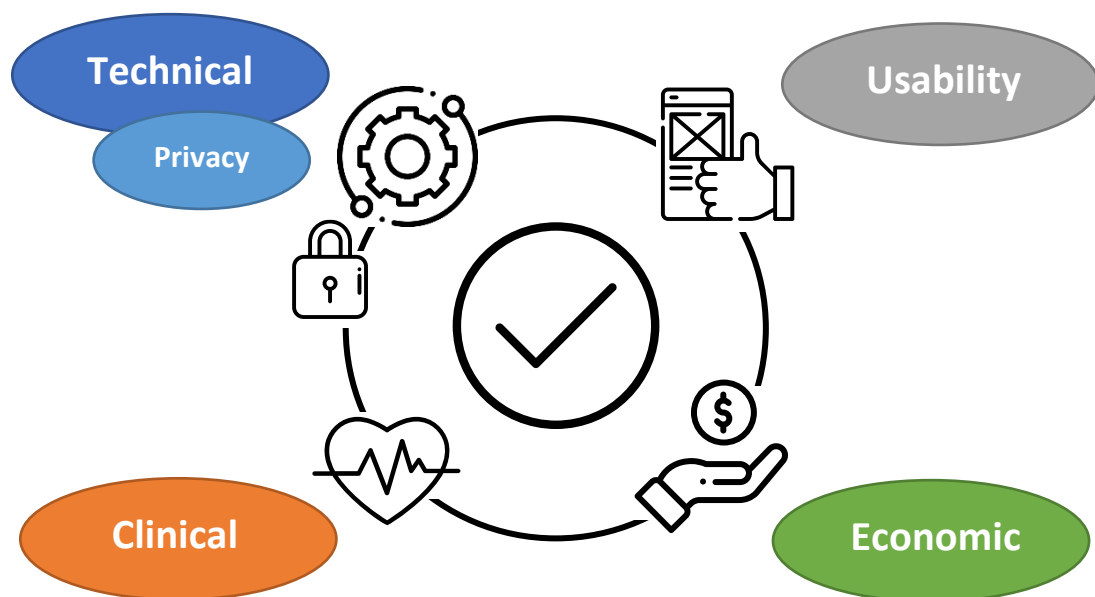
Figure 5 Elements of validation process for digital health products. Own illustration with free icons from https://www.flaticon.com/.

Technical validation would answer whether the product does what it is expected/promised to do. An important part of the technical validation is data security, privacy and confidentiality assessment. Clinical validation answers whether the product improves clinical outcome, how it fits into the existing clinical workflow and potentially compares it to existing solutions. Testing of usability focuses on the user experience; from the perspectives of both patients and operators (clinicians, doctors, nurses), while economic validation explores the cost-value ratio.

There is no formal requirement for such a comprehensive validation, different institutes regulate the different aspects and regulated requirements depend on geographic location (e.g. GDPR in EU), risk profile of the product (see risk classes) and health insurance systems (private versus public). Recently the Digital Health Scorecard system was proposed to aid the discrimination between different products and push "digital health companies to build impactful products that work for real patients, providers, and healthcare systems"(Mathews et al., 2019 p.7.). In the UK, the National Institute for Health and Care Excellence (NICE) developed an evidence standards framework for digital health technologies that provide standards to ensure the clinical and economic value of new solutions(National Institute for Health and Care Excellence, 2019). For this, a pragmatic, functional classification of digital health products was developed and connected this to the level of evidence needed to demonstrate their value (Fig. 6)(National Institute for Health and Care Excellence, 2019).
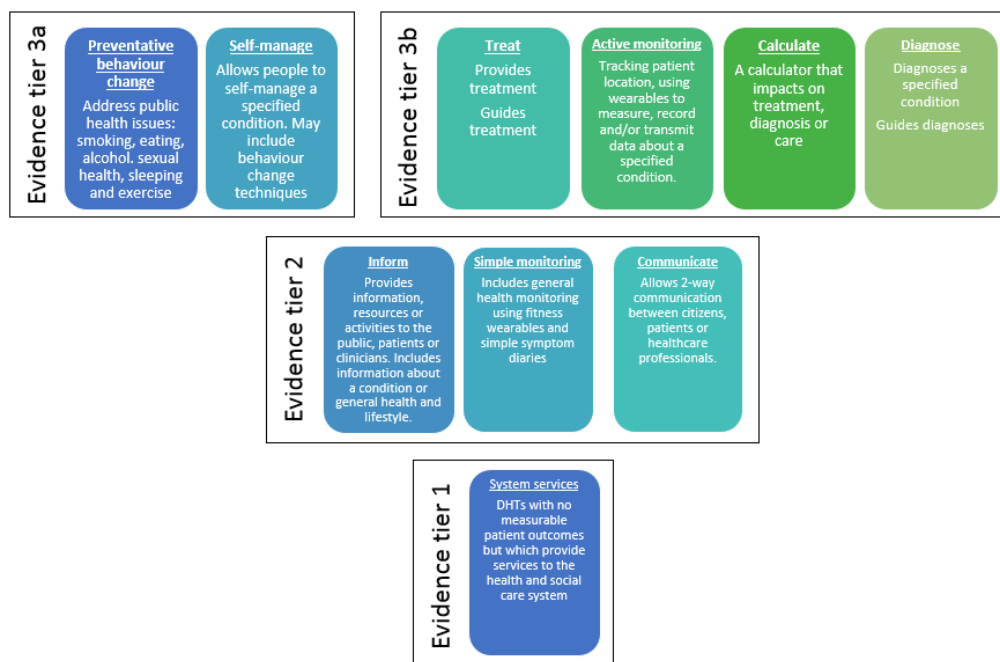
Figure 6 Evidence tiers defined by NICE. Source: (National Institute for Health and Care Excellence, 2019, p. 7)

For mHealth, the Working Group on mHealth assessment guidelines developed a comprehensive overview of existing guidelines for the assessment of mHealth products (Working Group on mHealth assessment guidelines, 2017). There is plan for a Working Group on AI/ML Clinical Evaluation by the ITU/WHO Focus Group on artificial intelligence for health (*Focus Group on "Artificial Intelligence for Health,"* n.d.; Wiegand et al., 2019). Further examples of guidelines developed for mHealth validation are in (Rowland et al., 2020).

Similar to the lack of accepted standards, there is no public source where the results of such broad assessments are collected and where the healthcare customers (patients, clinicians, etc.) could assess and compare the different digital health products. Various (mainly not-for-profit) organizations try to provide systematic information on digital health products or at least an overview of validated products (Cohen et al., 2020; Van Winkle et al., 2019). Additionally, there is a plethora of frameworks developed with the aim to aid the assessment of digital health products: a recent review identified 45 frameworks to assess health apps (none of them comprehensive enough for health technology assessment) (Moshi et al., 2018). Recently an interesting aspect of evaluation frameworks was identified. Kowatsch et al. reviewed 36 publication to consolidate the evaluation criteria published for digital health intervention (Kowatsch et al., 2019). Interestingly, the authors found that among the 331 evaluation criteria only 17 was related to effectiveness (defined as "the degree to which the DHI contributes to the enhancement of an individual's health behaviour/condition"(Kowatsch et al., 2019, p. 256)) and it was only the 8th in the ranking of evaluation criteria after ease of use, content quality, privacy and security, accountability, adherence, aesthetics and perceived benefit (Appendix 2). Even more interesting is their finding, that safety was the most neglected criterium, however one can argue, that it is strictly evaluated by regulatory agencies, therefore, other frameworks developed by the scientific community does not need to include this aspect.

The growing interest in (systematic) validation of digital health products is due to several factors:

a) **Increasing awareness on the limited resources in health care**

The current Coronavirus pandemic shed a clear light on the limited nature of health care resources and how the inappropriate use of these resources can lead to death of people. Allocation of (financial and human) resources must be appropriate according to the contribution of the technology to the health and well-being of the humanity.

While there is a consensus, that eHealth and digital health has large potential in enhancing health care efficiency (and consequently free up resources), this promise must be demonstrated. According to the consensus statement of the WHO Bellagio eHealth Evaluation Group, "To improve health and reduce health inequalities, rigorous evaluation of eHealth is necessary to generate evidence and promote the appropriate integration and use of technologies."(World Health Organization, 2019a p. i.).

Additionally, the allocation of private and public investment should not be inappropriately diverted from non-digital approaches to digital approaches due to a hype and a large, but unproven promise.

Value-based care model is expected to change the resource allocation in healthcare; this model promotes the increase of quality over the quantity of service provided to patients and reimburses health care providers based on quality metrics. CMS have introduced 7 value-based programs in the last decade[1]. While value-based care model can be a big catalyst for digital health innovations, it also puts pressure on innovators to focus on and demonstrate the improvement of specific quality metrics with their solutions.

b) **Overwhelming amount of new digital health products**

The number of available digital health solutions are growing rapidly. The number of health and fitness apps available in the Google Play and the Apple AppStore surpassed the 300,000 mark in 2017 with 40% of those apps focused on health condition management (IQVIA Institute for Human Data Science, 2017). The same report counted over 340 different consumer wearable devices (IQVIA Institute for Human Data Science, 2017). These numbers demonstrate that patients and operators are overwhelmed with the options and suggest, that product differentiation is becoming increasingly difficult for digital health innovators. An important and valuable differentiation strategy can be the (broad) validation of these products.

c) **Consumer expectation**

Clinicians vowed not to do harm; their main concern is likely about the risks that the use of digital health products may pose to patients' health. Therefore, the

---

[1] The actual value-based programs are described at https://www.cms.gov/Medicare/Quality-Initiatives-Patient-Assessment-Instruments/Value-Based-Programs/Value-Based-Programs (last accessed 02.05.2020)

demonstration of clinical safety and efficacy is essential for them to use these solutions. On the other hand, hospitals, as operators expect the demonstration of the easy integration of the solution into the workflow and a favourable cost-benefit ratio compared to gold standard methods. In general there is an increasing awareness on the protection of sensitive data from both the operators and the patients side; on one hand the compliance with data protection rules is a legal requirement in certain geographic regions, on the other hand an even more stringent data protection is expected by users where health related data are involved (Vayena et al., 2018).

Below, I will provide further details on the clinical and economic validation of digital health products and on a special form of validation methods, the testbeds.

2.3.1. Clinical validation

In the classical drug and medical device clinical development, products go through 4 clinical phases. In phase 1 studies, safety and toxicity is tested in a small, usually healthy population. In phase 2 studies, the safety is tested in the target population (typically sick patients), and the behaviour of the drug/device in the body is monitored (e.g. administration, dosage, distribution). Phase 3 studies are usually randomized controlled trials (RCTs), where patients are randomly assigned to a group using the new drug/device or a group getting standard care (or alternative solutions as control). At the end of the study, the measured outcomes are compared between the two groups to find statistically significant differences. Phase 4 studies are post-marketing observational studies to monitor safety, costs and effectiveness on large scale.

The analogues of the classical staged clinical testing were proposed by NODE.Health to aid the clinical validation of digital health (Sheon et al., 2018). In summary, the equivalent of phase 1 study would involve a prototype, which is being tested to identify use cases, missing features. The analogue of a phase 2 study could involve large scale feasibility testing in end users to assess usability and indication of efficacy. The phase 3 equivalent study would focus on assessing efficacy of the solution in the target users and potential financial benefits of the usage. The analogue of the phase 4 study would be the actual implementation where the digital product would be further refined to increase adoption, integration and interoperability with existing solutions. An overview and comparison of classical and digital clinical testing phases is in Appendix 3.

Clinical validation of digital health can happen through different ways (Coly & Parry, 2017). On one hand, a classical randomized controlled trial (RCT) can be used. However, for complex health interventions, more innovative study designs can be used, like quasi-experimental designs or observational study design (also called natural experiment) (Coly & Parry, 2017; Jandoo, 2020). A special form of natural experiments is the testbed, which will be further discussed in Chapter 2.3.3. The comparison of the study methods is not scope of this thesis, the advantages and challenges of each design are summarized in (Coly & Parry, 2017).

Regulations by trade commissions prohibit deceptive acts including false or misleading claims about a product or services. In the US the Federal Trade Commission (FTC) strongly emphasizes the need for proven claims in advertisement in case of health-related products (Federal Trade Commission, n.d., 2013). The EU advertising standards are described in the Unfair Commercial Practices Directive (UCPD) and the Misleading and Comparative Advertising Directive (2006/114/EC) (Piotr Arak & Anna Wójcik, 2017). These general rules imply that any health-related claims of a digital health product should be proven.

Besides the advertisement regulations, specific regulations apply to digital health products belonging to the regulatory category of "medical device".

2.3.1.1. *Digital health products classified as medical devices*

In the US, the FDA requires a 510(k) application for medical device in risk category Class I or II and a premarket approval application (PMA) for Class III device (FDA, 2020a).

In the EU, according to the medical device directive (MDD) and the more recent medical device regulation (MDR), a medical device cannot be marketed without a CE mark. The difference between the EU regulation and other territories is that the CE mark is affixed to the product by its manufacturer based on a conformity assessment either performed by the manufacturer itself (in case of Class I medical devices as Declaration of Conformity) or by an organization appointed by the competent authorities to conduct such assessment ("notified body", in case of Class II-III devices). All liability regarding the product conformity ultimately lies with the manufacturer.

In both territories, product verification and validation of performance data are necessary to achieve the medical device certification (European Commission, 2016; FDA, 2020b). In most cases this means that clinical validation is needed, however the quality requirements of that validation may vary (Rowland et al., 2020).

In case of medical devices, the clinical evaluation is undertaken during the development of the product (premarket) and – as an ongoing process – throughout the life cycle of the product (post-market surveillance and reporting) (European Commission, 2016). If a highly similar product has been already validated for the same purpose, the developers can claim equivalence (or substantial equivalence). In this case, after demonstrating the clinical, technical (and maybe biological) equivalence, the clinical validation data generated for the alternative product can be used for the new product as well and no repeated testing is needed (Murray et al., 2016) (European Commission, 2016).

The regulatory landscape is continuously evolving as new technologies arise and pressure builds from all stakeholders for clear and realistic regulations. For specific cases, specific guidelines are developed to aid the design of clinical evaluation of digital health products. As an example, the IMDRF developed principles for the clinical evaluation of SaMD in 2017 to "establish a common and converged understanding of clinical evaluation and principles for demonstrating the safety, effectiveness and performance of SaMD"(IMDRF Software as a Medical Device Working Group, 2017, p. 7). The document proposes a systematic clinical evaluation process, where clinical validation is the last step (Fig. 7). It strongly emphasizes that the high level of connectivity in SaMD provides a unique opportunity to the developers to continuously monitor its safety and effectiveness and modify to achieve highest performance in real-world.
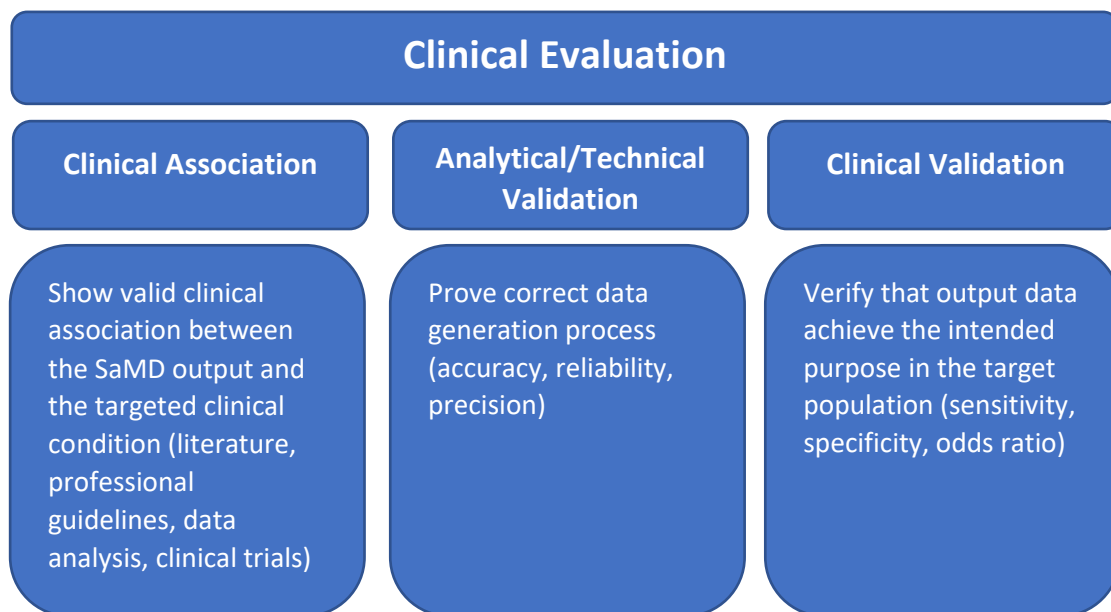
Figure 7 Comprehensive clinical evaluation of SaMD proposed by the IMDRF. Own illustration based on figure in (IMDRF Software as a Medical Device Working Group, 2017, p. 4)

While the regulatory landscape and requirements for clinical validation are changing periodically and may remain unclear for emerging technologies, both the FDA and the European Medicines Agency (EMA) promotes openness to allow successful interaction of developers with the agencies even at an early stage of development (Cerreta et al., 2020).

Besides the territorial regulatory agencies, the International Organization for Standardization (ISO) has several standards applicable for digital health products in the category of medical device: the standard on software for medical devices (IEC 62304:2006 "Medical device software—Software life cycle processes") and the main standards for medical devices (ISO 13485:2016 "Medical devices—Quality management systems—Requirements for regulatory purposes" and ISO 14971:2007 "Application of risk management to medical devices") (van Velthoven et al., 2018).

2.3.1.2.   *Digital health products outside of the category of medical devices*

Currently there is a low percentage of non-regulated digital health products (mainly health apps), which were tested in clinical setting and even in those cases, evidence tends to be of low quality (for an overview see (Gordon et al., 2020)). Similarly, a recent study focusing on the 20 top-funded US-based digital health company found that companies have yet failed to demonstrate value on outcome, cost or access to care (Safavi et al., 2019). On the other hand, there are growing safety, quality and ethical concerns about non-regulated digital health products (e.g. heart rhythm monitors, neurostimulation devices, and novel mental health tools, as cited in (Cohen et al., 2020 p. e164)). According to Cohen et al., "The paucity of published, high quality clinical data is perhaps the biggest contributor to the potential risk related to digital health companies" (Cohen et al., 2020 p. e174).

While clinical validation of non-medical devices is apparently still rare, it has potential advantages:

- **Differentiation:** separation of legit offerings from "snake oil" (Mathews et al., 2019) and using for marketing purpose to differentiate among the overwhelming number of products with this unique selling point (USP).

- **Creation of trust:** public trust is particularly important, if there is a need to build large-scale databases and customer consent in data sharing (Vayena et al., 2018)

- **Iterative improvement possibilities:** better integration into the healthcare system, higher efficacy, building dialog with clinicians, patients (potential to identify new opportunities, user innovation)

- **Accreditation:** several initiatives offer accreditation based on specific criteria (a representative collection of examples for such initiatives can be found in Table 1 of (Mathews et al., 2019)), clinical validation offers the possibility to get into a curated collection of "validated" products, e.g. Ranked Health Curated Health Apps and Devices collection[2] or the NHS Apps Library[3]

2.3.1.3.   Challenges of clinical validation of digital health products

Although in most cases clinical validation is a necessary step for bringing digital health products to the market and a meaningful validation process has several advantages (see above), there are major challenges with the planning and management of digital health clinical validation:

- **Clashes of culture:** fast-paced experimentation of digital companies vs. careful, systematic and complex testing of healthcare innovation

- **Products focusing on complex, typically chronic health conditions** (Murray et al., 2016)**:** long term follow-up and complex read-out methods might be needed

- **Prove the "obvious":** test and prove well-accepted dogmas (e.g. effect of regular sport on hypertension)

- **Lack of specialists with knowledge bridging both worlds** (Goldsack et al., 2020)

- **Need for multidisciplinary team**: for multidisciplinary products, as digital health, collaboration of specialists from different disciplines is needed. It might be necessary among product developers, and at regulatory agencies and investors evaluating digital health products.

- **Financial challenges** (Rowland et al., 2020)**:** typical IT start-up/SME budget vs. costly (long) clinical testing

- **Increased development risk:** compared to typical IT products, there is a much higher development risk, if clinical testing is needed

---

[2] http://www.rankedhealth.com/ last accessed 03.05.2020.
[3] https://www.nhs.uk/apps-library/ last accessed on 03.05.2020.

- **Continuously evolving standards and fragmented landscape of regulations:** as digital health products (particularly health apps) can be easily used globally, multiple guidelines and requirements, as well as different regulatory agencies make compliance difficult (Ferretti et al., 2019).

- **Fast changes of current and emergence of new technologies** (Murray et al., 2016)**:** companies must define the need and the extent of re-testing upgrades/updates. On the other hand, by the time of the completion of a lengthy clinical trial, technology may go through several updates to remain usable (see health apps staying compatible with smartphone operation systems)

- **Learning algorithms:** how to test continuously changing algorithm

- **Complex products:** products may fit several categories of regulations, therefore different rules could apply to different parts of a product

2.3.2. Economic validation and reimbursement

In the EU, ~77% of health care spending is on the delivery of care (eHSG SubGroup on Reimbursement, 2019). Digital health has large potential in eliminating or significantly decreasing the costs of delivery of care through e.g. distant monitoring. Additionally, digital health can manage the whole patient pathway through health care with higher efficiency, ultimately leading to decreased costs or at least higher value for same cost.

However, the European Commission highlighted in its eHealth Action Plan 2012-2020 (European Commission, 2012) that limited large-scale evidence on the cost-effectiveness of eHealth solutions and the inadequate/fragmented legal framework (particularly the lack of reimbursement schemes) are among the key barriers for the complete deployment of eHealth. This calls for urgent action by the developers (generation of economic evidence) as well as by policy makers, insurance companies and regulators (creating clear framework for reimbursement).

