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Lars Stegemann

Rahel Gubser

Martin Gersch

Alexander Bartschke

Andreas Hoffmann

See next page for additional authors

Authors

Lars Stegemann, Rahel Gubser, Martin Gersch, Alexander Bartschke, Andreas Hoffmann, Michael Wagner, and Daniel Fürstenau

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Research Paper

Lars, Stegemann, Freie Universität Berlin, Germany, lars.stegemann@fu-berlin.de

Rahel, Gubser, Charité – Universitätsmedizin Berlin, Germany, rahel.gubser@charite.de

Martin, Gersch, Freie Universität Berlin, Germany, martin.gersch@fu-berlin.de

Alexander, Bartschke, Berlin Institute of Health at Charité – Universitätsmedizin Berlin, Germany, alexander.bartschke@bih-charite.de

Andreas, Hoffmann, Fraunhofer FOKUS, Germany, andreas.hoffmann@fokus.fraunhofer.de

Michael, Wagner, Fraunhofer FOKUS, Germany, michael.wagner@fokus.fraunhofer.de

Daniel, Fürstenau, IT University of Copenhagen, Denmark & Charité – Universitätsmedizin Berlin, Germany, daniel.fuerstenau@itu.dk

Abstract

This paper focuses on the integration of digital therapeutics (DTx) into future-oriented and patient-centric care pathways. Based on a workshop series and problem-centered interviews in Germany, the current state-of-the-art of regulatory and technical integration of DTx was mapped as a landscape of DTx interoperability. The results focus on key interfaces of DTx, namely with Electronic Health Records (EHRs), devices, and other digital health innovations such as telemedicine, and highlight current challenges and potentials for future development. On a broader level, the results point to unresolved issues of care coordination, the optional role of the EHRs as regulated platforms for care, and the importance of integrating DTx data into public data spaces for research.

Keywords: Digital Therapeutics, DTx, Digital Health, Interoperability, Electronic Health Records, EHRs, Data Infrastructures.

1 Introduction

Digital therapeutics (DTx) refer to *software-driven, evidence-based therapeutic interventions for the prevention, management or treatment of a medical disease or disorder* (DTx Alliance, 2021). DTx represent a new, innovative product category within the broader landscape of digital health (Makin, 2019; Fürstenau et al., 2023) that complements regular therapeutic services. Germany, a country with a significant burden of healthcare costs, introduced prescription models for DTx in 2019. By the end of 2022, a total of 203,000 DTx prescriptions had been issued (GKV-SV, 2023), indicating a growing acceptance of DTx in the country. Notably, 4% of physicians or psychotherapists were responsible for issuing these prescriptions (TK, 2022). DTx, in contrast to many health apps, are evidence-based therapies that undergo a regulatory review process, typically involving clinical trials to establish their effectiveness and risk assessments (DTx Alliance, 2021; Dang et al., 2020). InVirto provides a notable instance of a DTx, featuring an app-based virtual reality training program designed as an exposure therapy intervention for individuals diagnosed with panic disorder and phobias (Planert et al., 2022).

Previous research has primarily focused on DTx as a stand-alone application for specific indications, with promising outcomes such as inducing desired behavioral changes (e.g., Ghose et al., 2022), reducing waiting times for other treatments (Weightman, 2020), improving adherence to traditional medications (e.g., Makin, 2019; Dang et al., 2020), increasing health literacy (e.g., Wicks et al., 2018), promoting patient autonomy and sovereignty (e.g., Zill et al., 2019; Oh et al., 2020), and reducing treatment-related disease burden (e.g., Berger et al., 2017). However, little attention has been paid to the effective integration of DTx technologies into existing and yet-to-be built care pathways (Fürstenau et al., 2023). Through a problem-driven analysis (Monteiro et al., 2022) of current DTx regulations and architectures, we respond to previous calls for research on the technical and social process integration of DTx (Wang et al., 2023; Fürstenau et al., 2023) and observe how DTx are and should be integrated into treatment processes. This is an important topic for research because a lack of analysis can lead to architecture and interoperability decisions that introduce harmful path dependencies and lock-ins, ranging from the creation (or reinforcement) of siloed architectures to vendor monopolies on data. It could also squander opportunities for digital medicine, personalized care and better care coordination. Aside from the implications for healthcare, existing architecture-inspired research in Information Systems (IS) has not systematically addressed this issue (e.g., Hodapp and Hanelt, 20-22). Moreover, IS research has rarely bridged the gap between uncovering conflicting expectations and logics in cross-organizational or nationwide electronic health records (EHRs) and eHealth infrastructures (e.g., Aanestad and Jensen, 2011; Winkler et al., 2020; Hansen and Baroody, 2020) and investigating individual therapeutic interventions that are not fully self-managed, as most research foci suggest (e.g., Dadgar and Joshi, 2018; Bardhan et al., 2020). From a patient-centered perspective, this leaves the crucial interaction between the individual and societal levels largely conceptually underdeveloped and understudied.