Economic validation of health products and services can happen through health technology assessment, defined as a "multidisciplinary process that uses explicit methods to determine the value of a health technology at different points in its lifecycle. The purpose is to inform decision-making in order to promote an equitable, efficient, and high-quality health system" (O'Rourke et al., 2020, p. 2).

Drummond et al defines economic evaluation in health care "as a comparative analysis of alternative courses of action in terms of both their costs and consequences" (M. E. Drummond, 2005).

These definitions imply, that for a proper economic evaluation, one has to analyse both the costs of the technology and the consequences (i.e. efficacy, benefits) of it.

For the efficacy/benefit testing, clinical trials can be used (see Chapter 2.3.1.).

Among costs, beyond the actual price of the intervention one needs to evaluate the cost consequences of all resources needed for the implementation, for the use and the follow-up, as well as potential costs of missed opportunities. In case of health technologies cost may appear from highly unexpected sources; a recent comment of Rahimi pointed out, that a cheaper solution (e.g. diagnostic solution) increase the access for broader population, which results in more frequent use of the solution and ultimately in a net rise in total expenditure (Rahimi, 2019). For economic evaluation, data on costs and value/benefit can derive from direct data collection (i.e. information from clinical trial) or from modelling.

The traditional economic evaluation methods developed for health care interventions have been already used for digital health as well, and their value - in certain cases - has been demonstrated (Bergmo, 2015). An overview of traditional economic evaluation methods is provided in Table 1. The evaluation can be a full evaluation, where two or more alternative solutions are compared or a partial evaluation, when no alternative solution is available for comparison.

Table 1 Overview of methods for full and partial economic evaluation

Full economic evaluation	Partial economic evaluation
Cost effectiveness analysis (CEA)	Costing analysis
Cost utility analysis (CUA)	Cost description analysis
Cost benefit analysis (CBA)	Cost outcome description analysis
Cost consequence analysis (CCA)	
Cost minimization analysis (CMA)	

The most commonly used method is CUA, where the outcome is measured as "healthy years" and valued as quality-adjusted life years (QALYs). QALYs are effective in comparing health gains of different solutions and they are considered the gold standard when deciding on reimbursement (Bergmo, 2015).

However, the traditional economic evaluation methods were developed for pharmaceutical products, medical devices or medical procedures and have severe limitations when used for digital health.

On one hand, digital health often generate value, which cannot be expressed as health benefit or QALY. For example, they often improve access to health care and information, reduce waiting time, or result in time saved by health care professionals (McNamee et al., 2016). In the current COVID-19 pandemic, a previously unrecognize or at least undervalued benefit of telemedicine was clearly demonstrated: the reduction in face-to-face interaction between patients and doctors may reduce the spread of the virus and limit the epidemic.

On the other hand, most digital health solutions can be considered complex interventions (McNamee et al., 2016). They are likely to change over time (updates, improvements), their outcome is complex (e.g. influencing the health of family members as well), they can be "socially contagious" (influencing the use of the intervention by others) and they have complex causal pathway (strong influence of setting on value, non-linear relationship between intervention input and output). For such complex digital health products, the use of complex evaluation methods was proposed (McNamee et al., 2016). Such an alternative study design is natural experiment (Craig et al., 2017), or a special form of that, called testbed (see Chapter 2.3.3.). In a natural experiment effectiveness and cost can be assessed in the real-world, where these complex interactions are present. Similar to the complex study design, complex modelling may be needed, which can be achieved through agent-based modelling (ABM) (J Chen, 2018).

LeFevre et al developed a flow-chart to guide selection of the right traditional evaluation method for mHealth, which can be used for other digital health solutions as well(LeFevre et al., 2017). Furthermore, they proposed a stage-based process for the economic evaluation and provide guidance on which steps are critical at the different stages of development (Fig. 8).
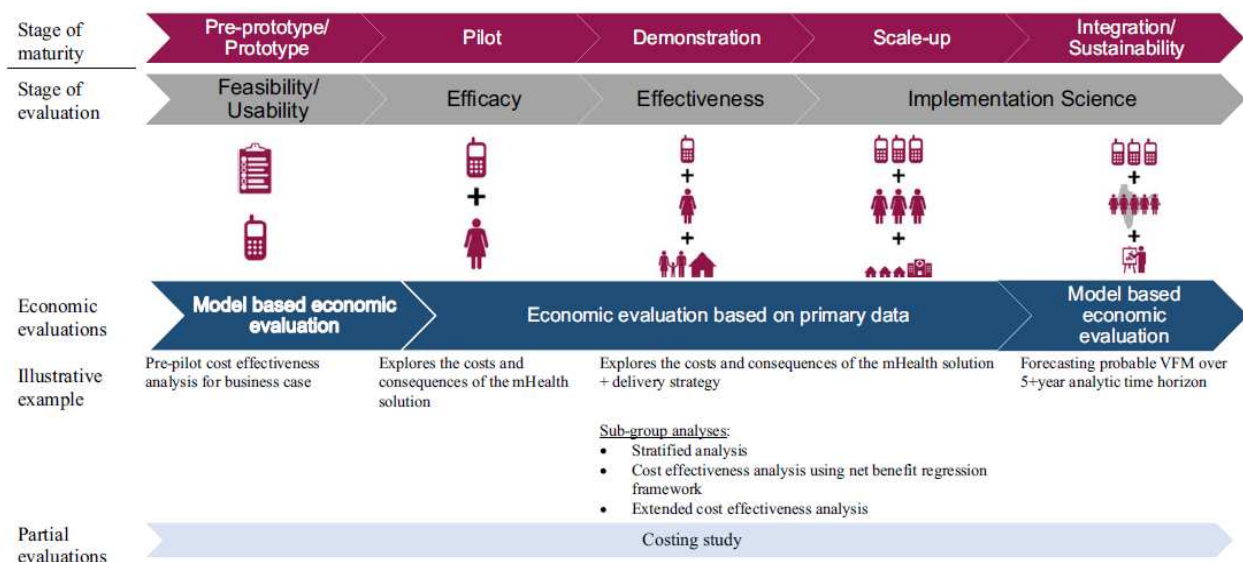
Figure 8 Economic evaluation methods recommended for the different stages of development. Source: (LeFevre et al., 2017, p. 13)

For a meaningful economic validation, developers need clear standards/guidelines and most importantly a clear path towards reimbursement. Reimbursement is seen as a key element for digital health to reach its full potential. In case of mobile apps, the lack of reimbursement was shown to lead to several harmful phenomena (Gordon et al., 2020). First, if developers need to charge patients, it can result in divide between patients who can afford the apps and those, who cannot. Second, to keep price low (or even provide the app for free) developers may rely on alternative revenue sources through advertisement and data mining, compromising privacy and performance. Third, the lack of reimbursement can discourage innovation and improvement of technologies.

The Reimbursement Subgroup of the eHSG developed an action plan to facilitate the implementation of clinically and economically useful digital health products and solutions through fair reimbursement in the EU (eHSG SubGroup on Reimbursement, 2019). The plan builds on 4 pillars.

1) Develop specific criteria to make appropriate reimbursement decisions for digital health products and solutions.

2) Setting up innovation investment funds for digital health products on an EU and on national level.

3) Develop European guidelines on how to generate relevant evidence for digital health products and solutions.

4) Develop instruments specific and fitting to digital health for the assessment and rewarding the value that digital health products and solutions provide for all stakeholders.

Examples of reimbursement of digital health products and solutions in EU countries are in Appendix 4.

2.3.3. Real-world testbed as a tool for digital health validation

In a broad sense, testbed (or test bed) is any device, facility or platform to test a theory, tool or new technology in development (*Testbed - Wikipedia*, n.d.). Nesta provides a specific definition for real-world testbeds as "Controlled or bounded environments for testing innovation in real-world, or close to real-world, conditions in the manner (or close to the manner) in which they will be used or operated." (Arntzen et al., 2019, p. 6). Unlike laboratories or simulated environment, real-world testbeds do not reduce the complexity of the environment but retain it to allow the (close to) real-world testing and adaptation.

In health care, the expression is used for an observational study, where real-world sites (e.g. whole cities or hospitals) are used for evaluating multiple 'combinatorial' innovations simultaneously (NHS England, 2015) "to evaluate both integration and impact within the existing working practices and systems of our health services" (CHF and The George Institute for Global Health, 2018, p. 5). Testbeds provide a platform for multiple stakeholders (innovators, health care professionals, patients, not-for-profit organization, industry partners) to work together at all stages from ideation until scale-up in a continuously evolving "living lab".

A similar concept exists as Living Lab for Healthcare and Independent Living (Robert Picard, 2017). Based on the definitions Living Labs are rather co-design spaces where innovators can incorporate user feedback early during development, while test beds are more upstream, where market-ready solutions can be tested, improved and scaled. As both concepts can be used for the evaluation of complex digital health products, in this thesis I will analyse the use of Living Labs along with test beds.

The relation of testbeds to other testing methods is shown in Figure 9.
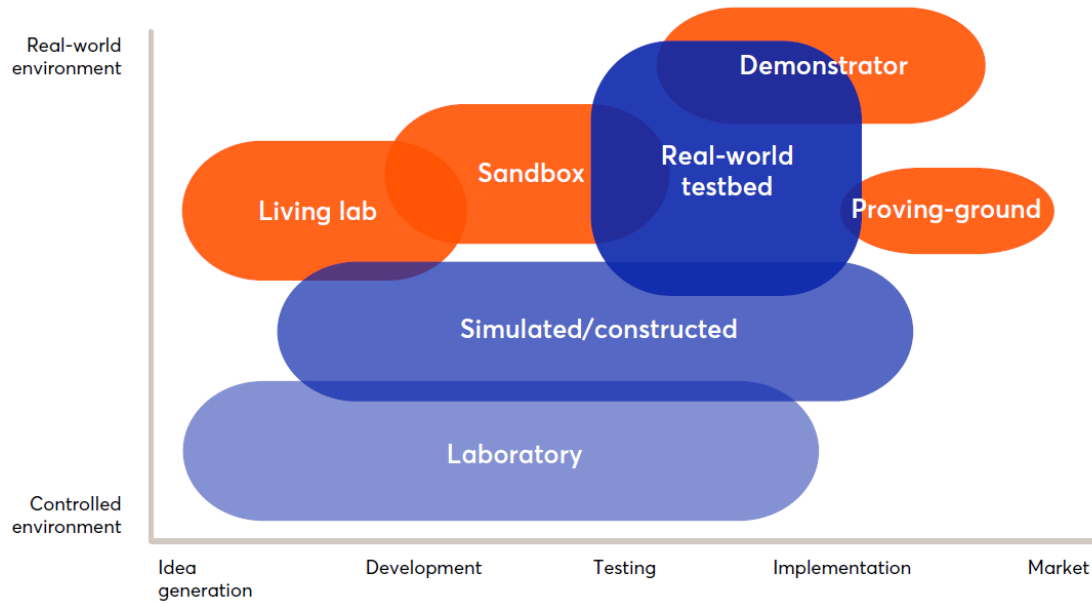
Figure 9 The relationship of the different testing methods based on the level of control in the environment and the technology readiness of tested innovations. Source: (Arntzen et al., 2019, p. 16)

The use of testbeds for innovation testing provide numerous benefits (Arntzen et al., 2019, p. 15):

- increase the access of innovators to testing, by providing special infrastructure with user groups, physical environment and special regulations

- allows the management of risk, experimentation also for technologies in complex ethical context

- they encourage investment into innovation, by allowing the real-world testing of innovation

Additionally, testbeds are highly valuable for the location, where they are established (e.g. cities, regions). As summarized by Arntzen et al., they help these places with:

- "Strengthening collaboration between the public sector, business, universities and other research-intensive organisations within a clear and structured framework, which is necessary for developing an innovation-driven growth ecosystem.

- Focusing and attracting investment and resources in innovation in specific technologies, sectors, and research areas where the local area is seeking to develop and strengthen competitive advantage.

- De-risking the process of developing new products and processes for firms, providing a safe space for them to iterate, fail, influence regulatory and policy change needed, and supporting them to develop to an investment-ready stage.

- Promoting an area as a good place to invest and develop knowledge-intensive functions, giving potential investors and existing firms in the area confidence there is a supportive and enlightened local innovation ecosystem.

- Improving the delivery of (or reducing the demand for) public services through creating the right policy, governance and regulatory systems.

- Maximising the economic potential and value of research done locally, and of other assets such as public sector data.

- Providing a framework for innovation policy that enables a more systemic approach to evaluation of effectiveness.

- Making better use of publicly available infrastructure." (Arntzen et al., 2019, p. 21)

Real-world testing, and consequently testbeds can be particularly useful in case of complex innovation, like most digital health products. As phrased by Nesta, "Innovation may work well in laboratory conditions, but they could fail or behave differently when introduced into the environments they are intended for – often complex, adaptive, real-world systems" (Arntzen et al., 2019, p. 8). Not surprising, that the three large scale testbed projects in healthcare are largely focused on evaluating the real-world impact of digital health (CHF and The George Institute for Global Health, 2018) (NHS England, 2015) (EIT Health, n.d.).

Interestingly, the recent developments in the German reimbursement scheme of digital health can be seen as a national scale test bed: registered low risk digital health solutions can be reimbursed by statutory health insurance, even without pre-existing evidence on a positive impact on health care provision and need to develop such evidence within 12 month of test period (Schickert et al., 2019).

Below the three large testbed programs are further analysed.

2.3.3.1.   National Health Service (NHS) England test bed programs

The NHS announced the wave 1 of its testbed projects in 2016 with 51 digital technologies over 4000 patients in 7 testbed programs (*NHS England Launch Second Phase of Test Bed Programme*, n.d.). The wave 2 was started in 2018 with 7 sites selected: 4 funded by the

government and 3 by the NHS England (NHS England, 2018b)(*NHS Accelerated Access Collaborative » Test Beds*, n.d.). These testbeds focus on long-term or chronic conditions and test tools and services promoting patient empowerment, early diagnosis, increased accessibility and more effective and efficient care. The overall aim is to generate "evidence to inform decisions about where and how the uptake of digital innovations at scale and pace across the health and care system is most likely to improve outcomes for patients and service users at a similar or lower cost" (NHS England, 2018a p. 1.). Importantly, these testbeds evaluate digital innovations not in isolation (and on top of existing care), but in combination with organizational changes to maximize benefits and minimize costs. As a multi-stakeholder tool, NHS testbeds bring together NHS, academia, industry, patient groups as well as charities. While the main aim of the NHS testbed program is to evaluate and validate new innovations, the first wave also provided key leanings about the method itself (NHS England, 2018a).

Here I summarize the key learnings of the wave 1 related to the whole testbed ecosystem (NHS England, 2018a):

- Importance of the early on-boarding of all parties, who are needed for the evaluation process (sponsors, designer/implementer of the project, people involved in the delivery of services, patient representatives and data and information governance specialist)

- Importance of identifying the purpose and goals of the individual stakeholders, build a consensus and manage expectations

- Set realistic budget and time requirement (e.g. realistic speed of patient recruitment)

- Set up data collection and sharing platforms/processes early (in the setting up phase) and keep communication channels open throughout the projects

- Define clear governance arrangement (including role of advisory board)

2.3.3.2. *Test bed systems in Australia*

The Australian Digital Health Agency (ADHA) started a $8.5 million testbed project in 2018 at 15 sites throughout Australia (*Digital Health Test Beds Program | NATIONAL DIGITAL HEALTH STRATEGY*, n.d.). These testbeds are part of the National Digital Health Strategy announced in 2017 that describes "digital health as key to improving service delivery and health outcomes (*Australia's National Digital Health Strategy | NATIONAL DIGITAL HEALTH STRATEGY*, n.d.)". The testbeds focus on chronic care, emergency care, end of life care and

residential aging as proposed by a recommendation of The George Institute for Global Health and the Consumers Health Forum of Australia (CHF and The George Institute for Global Health, 2018). Similar to the NHS England testbed project, the Australian system is also building a multi-stakeholder platform to assess "new digital-enabled models of care that are instigated and delivered cooperatively through sustainable and viable partnerships between industry, government and other organisations" (Biggs et al., 2019 p. s11.). Along with the testbeds, the ADHA developed a framework for the complex evaluation of e.g. the My Health Record system (patient record system) and emphasized the need for sophisticated methodology and measures for scaling up (Biggs et al., 2019).

2.3.3.3. *European Institute of Innovation and Technology (EIT) Health Accelerator program*

There is limited information available on the Living Labs and Test Beds Accelerator program of EIT Health (EIT Health, n.d.). The program seems to leverage an existing network of Living Labs (*Forum LLSA > Accueil*, n.d.) in Europe to provide an "open innovation ecosystems where stakeholders, including healthcare professionals and patients, cooperate on solutions to healthcare challenges". The program invites any European organization (start-up SME, innovators) with a market ready product/service on the field of MedTech, digital health or biotech and supports all stage of development from co-creation with users through validation until scale-up. Organizations can join with their own financial fund or can request funding from EIT. Additionally, EIT Health invites testbeds and living labs outside of its current network to join the program. The calls for funding requests were open until May 2020, more information on the projects might be available later this year.

2.3.3.4. *Challenges of real-world testbeds*

Based on the literature and the published experience on testbeds as tools for the evaluation of digital health, the following challenges were identified:

- **Timeframe:** the published digital health testbed projects run for a minimum of 2 years. During this time, short- and medium-term effects could be assessed and for long term effects interim results and projection were proposed to be used. On the other hand, digital health solutions typically change fast, therefore during a 2-year-period several

changes of the product or service might be used (especially in case of less matured technologies)(Shana Vijayan, 2019). Third, it opens a question, how the developing companies should survive this period financially: similar how pharma companies finance clinical testing (through investments, which significantly increase investment need and consequently price) or should they be reimbursed during the testing (similar to the German model).

- **Historicity or path dependence:** it seems critical, when the study is performed (public acceptability or attitude towards technology, disease, status may change in time e.g. drastic change in attitude towards smoking/obesity in the USA) (McNamee et al., 2016)

- **Reproducibility:** from a scientific point of view, reproducibility of real-world results is very low (Craig et al., 2017)

- **Cost** (NHS England, 2018a)

- **Effect of unobserved variables:** in such a complex system, one cannot rule out the effect of variables, which were not followed (observed) during the experiment. Therefore, very thorough planning is needed to define all measured variables upfront and complex measurement is needed (McNamee et al., 2016)

- **Multi-stakeholder team:** the advantage of the real-world experiment is, that a broad set of stakeholders can participate at all stages of the project. This advantage can bring along the challenge of managing the often-diverting goals and expectations of the stakeholders (NHS England, 2018a).

- **Project management difficulties:** beyond the challenge of managing the various stakeholders, project management may face further difficulties, as observed in the wave 1 of the NHS testbed systems: among the important learnings, it was mentioned, that i) clinicians buy-in is key for a successful implementation, ii) too enhance patient recruitment, new strategies had to be tested and implemented, iii) high flexibility was needed especially due to the iterative changes of tested technologies (NHS England, 2018a)

- **Use of statistical methods:** in test beds there is high interaction between patients in a particular cluster (social group, friends), that can lead to correlation between the

results of those patients. Therefore, statistical methods insensitive to correlation are needed (Sanson-Fisher et al., 2014)

- **Ethical issues:** it is essential to clarify, if consent is needed from participant, as the range of affected individuals is much broader and arranging the consent can take longer (NHS England, 2018a).

- **Need for prior validation:** products and services evaluated in testbeds need some validation a-priory to be included (McNamee et al., 2016)

- **Data collection, analysis and security**: these were mentioned as key in all cases (NHS England, 2018a)(CHF and The George Institute for Global Health, 2018)

- **Top level commitment:** need for national leadership, strong top-level commitment from the state/sponsor is important (NHS England, 2018a)

- **Need for pre-existing high-quality data** (surveys, databases) (NHS England, 2018a)

- **Need for digital literacy** (Topol Review, 2019): if the level of literacy needed for the maximum exploitation of the technology is not available, technical training must be incorporated into the project (prolongation of timelines, increased costs). On the other hand, once a high level of digital literacy is achieved in the test bed, it can be used for further projects and market the testbed community based on the existence of the testbed (Arntzen et al., 2019).

2.4. Digital health and eHealth in Austria

In 2019 a country health profile was published about Austria (OECD/European Observatory on Health Systems and Policies, 2019). According to this report, life expectancy at birth is slightly above the EU average (81.7 years vs. 80.9 years in 2017), however the healthy life years at birth is significantly lower, than the EU average (57 years free of disability or disease versus 64 years in the EU). While cancer death was reported to decrease since 2000, mortality due to diabetes has strongly increased and heart diseases were still the main cause of death. These numbers suggest an increase prevalence and effect of chronic diseases on health. At the same time, health spending in Austria was 10.4% of the GDP in 2017 (3rd highest in the EU). The outlooks for health care in Austria emphasize the population ageing putting pressure on health care expenditure and particularly on long-term care.

The latest survey by the WHO on eHealth was performed in 2015 to assess the use of eHealth in support of universal health coverage globally (WHO Global Observatory for eHealth & World Health Organization, 2016). This book provides a snapshot from 2015 about the use of telehealth, mHealth, eLearning, electronic health record system and the strategic use of ICT to increase health care efficiency (including social media and big data) in 125 countries. While much has changed in eHealth since 2015, importantly the electronic health record system was already better developed compared to other countries and the country ranked 21th in the ICT Development Index.