In the area of IS in healthcare, we suggest that in order to increase patient value, it is important to consider not only the use of DTx by patients, but also their intersection with the broader digital health infrastructure and current environment. This includes analyzing how data flows between different DTx and health applications, how DTx can be combined with different devices in a patient-centric "plug-and-play" manner, and how the data generated can be used beyond its immediate care coordination purpose and for research. A critical aspect of improving the uptake and use of DTx is ensuring their easy and seamless integration into care pathways while maintaining transparency around privacy and patient empowerment. This is particularly important given the widespread availability and national regulation of EHRs, which is a prominent topic in IS in healthcare research (e.g., Aanestad and Jensen, 2011; Hoyt and Hersh, 2018; Stegemann and Gersch, 2021), and the increasing number of wearable and personal health devices (e.g., Witte et al., 2020).

The purpose of this paper is to *analyze how to create future-oriented and patient-centric care pathways regarding DTx and their interoperability*. From a **patient-centric interoperability perspective**, we focus on the intersection of DTx and (1) EHRs, (2) devices, and (3) other digital health innovations such as telemedicine. Our decision to adopt this perspective is grounded in the existing literature on interoperability, which has a longstanding tradition of exploring the subject (e.g., Kohli and Tan, 2016; Lehne et al., 2019; Hodapp and Hanelt, 2022). *Patient-centric interoperability* considers interoperability from the patient's perspective along the care pathway, examining both vertical interoperability (across layers of hardware-software abstraction) and horizontal interoperability (across interconnected activity domains such as leisure, health-related matters, and mobility) (Hodapp and Hanelt, 2022). As such, it encompasses the integration of technical and social aspects to achieve seamless processes (e.g., Sadeghi et al., 2012). To approach our research question, we conducted workshops and semi-structured, problem-centric interviews with key stakeholders in the digital health market and infrastructure. Our research was conducted within the context of Germany, where DTx were introduced early on as an innovative approach to patient care. This afforded us the opportunity to conduct an in-depth exploration of our research question, resulting in an instructive and highly relevant example for other contexts.

Our contribution is a landscape of DTx interoperability from a patient-centric perspective, mapping the key interfaces between the main important digital technologies supporting digital medicine. This

mapping can serve as an analytical tool to understand and target architectural and regulatory interoperability measures. In addition, we highlight areas of future research for interoperability as a distinct research focus (e.g., Hodapp and Hanelt, 2022), introducing a patient-centric focus. This discussion is sensitive to digital options and debts with respect to current regulatory and technical approaches to DTx interoperability. It supports reimagining future care journeys and helps in the future-oriented design of key interfaces of the DTx landscape.

2 Conceptual Background

2.1 Interoperability: Concept and DTx-Specific Background

Interoperability is a core concept in digital medicine (Lehne et al., 2019), given the various stakeholders involved in healthcare (e.g., Kohli and Tan, 2016). It has long been discussed regarding several sub-challenges, such as terminologies, exchange formats and models (Benson and Grieve, 2016; Hodapp and Hanelt, 2022). Interoperability can be defined as "the ability of two or more systems or components to exchange information and to use the information that has been exchanged" (IEEE, 2002). Achieving interoperability through common consensus on standards and interfaces between heterogeneous systems and IT architectures is a challenge that increases significantly with the number of actors (e.g., Kohli and Tan, 2016; Benson and Grieve, 2016), especially when considering the integration of DTx data into existing complex health IT systems. Depending on the type and nature of the data/information exchanged and reused, interoperability can be distinguished at different levels: technical, syntactic, semantic and pragmatic/organizational.