A report about the European eHealth scenery in 2016 showed a different picture of the country (Piotr Arak & Anna Wójcik, 2017): a summary measure in availability of online appointment booking, e-Prescription status, 24/7 healthcare info service availability, usage of online appointments and usage of ePrescriptions by GPs ranked Austria 29th among 37 European countries (Fig. 10).
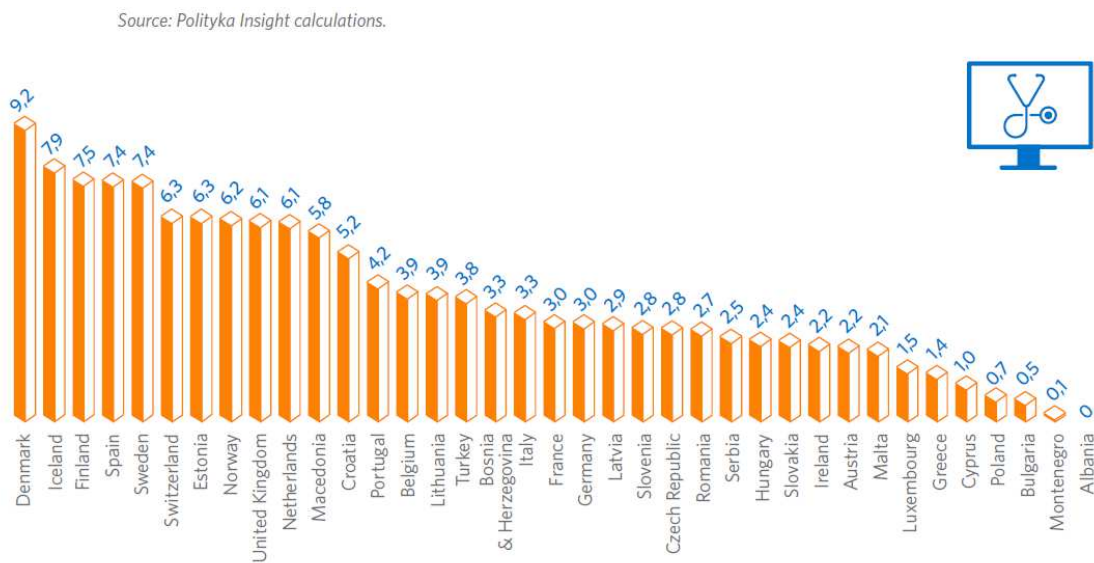
Figure 10 eHealth index of 37 European countries in 2016. Source: (Piotr Arak & Anna Wójcik, 2017, p. 11))

The latest international benchmarking study that included and analysed the Austrian healthcare digitalization strategy was carried out in 2018 (Rainer Thiel et al., 2018). The study established a Digital Health Index based on 34 indicators on three levels: i) the level of policy activity, ii) the level of maturity and the state of technical implementation, and iii) the level of actual use of digital health technologies, entailing the exchange of data (Fig. 11).
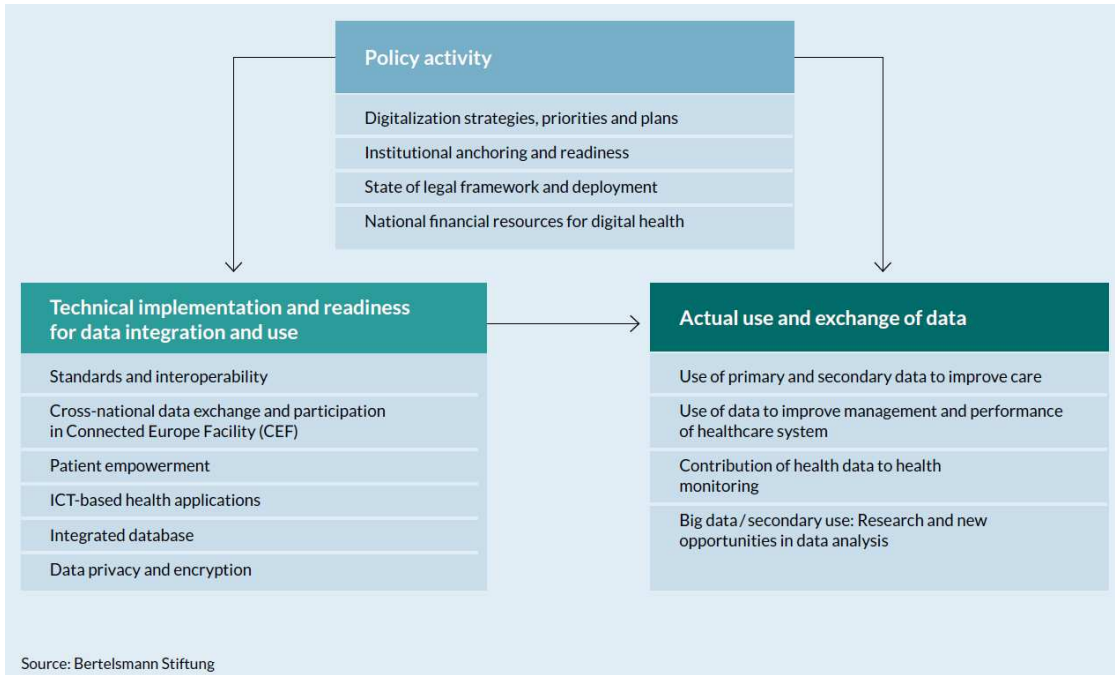
Figure 11 Levels of the Digital Health Index developed by the Bertelsmann Stiftung. Source: (Rainer Thiel et al., 2018, p. 30)

In this analysis, Austria ranked 10th among the 17 countries examined: the level of policy activities being the strongest, followed by technical readiness and the actual use of data (Fig. 12).
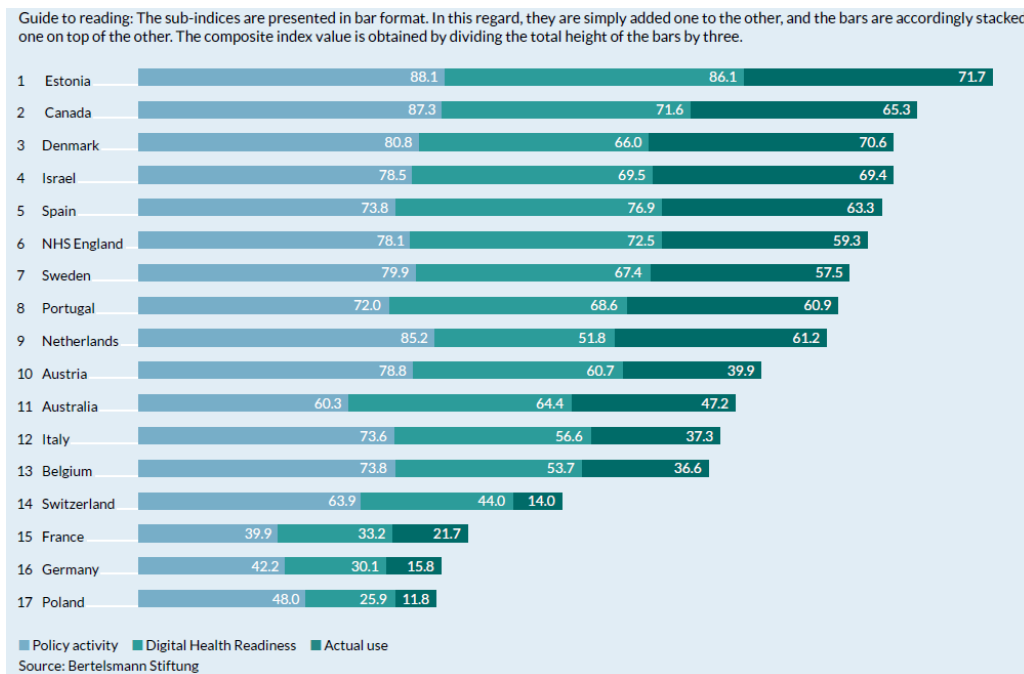
Figure 12 Digital Health Sub-indicis on the 3 levels. Source: (Rainer Thiel et al., 2018, p. 222)

The differences in the ranking of the Austrian digital health scenery may result from the different emphasis to the electronic health record system when establishing the ranking index in the mentioned studies.

As mentioned already in the country eHealth profile in 2015 (WHO Global Observatory for eHealth & World Health Organization, 2016), Austria has an Electronic Health Record system in place, called ELGA (or elektronische Gesundheitsakte) (*ELGA: About*, n.d.). The implementation started in December 2015, and it is currently being rolled out to the different healthcare facilities and federal states throughout Austria. The patient records are growing gradually, as more and more institutes join the system. The system is planned to serve as a "backbone" of the Austrian eHealth system, it will incorporate further modules, like eMedikation (interim implementation in all states due to the COVID-19 pandemics) and eVaccination (vaccination documentation). Currently, ELGA is voluntary for citizens through an opt out method: it is available for everybody who has access to the Austrian health care system, those who do not want to have access to it can opt out anytime. The system is operated by ELGA GmbH, that was responsible for the development of the current record as well as will be responsible for the development of the future modules.

With the aim to fully exploit the potential of digitalization, the Federal Ministry for Digital and Economic Affairs coordinated the Digital Roadmap Austria initiative established in 2017. An even more ambitious strategy is currently under development under the framework Digital Austria[4] with the aim "to establish and further ensure Austria's role as a leading digital nation to guarantee and expand prosperity, and job opportunities, as well as the quality of life in the long term" (European Commission, 2019a). A Digitalization Agency was developed in 2018 to be a knowledge and project platform to implement digitalization projects, provide expertise and know-how, communicate opportunities and network and coordinate stakeholders[5].

In the Digital Roadmap Austria, the following aims were defined for the health care and social affairs (Federal Ministry for Digital and Economic Affairs, nd):

- "Implement and continue to develop the electronic health record scheme (ELGA) nationwide

---

[4] Available in German at https://www.digitalaustria.gv.at/ (last accessed on 07.06.2020)
[5] https://www.ffg.at/en/node/70661 last accessed on 22.03.2020.

- Design an electronic vaccination record, electronic mother-and-child medical card and electronic prescription (ePrescription)

- Set up contact and advice centres for the whole population, e.g. in the form of an electronically supported initial contact and advisory service (TEWEB)

- Develop a patient summary that contains key medical data on the patient (e.g. blood group, allergies and drug intolerances), and can be viewed in other countries subject to the patient's consent

- Encourage the widespread use of assistance systems to help elderly people and people with special needs

- Prepare a framework for electronic health services e.g. telemedicine" (Federal Chancellery and Federal Ministry of Science, Research and Economy, 2016 p.30)

2.4.1. Digital health companies in Austria

Austria/Vienna has a goal to be life science leader in Europe[6]. There is a broad, supportive ecosystem built out to offer an attractive location for biotech start-ups. The Austrian Life Science Directory[7] lists all life science/biotech/MedTech companies, suppliers, service providers and research and education institutes in Austria, including medical device developers. Currently[8], there are 63 developer companies in the directory working on software for medicine, telemedicine and eHealth proving a dynamic life science environment in the country.

Digital health start-ups can get special support at the open innovation platform, Health Hub Vienna[9], and it's accelerator program organized by the Viennese high-tech incubator INiTS Universitäres Gründerservice Wien GmbH. The accelerator program focuses on medical device, digital health, med tech start-ups with a team size of 8-10, and with a working prototype. Health Hub Vienna offers access to a network of pharmaceutical companies, medical device manufacturers, private and public insurance companies, healthcare suppliers, regulatory experts and selected investors. Besides connecting the start-ups with important

---

[6] https://www.lisavienna.at/life-sciences-in-vienna/for-start-ups/ last accessed on 11.06.2020
[7] http://www.lifesciencesdirectory.at/ last accessed on 11.06.2020.
[8] Stand on 11.06.2020.
[9] https://healthhubvienna.at/ last accessed on 11.06.2020.

stakeholders and mentors, the accelerator program also gives specific support on regulatory affairs, certification processes and fundraising.

3. Methods

3.1. Establishing a model for digital health validation ecosystem

To define the "digital health validation ecosystem", the definition of innovation ecosystem by Granstrand and Holgersson was used (Granstrand & Holgersson, 2020). As defined in their paper, "innovation ecosystem is the evolving set of actors, activities, and artifacts, and the institutions and relations, including complementary and substitute relations, that are important for the innovative performance of an actor or a population of actors" (Granstrand & Holgersson, 2020 p.3.). Based on this, in this thesis a digital health validation ecosystem is used as the **evolving set of actors, activities and aftifacts and the institutions and relations, that are important for the clinical and economic validation of digital health innovations**. Artifacts are according to Granstrand and Holgersson "products and services, tangible and intangible resources, technological and non-technological resources, and other types of system inputs and outputs, including innovation" (Granstrand & Holgersson, 2020 p. 3.).

To analyse the Austrian landscape, the elements of the digital health validation ecosystem were put into a model. To get the basic structure of the model, I used the one proposed by the WHO on the components enabling the implementation of digital health interventions (World Health Organization, 2019a, p. xiii). The elements of the digital health validation ecosystem were added to this model based on the publication of Kowatsch et al. describing barriers of successful digital health evaluation (Kowatsch et al., 2019).

3.2. Literature review

Literature review was used to identify institutes in Austria actively involved in the clinical testing of digital health. Relevant peer-reviewed scientific publications were retrieved from PubMed®[10] on May 2020. Search terms were combinations of standard expression for (clinical) evaluation (term: trial), the geographic area (term: Austria) and variations of broad digital health innovation terms (terms: "digital health" or eHealth or mHealth). All publications indexed on PubMed until 27. May 2020 were screened with this strategy. All

---

[10] Biomedical library of the National Institute of Health https://pubmed.ncbi.nlm.nih.gov/ last accessed on 27.05.2020.

titles, author lists and abstracts were read to identify relevant publications. Where necessary, full text was screened. The inclusion and exclusion criteria are described in Table 2.

Table 2 Summary of inclusion and exclusion criteria in the literature review

Inclusion criteria	- Description of a planned or performed clinical or field testing of a digital health product or service supporting the diagnosis, monitoring, follow-up, management or the treatment of a human disease or disease predisposing condition (e.g. obesity) - Description of a planned of performed institutional or field testing of a digital health product or service supporting elderly people or childcare - Testing is done in at least one Austrian clinical or institutional site - No restriction on time of the publication or the trial - No restriction on the results or successful execution of the testing
Exclusion criteria	- Testing or description of information management systems or clinical decision management software as stand-alone product - Clinical trials performed **in order to develop** digital health product or services (e.g. collect data to establish predictive algorithms or diagnostic tools)

To identify the Austrian institutes involved in the testing, Austrian affiliations of authors were retrieved, however only the highest organizational level was considered (e.g. in case of a university professor, only the university and not the department or research group). Where an author had multiple affiliations from different institutes, all institutes were considered, but if the affiliations were from the same highest institutional level and only the divisions were different, only the highest institutional affiliation is shown once.

The full review of the digital health solutions, the methods and the results of these projects is not scope of this thesis.

3.3. Qualitative expert interviews

Qualitative content analysis (Mayring, 2014) of expert interviews was used to identify the elements of the Austrian ecosystem. Structured interviews were conducted with local experts to explore supportive factors and barriers while planning and conducting validation of digital health.

As expert, a person was defined as someone with **experience in planning and/or conducting clinical or field validation of digital health or a key member of the ecosystem, who works or worked with innovators planning of conducting validation**. Only experts active in Austria were selected.

Four experts were chosen, two working at companies developing digital health products and two working at key institutes supporting validation of digital health. However, only two experts agreed on participating in an interview, while a third expert answered two direct questions via email briefly. No contact could be made with the fourth expert selected. Brief summary of work experience (anonymized) of the two interviewed experts is provided in Appendix 5.

The first contact was made via emails, where the topic and the research questions were described. After agreeing to the interview, appointments were made for a Skype (Expert #1) or a phone call (Expert #2) and the interview checklist questions (see below) were sent at least 3 days in advance. The interview with Expert #1 was conducted in 07.04.2020, with Expert #2 on 04.06.2020.

Interviewees signed a Declaration of Consent (template of the Declaration of Consent is in Appendix 6). Interviews were recorded either with the built-in function of Skype or with the voice recorder of a smartphone. Both interviews lasted for ~1 hour (49 minutes and 48.5 minutes) without interruption.

For transcription of the interviews, a mixture of clean read and selective protocols were used (Mayring, 2014). For selection, all parts of the interview, which were unrelated to the research (e.g. introductory parts, excurses on topics that naturally arose due to the COVID-19 pandemics) were removed. For the rest of the discussion the following rules were used:

- The interview was transcribed literally in English
- Passages by the interviewer are marked with VSZ, those of the Expert #1 with E#1 , those of Expert #2 with E#2

- Language and punctuation were slightly modified to retain clarity

- Excessive expletives, decorating words were removed

- Where the expert used an English word incorrectly, a right or more fitting word was added in parenthesis and marked with the author initials (VSZ)

- Comments by the expert, which could reveal the identity of the interviewees were removed or modified to retain the main message but maintain anonymity

Scripts of the interview were sent to the experts and at least one-week time was offered for review and approval. Interview transcripts are provided in Appendix 7 (E #1) and 8 (E #2).

3.3.1. Interview checklist

To ensure that all topics are discussed during the interviews, an interview checklist was developed with questions. The checklist was solely used as a frame and it allowed to ask additional or omit certain questions, according to the information gained during the interview. As the experience of expert working at an institution in the ecosystem (E #1) covers slightly different angles of the topic compared to the one working at a digital health company (E#2), two variants of interview questions were developed (indicated as E #1 and E #2).

The topics and the questions are summarized in Table 3.

Table 3 Interview checklist with topics and questions

1. Introduction	E #1: In your experience what is the attitude of the start-ups to clinical/economic testing? E #2: What is your experience with clinical and economic validation of digital health?
2. Factors pushing digital health companies towards validation	E #1: If you consider companies, which are roughly working on similar products and one considers running a clinical testing and one does not consider running it. Do you see any critical factors among the founders, among the investors, what makes this difference between these companies? E #2: Do you have anyone on the team, who had already experience with clinical testing (of digital health)?
3. Internal and external expertise on	E #1: What is your opinion, in Austria do you have clinicians and CROs with open mind for digital innovation testing? Do

	conducting validation in Austria	you see the emergence of specialists in digital health among clinicians in Austria? If yes, could you name a few? How is your organization supporting digital health validation? E #2: Do you plan to design/organize and manage the study with internal people, or do you get a CRO/consultants to do it? Who will be the internal coordinator (which function) of the study? Do you reach out to external advisors?
4.	Policies (regulatory, insurance) in digital health validation	E #1: Do you see the emergence of specialists in digital health among regulators in Austria? E #2: Do you know about local policies/frameworks/recommendations of regulators or insurance companies on digital health? If yes, where did you get information about them?
5.	Financing and validation in Austria	E #1: Do you see any financial benefits for companies (public funding or from VCs) that they get easier funding if there are such validations in place? E #2: Do you have among your investors people supporting/pushing for validation of your innovation? Do you know about public funding that would support validation?
6.	Ecosystem elements supporting application for reimbursement	E #1: How much, do you think companies plan to go for reimbursement by insurance companies? E #2: Do you plan to go for reimbursement? If yes, which external parties support you in this process?
7.	Challenges during validation	E #1: What are the major challenges for companies in your experience going for validation?[11] E #2: Based on your experience, which part do you expect to be the most challenging during the study: designing, organizing, executing/managing or financing?

---

[11] This question was not asked, as the expert discussed the topic during the interview without specifically asking about it.

8. International comparison	E #1: Are there any good practices internationally, that you think are important regarding clinical and economic validation of digital health? E #2: Do you see any international practice/institute/evaluation method that would be useful to have in Austria to support digital health testing?

3.3.2   Content analysis

Interviews were summarized and key points were collected before further analysis. For the analysis of the interviews structuring was used (Mayring, 2014). Briefly, categories were established based on the research questions and the theoretical background. During the run-through of the interview transcripts, all parts of the interview addressing a certain category were marked. Parts within each category were collected from both interviews and summarized for analysis. Anchor samples (passages quoted from the interviews) were selected to illustrate the categories (Mayring, 2014).

4. Model of a digital health validation ecosystem

This section aims to collect the elements of an ecosystem supporting the clinical and economic validation of digital health innovation.

As described above, digital health innovations are complex products, their development involves multidisciplinary team and to their clinical and economic validation complex evaluation methods are needed. Therefore, a complex ecosystem might be necessary for the successful validation and consequently integration of digital health. As stated by the WHO, "in the absence of a robust enabling environment, there is the risk of a proliferation of unconnected systems and a severe impact on the effectiveness and sustainability of the health intervention" (World Health Organization, 2019a, p. xiv).

To build the ecosystem model, I used two recent publications on digital health intervention (Kowatsch et al., 2019)(World Health Organization, 2019a).

According to the WHO, the following components of an ecosystem are contributing to the implementation of digital health products (Fig. 13) (World Health Organization, 2019a):

- Health content: information aligned with recommended health practices and validated health content
- Digital health interventions and technologies
- Digital applications: ICT systems and communication channels facilitating delivery of the intervention and health content
- Foundation layer: enabling environment through leadership and governance

LEADERSHIP & GOVERNANCE			
STRATEGY & INVESTMENT	SERVICES & APPLICATIONS	LEGISLATION, POLICY& COMPLIANCE	WORKFORCE
	STANDARDS & INTEROPERABILITY		
	INFRASTRUCTURE		

Source: WHO (World Health Organization, 2019)

Figure 13 Components of an enabling ecosystem for the implementation of digital health interventions. Source: (World Health Organization, 2019a, p. xiii)

According to Kowatsch et al., main barriers of the evaluation phase are funding, costs (maintenance), guidelines and methodology (Kowatsch et al., 2019). These barriers can be managed by different parties of the ecosystem:

- Funding: public and private funding opportunities tailored to the evaluation phase
- Costs (maintenance): existing infrastructure and delivery channels for testing digital health innovation, high quality pre-existing health data sets
- Guidelines: support through standards developed by national and international institutes, regulatory policies and legislations
- Methodology: support of academic institutes, statisticians and data analysts specialized to digital health evaluation; expert advisors and CROs

These stakeholders were placed into the basic model structure proposed by the WHO, except, that below the leadership and governance layer, an additional foundation layer "patients and patient representatives" were added to represent the patients in the ecosystem (Fig. 14). The individual elements of the model are analysed below.
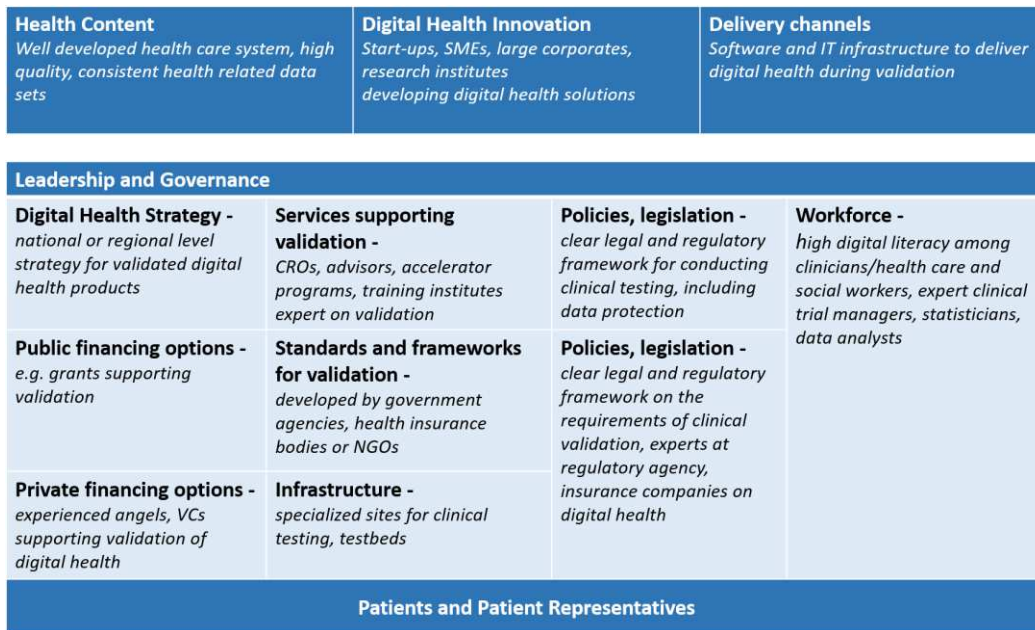
Health Content	Digital Health Innovation	Delivery channels
Well developed health care system, high quality, consistent health related data sets	*Start-ups, SMEs, large corporates, research institutes developing digital health solutions*	*Software and IT infrastructure to deliver digital health during validation*

Leadership and Governance

Digital Health Strategy - *national or regional level strategy for validated digital health products*	**Services supporting validation -** *CROs, advisors, accelerator programs, training institutes expert on validation*	**Policies, legislation -** *clear legal and regulatory framework for conducting clinical testing, including data protection*	**Workforce -** *high digital literacy among clinicians/health care and social workers, expert clinical trial managers, statisticians, data analysts*
Public financing options - *e.g. grants supporting validation*	**Standards and frameworks for validation -** *developed by government agencies, health insurance bodies or NGOs*	**Policies, legislation -** *clear legal and regulatory framework on the requirements of clinical validation, experts at regulatory agency, insurance companies on digital health*	
Private financing options - *experienced angels, VCs supporting validation of digital health*	**Infrastructure -** *specialized sites for clinical testing, testbeds*		

Patients and Patient Representatives

Figure 14 Model of a supportive ecosystem for the clinical and economic validation of digital health. Own illustration.

Health Content:

The value of digital health innovation depends on the health care system, where it is implemented. On one hand, users may not be able to fully exploit the benefits of the new products/services (e.g. low level of digital literacy, necessary IT infrastructure missing, low speed and instable internet connection). The same factors influence the evaluation of digital health innovation, since only those benefits can be measured in practice (also during testing), which are deployed. In a supportive ecosystem the health care system is well developed, and the basic system requirements are available.

A special element of this element is the existence of quality data sets in health care. As mentioned above, for real-life testing of digital health (e.g. testbed projects) such (historical) data sets are needed (NHS England, 2018a). These data might be used during the planning, set up or during the analysis of validation. Health content is particularly important for new, emerging digital health technologies, like AI or data analysis (big data). As described recently in the Topol review, these technologies open new possibilities in analysing, interpreting and making decisions, however "(u)neven NHS data quality, gaps in information governance and lack of expertise remain major barriers to the adoption of these advances" (Topol Review, 2019, p. 11). Based on this, the lack of even, high quality data would pose a barrier during clinical and economic validation as well, as the full potential of these technologies could not be recognized.

Digital Health Innovation:

Digital health innovators (start-ups, SMEs, large corporates) are important elements of the ecosystem. They may share experience with each other on digital health validation in a direct way or - through the move of the workforce from one company to the other – indirectly. Similarly, research institutes, universities developing and testing digital health solutions may educate other members of the ecosystem, particularly because they are used to conduct scientifically solid studies and share the results in publications.

Delivery Channels:

Software and communication channels to deliver digital health interventions are already necessary during the validation of digital health. If new channels need to be built for the testing, it does not only increase the costs of the testing but adds an additional level to the complexity during the testing (users need to learn and use the new channels). Additionally, if interim communication channels are used during validation, it reduces the ability to translate the results and experience during the study for a later, real-life use

Strategy and Investment:

Validation of digital health is a complex task, where the interest and aim of several different stakeholders need to be maintained. Therefore, a national or state level strategy for the support of digital health validation might be needed. This is particularly true, if large-scale evaluation methods (e.g. testbeds) are developed, where the large financial and institutional resource need necessitates state or national level commitment.

In general, a strategic approach is necessary "to support a cohesive approach to implementation, in which different digital interventions can leverage one another, as opposed to operating as isolated initiatives" (World Health Organization, 2019a, p. xiii). Additionally, a recent report compared digitalization of health care in 17 countries and concluded, that digital transformation needs political leadership: as described by the #SmartHealthSystems report, "(s)uccessful countries are characterised by a trio of effective strategy, political leadership and coordinating national institutions" (Rainer Thiel et al., 2018, p. 4).

Naturally, digital health validation needs to be financed, the availability of public and private funding for this purpose is essential. In the private sector it can be supported by angel investors experienced in digital health validation or VCs supporting the testing (and understanding the time and financial requirements of such testing). Large scale and

simultaneous testing of digital health inventions is likely to require public financing, e.g. in the form of grants or government programs establishing the testing environment.

Services:

Services supporting the validation of digital health can be Contact Research Organizations (CROs) specialized for this field, advisors or consultants supporting the planning/execution of such validation, institutes providing training and accelerators specialized for digital health companies. In a broad sense, research institutes and universities conducting research on the field of digital health evaluation can be included into this section.

Standards and Frameworks:

Standards and frameworks can provide developers with clear guidance on planning a meaningful evaluation of digital health. Such guidance can come from international institutes (e.g. the guidance of the IMDRF on SaMD (IMDRF Software as a Medical Device Working Group, 2017)) or from national institutes (e.g. the evidence standards for digital health developed in the UK by NICE (NICE, 2019)).

Infrastructure:

Clinical and economic validation of digital health may require special infrastructure: clinical sites specialized for the testing with necessary hardware (e.g. dedicated servers), natural experiment sites (testbeds, living labs).

Policies and legislation on conducting clinical testing:

Developers need an understanding on the legal and regulatory background on conducting clinical testing. These include compliance with national clinical trial regulations, understanding the requirements of getting ethical committee approval at testing sites, and applicable legislation on data protection. Institutes involved in the approval can provide guidance, centralized information platforms can help gaining understanding and clinical trial managers, contract research organizations can plan the process.

Policies and legislation on the requirements of clinical validation:

Besides a clear legal background on conducting clinical testing, developers should also know about the legal and regulatory requirements of certification, approval and reimbursement in advance. This knowledge will guide the design of the clinical test and inform developers on how they can generate evidence for economic value and get reimbursed. The challenge of the legislation and policy might be that it needs to be flexible to accommodate future technologies, specific to diverse digital technologies and stable, so companies can plan ahead.

Such stability is particularly important when long-term evaluation methods are used for the validation. Additionally, dedicated departments, groups or experts on digital health might be needed at regulatory bodies and insurance companies, who can advise innovators.

Workforce:

In a supportive ecosystem, workforce needed to the validation is available. This requires that teaching facilities exist: medical universities include digital health and its validation in the curriculum, other health care professionals are trained to gain necessary digital literacy, clinical trial managers get experience on digital health testing, and statisticians, data analysts can support the planning, modelling and analysis of new, complex experimental schemes (e.g. agent based modelling (J Chen, 2018)). Important aspect of the training is understanding ethical considerations.

Additionally, continuous education on the field is necessary for all parties to remain up to date in this dynamically developing field[12].

A recent review analysed the impact of new technologies on the NHS workforce and identified that "(t)he healthcare workforce needs expertise and guidance to evaluate new technologies, using processes grounded in real-world evidence" (Topol Review, 2019, p. 10).

Patients and Patient Representatives:

Similar to the importance of digitally native healthcare workforce, high digital literacy of patients can support the validation of digital health. Low digital literacy may lead to inconvenience, which result in higher patient dropout (Alexander Walter, 2013). Low understanding can also result in mistrust of the technology, which again leads to lower retention or even low willingness to participate (recruitment rate) (Alexander Walter, 2013). Finally, it can also cause incorrect use of the technology and consequently no or low benefits registered from it. All these lead to low quality clinical data, longer trial and higher costs.

Involvement of patients (or patient representatives) throughout the development of digital health was identified as an important facilitator of the successful and sustainable adoption of patient facing digital health innovation (van Velthoven et al., 2019). This finding implies that their involvement in the planning and execution may support digital health validation and they are important partners in the ecosystem.

---

[12] See point 38 in the European Parliament resolution on enabling the digital transformation of health and care in the Digital Single Market; empowering citizens and building a healthier society (2019/2804(RSP)) available at https://www.europarl.europa.eu/doceo/document/B-9-2019-0239_EN.html (last accessed on 07.06.2020)

Patient representatives are patients' organizations and self-help groups. According to the EMA, "(p)atients' organisations are defined as not-for-profit organisations which are patient focused, and whereby patients and/or carers (the latter when patients are unable to represent themselves) represent a majority of members in governing bodies" (Sienkiewicz & van Lingen, 2017, p. 3).

The activities of patient organizations can focus on policy, capacity-building and education, peer support and research & development (Sienkiewicz & van Lingen, 2017).

Related to policy development, patient organizations can help policy makers to learn about the "end-user view" on digital health validation (e.g. which factors are important to test for the patients).

On the capacity-building and education field, patient organizations might support digital health evaluation through arranging patient education on technologies, aiding the generation and dissemination of product/service-related information material and through educating the various stakeholders (including digital health developers, health care workforce) on the end-user view. All these activities may enhance patient recruitment, engagement and retention during the validation of digital health.

As described by the European Patients Forum (Sienkiewicz & van Lingen, 2017), patient organizations are increasingly involved in the research and development (including clinical testing) of pharmaceuticals e.g. through data collection from patients or sometimes even through funding of development costs. This activity could highly support real-life evaluation of digital health as well, through realistic planning, incorporating end-user view early on to increase user experience and therefore, success of the testing.

Based on this complex role of patients and patient organizations during digital health validation, they were placed in the ecosystem model as a foundation level similar to the leadership and governance block.

5. Validation of digital health in Austria

5.1. Institutes involved in published clinical trials for digital health in Austria

Literature review was used to identify institutes in Austria which actively involved in the testing of digital health. Therefore, I analyse peer-reviewed scientific publications indexed on PubMed describing digital health trials in Austria. With the search terms "digital health" AND trial AND Austria 6, with the terms eHealth AND trial AND Austria 64, with the terms mHealth AND trial AND Austria 64 publications were identified which were published until 27. May 2020. After screening of all publications, 16 published trials were identified (Table 4).

Table 4 Published clinical trials for digital health in Austria

Project description	Affiliations of authors in Austria	Reference
Palliative care of oncology patients with telemedicine	Medical University of Vienna, Hospital Sankt Josef	(Nemecek et al., 2019)
Telemonitoring for the diagnosis and treatment of sleep apnea (HOPES study)	NRZ Rosenhügel, Vienna, Medical University of Vienna	(Kotzian et al., 2018)
Real-time remote symptom monitoring of cancer patients (eSMART Study)	Medical University of Vienna	(Maguire et al., 2017)
Telehealth nutrition solution for diabetes	AIT Austrian Institute of Technology GmbH, Versicherung für Eisenbahnen und Bergbau, Medical University of Graz	(Schusterbauer et al., 2018)
Telehealth delivered feedback system for behaviour change after amyotrophic heart infarct	AIT Austrian Institute of Technology GmbH, Medical University of Innsbruck, UMIT - University for Health Sciences, Medical Informatics and Technology	(Kreiner et al., 2015)
App based assistance service for elderly	Salzburg Research Forschungsgesellschaft m.b.H., MOWI, Salzburger Hilfswerk	(Willner et al., 2015)
Web-based follow-up intervention for obesity treatment in women	FEM Süd, Kaiser Franz Josef - Hospital Vienna, Medical University of Vienna	(Rader et al., 2017)
Net coaching to support weaning children off enteral nutrition	Medical University of Graz	(Marinschek et al., 2014)
Clinical Decision Support System complemented with a mobile app to monitor nutritional status of cancer patients	Medical University of Vienna, Vienna General Hospital, Krankenhaus Rudolfstiftung, Hospital of the Brothers of St. John of God (Salzburg)	(de Bruin et al., 2018)
Mobile teledermatology in acne patients	Medical University of Graz, Private Dermatology Practice	(Frühauf et al., 2015)
MyCor telemonitoring program for chronic heart disease	UMIT - University for Health Sciences, Medical Informatics and Technology Medical University of Innsbruck, AIT Austrian Institute of Technology, Institute	(Ammenwerth et al., 2015)

	of Health Care Engineering with European Notified Body of Medical Devices, Graz University of Technology	
Smart blister and mHealth solution to monitor medication adherence	AIT Austrian Institute of Technology, Science Consulting & Clinical Monitoring, Health Centre South, Vienna	(Brath et al., 2013; Morak et al., 2012)
Telemedical follow-up of pacemaker	AIT Austrian Institute of Technology GmbH, Medical University of Graz	(Hayn et al., 2013)
Telemonitoring after acute heart failure (Mobitel)	Medical University of Graz, AIT Austrian Institute of Technology GmbH, various hospitals through Austria	(Scherr et al., 2009)
Telemedical support in diabetes in adolescents	Medical University of Vienna	(Rami et al., 2006)
Diab-Memory mHealth application for assisting insulin treatment in diabetes	Austrian Research Centers GmbH (former name of the Austrian Institute of Technology), Medical University of Vienna	(Kollmann et al., 2007)

a)   affiliation is only indicated at the highest institutional level (e.g. department not shown, only university)

The full review of the digital health solutions, the methods and the results published for these projects is not scope of this thesis.

All, but one trial tested telemedicine solutions: either to monitor, follow-up or coach patients remotely. There was only one trial where mHealth applications were used to aid self-management of patients (Kollmann et al., 2007)[13]. Three trials involved cancer patients, 3 trials patients with diabetes, 4 focused on circulatory diseases, and one trial for each skin disease, stroke, medication monitoring, obesity and elderly assistance.

When analysing the authors, I identified, that the Austrian Institute of Technology GmbH (AIT) was involved in 7 studies, medical universities in 14 studies, (the Medical University of Vienna in 7, the Medical University of Graz in 5, the Medical University of Innsbruck in 2 studies), non-medical universities in 2 studies, non-university hospitals in 6 studies, other research institute in 1 study. There was only one private consulting firm (Science Consulting & Clinical Monitoring) among the authors, one health insurance institute (Versicherung für Eisenbahnen und Bergbau), one private doctor practice and one author with affiliation to the European Notified Body of Medical Devices at the University of Technology, Graz. In the 15 studies identified by literature review, none of the authors had an affiliation to digital health developing companies (start-ups, SMEs or large corporates).

---

[13] mHealth was used in other trials as a tool for telemedicine and not as the main tested product

5.2. Results of expert interviews

5.2.1. Summary of interviews

Expert #1:

Due to the vast expertise of E #1 with start-ups, the interview largely focused on the experience of digital health start-ups in Austria. As E#1 highlighted, each digital health start-up is different; depending on the technology, business model, experience of the team their attitude towards clinical testing varies. According to her, experience in life science industry helps, however, too much experience may hinder innovation and make people blind to new paths. She discussed the role of the Health Hub Vienna accelerator program in the digital health validation ecosystem: the program may provide specific support for validation, if it is needed to the success of the start-up. She highlighted, that the program can support start-ups coming from non-EU countries understand the certification process. Additionally, it offers networking opportunity with open minded members of the local ecosystem. She also named experts among clinicians for digital health, but mentioned, that these experts are still rare. On the other hand, she highlighted, that the COVID-19 pandemics changed the attitude towards digital health. She brings the example of the immediate introduction of ePrescription. She predicted a fundamental and highly positive change in attitude towards digital health solutions. Regarding regulations, she concluded, that the lagging of the regulations compared to technological development is inevitable and it is particularly so in Europe. She mentioned, that clinical validation can bring financial benefit for the start-ups, investors understand that complying with the rules of healthcare is needed. Clinical testing can also become a unique selling point (brought the example of mySugr, the first FDA approved app, acquired by Roche). However, as she stated, clinical testing may not be so important in case of over-the-counter solutions. When discussing reimbursement, she highlights that not everything can be reimbursed, but reimbursement is a particularly large economic driving force in Austria, due to the patients' expectation of free healthcare. She brought up the topic of regulatory testbeds twice during the interview: once as a possibility to make regulations more effective, and second, when asking about international practices, that could be useful in Austria as well.

Digital health ecosystem elements identified during the interview:

- Health Hub Vienna (accelerator program)

- Expert clinicians (e.g. Programmdirektor für E-Health, Telemedizin und Komplexitätsforschung, Medical University of Vienna)
- Telemed Austria

Potential gaps or barriers identified:

- Lack of specialists among clinicians and regulators
- Lack of regulatory testbeds
- Lagging and particularly strict regulations
- Resistance of doctors (fear of becoming obsolete)

Expert #2:

As E #2 works at a digital health company, which is going for reimbursement and may plan clinical validation of certain products, the interview focused on their experience in these areas so far. Regarding internal and external functions supporting their plans, he mentioned, that they have internal expertise in clinical testing, and plan to hire clinical trial manager or clinical research assistant soon. This internal expertise can be enough, in his opinion, so they would not need external advisors. Still, they would outsource the actual clinical trial management to a CRO, that they would search internationally (with a preference for an Austrian partner). Although he could not name any potential local CROs, he highlighted, that it is still possible that such CROs exist, he just did not know about them. Until now, they find the reimbursement process complicated and bureaucratic (as he said, the latter is typical to Austria), they have no external support in this, but he thinks that another company, who already went through this process could help them. He also finds large international companies helpful to spread the word about their product and promote its use. Instead of contacting local regulators, they discuss regulatory questions with the European Medicines Agency (EMA) due to existing relationship. According to him, the topic of validation was not discussed with investors, neither had public support, but he thinks that the Austrian Research Promotion Agency (FFG) could be a partner for public financing options. As biggest challenge for clinical testing, he mentioned the resistance of clinicians towards digital health. To overcome this barrier he confirmed, that clinical validation results could help and the support of key opinion leaders. Based on his experience, political debates in state institutes and bureaucracy are barriers in Austria.

Digital health ecosystem elements identified during the interview:

- Other digital health companies

- Large international pharma companies

- FFG (Österreichische Forschungsförderungsgesellschaft (Austrian Research Promotion Agency))

Potential gaps or barriers identified:

- Political debates in state institutes

- Bureaucracy, complicated processes

- Lack of external support in getting reimbursement

- Resistance of doctors

5.2.2. Analysis of interviews

Structured interviews were conducted with two experts to identify relevant players and elements in the Austrian digital health validation ecosystem.

1. Experience with digital health validation

Expert #1 is working with numerous digital health start-ups in Austria and globally through an accelerator program. In her experience, the attitude of start-ups towards validation varies; some are very strategic about it (either strategically deciding to do clinical validation or making a conscious decision about not to do), some are more naïve. In her experience, even those, who make the decision to get clinical validation, may underestimate the resource need of this decision.

Expert #2 is working at a digital health company in Austria, developing Class 1 medical devices. He has large experience in clinical studies where their digital health product is used as a tool. Currently the company is planning to go for reimbursement with one of their digital health products and may run a clinical validation as well with a partner organization.

2. Factors driving companies towards validation

When discussing, why certain start-ups decide for validation and why others do not, Expert #1 mentioned the following factors:

- product/service

"it may not make sense to go for a clinical validation if I have a solution that is in the preventive care. We all know, that doing sports helps to stay healthier, but you will

feel it only, when you are 50. It does not make sense to go for clinical validation in that sense in such a case." (E #1)

- team experience, awareness

"It can be on every level; on the founders' level, if there is one really experienced in the health domain and has come maybe from a pharmaceutical background, they have an easier time taking the right decision." (E #1)

3. <u>Internal and external expertise on conducting validation in Austria</u>

Expert #2 confirmed, that they already have internal expertise in running clinical trials at the company, although they are still just considering clinical validation of their product. He believes, that they will not need external advisors for the study, but interestingly, he was confident, that they would work with a CRO on the clinical validation and a clinical research assistant or clinical trial manager would coordinate the study internally.

As Expert #1 mentioned, clinicians and CROs open to digital health are still rare in Austria, however, she sees that due to COVID-19, this may change:

"So all of a sudden digital solutions have become very, very interesting. And it pushed open many closed doors in one go. It will radically change; we are in a very radical change." (E #1)

This rarity of specialized experts or at least the lack of visibility of specialized experts might contribute to the fact, that E #2 could not name local CROs active on this field.