Technical interoperability at the first and lowest level enables basic data exchange based on network protocols in an organization, IT infrastructure or ecosystem (e.g. Lehne et al., 2019; European Commission, 2017; Benson and, Grieve 2016; Oemig and Snelic, 2016). Standards and formats, e.g. HL7, FHIR, IHE (for medical data), are used to ensure *syntactic interoperability*. This structured data/information exchange enables applications to process the exchanged data/information (e.g. Lehne et al., 2019; European Commission, 2017; Benson and Grieve, 2016; Oemig and Snelic, 2016). At the next higher level, *semantic interoperability* implies an unambiguous understanding of the exchanged information in order to be able to interpret it without fiction. This is ensured by classification systems and terminologies such as SNOMED CT and LOINC (e.g. Lehne et al., 2019, European Commission, 2017; Benson and Grieve, 2016). *Pragmatic/organizational interoperability* at the highest level of interoperability means harmonized processes and procedural instructions to ensure, on the one hand, the reliability of the exchanged data/information through documentation of actions and observations and, on the other hand, compliance with common goals and principles, such as evidence-based medical guidelines (e.g. Lehne et al., 2019; European Commission, 2017; Benson and Grieve, 2016).

The levels build on each other and as the level of interoperability increases, the extracted data/information and knowledge (fragments) offer increasing potential for integration and automation (Oemig and Snelic, 2016). Interoperability has enormous potential for innovation in a digital business ecosystem (Hodapp and Hanelt, 2022), especially as the level of interoperability increases, algorithms can process data better and more accurately (Lehne et al., 2019). The consideration of measures for the first three levels of interoperability tends to come from a more technical viewpoint. Based on a long-standing discussion, there are more dimensions, i.e. perspectives of interoperability measures, to address different challenges, such as economic dimensions like cost-benefit trade-offs, legal dimensions through compliance with laws and regulations, and care process alignment from an organizational dimension (European Commission, 2017; eHealth Network, 2015). According to Hodapp and Hanlet's (2022) model of interoperability, questions about interoperability issues include where interoperability is increasing (e.g., at what level), who is increasing interoperability (regulators, standard-setting organizations, platform leaders), and what is the unit of analysis (individual, organization, ecosystem). But our focus is not on a single static unit, but on the process. As we argue in alignment with the European Interoperability Framework (eHealth Network, 2015; European Commission, 2017; Kouroubali and Katehakis, 2019) and the frameworks of Sadeghi et al. (2012) and Gohar et al. (2021),

a patient-centric interoperability perspective must also capture the connectedness in the care process/patient journey.

In the context of DTx, standards such as HL7 (v2, v3/CDA, FHIR), IHE (XDS) on the technical/syntactic level and ICD-10, LOINC, and SNOMED-CT on the semantic level, among many others, need to be recognized. These standards have been tailored to domains such as ISO/IEEE 11073 for devices, which is differentiated for service-oriented device connectivity in the context of point-of-care versus personal health devices. Different countries have partially adopted national standardization routes, which may partially extend or even counteract international standardization activities (e.g. Payne et al., 2019). In this context, interoperability is important from the patient's perspective, as it is a condition for the right to data portability (Hert et al., 2018) and enables certain use cases, such as switching from one digital health app to another, changing health insurance (if more than one exists in a country), and migrating personal health data and preventing lock-in effects (e.g., Stegemann and Gersch, 2021). Using multiple digital health apps together, e.g. for multi-morbid profiles such as diabetes, obesity and depression, or using a specific personal health device (not the bundled one) in conjunction with a specific digital health app.

While previous research has often examined private firm settings where interfaces are controlled by key firms, such as Apple (Ghazawneh and Henfridsson, 2010 & 2013; Eaton et al., 2015; Gleiss et al., 2021), in our context, key interfaces or data flows are governed by publicly-mandated regulations. While there is no reason to believe that the findings of Eaton et al. (2015) and Ghazawneh and Henfridsson (2010) on the interest-driven and contested nature of interfaces do not apply in such an environment, regulatory directives can influence and channel the interests. Interoperable interfaces can create new options and resolve path dependencies, as discussed below.