"We do not know about such partner in Austria, who could support us in this study, but it does not mean, that with a little bit of search we will not find someone. I cannot answer with certainty." (E #2)

The following components of the Austrian digital health validation ecosystem could be identified during the interviews:

- expert clinicians at university clinics: e.g. Program director for E-health, Telemedicine and Komplexitätsforschung at the Medical University of Vienna (E #1)

- Telemed Austria (E #1)

- Health Hub Vienna: providing networking and support tailored to the start-ups needs in the accelerator program.

"And this is one of the expectations in the program, to help them to do the right thing, approach the right people, to get into the clinics, to get into the European certification process etc." (E #1)

- digital health companies experienced in validation (E #2)

- large pharma companies using digital health (E #2)

4.   <u>Policies (regulatory, insurance) in digital health validation</u>

Based on the interviews, regulatory policies are lagging behind technology, in Europe this area seems to be overregulated:

"And in Europe, we tend to overregulate everything, which is good for the patient, but it is bad for the speed of innovation." (E #1)

However, this lag might be inevitable, as Expert #1 phrased it,

"Well, what is always the case is that the regulatory bodies lag behind the technology. There is always a new technology coming up, they have not seen before, so there are no rules how to go through the process." (E #1)

In case of the company of Expert #2, they rather went to the European Medicine Agency (EMA) for regulatory advice, because of an existing connection with the Agency:

"No, when this topic came up or when we decided to take this path, we went to the EMA directly to ask. We already established a working relationship with them, there they know about us already." (E #2)

5.   <u>Financing and validation in Austria</u>

Whether or not the (clinical) validation is of the financial benefit of start-ups depends on the solution and the business model. As E #1 summarized:

"There is a very close link between the technological solution (what does it do) to the business model (how do I bring the solution to the patient or the customer) and the certification process. And they need to go hand in hand." (E #1)

According to E #1, in case of over the counter model, the resources should be rather focused on marketing, whereas in other cases validation can be an asset and a unique selling point (USP) (she brought the example of MySugr, which was acquired by Roche).

Among the investors of the digital health company where Expert #2 works, the topic of validation was not discussed yet. Additionally, Expert #2 did not know about specific public funding opportunities for this topic, but speculated, that the Austrian Research Promotion Agency could be a potential source of such funding.

> "I do not know about specific grants for it, but we had good experiences with FFG (VSZ: Österreichische Forschungsförderungsgesellschaft (Austrian Research Promotion Agency)) and I think they could be a partner in this, to support such clinical validation, maybe within KLIPHA." (E #2)

6. Ecosystem elements supporting application for reimbursement

As E #1 concluded, reimbursement is a big economic driving force, which in her opinion is particularly so in Austria. Due to the social health insurance system, in her experience, Austrian patients and doctors expects that everything is reimbursed by the government. Exceptions are the – rare – private patients.

> "So, in Austria in particular, it is a normal attitude of the patient that the government "has to take care of my health"." (E #1)

Applying for reimbursement is also a topic at the company of Expert #2, and in his experience, the process is unclear and bureaucratic in Austria. He also confirmed, that they did not receive any external help during the process.

> "It seems to be a complicated, bureaucratic process at the moment, according to our recent experience. It is typical to Austria, it is rather unclear and difficult." (E #2)

7. Challenges during validation

E #1 mentioned during the interview, that resource needs of clinical validation is very high:

> "Because it costs a lot of time and it costs a lot of resources, and it costs a lot of energy also to record everything the right way, etc." (E #1)

Another challenge might be the lack of experience in start-ups:

"Those people, who approach this problem in a very naive way, they most likely will fail, if they do not buy in expertise." (E #1)

Resistance of health care users was mentioned by both interviewees:

"Because they (VSZ: digital health companies) were stumbling over the "we used to do it differently" attitude in the healthcare system everywhere on every level: doctors were afraid of all solution, because it might be that they can be squeezed out of the system and become obsolete." (E #1)

"If you were asking about the most challenging part, but without listing any examples, I would say, that the most challenging is to make the doctors accept these applications." (E #2)

"Some (VSZ: doctors) are really negative and say 'a digital health application should never replace their knowledge and experience'. So, they do not look at such application as a tool, that can make their work easier, but rather something that is a threat and could replace them." (E #2)

Interference of politics: based on the experience of Expert #2, the interference of politic with the ecosystem creates a challenge while navigating it.

8. International comparison

E #1 mentioned during the interview, that regulatory test beds could be an improvement of the Austrian ecosystem.

"I think one of the domains they (VSZ: Federal Ministry for Digital and Economic Affairs) should really focus on is eHealth regulatory test beds." (E #1)

As she concluded, these test beds could support the system at several level:

"I think that (VSZ: test-beds) should be a focus area, to help and create an ecosystem and really speed up everything: saving money in the system, creating an ecosystem, where digital innovations can thrive and also create the halo and make Austria visible, because there are not a lot of nations who did that." (E #1)

5.3. Austrian digital health validation ecosystem

This section collects the elements of the digital health validation ecosystem in Austria, to identify strength and potential gaps in the country. Ecosystem members identified by the literature review and through interviews were put in the model established in Chapter 4. Additional members were added based on available public information on the respective ecosystem elements. These members are:

Health content and Delivery channel:

- ELGA: the Austrian Patient Record System, ELGA is described in details in Chapter 2.4.

Digital health innovation:

- Ludwig Boltzmann Institute (LBI) for Digital Health and Patient Safety: the research institute located at the Medical University of Vienna aims "to develop, and later introduce, digital tools that will enhance patient safety by: (I) empowering patients; (II) empowering HCP [VSZ: health care professionals]; (III) assisting decision-making"(*Ludwig Boltzmann Institut for Digital Health and Patient Safety | Ludwig Boltzmann Gesellschaft*, n.d.). The institute was established in 2019 together with the LBI for Digital Health and Prevention, "not only to deliver excellent results in these currently under-researched areas, but to provide fertile grounds for interdisciplinary and trans-sectoral teams with the ambition to impact society and generate knowledge with high relevance for patients, caregivers and their families" (Medizinische Universität Innsbruck, 2018, p. 1).
- Large pharma companies active in Austria (Boehringer Ingelheim, Sanofi, Pfizer, Novartis): large pharma companies are part of the life science scene of Austria. As mentioned by Expert #2, these companies can support digital health start-ups and SMEs through various ways. They also delegate mentors to the accelerator program of Health Hub Vienna (state as of 05.06.2020).

Digital health strategy:

- Digital Health in Wien: as part of the HEALTH.DigitalCity.Wien[14] initiative there is an online platform to submit ideas and public view on how Vienna can become a leading "digital health city". Anyone interested can submit his or her opinion after registration on the website[15]. The inputs will be used to develop a digital health strategy for the city.

Public funding:

- Österreichische Forschungsförderungsgesellschaft (FFG): the FFG or Austrian Research Promotion Agency was mentioned as potential source of public funding of digital health validation. To identify funding opportunities at FFG fitting a certain topic, there are 2 easy methods provided by the Agency. One is the Förderservice[16] –to contact the agency and discuss funding possibilities. The second is the QuickCheck[17]: it is an online form, where one can submit basic information (e.g. project title, planned start and end, approximate costs) and a brief project sketch, and receives expert feedback on the fitting funding options.

- Förderpilot: a centralized online platform to find grants, loans, bank guarantee, investment, incubator/accelerator and coaching opportunities provided by many national and regional institutes in Austria[18]. There are two possibilities on the website to receive personalized recommendation; one can provide basic information about the project (in the form of a drop-down menu) and get immediately an automatic selection of options. The other option is a personalized search by experts in the background, where – like the QuickCheck option at FFG – one receives feedback and recommendation after a short period of time, however here the information will come from all partner institutes in the background.

- Fonds zur Förderung der wissenschaftlichen Forschung (FWF): the FWF (or Austrian Science Fund) funds non-commercial clinical research in the Programme Clinical Research

---

[14] Limited information on the initiative is available in German at https://health.digitalcity.wien/ (last accessed on 05. 06. 2020)

[15] platform is in German at https://www.partizipation.wien.at/de/consultation/8900 (last accessed on 05.06.2020)

[16] https://www.ffg.at/foerderservice last accessed on 05.06.2020.

[17] https://www.ffg.at/quickcheck last accessed on 05.06.2020.

[18] The actual list of all partners behind Förderpilot is available at: https://www.foerderpilot.at/foerderstellen.html (last accessed on 05.06.2020)

(KLIF). Projects need to "generate new scientific knowledge and insights that improve clinical practice and patient treatment"[19] to be supported. The fund would also finance the clinical validation of digital health products or services (only non-commercial), after the positive evaluation of external reviewers on the project proposal. It must be noted, that in the database of the funded clinical trials no digital health validation project was identified (as of 02.06.2020)[20]. Only one project was found, where clinical trial was funded to support the development of a digital health solution (Virtual and Augmented Reality Module for 3D Reconstruction, project number: KLI 678).

Services supporting validation:

- Mentors at Health Hub Vienna: the role of Health Hub Vienna in the digital health scene of Vienna is described in Chapter 2.4. Among the mentors in the accelerator program, key ecosystem members were identified.
- DEXHELPP[21]: working with several partner institutes[22], DEXHELPP aims to support analysis, planning and control of health care systems. This is achieved by using existing and new data to analyse the current status quo, forecast future development and develop scenarios based on different interventions. Through the development of new models for digital health, DEXHELPP could help to calculate economic benefit of digital health products and become an important element of the Austrian digital health validation ecosystem.

Infrastructure:

- LBI for Digital Health and Prevention[23]: the institute hosted by the University Institute of Sports Medicine, Prevention and Rehabilitation in Salzburg aims to improve the sustainability of lifestyle changes to reduce the risks and consequences of cardiovascular

---

[19] https://www.fwf.ac.at/en/research-funding/fwf-programmes/programme-clinical-research-klif/ last accessed on 14.06.2020.

[20] https://pf.fwf.ac.at/en/research-in-practice/project-finder/?search%5Bwhat%5D=&search%5Bscience_discipline_id%5D=&search%5Bpromotion_category_id%5D=13457 last accessed on 02.06.2020.

[21] Information translated from German at www.dexhelpp.at (last accessed on 05.06.2020)

[22] List of the actual partners can be found at http://www.dexhelpp.at/en/partners/ (last accessed on 05.06.2020)

[23] The website of the institute is available in German language at https://www.lbg.ac.at/lbi-dhp (last accessed on 05. 06. 2020)

diseases(Niebauer J & Stütz T, 2019). During the 7 years of the project, the institute will work together with several consortium partners to develop and concurrently implement new and existing digital techniques and tools in the model region of Salzburg. First, the project will involve patients in outpatient cardiological rehabilitation units and if successful, roll out for other patients and potentially even for healthy individuals. Although it is not explicitly mentioned in publicly available descriptions of the Institute, the project seems to be similar to a cardiovascular disease prevention and management test bed.

- Zentrum für Präzisionsmedizin (Centre for Precision Medicine): there is a plan to build a Centre for Precision Medicine in Vienna in 2022 (together with a Centre for Translational Medicine and Therapy and a Centre for Technology Transfer). The aim is to establish a location for the 21. Century Medicine, where the focus is on biomedical research, clinical studies, genome technology, bioinformatic and IT[24]. Based on this information, this Centre could become an important infrastructural element (to run clinical trials) of the digital health validation ecosystem.

Policies, legislation:

- Legal and regulatory framework for conducting clinical testing: Austria, as part of the EU, has adopted and will apply the new EU Clinical Trial Regulation (Regulation (EU) No 536/2014)(European Commission, 2014). This new regulation aims to create an environment, that is favourable to conduct clinical trial, but at highest safety and increased transparency (European Commission, 2014). The Austrian Federal Office for Safety in Health Care (Bundesamt für Sicherheit im Gesundheitswesen (BASG)) has a centralized information page where all applicable laws and regulations related to medical devices are collected (Austrian Federal Office for Safety in Health Care, 2020). Regarding data protection during clinical trials, GDPR is applicable for all parties involved (including data of clinicians, nurses involved).

- Digital Health and Innovation at Austrian National Public Health Insurance (Gesundheit Österreich GmbH (GÖG)): the Austrian National Public Health Insurance is responsible for the planning and researching the public healthcare in Austria. Its three business units are

---

[24] Information translated from German from the project website: https://www.zpm.at/de/das-zentrum/zentrum-fuer-praezisionsmedizin/ (last accessed on 05.06.2020)

responsible for innovation facilitation through data analysis (The Austrian National Institute for Health Services Research), for developing standards and registries to maintain high quality health care (The Austrian National Institute for Quality in Health Care) and for providing financial support for projects to increase knowledge, competences, and networks (The Austrian Health Promotion Fund). As mentioned on their website, they have a special expertise in digital health. The Head of Digital Health and Innovation directly reports to the Executive Board[25] and is listed as a mentor of Health Hub Vienna[26]. GÖG has performed an economic evaluation of telemedicine in Austria[27].

Patients and Patient Representatives:

- Digital literacy of citizens: the European Commission monitors the digitalization of EU member states with the Digital Economy and Society Index (DESI). According to the latest report in 2020 (European Commission, 2020), Austria is above the EU average (rank 9th) on the human capital part, which covers essentially the digital skills of citizens. As mentioned, 66% of citizens between 16 and 74 years of age have at least basic digital skills (versus 58% as the EU average). Despite this relatively high digital literacy, Austria continues to invest into the development of digital skills of broad citizen groups (European Commission, 2019b).

- Bundesverband Selbsthilfe Österreich (BVSHOE): the Federal Association of Self-Help Austria is an umbrella organization for disease specific Self-Help groups and Patient Organizations in Austria. It is a not-for-profit organization funded by the Österreichische Sozialversicherung (Austrian Social Insurance) and by the Federal Ministry of Social Affairs, Health, Care and Consumer Protection. The Association is already involved in digital health project as a representative of its member organizations: BVSHOE has the right to express opinion about the ELGA system and to form a direct communication channel between Patient Organizations and ELGA GmbH. As stated on the website of the Association[28], their aim is to bring the patient's view in how ELGA works. This mission is very much in line with

---

[25] Organization chart available at https://goeg.at/Organization_Chart (last accessed on 05.06.2020)
[26] Information from https://healthhubvienna.at/ (last accessed on 05.06.2020)
[27] Description of the project is available in German at https://goeg.at/Telegesundheitsdienste_oekonom_Eval (last accessed on 05.06.2020)
[28] Translated from German from the Association website at https://www.bundesverband-selbsthilfe.at/leuchtturmprojekte/ (last accessed on 05. 06. 2020)

how patient organizations can support development and validation of digital health by providing patient focused criteria.

- ProRare: ProRare (Alliance for Rare Diseases) supports the initiative of BVSHOE, to incorporate the patient's view into the development of ELGA (Pro Rare Austria, 2019). Additionally, the umbrella organization for Rare Disease Patient Organizations and Self-Help Groups acts as an intermediary between patients and politics, authorities, health care providers, research and national and international pharma companies[29]. This position of the Alliance makes it a strong partner in the ecosystem of digital health validation.

The summary of the Austrian digital health validation ecosystem is in Figure 15.

---

[29] Information available in German at https://www.prorare-austria.org/projekte/strategiepapiere/ last accessed on 05.06.2020.

Health Content – *High quality, consistent health related data sets* <u>Austrian example:</u> Data from ELGA (Electronic Health Record)	**Digital Health Innovation** – *Start-ups, SMEs, large corporates, research institutes* <u>Austrian examples</u>: AIT*, Universities* (MedUni Wien, Graz), large pharma** (BI, Sanofi, Pfizer, Novartis), Ludwig Boltzmann Institut for Digital Health and Patient Safety, start-ups and SMEs**	**Delivery Channels** – *Software and IT infrastructure to deliver digital health* <u>Austrian example:</u> Different modules of ELGA

Leadership and Governance

Digital Health Strategy – *national or regional strategy supporting validation and validated digital health products* <u>Austrian example:</u> Digitalization Agency, Digital Roadmap Austria, Digital Health in Wien (population consultation)	**Services Supporting Validation** – *CROs, advisors, accelerator programs, training institutes expert on validation* <u>Austrian example:</u> Health Hub Vienna**, DEXHELPP	**Policies & Legislation** – *clear legal and regulatory framework for conducting clinical testing* <u>Austrian example:</u> Clinical Trial Regulation (Regulation (EU) No 536/2014), Bundesamt für Sicherheit im Gesundheitswesen (BASG, Austrian Federal Office for Safety in Health Care)[d], AGES Medizinmarktaufsicht (Austrian Medicines Agency), GDPR	**Workforce** – *high digital literacy among clinicians/health care and social workers, expert clinical trial managers, statisticians, data analysts* <u>Austrian example:</u> Programmdirector for E-health, Telemedizin and Komplexitätsforschung at the Medical University of Vienna, Telemed Austria, hospitals[c]**
Public Financing Options (e.g. grants) – *National grants supporting validation* <u>Austrian example:</u> FFG**, FWF, Förderpilot.at	**Standards and Frameworks for Validation** - *developed by government agencis, health insurance bodies or NGOs* <u>Austrian example:</u> Methodological recommendations for the economic evaluation of eHealth applications in Austria 2018[a]	**Policies & Legislation** – *clear legal and regulatory framework on the requirements of clinical validation, experts at regulatory agency, insurance companies on digital health* <u>Austrian example:</u> European Notified Body of Medical Devices at University of Technology, Graz*; Digital Health and Innovation at Austrian National Public Health Insurance (GÖG), Versicherung für Eisenbahnen und Bergbau*	
Private Financing Options – *experienced angels, VCs supporting validation of digital health* <u>Austrian example:</u> ?	**Infrastructure** – *specialized sites for clinical testing, testbeds* <u>Austrian example:</u> Zentrum für Präzisionsmedizin, Ludwig Boltzmann Institut Digital Health and Patient Safety (Salzburg)		

Patients and Patient Representatives –
 <u>Austrian example:</u> high digital literacy of citizens, ~160 Self-Help and Patient Organizations („Selbsthilfe- und Patientenorganisationen"), Allianze for Rare Diseases (ProRare), Federal Association of Self-Help Austria (Bundesverband Selbsthilfe Österreich)[b]

a) Österreichise Sozialversicherung
b) https://www.bundesverband-selbsthilfe.at/ and https://oekuss.at/selbsthilfelandschaft_oesterreich
c) Complete list of Austrian hospitals involved in published digital health trials is in Chapter 5.1.
d) Collection of national and EU laws and regulations for medical device available at https://www.basg.gv.at/en/about-us/legal-basis#c12785

*Figure 15 Members of the digital health validation ecosystem in Austria (own illustration). *Elements identified by literature review, **Elements identified from expert interviews*

5.4. Limitations

This study of the Austrian digital health validation ecosystem has limitations.

On one hand, there were only 2 experts interiewed to identify elements of the ecosystem. However, one of the experts has worked with several digital health companies (some of those went through clinical testing or reimbursement) and she has probably one of the largest network in the Austrian digital health industry.

The second limitation is, that no expert was interviewed, who actually did clinical and economic validation; Expert #2 is in the process of applying for reimbursement and has experience in clinical use, but not in validation. However, accessibility to experts experienced in both clinical and economic validation of digital health is problematic even globally, as there are not many companies, who did proper validation (probably only one such company exists in Austria (MySugr[30])).

The third limitation is that with the review of scientific literature only those ecosystem members can be identified, who are i) interested in publishing the results in peer-reviewed journals (mainly academic research institutes), ii) experienced in how to publish a scientific journal and finally iii) satisfied with the results of the clinical testing (as negative results are rarely published, particularly not by non-academic institutes).

Finally, a limitation of the study is that it approached digital health in general, however the term covers highly different technologies, products and services, which – as Expert #1 pointed out –may not require clinical testing and may not have a chance for reimbursement (and consequently may become indifferent to economic validation). Further studies are needed to answer the same research questions from the perspectives of disjunct categories of digital health.

---

[30] Diabetes management app developed in Austria, acquired by Roche in 2017 https://www.mysugr.com/en/ last accessed on 14.06.2020.

6. Discussion

This chapter will conclude the strengths and gaps identified in the Austrian digital health ecosystem and propose international good practices to further strengthen it.

Strengths:

The Austrian digital health validation ecosystem benefits from a strong national commitment and comprehensive strategy on deploying digital health in the country. Additionally, the initiative of the capital, Vienna to become a leading digital city of the world could warrant support for further development of the ecosystem. The Electronic Health Record system can become a good source for consistent, high quality data and could serve as a delivery channel for the validation of new innovations (if modules developed by external companies can become integrated into ELGA).

The strong research and development activity of the universities and research institutes, as well as their active involvement in the clinical testing of digital health can form a fertile ground for validated innovations; these activities help building experts on the field, their publications can guide digital health companies designing their validation strategy and finally their involvement in international projects helps the import of good-practices to Austria.

The presence of centralized online platforms on the various public financing opportunities aid developers to find financial support for the validation easily.

A remarkable element of the ecosystem is the platform and accelerator program of the Health Hub Vienna; it is a one-stop-shop for digital health companies (particularly start-ups) to contact and network with most of the relevant stakeholders of the validation ecosystem. It can be particularly attractive for start-ups coming from outside of the EU to get information on the requirements in the EU.

Finally, the ecosystem is strengthened by high digital literacy of Austrian citizens and by the strong network of patient representative organizations.

Gaps:

This study identified two major gaps and a few segments, where the ecosystem could benefit from further development.

One clear gap is the lack of – visible – private investment options financing validation process. However, it is easy to imagine that current investors in digital health companies would support validation as well, however this study could not evaluate their willingness.

A second gap is in the infrastructure necessary for the clinical testing and validation of digital health. Although the Centre for Precision Medicine was identified as a potential site specialized on such clinical trials, the establishment of the institute is still in the planning phase. Additionally, the LBI Digital Health and Patient Safety seems to be a real-world testbed, however it is not clear, if the platform is still open for external digital health products or only aims to test internally developed solutions.