2.2 Future-Oriented Design

The notion of future-oriented design implies the availability of options for the future, despite unknown or risky developments. Options have been a recurrent issue in architectural research in IS (e.g., Rolland et al., 2018; Woodard et al., 2013). Rolland et al. (2018) proposed that, analogous to financial options, digital options refer to future possibilities that can be realized by making a certain architectural choice now. In their paper, they contrast digital options with digital debt. Digital debt refers to obligations that take effect later but are implied in current architectural decisions. The authors refer to the paradoxical nature of digital options and digital debt. The realization of digital options often implies a certain amount of digital debt, while the realization of options cannot be avoided. Research on digital options and digital debt is sensitive to *path dependencies and lock-ins* (e.g., Arthur, 1994; Shapiro and Varian, 1999). Certain decisions and actions will put a system (such as a national eHealth infrastructure) on a trajectory that enables the realization of certain options (while not realizing others) and simultaneously implies a certain amount of digital debt. Self-reinforcing processes can therefore create a momentum beyond the agency of individuals or social groups (Hughes et al., 1987). Path dependency thereby characterizes the non-ergodicity of such processes, meaning that, based on an initial contingent state, decisions and actions in the process lead to trajectories that may become irreversible over time. In the context of national eHealth infrastructures, these decisions and actions are regulatory and mostly technical in nature, such as on which architecture and standard to base a nationwide EHR on, which mandatory interface standards to use for data extraction and exchange between key systems, or how to connect devices to digital health apps, the EHR, or primary systems of physicians in ambulatory and hospital settings, psychotherapists, or other medical professionals. Germany has chosen to set EHRs as a central, intersectoral data hub through regulatory mandates. With this knowledge, we sharpen our perspective for studying the long-term impact of the design of the DTx interface landscape.

2.3 Patient-Centric Interoperability

While preservation of digital options has been studied as an outcome (Rolland et al., 2018), the goal of optionality is to provide an IT artifact with some degree of adaptability to the requirements of specific stakeholders. Among them, in healthcare, the goal of patient-centricity includes achieving high-quality,

cost-efficient, accessible, and interconnected healthcare services while promoting principles such as (data) sovereignty, empowerment, or data protection (Berwick et al., 2008; Hert et al., 2018). Previous interoperability approaches have tended to be provider-centric (Gohar et al., 2021). Increasing patient empowerment over their data and a more active involvement of patients in the treatment process (e.g., through DTx therapies) also requires a rethinking of interoperability considerations. By adopting a patient-centric perspective of interoperability, interfaces that are relevant to the patient's treatment process are considered, providing different options for an optimal outcome, not only for services along the patient journey, but also for health management (e.g., prevention through multi-channel nudging of healthy behaviors).

A patient-centric perspective should promote better adherence (where the therapy is effective), empower patients, and facilitate use. It should do this by elimination of redundancies (e.g., avoiding multiple places where to enter the same information) and providing a more comprehensive picture of health status, e.g., providing self-collected data from the DTx in the form of patient-reported outcomes (PROMs) or vital signs. From an individual patient perspective, care processes should be high quality, efficient, and integrated way, reducing structural and organizational friction. It means designing processes and solutions around the patient's needs, and encompasses all phases from design to rollout of solutions (Jandoo, 2020), as well as along more or less integrated patient care pathways.

3 Methods

3.1 Research Context and Research Approach

In a research project funded by the German Federal Ministry of Health, we studied the national technical and regulatory developments around DTx. The selected setting was chosen for its high relevance and uncertain nature, as described by Patel and Butte (2020), which makes it a revelatory environment. Additionally, the lack of international comparisons on meaningful interoperability architectures and regulations further justifies the choice of this setting. The key interfaces of DTx, particularly from the patient's perspective and along care pathways, were the specific units of analysis. These interfaces included EHRs, devices, and other digital health innovations such as telemedicine. The choice of these specific units of analysis was motivated in each case by conceivable regulatory options (reflected by the federal ministry of health), which created a high degree of uncertainty among stakeholders and thus contested terrain, creating important inflection points for future developments. The research conducted on these specific topics was *problem-driven* (Monteiro et al., 2022) and *exploratory* (Sarker et al., 2018). Therefore, it was suitable for qualitative, exploratory methods (Sarker et al., 2018), as there were limited previous structured reports and analyses available.

During the research project, data (transcripts, protocols, and field notes) from a series of workshops (from October 2021 till April 2022) and additional problem-centered interviews (Witzel and Reiter, 2013) were continuously collected and analyzed in order to, first, generate new insights and questions from the literature and interviews and, second, to explore the emerging insights within the workshops. We used phenomenon-focused problematization (Monteiro et al., 2022; Gkeredakis and Constantinides, 2019) and in doing so gained insights into more abstract concepts such as interoperability. The aim of our study is to provide a snapshot of the early phase of DTx adoption in Germany and to further elaborate the concept of DTx. This will help to understand the importance of designing interoperability along patient pathways to improve the value of care for patients and all stakeholders in the healthcare system.