The ecosystem could be strengthened by developing additional Standards and Frameworks for Validation (particularly aiding the application for reimbursement) and by the targeted training of healthcare workers towards digital health validation. It is striking, that both interviewees mentioned the resistance of doctors towards digital health as a key challenge. Furthermore, the lowering of bureaucracy and the reduction of the impact of political debates on the ecosystem could be valuable for digital health companies.

<u>Potential good-practices to support the Austrian digital health validation ecosystem:</u>

Based on the literature overview in Chapter 2, three elements were identified, to support the ecosystem in Austria.

- **Testbeds:** as Expert #1 mentioned, real-world testbeds could be useful infrastructure elements to make validation of digital health easier and more efficient. This would also mean, that the scene supports the development of new innovations with higher value and with higher likelihood of successful implementation. Additionally, such testbeds could make Austria even more attractive for digital health innovators (Arntzen et al., 2019).

- **National evidence standard for digital health:** similar to the evidence standard framework developed by NICE in the UK, a pragmatic framework describing the evidence necessary for reimbursement could help developers in their journey through the process(NICE, 2019). This evidence framework could be supplemented with establishing **a collection of "approved" digital health solutions** (particularly wearables and apps) by Austrian institutes[31]. This collection could guide patients and healthcare providers

---

[31] Similar to the NHS app library (https://www.nhs.uk/apps-library/) last accessed on 14.06.2020.

selecting valuable and validated digital health solutions. Additionally, it could be an incentive for digital health companies to fulfil the necessary requirements and perform the necessary validation to get into the collection.

Bibliography

Accenture. (2018). *Accenture 2018 Consumer Survey on Digital Health*.
    https://www.accenture.com/_acnmedia/PDF-71/Accenture-Health-Meet-Todays-Healthcare-
    Team-Patients-Doctors-Machines.pdf#zoom=50

Alexander Walter. (2013). The Uphill Path to Successful Clinical Trials. *Pharmacy and Therapeutics*,
    38(4), 225–227. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3684189/?report=classic

Ammenwerth, E., Woess, S., Baumgartner, C., Fetz, B., van der Heidt, A., Kastner, P., Modre-Osprian,
    R., Welte, S., & Poelzl, G. (2015). Evaluation of an integrated telemonitoring surveillance
    system in patients with oronary heart disease. *Methods of Information in Medicine*, *54*(5), 388–
    397. https://doi.org/10.3414/ME15-02-0002

Arntzen, S., Wilcox, Z., Lee, N., Hadfield, C., Rae, J., Hadfield, C., & Rae, J. (2019). *Testing Innovation
    in the Real World - Real-world testbeds*. https://www.nesta.org.uk/report/testing-innovation-
    real-world/

Australia's National Digital Health Strategy | NATIONAL DIGITAL HEALTH STRATEGY. (n.d.). Retrieved
    May 19, 2020, from https://conversation.digitalhealth.gov.au/australias-national-digital-health-
    strategy

Austrian Federal Office for Safety in Health Care. (2020). *Legal Basis*.
    https://www.basg.gv.at/en/about-us/legal-basis#c12785

Bergmo, T. S. (2015). How to measure costs and benefits of ehealth interventions: An overview of
    methods and frameworks. In *Journal of Medical Internet Research* (Vol. 17, Issue 11). Journal of
    Medical Internet Research. https://doi.org/10.2196/jmir.4521

Biggs, J. S., Willcocks, A., Burger, M., & Makeham, M. A. B. (2019). Digital health benefits evaluation
    frameworks: building the evidence to support Australia's National Digital Health Strategy.
    Medical Journal of Australia, *210*(S6), S9–S11. https://doi.org/10.5694/mja2.50034

Brath, H., Morak, J., Kästenbauer, T., Modre-Osprian, R., Strohner-Kästenbauer, H., Schwarz, M.,
    Kort, W., & Schreier, G. (2013). Mobile health (mHealth) based medication adherence
    measurement - a pilot trial using electronic blisters in diabetes patients. *British Journal of
    Clinical Pharmacology*, *76*(S1), 47–55. https://doi.org/10.1111/bcp.12184

Cerreta, F., Ritzhaupt, A., Metcalfe, T., Askin, S., Duarte, J., Berntgen, M., & Vamvakas, S. (2020).
    Digital technologies for medicines: shaping a framework for success. In *Nature Reviews Drug
    Discovery*. Nature Research. https://doi.org/10.1038/d41573-020-00080-6

CHF and The George Institute for Global Health. (2018). *Going Digital to deliver a healthier Australia
    - a health policy report*. https://chf.org.au/sites/default/files/gdigital_report_j060618.pdf

Cohen, A. B., Mathews, S. C., Ray Dorsey, E., Bates, D. W., & Safavi, K. (2020). Direct-to-consumer
    digital health. *The Lancet Digital Health*, *2*(4), e163–e165. https://doi.org/10.1016/S2589-
    7500(20)30057-1

Coly, A., & Parry, G. (2017). *Evaluating Complex Health Interventions: A Guide to Rigorous Research
    Designs*. https://www.academyhealth.org/files/AH_Evaluation_Guide_FINAL.pdf

Craig, P., Katikireddi, S. V., Leyland, A., & Popham, F. (2017). Natural Experiments: An Overview of
    Methods, Approaches, and Contributions to Public Health Intervention Research. *Annual*

Review of Public Health, *38*(1), 39–56. https://doi.org/10.1146/annurev-publhealth-031816-044327

de Bruin, J. S., Schuh, C., Seeling, W., Luger, E., Gall, M., Hütterer, E., Kornek, G., Ludvik, B., Hoppichler, F., & Schindler, K. (2018). Assessing the feasibility of a mobile health-supported clinical decision support system for nutritional triage in oncology outpatients using Arden Syntax. *Artificial Intelligence in Medicine*, *92*, 34–42. https://doi.org/10.1016/j.artmed.2015.10.001

Digital Health Test Beds program | NATIONAL DIGITAL HEALTH STRATEGY. (n.d.). Retrieved May 19, 2020, from https://conversation.digitalhealth.gov.au/digital-health-test-beds-program

eHSG SubGroup on Reimbursement. (2019). *Proposed Guiding Principles for Reimbursement of Digital Health Products and Solutions*. https://www.medtecheurope.org/wp-content/uploads/2019/04/30042019_eHSGSubGroupReimbursement.pdf#page=14

EIT Health. (n.d.). *Living Labs and Test Beds - EIT Health*. Retrieved May 19, 2020, from https://eithealth.eu/project/living-labs-and-test-beds/

ELGA: About. (n.d.). Retrieved June 11, 2020, from http://www.elga.gv.at/en/about-elga/

European Commission. (2012). *eHealth Action Plan 2012-2020 - Innovative healthcare for the 21st century*. https://eur-lex.europa.eu/legal-content/HR/ALL/?uri=CELEX%3A52012DC0736

European Commission. (2014). Regulation (EU) No 536/2014 of the European Parliament and of the Council on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC. *Official Journal of the European Union*, *L 158/1*. https://ec.europa.eu/health//sites/health/files/files/eudralex/vol-1/reg_2014_536/reg_2014_536_en.pdf

European Commission. (2016). *Guidelines on Medical Devices - Clinical Evaluation: A guide for manufacturers and notified bodies under directives 93/42/EEC and 91/385/EEC*.

European Commission. (2019a). *Digital Government Factsheet 2019 Austria*. https://joinup.ec.europa.eu/sites/default/files/inline-files/Digital_Government_Factsheets_Austria_2019_3.pdf

European Commission. (2019b). *Monitoring progress in national initiatives on digitising industry (Country report Austria)*.

European Commission. (2020). *Digital Economy and Society Index (DESI) 2020 Austria*. https://ec.europa.eu/digital-single-market/en/scoreboard/austria

FDA. (2019). *Software Precertification Program 2019 Mid-Year Update*. https://www.fda.gov/media/129047/download

FDA. (2020a). *Classify Your Medical Device*. https://www.fda.gov/medical-devices/overview-device-regulation/classify-your-medical-device

FDA. (2020b). *Content of a 510(k)*. https://www.fda.gov/medical-devices/premarket-notification-510k/content-510k#link_12

Federal Chancellery and Federal Ministry of Science Research and Economy, Digital Roadmap Austria (Vienna, 2016)

<https://www.digitalroadmap.gv.at/fileadmin/downloads/digital_road_map_broschuere_eng.pdf>.

Federal Ministry for Digital and Economic Affairs, "Health, Care and Social Affairs: Digital Roadmap Austria" <https://www.digitalroadmap.gv.at/en/fields-of-action-and-measures/health-care-and-social-affairs/> [accessed 20 June 2020].

Federal Trade Commission. (n.d.). *Health Claims*. Retrieved June 13, 2020, from https://www.ftc.gov/tips-advice/business-center/advertising-and-marketing/health-claims

Federal Trade Commission. (2013). *Marketing Your Mobile App: Get It Right from the Start*. https://www.ftc.gov/tips-advice/business-center/guidance/marketing-your-mobile-app-get-it-right-start

Ferretti, A., Ronchi, E., & Vayena, E. (2019). From principles to practice: benchmarking government guidance on health apps. In *The Lancet Digital Health* (Vol. 1). https://doi.org/10.1016/S2589-7500(19)30027-5

Focus Group on "Artificial Intelligence for Health." (n.d.). Retrieved May 29, 2020, from https://www.itu.int/en/ITU-T/focusgroups/ai4h/Pages/default.aspx

Forum LLSA > Accueil. (n.d.). Retrieved May 19, 2020, from https://www.forumllsa.org/

Frühauf, J., Kröck, S., Quehenberger, F., Kopera, D., Fink-Puches, R., Komericki, P., Pucher, S., Arzberger, E., & Hofmann-Wellenhof, R. (2015). Mobile teledermatology helping patients control high-need acne: A randomized controlled trial. *Journal of the European Academy of Dermatology and Venereology*, *29*(5), 919–924. https://doi.org/10.1111/jdv.12723

Gathani, R., & Cowlishaw, S. (2019). *EU Medical Device Coordination Group Publishes Guidance on the Qualification and Classification of Software under Upcoming Medical Device Regulations | Covington Digital Health*. https://www.covingtondigitalhealth.com/2019/10/eu-medical-device-coordination-group-publishes-guidance-on-the-qualification-and-classification-of-software-under-upcoming-medical-device-regulations/

Goldsack, J. C., Coravos, A., Bakker, J. P., Bent, B., Dowling, A. v., Fitzer-Attas, C., Godfrey, A., Godino, J. G., Gujar, N., Izmailova, E., Manta, C., Peterson, B., Vandendriessche, B., Wood, W. A., Wang, K. W., & Dunn, J. (2020). Verification, analytical validation, and clinical validation (V3): the foundation of determining fit-for-purpose for Biometric Monitoring Technologies (BioMeTs). *Npj Digital Medicine*, *3*(1), 1–15. https://doi.org/10.1038/s41746-020-0260-4

Gordon, W. J., Landman, A., Zhang, H., & Bates, D. W. (2020). Beyond validation: getting health apps into clinical practice. *Npj Digital Medicine*, *3*(1), 1–6. https://doi.org/10.1038/s41746-019-0212-z

Granstrand, O., & Holgersson, M. (2020). Innovation ecosystems: A conceptual review and a new definition. In *Technovation* (Vols. 90–91, p. 102098). Elsevier Ltd. https://doi.org/10.1016/j.technovation.2019.102098

Hayn, D., Kollmann, A., Perl, S., Kos, C., Rotman, B., Lercher, P., Tscheliessnigg, K. H., & Schreier, G. (2013). A randomized controlled clinical trial of pacemaker follow-up in clinic and by telemedical interpretation of the pacemakers' magnet mode. *Journal of Telemedicine and Telecare*, *19*(8), 456–465. https://doi.org/10.1177/1357633X13512066

Hillestad, R., Bigelow, J., Bower, A., Girosi, F., Meili, R., Scoville, R., & Taylor, R. (2005). Can electronic medical record systems transform health care? Potential health benefits, savings, and costs. *Health Affairs*, *24*(5), 1103–1117. https://doi.org/10.1377/hlthaff.24.5.1103

IMDRF SaMD Working Group. (2013). *Software as a Medical Device (SaMD): Key Definitions*. http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-131209-samd-key-definitions-140901.pdf

IMDRF Software as a Medical Device Working Group. (2017). *Software as a Medical Device (SAMD): Clinical Evaluation - Guidance for Industry and Food and Drug Administration Staff*.

IQVIA Institute for Human Data Science. (2017). *The Growing Value of Digital Health*. https://www.iqvia.com/insights/the-iqvia-institute/reports/the-growing-value-of-digital-health

Istepaniana, R. S. H., & AlAnzi, T. (2020). Mobile health (m-health): evidence-based progress or scientific retrogression. In D. D. Feng (Ed.), *Biomedical Information Technology* (pp. 717–733). Academic Press.

J Chen. (2018). *Agent-based Modelling in Healthcare Operations: A Systematic Review of its Scope, Quality and Implementation*. https://ora.ox.ac.uk/objects/uuid:9b71bc9f-61c1-4485-93b2-0b7e17e0e62f/download_file?file_format=pdf&safe_filename=SysReview%2Bof%2BABM%2Bin%2BHealthcare%2BOperations%2B%25281010130%253B%2B2017-2018%2BDissertation%2529.pdf&type_of_work=Thesis

Jandoo, T. (2020). DIGITAL HEALTH WHO guidance for digital health: What it means for researchers. *Digital Health*, *6*, 1–4. https://doi.org/10.1177/2055207619898984

Jörg Schickert and others, "Digital Health Solutions to Become Reimbursable in Germany – Milestone for Patients and Providers | Focus on Regulation," 2019 <https://www.hlregulation.com/2019/11/15/digital-health-solutions-to-become-reimbursable-in-germany-milestone-for-patients-and-providers/> [accessed 1 June 2020].

Keesara, S., Jonas, A., & Schulman, K. (2020). Covid-19 and Health Care's Digital Revolution. *New England Journal of Medicine*, *382*(23), e82(1)-e82(3). https://doi.org/10.1056/nejmp2005835

Kellermann, A. L., & Jones, S. S. (2013). What It Will Take To Achieve The As-Yet-Unfulfilled Promises Of Health Information Technology Care Transformation. *Health Affairs*, *32*(1), 63–68. https://doi.org/10.1377/hlthaff.2012.0693

Kollmann, A., Riedl, M., Kastner, P., Schreier, G., & Ludvik, B. (2007). Feasibility of a mobile phone-based data service for functional insulin treatment of type 1 diabetes mellitus patients. *Journal of Medical Internet Research*, *9*(5). https://doi.org/10.2196/jmir.9.5.e36

Kotzian, S. T., Schwarzinger, A., Haider, S., Saletu, B., Spatt, J., & Saletu, M. T. (2018). Home polygraphic recording with telemedicine monitoring for diagnosis and treatment of sleep apnoea in stroke (HOPES Study): study protocol for a single-blind, randomised controlled trial. *BMJ Open*, *8*, 18847. https://doi.org/10.1136/bmjopen-2017-018847

Kowatsch, T., Otto, L., Harperink, S., Cotti, A., & Schlieter, H. (2019). A design and evaluation framework for digital health interventions. *IT - Information Technology*, *61*(5–6), 253–263. https://doi.org/10.1515/itit-2019-0019

Kreiner, K., Welte, S., Modre-Osprian, R., Fetz, B., Heidt, A., Kropf, M., Ammenwerth, E., Pölzl, G., & Kastner, P. (2015). A Personalized Feedback System for Supporting Behavior Change for

Patients after an Acute Myocardial Infarction. *Studies in Health Technology and Informatics*, *212*, 50–56. https://doi.org/10.3233/978-1-61499-524-1-50

LeFevre, A. E., Shillcutt, S. D., Broomhead, S., Labrique, A. B., & Jones, T. (2017). Defining a staged-based process for economic and financial evaluations of mHealth programs. *Cost Effectiveness and Resource Allocation*, *15*(1). https://doi.org/10.1186/s12962-017-0067-6

Ludwig Boltzmann Institut for Digital Health and Patient Safety | Ludwig Boltzmann Gesellschaft. (n.d.). Retrieved May 26, 2020, from https://www.lbg.ac.at/lbi-dhps

Maguire, R., Fox, P. A., Mccann, L., Miaskowski, C., Kotronoulas, G., Miller, M., Furlong, E., Ream, E., Armes, J., Patiraki, E., Gaiger, A., Berg, G. v, Flowerday, A., Donnan, P., Mccrone, P., Apostolidis, K., Harris, J., Katsaragakis, S., Buick, A. R., & Kearney, N. (2017). The eSMART study protocol: a randomised controlled trial to evaluate electronic symptom management using the advanced symptom management system (ASyMS) remote technology for patients with cancer. *BMJ Open*, *7*, 15016. https://doi.org/10.1136/bmjopen-2016-015016

Marinschek, S., Dunitz-Scheer, M., Pahsini, K., Geher, B., & Scheer, P. (2014). Weaning children off enteral nutrition by netcoaching versus onsite treatment: A comparative study. *Journal of Paediatrics and Child Health*, *50*(11), 902–907. https://doi.org/10.1111/jpc.12662

Mathews, S. C., Mcshea, M. J., Hanley, C. L., Ravitz, A., Labrique, A. B., & Cohen, A. B. (2019). Digital health: a path to validation. *Npj Digital Medicine*, *2*(38). https://doi.org/10.1038/s41746-019-0111-3

Mayring, P. (2014). *Qualitative Content Analysis Theoretical Foundation, Basic Procedures and Software Solution*. http://nbn-resolving.de/urn:nbn:de:0168-ssoar-395173

McNamee, P., Murray, E., Kelly, M. P., Bojke, L., Chilcott, J., Fischer, A., West, R., & Yardley, L. (2016). Designing and Undertaking a Health Economics Study of Digital Health Interventions. *American Journal of Preventive Medicine*, *51*(5), 852–860. https://doi.org/10.1016/j.amepre.2016.05.007

Medizinische Universität Innsbruck. (2018). *Ludwig Boltzmann Digital Health Institutes on Patient-Centered Health Systems*. https://www.i-med.ac.at/forschung/files/Fact-Sheet-LBI-Digital-Health-Institutes.pdf

Mercom Capital Group. (2019). *Digital Health Funding and M and A: 2019 Fourth Quarter and Annual Report*. https://mercomcapital.com/wp-content/uploads/2020/01/MercomDigitalHealthFundingMAQ42019ExecSumm.pdf

Mercom Capital Group. (2020). *Q1 2020 Digital Health (Healthcare IT) Funding and M and A Report*. https://mercomcapital.com/product/q1-2020-digital-health-healthcare-it-funding-ma-report/

MobiHealthNews, "MobiHealthNews' Predictions for 2020: Big Tech's Here to Stay, Digital Health Moves through Gartner Hype Cycle and More | MobiHealthNews," 2020 <https://www.mobihealthnews.com/news/mobihealthnews-predictions-2020-big-techs-here-stay-digital-health-moves-through-gartner-hype> [accessed 7 June 2020].

Morak, J., Schwarz, M., Hayn, D., & Schreier, G. (2012). Feasibility of mHealth and Near Field Communication technology based medication adherence monitoring. *Proceedings of the Annual International Conference of the IEEE Engineering in Medicine and Biology Society, EMBS*, *2012*, 272–275. https://doi.org/10.1109/EMBC.2012.6345922

Moshi, M. R., Tooher, R., & Merlin, T. (2018). Suitability of current evaluation frameworks for use in the health technology assessment of mobile medical applications: A systematic review. *International Journal of Technology Assessment in Health Care*, *34*(5), 464–475. https://doi.org/10.1017/S026646231800051X

Murray, E., Hekler, E. B., Professor, A., Andersson, G., Collins, L. M., Doherty, A., Hollis, C., Rivera, D. E., West, R., of Health Psychology, P., Wyatt, J. C., Director, F., & Murray FRCGP FRCP, E. (2016). Evaluating digital health interventions: key questions and approaches HHS Public Access. *Am J Prev Med*, *51*(5), 843–851. https://doi.org/10.1016/j.amepre.2016.06.008

National Institute for Health and Care Excellence. (2019). *Evidence Standards Framework for Digital Health Technologies Contents*. https://www.nice.org.uk/about/what-we-do/our-programmes/evidence-standards-framework-for-digital-health-technologies

Nemecek, R., Huber, P., Schur, S., Masel, E. K., Baumann, L., Hoeller, C., Watzke, H., & Binder, M. (2019). Telemedically augmented palliative care: Empowerment for patients with advanced cancer and their family caregivers. *Wiener Klinische Wochenschrift*, *131*(23–24), 620–626. https://doi.org/10.1007/s00508-019-01562-3

NHS Accelerated Access Collaborative » Test beds. (n.d.). Retrieved May 19, 2020, from https://www.england.nhs.uk/aac/what-we-do/how-can-the-aac-help-me/test-beds/

NHS England. (2015). *Real world testing of "combinatorial innovation" A global invitation to innovators*. https://www.england.nhs.uk/wp-content/uploads/2015/03/test-bed-prospectus.pdf

NHS England. (2018a). *NHS England Test Beds Programme: Evaluation learning from Wave 1*. https://www.england.nhs.uk/wp-content/uploads/2018/11/test-beds-programme-evaluation-learning-from-wave-1.pdf

NHS England. (2018b). *Test Beds Programme Information to support the launch of wave 2*. https://www.england.nhs.uk/wp-content/uploads/2018/04/test-beds-supporting-information-wave-2-competition.pdf

NHS England launch second phase of Test Bed programme. (n.d.). Retrieved May 19, 2020, from https://www.digitalhealth.net/2018/02/nhs-england-office-life-sciences-launch-second-phase-test-bed/

NICE. (2019). *Evidence Standards Framework for Digital Health Technologies*.

Niebauer J, & Stütz T. (2019). Neues Ludwig-Boltzmann-Institut für digitale Gesundheit am Universitätsinstitut für Sportmedizin in Salzburg. *German Journal of Sports Medicine*, *70*, 143–144.

O'Dea, S. (2020). *Smartphone users worldwide 2016-2021*. https://www.statista.com/statistics/330695/number-of-smartphone-users-worldwide/

OECD/European Observatory on Health Systems and Policies. (2019). *Austria: Country Health Profile 2019, State of Health in the EU*. http://www.euro.who.int/__data/assets/pdf_file/0005/419450/Country-Health-Profile-2019-Austria.pdf?ua=1

O'Rourke, B., Oortwijn, W., & Schuller, T. (2020). The new definition of health technology assessment: A milestone in international collaboration. *International Journal of Technology Assessment in Health Care*, 1–4. https://doi.org/10.1017/S0266462320000215

Piotr Arak, & Anna Wójcik. (2017). *Transforming eHealth into a political and economic advantage*. https://ec.europa.eu/digital-single-market/en/news/transforming-ehealth-political-and-economic-advantage

Pro Rare Austria, Patientenstrategie ELGA - Eine Initiative von BVSHÖ Und Pro Rare Austria, 2019 <https://www.prorare-austria.org/fileadmin/user_upload/project/BVSHOEPRA_StrategiepapierELGA_20190723.pdf>.

Rader, S., Thomas, ·, Dorner, E., Schoberberger, R., & Wolf, H. (2017). Effects of a web-based follow-up intervention on self-efficacy in obesity treatment for women. *Wien Klin Wochenschr*, *129*, 472–481. https://doi.org/10.1007/s00508-017-1198-7

Rahimi, K. (2019). Digital health and the elusive quest for cost savings. In *The Lancet Digital Health* (Vol. 1, Issue 3, pp. e108–e109). Elsevier Ltd. https://doi.org/10.1016/S2589-7500(19)30056-1

Rainer Thiel, Lucas Deimel, Daniel Schmidtmann, Klaus Piesche, Tobias Hüsing, Jonas Rennoch, Veli Stroetmann, & Karl Stroetmann. (2018). *#SmartHealthSystems International comparison of digital strategies*. https://www.bertelsmann-stiftung.de/fileadmin/files/Projekte/Der_digitale_Patient/VV_SHS-Studie_EN.pdf

Rami, B., Popow, C., Horn, W., Waldhoer, T., & Schober, E. (2006). Telemedical support to improve glycemic control in adolescents with type 1 diabetes mellitus. *European Journal of Pediatrics*, *165*(10), 701–705. https://doi.org/10.1007/s00431-006-0156-6

Robert Picard. (2017). *Co-design in Living Labs for Healthcare and Independent Living: Concepts, Methods and Tools* (Robert Picard, Ed.). Wiley ISTE.

Rowland, S. P., Fitzgerald, J. E., Holme, T., Powell, J., & Mcgregor, A. (2020). What is the clinical value of mHealth for patients? *Npj Digital Medicine*, *3*(4). https://doi.org/10.1038/s41746-019-0206-x

Safavi, K., Mathews, S. C., Bates, D. W., Ray Dorsey, E., & Cohen, A. B. (2019). Top-funded digital health companies and their impact on high-burden, high-cost conditions. *Health Affairs*, *38*(1), 115–123. https://doi.org/10.1377/hlthaff.2018.05081

Sanson-Fisher, R. W., D'Este, C. A., Carey, M. L., Noble, N., & Paul, C. L. (2014). Evaluation of Systems-Oriented Public Health Interventions: Alternative Research Designs. *Annual Review of Public Health*, *35*(1), 9–27. https://doi.org/10.1146/annurev-publhealth-032013-182445

Scherr, D., Kastner, P., Kollmann, A., Hallas, A., Auer, J., Krappinger, H., Schuchlenz, H., Stark, G., Grander, W., Jakl, G., Schreier, G., & Fruhwald, F. M. (2009). Effect of home-based telemonitoring using mobile phone technology on the outcome of heart failure patients after an episode of acute decompensation: randomized controlled trial. *Journal of Medical Internet Research*, *11*(3). https://doi.org/10.2196/jmir.1252

Schickert, J., Goehl, B., Thiermann, A., & Welter-Birk, T. (2019). *Digital health solutions to become reimbursable in Germany – milestone for patients and providers | Focus on Regulation*. https://www.hlregulation.com/2019/11/15/digital-health-solutions-to-become-reimbursable-in-germany-milestone-for-patients-and-providers/

Schusterbauer, V., Feitek, D., Kastner, P., & Toplak, H. (2018). Two-Stage evaluation of a telehealth nutrition management service in support of Diabesity therapy. *Studies in Health Technology and Informatics*, *248*, 314–321. https://doi.org/10.3233/978-1-61499-858-7-314

Sean, D. (2020). *In 2019, digital health celebrated six IPOs as venture investment edged off record highs*. https://rockhealth.com/reports/in-2019-digital-health-celebrated-six-ipos-as-venture-investment-edged-off-record-highs/

Shana Vijayan. (2019). *Test Beds: Digital Health Technologies in the NHS: The case for agile regulation, experimentation, implementation and evaluation.* www.england.nhs.uk

Sheon, A. R., Van Winkle, B., Solad, Y., & Atreja, A. (2018). An Algorithm for Digital Medicine Testing: A NODE.Health Perspective Intended to Help Emerging Technology Companies and Healthcare Systems Navigate the Trial and Testing Period prior to Full-Scale Adoption. *Digital Biomarkers*, *2*(3), 139–154. https://doi.org/10.1159/000494365

Sienkiewicz, D., & van Lingen, C. (2017). *The added value of patient organizations*. https://www.eu-patient.eu/globalassets/library/publications/epf_added_value_report_final.pdf

Testbed - Wikipedia. (n.d.). Retrieved May 18, 2020, from https://en.wikipedia.org/wiki/Testbed

The European Parlament and the Council of the European Union. (2017). *Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/4*.

Topol Review. (2019). *Preparing the healthcare workforce to deliver the digital future*. https://topol.hee.nhs.uk/wp-content/uploads/HEE-Topol-Review-2019-printable.pdf

Title 21 - FOOD AND DRUGS CHAPTER 9 - FEDERAL FOOD, DRUG, AND COSMETIC ACT SUBCHAPTER II - DEFINITIONS Sec. 321 - Definitions; generally, Pub. L. No. 21 U.S.C. 321 (2006). https://www.govinfo.gov/content/pkg/USCODE-2010-title21/pdf/USCODE-2010-title21-chap9-subchapII-sec321.pdf

U.S. Department of Health and Human Services, Food and Drug Administration, Center for Devices and Radiological Health, C. for B. E. and R. (2019). *Policy for Device Software Functions and Mobile Medical Applications Guidance for Industry and Food and Drug Administration Staff Preface Public Comment*. https://www.fda.gov/media/80958/download

Validic. (2019). *What CMS's Latest Ruling Means for RPM*. https://validic.com/what-cmss-latest-ruling-means-for-rpm/

van Velthoven, M. H., Carlos Cordon, ;, Helena, M., & Velthoven, V. (2019). Sustainable Adoption of Digital Health Innovations: Perspectives From a Stakeholder Workshop. *Journal of Medical Internet Research*, *21*(3), e11922. https://doi.org/10.2196/11922

van Velthoven, M. H., Smith, J., Wells, G., & Brindley, D. (2018). Digital health app development standards: A systematic review protocol. *BMJ Open*, *8*(8). https://doi.org/10.1136/bmjopen-2018-022969

Van Winkle, B., Solad, Y., Vaswani, N., & Rosner, B. I. (2019). Navigating the Digital Health Ecosystem to Bridge the Gap from Innovation to Transformation: A NODE.Health Perspective on Digital Evidence. *Digital Biomarkers*, *3*(2), 83–91. https://doi.org/10.1159/000500194

Vayena, E., Haeusermann, T., Adjekum, A., & Blasimme, A. (2018). Digital health: meeting the ethical and policy challenges. In *Swiss medical weekly* (Vol. 148, Issue 0304, p. w14571). EMH Media. https://doi.org/10.4414/smw.2018.14571

WHO Global Observatory for eHealth, & World Health Organization. (2016). *Atlas of eHealth country profiles : the use of eHealth in support of universal health coverage : based on the findings of the third global survey on eHealth, 2015*. WHO Document Production Services.

Wiegand, T., Krishnamurthy, R., Kuglitsch, M., Lee, N., Pujari, S., Salathé, M., Wenzel, M., & Xu, S. (2019). WHO and ITU establish benchmarking process for artificial intelligence in health. In *The Lancet* (Vol. 394, Issue 10192, pp. 9–11). Lancet Publishing Group. https://doi.org/10.1016/S0140-6736(19)30762-7

Willner, V., Schneider, ; C, Feichtenschlager, ; M, Willner, V., Research, S., Jakob, F. M. B. H., & Straße, H. (2015). eHealth 2015 Special Issue: Effects of an assistance service on the quality of life of elderly users. *Appl Clin Inform*, *6*, 429–442. https://doi.org/10.4338/ACI-2015-03-RA-0033

Working Group on mHealth assessment guidelines. (2017). *Report of the Working Group on mHealth assessment guidelines | Shaping Europe's digital future*. https://ec.europa.eu/digital-single-market/en/news/report-working-group-mhealth-assessment-guidelines

World Bank. (2012). *Information and Communications for Development 2012: Maximizing Mobile*. https://doi.org/10.1596/978-0-8213-8991-1

World Health Organization. (2018). *Classification of digital health interventions v1. 0: a shared language to describe the uses of digital technology for health*.

World Health Organization. (2019a). *Recommendations on digital interventions for health system strengthening (WHO/RHR/19.8). Licence: CC BY-NC-SA 3.0 IGO.* https://apps.who.int/iris/bitstream/handle/10665/311977/WHO-RHR-19.8-eng.pdf?ua=1

World Health Organization. (2019b). *WHO guideline: recommendations on digital interventions for health system strengthening. Executive summary.*

World Health Organization. (2020). *COVID-19 and digital health: What can digital health offer for COVID-19?* https://www.who.int/china/news/feature-stories/detail/covid-19-and-digital-health-what-can-digital-health-offer-for-covid-19

World Health Organization Executive Board 142. (2017). *mHealth - Use of appropriate digital technologies for public health: report by the Director-General.* https://apps.who.int/iris/handle/10665/274134

Appendix

Appendix 1 Classification of Digital Health Interventions v.1.0. Source: (World Health Organization, 2018, pp. 6–9)

1.0 CLIENTS

1.1 Targeted client communication
- 1.1.1 Transmit health event alerts to specific population group(s)
- 1.1.2 Transmit targeted health information to client based on health status or demographics
- 1.1.3 Transmit targeted alerts and reminders to client(s)
- 1.1.4 Transmit diagnostics result, or availability of result, to clients

1.2 Untargeted client communication
- 1.2.1 Transmit untargeted health information to an undefined population
- 1.2.2 Transmit untargeted health event alerts to undefined group

1.3 Client to client communication
- 1.3.1 Peer group for clients

1.4 Personal health tracking
- 1.4.1 Access by client to own medical records
- 1.4.2 Self monitoring of health or diagnostic data by client
- 1.4.3 Active data capture/ documentation by client

1.5 Citizen based reporting
- 1.5.1 Reporting of health system feedback by clients
- 1.5.2 Reporting of public health events by client

1.6 On-demand information services to clients
- 1.6.1 Client look-up of health information

1.7 Client financial transactions
- 1.7.1 Transmit or manage out of pocket payments by client
- 1.7.2 Transmit or manage vouchers to client for health services
- 1.7.3 Transmit or manage incentives to clients for health services

2.0 HEALTHCARE PROVIDERS

2.1 Client identification and registration
- 2.1.1 Verify client unique identity
- 2.1.2 Enrol client for health services/clinical care plan

2.2 Client health records
- 2.2.1 Longitudinal tracking of client's health status and services received
- 2.2.2 Manage client's structured clinical records
- 2.2.3 Manage client's unstructured clinical records
- 2.2.4 Routine health indicator data collection and management

2.3 Healthcare provider decision support
- 2.3.1 Provide prompts and alerts based according to protocol
- 2.3.2 Provide checklist according to protocol
- 2.3.3 Screen clients by risk or other health status

2.4 Telemedicine
- 2.4.1 Consultations between remote client and healthcare provider
- 2.4.2 Remote monitoring of client health or diagnostic data by provider
- 2.4.3 Transmission of medical data to healthcare provider
- 2.4.4 Consultations for case management between healthcare providers

2.5 Healthcare provider communication
- 2.5.1 Communication from healthcare provider to supervisor
- 2.5.2 Communication and performance feedback to healthcare provider
- 2.5.3 Transmit routine news and workflow notifications to healthcare provider(s)
- 2.5.4 Transmit non-routine health event alerts to healthcare providers
- 2.5.5 Peer group for healthcare providers

2.6 Referral coordination
- 2.6.1 Coordinate emergency response and transport
- 2.6.2 Manage referrals between points of service within health sector
- 2.6.3 Manage referrals between health and other sectors

2.7 Health worker activity planning and scheduling
- 2.7.1 Identify clients in need of services
- 2.7.2 Schedule healthcare provider's activities

2.8 Healthcare provider training
- 2.8.1 Provide training content to healthcare provider(s)
- 2.8.2 Assess capacity of healthcare provider

2.9 Prescription and medication management
- 2.9.1 Transmit or track prescription orders
- 2.9.2 Track client's medication consumption
- 2.9.3 Report adverse drug effects

2.10 Laboratory and Diagnostics Imaging Management
- 2.10.1 Transmit diagnostic result to healthcare provider
- 2.10.2 Transmit and track diagnostic orders
- 2.10.3 Capture diagnostic results from digital devices
- 2.10.4 Track biological specimens

3.0 HEALTH SYSTEM MANAGERS

3.1 Human resource management
- 3.1.1 List health workforce cadres and related identification information
- 3.1.2 Monitor performance of healthcare provider(s)
- 3.1.3 Manage certification/ registration of healthcare provider(s)
- 3.1.4 Record training credentials of healthcare provider(s)

3.2 Supply chain management
- 3.2.1 Manage inventory and distribution of health commodities
- 3.2.2 Notify stock levels of health commodities
- 3.2.3 Monitor cold-chain sensitive commodities
- 3.2.4 Register licensed drugs and health commodities
- 3.2.5 Manage procurement of commodities
- 3.2.6 Report counterfeit or substandard drugs by clients

3.3 Public health event notification
- 3.3.1 Notification of public health events from point of diagnosis

3.4 Civil Registration and Vital Statistic
- 3.4.1 Notify birth event
- 3.4.2 Register birth event
- 3.4.3 Certify birth event
- 3.4.4 Notify death event
- 3.4.5 Register death event
- 3.4.6 Certify death event

3.5 Health financing
- 3.5.1 Register and verify client insurance membership
- 3.5.2 Track insurance billing and claims submission
- 3.5.3 Track and manage insurance reimbursement
- 3.5.4 Transmit routine payroll payment to healthcare provider(s)
- 3.5.5 Transmit or manage incentives to healthcare provider(s)
- 3.5.6 Manage budget and expenditures

3.6 Equipment and asset management
- 3.6.1 Monitor status of health equipment
- 3.6.2 Track regulation and licensing of medical equipment

3.7 Facility management
- 3.7.1 List health facilities and related information
- 3.7.2 Assess health facilities

4.0 DATA SERVICES

4.1 Data collection, management, and use
- 4.1.1 Non routine data collection and management
- 4.1.2 Data storage and aggregation
- 4.1.3 Data synthesis and visualization
- 4.1.4 Automated analysis of data to generate new information or predictions on future events

4.2 Data coding
- 4.2.1 Parse unstructured data into structured data
- 4.2.2 Merge, de-duplicate, and curate coded datasets or terminologies
- 4.2.3 Classify disease codes

4.3 Location mapping
- 4.3.1 Map location of health facilities/structures
- 4.3.2 Map location of health events
- 4.3.3 Map location of clients and households
- 4.3.4 Map location of healthcare provider(s)

4.4 Data exchange and interoperability
- 4.4.1 Data exchange across systems

Appendix 2. Ranking of digital health intervention evaluation criteria based on their frequency in published evaluation frameworks. #EC shows the number of evaluation criteria in that category (in % of all criteria i.e. 331). Source: (Kowatsch et al., 2019)

Name	Description	# EC
Ease of use	The degree to which effort is required to take advantage of the DHI (e. g., using common interaction paradigms). [69, 72, 85]	87, 26.3 %
Content quality	The degree to which the content of a DHI is accurate, timely, complete, relevant, and consistent (e. g., real-time location-based pollen warnings for asthmatics). [45, 79, 81]	41, 12.4 %
Privacy & security	The degree to which the DHI considers legal requirements and aspects with respect to privacy and security aspects (e. g., a DHI is compliant with the General Data Protection Regulation). [17, 49, 74, 88]	41, 12.4 %
Account-ability	The degree to which information about the DHI is made explicit for usage decisions (e. g., details of the intervention author of a DHI are accessible). [23, 40, 44]	39, 11.8 %
Adherence	The ratio of actual usage to intended usage of a DHI (e. g., 4 out of 5 exercises are conducted per week). [2, 42, 80]	27, 8.2 %
Aesthetics	The degree to which the DHI interface applies design elements, colors and fonts in a logical way (e. g., consistent use of colors, figures and fonts). [45, 58]	19, 5.7 %
Perceived benefit	The degree to which a person believes that using a DHI improves his or her health behavior/health condition (e. g., a believe that a DHI helps to increase physical activity). [17, 73]	18, 5.4 %
Effective-ness	The degree to which the DHI contributes to the enhancement of an individual's health behavior/condition (e. g., significant reduction of fat mass). [17, 67, 73]	17, 5.1 %
Service quality	The extent to which support of a DHI is provided (e. g., a technical support line is made available). [49]	15, 4.5 %
Personal-ization	The degree to which the DHI adapts to the needs of an individual (e. g., the daily step goal of a DHI adapts to the capabilities of an individual). [14]	11, 3.3 %
Perceived enjoyment	The degree to which an individual believes that using a DHI is engaging (e. g., the use of game elements and level designs in a DHI). [73]	8, 2.4 %
Ethics	The degree to which the DHI addresses ethical aspects (e. g., the DHI was designed for individuals with various cultural backgrounds or disabilities). [88]	5, 1.5 %
Safety	The extent to which the usage of a DHI is safe with respect to side effects (e. g., interactions with a DHI are limited to account for addiction behavior). [88]	3, 0.9 %

Appendix 3. Analogues of clinical testing phases for classical and digital health products. Source: (Sheon et al., 2018, p. 6)

Drug and device trials			Digital medicine studies		
therapeutic and device testing phases			digital health (nonregulated) product testing phases		
phase	purpose	population	phase	purpose	population
Preclinical	Test drug safety and pharmacodynamics. Required to test new drug in humans	Animals	Pre-marketing	Classify device accessories into levels of risk (e.g., class I or class II). Ensure safety of radiation-emitting devices	Animals or lab only
Phase I: in vivo	Safety and toxicity	Healthy or sick volunteers (n = very small)	Phase I: in silico	Identify likely use cases. Rapidly determine whether and how a product is used. Identify desired and missing features	Healthy or sick volunteers (n = small)
Phase II: therapeutic exploratory	Safety, pharmacokinetics, optimal dosing, frequency and rout of administration, and endpoints. Generate initial indication of efficacy to determine sample size needed for phase III	Sick volunteers (n = small)	Phase II: feasibility	Develop/refine clinical work flow. Assess usability. Generate initial indication of efficacy to determine sample size needed for phase III	Volunteers reflecting Intended users (n = medium)
Phase III: pivotal or efficacy	Experimental study to demonstrate efficacy. Estimate incidence of common adverse events	Diverse target population (n = medium)	Phase III: pivotal or efficacy	Experimental study to demonstrate clinical effectiveness and/or financial return on investment	Intended users, defined settings and context (n = medium/large)
Phase IV: therapeutic use or postmarketing	Observational study to identify uncommon adverse events. Evaluate cost or effectiveness in populations	Reports collected from universe of real-world users (n = census)	Implementation	Observational or experimental design. Uses implementation science including change management and rapid cycle testing to deploy a tested intervention at scale. Assess effectiveness and unintended consequences in specific or real-world settings. Assess integration requirements, interoperability, staffing and staff training requirements for widespread adoption	Intended users, real-world setting and context (n = universe in a specific setting)
Pragmatic (effectiveness) trial	Understand effectiveness of drug or device in real-world settings	May use EHR or other "big data" sources. Diverse settings and patient population	Pragmatic (effectiveness) trial	Understand effectiveness of technology in real-world settings	May use EHR or other big data sources. Diverse settings and patient population. May be conducted completely independently from healthcare setting

Appendix 4 Examples for reimbursement of digital health products and solutions in the EU. Source: (eHSG SubGroup on Reimbursement, 2019, pp. 14–15)

Country	Product / Service	Level	Payer
Germany	Functional analyses of Cardiac Resynchronization Therapy (CRT) devices and implantable cardioverter-defibrillators (ICD)	National	Statutory Health Insurance (SHI)

Learning

- doctors need written consent of the patient
- dedicated reimbursement for functional analyses
- doctors can get 116,48 € for following up patients with CRT and ICD four times remotely (in addition they can charge one normal function analyses and three telephone calls)
- on top of this telemedical infrastructure (app or transmitter) is reimbursed (though further work is needed), which is needed for sending data to the doctors

Country	Product / Service	Level	Payer
Germany	Video Consultation	National	Statutory Health Insurance (SHI)

Learning

- doctors need written consent of the patient
- service provider needs certification in accordance with national law
- additional reimbursement on top of regular amount for online consultation
- quantitative imitation of video consultations

Country	Product / Service	Level	Payer
Netherlands	Teleconsults reimbursed since 2018	National	Statutory Health Insurance (SHI)

Learning

- Teleconsults are reimbursed as hospital visits
- this stimulates doctors to treat patients in a @home situation, with or without telemonitoring devices and or symptom based
- this is for all specialism within hospital care

88

Country	Product / Service	Level	Payer
France	Financial compensation for telemedicine in France	National	Statutory Health Insurance (SHI)

Learning

- 2015: introduction of compensation of Teleconsultation and tele-expertise performed by medical doctors by €28 and €14 per consultation respectively.
- 2016: introduction of compensation of teleconsultation and tele-expertise for "long term illness" patients and from home/medico-social care. Medical doctors were compensated per consultation; general practitioners: €26, specialists: €28 and psychiatrists: €43.70.
- Financial compensation for chronic heart failure (CHF), chronic kidney failure (CKF) and chronic respiratory failure (CRF) were later approved as an experiment through package and payment-for-performance schemes. These schemes pay medical doctors €110 for CHF, €73 for CKF and CRF per patient for 6 months.
- Routine financial compensation is currently only provided for one telemedicine service in France.
- The impact of financing still needs to be assessed.
- As of September 15th, 2018, the coverage for teleconsultation was generalized and became effective at the national level.

Country	Product / Service	Level	Responsible authority
France	HTA Framework for connected medical devices	National	Haute Autorité de Santé (HAS)

Learning

- Published in 2017, the Guide supports manufacturers seeking reimbursement for connected medical devices
- This guide contains all the information required to build the reimbursement application file, including examples of tables to be provided as well as list of links to search for epidemiological data.
- It aims at addressing the specificities of connected medical devices as well as the organisational aspects linked to these devices.
- The guide contains the information required to build the reimbursement application file for the approval by HAS
  This is a first version of a specific guide that will be adapted to the needs identified for the constitution of a dossier

Appendix 5. Professional experience of Experts interviewed for this thesis (anonymized summary)

Expert #1:

Expert #1 has a degree in molecular biology as well as in economy with focus on entrepreneurship and innovation. She has worked with life science start-ups for the last 16 years through the business incubator, INiTS and in Health Hub Vienna. She is currently in leading position in both institutes. She has broad experience with digital health start-ups, as well as a network in the Austrian digital health ecosystem through the accelerator program of Health Hub Vienna.

Expert #2:

Expert #2 is a medical doctor by training. He has over 20 years of experience in academic research and at pharma, biotech and digital health companies. His experience ranges from research and development, through project and grant management till clinical development and medical affairs. He is currently chief medical officer at a digital health SME in Austria. The company develops digital health applications, which were developed with the help of and used by clinicians already. The company is currently going for reimbursement with one of their products and may go for clinical validation of another product with a partner.

Appendix 6. Declaration of Consent template

Declaration of Consent

Dear Mr/Ms

As part of my master thesis, „Clinical and economic assessment of digital health innovations in Austria — an ecosystem view" at the WU Executive Academy, I would like to conduct interviews with experts on the field of digital health validation. With this Declaration of Consent, I would like to request your consent in recording the interview (recording and script will not be published) and using the interview results in my master thesis.

Thank you for your collaboration in this study,

_____

Valeria Szijarto

Hereby I declare my consent to the audio-recording of the interview and to the use of the results in the above described master thesis. I understand that in any report on the results my identity will remain anonymous. I understand, that the original audio recording, the signed consent and the written transcript of the interview (without any identifying information) will be retained by the author for 3 years after submitting the thesis.

_____   _____, on _____

Signature of Expert   place   date

Appendix 7. Interview transcript with Expert #1

VSZ: In your experience what is the attitude of the start-ups to the clinical testing: do they plan, did they run, what did they think about it?

E #1: It really varies a lot; it depends on many factors. If I start with a very good example, a very successful example, mySugr, they really took the strategic decision very early on, that the medical device certification will be one part of their unique selling proposition. They thought they have had taken that decision on a very early stage, when they were asked, "do you know, what you are up to if you do that? Are you aware of everything that you have to do if you do so?" Making them aware of what it really means, may shake such a decision again. Because it costs a lot of time and it costs a lot of resources, and it costs a lot of energy also to record everything the right way, etc. mySugr took it very seriously right from the beginning, because they were aware of it early on what it takes.

And there are others who very strategically take the decision not to do that. And now we are talking about certification as a medical device, and clinical validation is yet another level beyond that. It really varies, whether or not it makes sense. It does not make sense in every case, I think. As we started to discuss about the timeframe: it may not make sense to go for a clinical validation if I have a solution that is in the preventive care. We all know, that doing sports helps to stay healthier, but you will feel it only, when you are 50. It does not make sense to go for clinical validation in that sense in such a case. It does not make sense in all the cases and it always depends on the awareness of the team, whether they know exactly why or why not they should clinically validate, and of course it depends on the technology, the project, the innovation, they are trying to generate. There is no one for all answer to that.

VSZ: The accelerator program also supports the start-ups planning this kind of validation, certification process. How is it going? How much emphasis is given?

E #1: Again, it depends on whether there is a need for this emphasis or not. It depends on whether they had already done it in their respective countries or not, whether they are aware. Some of the start-ups from other countries which are e.g. not within Europe, in most cases they are not that aware yet, what needs to be done in Europe in order to get everything certified, to get into the system. Yet, this is the reason why they reach out, they want to get into the Health Hub Vienna, as that can help them becoming aware. And this is one of the

expectations in the program, to help them to do the right thing, approach the right people, to get into the clinics, to get into the European certification process etc. This is part of the acceleration program. But not everybody needs it, as they accomplished different things. Thus, this is also one of the questions to be answered when applying to the program: what are the main challenges, that you think you will face during the next couple of months and the next 2-3 years. Some of them are wise enough and are very aware of the fact, that they need to do this, and some are simply blue-eyed and do not see that they have to do it. And some of them give a great answer, why they have not done it. Not one solution is like the other, so it depends.

If you consider start-ups, which are roughly working on similar products and one considers running a clinical testing and one does not consider running it. Do you see any critical factors among the founders, among the investors, what makes this difference between these start-ups? (E.g the founders have a background, that they already did it? Are there certain investors who are typically pushing for it? More experienced investors vs less experienced investors?)

It comes back to the awareness of the team: what it brings to have clinical testing and what are the benefits and disadvantages. It can be on every level; on the founders' level, if there is one really experienced in the health domain and has come maybe from a pharmaceutical background, they have an easier time taking the right decision. Because if it is the same solution, it should be the same answer. Yet it might be, that the business model is different and needs different things. In general, having experience in the life sciences sector definitely helps to take the right decision. And these are the people, who are aware, who really think about the decision. The newbies, that do not know anything about the domain, what it really needs to be successful and how it really works, how sale cycles really work, how different it is between Austria and Germany and Switzerland, just to name the DACH region. (We now see it in Corona, the health systems work completely different in the USA vs EU and within EU there is lots of differences.) Those people, who approach this problem in a very naive way, they most likely will fail, if they do not buy in expertise. To access the expertise in the domain is certainly helpful. Yet, what can also be seen and also is true for other industries, is that radical innovation is usually not brought in by so called industry experts. Because they see certain patterns they have seen over and over again, this makes you blind for completely

new solutions and that is described as the "innovators dilemma". That is true not only in the health care, it is true in every industry. It is usually those, that come with a completely different angle, they come up with radical solutions, that really makes the entire industry walk completely different paths. And that is the reason why those, who walked the old paths over and over again, and know the path and all the trees and stones and gates on that path, they are blind to solutions that take completely different paths. Does not mean, that medical device certification questions and clinical validation questions are not relevant any longer, but you can fall off the horse on the other side, to have too much clinical expertise to be blind to these real radical solutions.

VSZ: What you just mentioned, that probably these digital health testings requires completely different mindset and approach compared to medical drug and even medical device clinical testing. And as you mentioned, you need people who are partially in and partially out, or at least with open eyes for the new things, it is probably also true for the clinicians who are running these tests, and also for the CROs, who are arranging these tests. What is your opinion, in Austria do you have such clinicians and CROs with open minds and eyes for digital innovation testing and not just follow the traditional clinical testing path of health care?

E #1: Yes, there are some, but they are still very rare. Let me put it differently: they used to be very rare before the Corona (VSZ: Coronavirus) crisis, now everybody is open for digital solutions, because everybody is scared of too much contact, everybody needs to shut down contacts as good as possible. So all of a sudden digital solutions have become very, very interesting. And it pushed open many closed doors in one go. It will radically change; we are in a very radical change. Just to give you one simple example: in Austria, handing out medication at a pharmacy to a patient, it had to be a physical recipee (VSZ: prescription) with a real signature before and there was no way around that. So, you had to go physically to the doctor to get that physical sheet of paper in order to get your medication. And this has radically changed just for the sheer need to get this done faster and to prevent social interaction. And now everybody says: we always said it was not so easy and now all of a sudden it works. This is also what I meant. Just because everybody in the pharmacy knows, that it works that way, they might be blind to the solution, that it could be so much easier in fact. This is the reason why we are in a very interesting phase right now. It is literally the El Dorado of all the digital health solutions. Because they were stumbling over the "we used to

94

do it differently" attitude in the healthcare system everywhere on every level: doctors were afraid of all solution, because it might be that they can be squeezed out of the system and become obsolete. But now they are even more afraid of Corona and everybody realizes, it is so easy and, yet, we are still needed. The brain cells need to be connected by the fear of Corona in a different way and all of the sudden we realize that 'oh yeah, in fact it always had been easier, we just never tried it. We would not have thought that it works, because we used to do the different way.' And this is something that will radically change the healthcare system in the next couple of months, I am sure.

VSZ: Often people blame regulators, policy makers or even insurance companies (public or private insurances) for holding back all these health innovations, because they want to be on the safe side. Just coming back to the clinical testing, you worked with regulatory advisors, or insurances – how do you see it in Austria. Are they still pushing for clinical testing or are they already loosening up a bit on this kind of things?

E #1: Well, what is always the case is that the regulatory bodies lag behind the technology. There is always a new technology coming up, they have not seen before, so there are no rules how to go through the process. And those regulatory bodies are the bodies, that the clinicians have to be aware of, because the clinicians are supposed to use only solutions, that went through regulatory processes. That is the reason why doctors were afraid of breaking the rules and using e.g. Skype, because data protection is not so easy, or at least people say, it is not safe. And there are many other rules, regulations, that doctors have to comply with. Being responsible for damages, doctors' law, hospital law and lots of legal frameworks they have to comply with, and they all try to protect the patient, which is important, but they all slow down the process. The documentation the doctors have to do in terms of 'what do I do, what have I done, did I tell the patient what can happen, side effects'. They have to document it all, and that is because of the regulatory bodies. So the entire process is always lagging behind. The clinicians are dependent on the regulatory bodies. And of course, the regulatory bodies cannot set the rules on how to take a new technology through the regulatory process if the technology is not yet there.

On top of all this, there was a difficulty in EU, that the regulatory process have been made more strict and it is the effect, that many years ago there was this case, that silicone implants of surgent providers of breast enlargement surgery used not medical device silicone but

industry silicone, which really led to horrific health problems of those ladies, that were affected. So, this led to the question, within Europe how can this be prevented in the future? And they redesigned of all the medical device certification processes. That led to that not only that regulatory bodies were lagging behind, on top of that they had to re-train and re-justify the new rules in their own regulatory body. So, the regulatory body had to be certified first and that really led to a certification bottleneck within Europe. There were not even enough regulatory bodies who were certified to check for the new rules and that was very difficult situation for everyone in that system. It shows, that on the regulatory side, we will always lag behind, there is no way around that. And in Europe, we tend to overregulate everything, which is good for the patient, but it is bad for the speed of innovation.

Yet, I think that there are more moves in the domain right now. Basically, a clinical study is nothing, but a setup, where the rules are set out in a very controlled manner, because what you have is a new technology, that is not yet proven to be safe. This is what you test first in a clinical study. In the different phases, one has to test different things. Basically, a clinical study is nothing else, but a very systematic way of describing domains and groups of people and ways of how to do that. It is kind of a test bed. And this is what the EU is now working on: creating test beds in many different domains, also in health care and I think that is the right way to go. How can we define clinical setups like test beds for a safe clinical trial, for a safe way of testing innovation on patients, in a real case scenario and make this faster. And I think, that is a good idea. There will always be need for clinicians who are open to that, and support that from the clinical side. And if it is really set up well, it might really speed up the process of the eHealth solutions to come.

VSZ: Do you see the emergence of specialists on digital health among clinicians and regulators in Austria?

E #1: Yes, definitely. There are some at the university clinics, there is e.g. Alexander Gaiger (VSZ: Programmdirektor für E-Health, Telemedizin und Komplexitätsforschung, Medical University of Vienna), Freddie Meryn. There is a couple more. There is the Association of Telemedicine in Austria (VSZ: Telemed Austria) and there is a couple of clinician members of that association.

VSZ: In the accelerator, do you network with these people?

E #1: Definitely! Because you still need this openness on the applier side. If it is really in the clinics, you need the clinicians. Just like there are clinics who are used to do clinical studies in the "normal" biotech, e.g. vaccine development, and there are other hospitals and doctors, who do not do clinical studies and the same is true for digital solutions.

VSZ: You mentioned, that in certain cases it brings the startups benefit to run such testing. And clinical testing I mean in the broad sense: not just testing the benefits for patients and health care workers, but also the clinical usability (integration). Do you see any financial benefits for the start-ups? Public funding or from VCs, that they are more willing to invest if they see that there are such validations in place?

E #1: Sure, because everybody who invests into start-ups knows that at the end you need either to have a very good explanation why you take the B2C route, or you need to integrate it into the healthcare system. And everybody knows, that if you do not comply with the rules in there, you simply will fail. So, it does not make sense to invest into solutions like that. Definitely this is a very important decision, which way do we take, why do we take it. There is a very close link between the technological solution (what does it do) to the business model (how do I bring the solution to the patient or the customer) and the certification process. And they need to go hand in hand. It might be that you take the Over the Counter route, where you have to invest differently into communication, rather invest into marketing. On the other hand, the load of the money you spend is much higher if you take clinical testing and certification, but at the end, you might have this USP that mySugr definitely had. They were bought by Roche and the fact that they were the first medical device certified app by the FDA in the US definitely drew up the price. They definitely worked it out with the regulatory body, as for the FDA it was also the first time, they certified an app. So they walked this new terrain together with the regulatory body, both learned a lot and this is the way to go and that is the reason why the investors invested initially and they were able to trace funds from Roche Venture (it was in the start-up as investor before Roche bought it). Definitely, it is an asset.

VSZ: You mentioned the different business models. How much, do you think the start-ups plan to go for reimbursement by insurance companies. Is it a dream or they take it granted or it is a no way, nobody will get reimbursed?

E #1: It depends on the solution, because not everything has the chance to get reimbursed. Yet of course reimbursement schemes are the big economic driving force of solutions to be accepted by the system. Particularly in Austria – also true for most of Europe – it is that the patients and the doctors are used to getting everything reimbursed. So, in Austria in particular, it is a normal attitude of the patient that the government "has to take care of my health". And it is a very bad attitude in fact, not to take your own responsibility. On the other hand, it is a very social attitude, because now we see all the problems in the USA, that the system is really cracking, because of exactly that "unsocial" attitude. So only those, who have insurance can afford the treatment, and the others are left out. At the moment, we are very happy that our system is so expensive, we have so many intensive care beds, etc. Couple of months ago people were discussing 'Do we really need that many beds?'. In general, I think the attitude of the patient, who is kind of the user in the business model, is used to getting it paid by the insurance, so remuneration schemes are really big economical driving forces. Also, the doctors will not prescribe a solution, which forces the patient to pay, which is not remunerated, because of that. Unless they are private patients, which are used to pay, but that is a relatively small percentage of the population, that is willing to pay themselves. Then, in Austria we have this discussion about 2 classes within the medical systems, which is important. It is there in fact, and still it is questionable, if it is good. On the other hand, we simply cannot afford everything as a system, as a government, and nobody can afford it. So, these are really difficult questions at the moment. But again: it is the big economic driving force.

VSZ: Are there any other points, that you think is important regarding clinical and economical validation of digital health?

E #1: The Austrian Federal Ministry of Digitalization and Economics has started to work on the question on how to create regulatory test beds. I think one of the domains they should really focus on is eHealth regulatory test beds. Recently the remuneration system in Germany has changed, because it enables eHealth start-ups to clinically test and be remunerated. It is one form of such a test bed that might be considered. It does not rule out all rules, but enables to fulfil all rules. I think that should be a focus area, to help and create an ecosystem and really speed up everything: saving money in the system, creating an ecosystem, where digital innovations can thrive and also create the halo and make Austria visible, because there are

98

not a lot of nations who did that. The introduction of the ePrescription is also a kind of a regulatory test bed enforced by COVID19. And now everybody says, 'It would have been possible, why did we have to wait for the crisis?'.

Appendix 8. Interview transcript with Expert #2

VSZ: As you mentioned, there is a possibility, that your product is getting tested in the clinic. You also have large experience on how to use your product in the clinic already and you may use this experience during the clinical validation. Do you have anyone on the team, who had already experience with clinical testing (of digital health)?

E #2: Yes, we have such person.

VSZ: Do you plan to design/organize and manage the study with internal people or do you plan to get a CRO/consultants to do it?

E #2: CRO, of course. It is rare that company of any size does not outsource such project.

VSZ: Who will be the internal coordinator (which function) of the study?

E #2: Clinical research assistant (CRA) or clinical trial manager (CRM).

VSZ: Does this function already exist within the company? Is there a person within the company, who could fulfil this function?

E #2: Exact such function does not exist, but the position was created and will be filled in the very near future.

VSZ: If you plan to work with a CRO on the study, do you know about a potential partner in Austria, who has experience with digital health and whom you could rely on or would you – also – look for such partners internationally?

E #2: We do not know about such partner in Austria, who could support us in this study, but it does not mean, that with a little bit of search we will not find someone. I cannot answer with certainty. But we would most likely search internationally. If we find a compatible CRO in Austria as well, we will choose that, also for the geographic reasons, i.e. convenience in logistics. So, we are open for every possibility.

VSZ: Do you plan to work with any external advisors? Someone, who could help planning, managing the whole procedure and selecting the CRO.

E #2: It is possible, that we have enough knowledge and experience already internally, so we won't need such dedicated advisor.

VSZ: Do you know about local policies/frameworks/recommendations of regulators or insurance companies on digital health? So, such things that really focus on how to run a digital health validation in Austria.

E #2: No, when this topic came up or when we decided to take this path, we went to the EMA directly to ask. We already established a working relationship with them, there they know about us already.

VSZ: So, you went there directly, to the European centre?

E #2: Yes.

VSZ: You mentioned, that you plan to go for reimbursement with one of your products. Do you know about any external partners, who helps you in this process? Any state or any private institutes?

E #2: The short answer is no. It seems to be a complicated, bureaucratic process at the moment, according to our recent experience. It is typical to Austria, it is rather unclear and difficult.

VSZ: Are you maybe in touch with other companies, digital health companies, who went through this process?

E #2: Yes, this would have been my next point. Maybe we could reach out to certain companies who have experience in this. This could be a possibility.

VSZ: In general, do you have investors who particularly push for validation and reimbursement, or if not particularly pushes for it, but at least supports it and understands that it requires time, effort, money.

E #2: This topic did not come up so far. No.

VSZ: Do you know about public funding opportunities to cover this process?

E #2: I do not know about specific grants for it, but we had good experiences with FFG (VSZ: Österreichische Forschungsförderungsgesellschaft (Austrian Research Promotion Agency)) and I think they could be a partner in this, to support such clinical validation, maybe within KLIPHA.

VSZ: I recently heard about a website, called Förderpilot.at. Have you heard about it?

E #2: No, I do not know it.

VSZ: All in all, when you look ahead and – based on your experience working with clinicians and running clinical trials – what do you think, what will be the most challenging part of a validation: designing, arranging and managing or the financial side, to get the money for it.

E #2: If you were asking about the most challenging part, but without listing any examples, I would say, that the most challenging is to make the doctors accept these applications. And really, we see that it depends on the countries, cultures, some are open for such applications and others are not. And it does not only depend on countries, but even on the specialties. Some are really negative and say 'a digital health application should never replace their knowledge and experience'. So, they do not look at such applications as a tool, that can make their work easier, but rather something that is a threat and could replace them. So, it is a big challenge and making such digital application accepted by clinicians always takes time and effort.

VSZ: I see. And when looking at methods how to get over this barrier, could that be helpful, if you said that 'it was validated this and this ways'? In your opinion, would clinicians accept it easier?

E #2: Validation would definitely help. If it works and there are data that demonstrate that it helps doctors either in diagnosis or during severity monitoring (as we discussed earlier), then it could help. And our experience is, that if we get close to a key opinion leader of that specialty, then it is a huge thing. Without being too concrete: if we have an opportunity to introduce the application to a key opinion leader and then he or she goes to a conference and talks about the experiences and recommends it, then it helps to get more people on board.

VSZ: When looking at international practices: you mentioned, that in Austria the system is very bureaucratic and maybe you would look for the CRO internationally. Are there any other international practices, institutes or companies, that works very well in supporting digital health companies running clinical validation, and that would be very useful in Austria as well?

E #2: In my opinion the large pharma companies are very helpful and will be very helpful. If they see the benefit of such application and start using it – usually on a narrow patient population – in my view it is a very good path. They can later spread the word, especially because these multinational pharma companies also communicate across the borders. So, if someone starts using it here, it can easily spread to the same patient population or for the same specialty but to another country. If large companies hear about such application and they have an e.g. phase 4 post marketing study running and they start using the app there, that is a huge help.

VSZ: Are the large pharma companies in Austria also partners in this?

E #2: Yes. They are. When I was talking about (VSZ: the challenges in) Austria before, I was specifically talking about state institutes, bureaucracy and not about international companies, or not even the AGES. Only those that can be a scene for political debate, like between Vienna and the government (led by different parties).