3.2 Data Collection

Data was gathered in a problem-driven way (Monteiro et al., 2022) through problem-centric interviews and workshops. We conducted six workshops (see Appendix A1). These workshops provided an opportunity to present and test certain ideas from the study team and from the problem-centered interviews, and to challenge tentative solutions developed by the study team. The workshops included a diverse set of invited high-profile subject matter experts from multiple perspectives, including

regulators and government agencies, national bodies representing physicians, patients, and health insurers, industry associations, DTx and medical device manufacturers, interoperability experts, among other stakeholders. Interviewees were selected based on thematic expertise (Meuser and Nagel, 2009), as we focused on the three interfaces mentioned above (EHR, devices, and other digital health innovations, i.e., telemedicine), specific to the respective workshop topic. We used illustrative indication scenarios such as diabetes, heart failure, back pain, and disorders such as depression and brought the concepts together in an explorative context (e.g., Sarker et al., 2018; Flick, 2009). In addition, the first workshop acted as a stage-setting event, and the final workshop synthesized the findings for feedback and discussion in this regard. To avoid bias in the data collection and ensuring the quality of the study, the minutes of the workshops were taken by at least two study members and consolidated afterwards.

We conducted 51 problem-centric interviews with different experts (e.g., Meuser and Nagel, 2009; Witzel and Reiter, 2012). For the interviews, we followed a similar approach in selecting high-profile subject matter experts based on their expertise and relevance to the topic at hand[1]. Before each interview, the interviewees were informed about the nature of the research project and gave their consent to participate in the study. Due to the exploratory and preliminary nature of the study, we refrained from recordings in most cases. Instead, at least two interviewers were present, one asking questions and the other taking notes. The interview was semi-structured and tailored to the specific topic at hand. The questions asked for specific expert opinions, viewpoints, and assessments of the current regulatory and technical landscape as well as specific options for future settings around DTx. At the end of the interview, the experts were invited to the workshops to further discuss their views. The length of the interviews varied between 25 and 60 minutes, with an average scheduled duration of 30 minutes. Interviews were conducted via phone or video conferencing tools. Besides the interviews and workshops, desk research methods were used, drawing on existing published data and literature. Relevant sources were identified and then evaluated. Examples include the analysis of device components of DTx listed in the national DTx directory, research on relevant standards (e.g., ISO/IEEE for DTx devices) and legal texts (e.g., §355a, §374a German Social Law SGB V).

3.3 Data Analysis

The analysis of the data occurred in multiple steps by several study members according to the quality criteria of qualitative research, in the style of open and selective coding (Saldaña, 2009; Witzel and Reiter, 2012), merging, and dropping of topics (Grodal and Holm, 2021). First, we read and discussed the interview notes in preparation for the workshops, synthesizing unbiased, relevant insights and findings into statements or theses that were subsequently presented to the workshop audience. Second, we took notes at the workshops, creating another layer of data that was used for subsequent discussion and analysis. Third, we synthesized interview and workshop notes into more aggregated statements and findings for the final workshop and for this paper. The research process was iterative and exploratory (e.g., Flick, 2009; Sarker et al., 2018), favoring depth over breath, as exemplified by the a priori selection of research topics and conceivable future settings. As another layer of analysis, we synthesized the findings into three overarching *topic areas* and 10 topical issues (Grodal and Holm, 2021). These topic areas and the resulting topics are presented in Table 1 and quotes in Appendix A2 using some categorization principles of qualitative content analysis (Mayring, 2014). The topics characterize the current state-of-the-art regarding DTx interoperability, and allowed us to derive implications for future technological and regulatory areas.

[1] Some of their roles included CEOs and interoperability experts from DTx vendors, trade union heads and experts in interoperability for DTx and MedTech companies, interoperability experts in government bodies responsible for the DTx process, interoperability, and national eHealth infrastructure, heads of digitalization and representatives from major health insurance companies, committee leaders in international interoperability working groups, representatives from medical associations and individual digital health experts, representatives from the pharmaceutical industry, and patient representatives.

4 Results

Figure 1 shows a DTx interoperability landscape that has been developed iteratively along the interfaces of DTx, EHR, devices, and other digital health innovations. This landscape includes specific features that are fixed and unchangeable in the medium term for Germany, such as the Telematics Infrastructure (TI) and the central position of an EHR as a data hub for health and medical data. This role is provided by the respective statutory insurance companies (Stegemann and Gersch, 2021). These regulatory and technical cornerstones are essential components of the interoperability landscape in Germany.

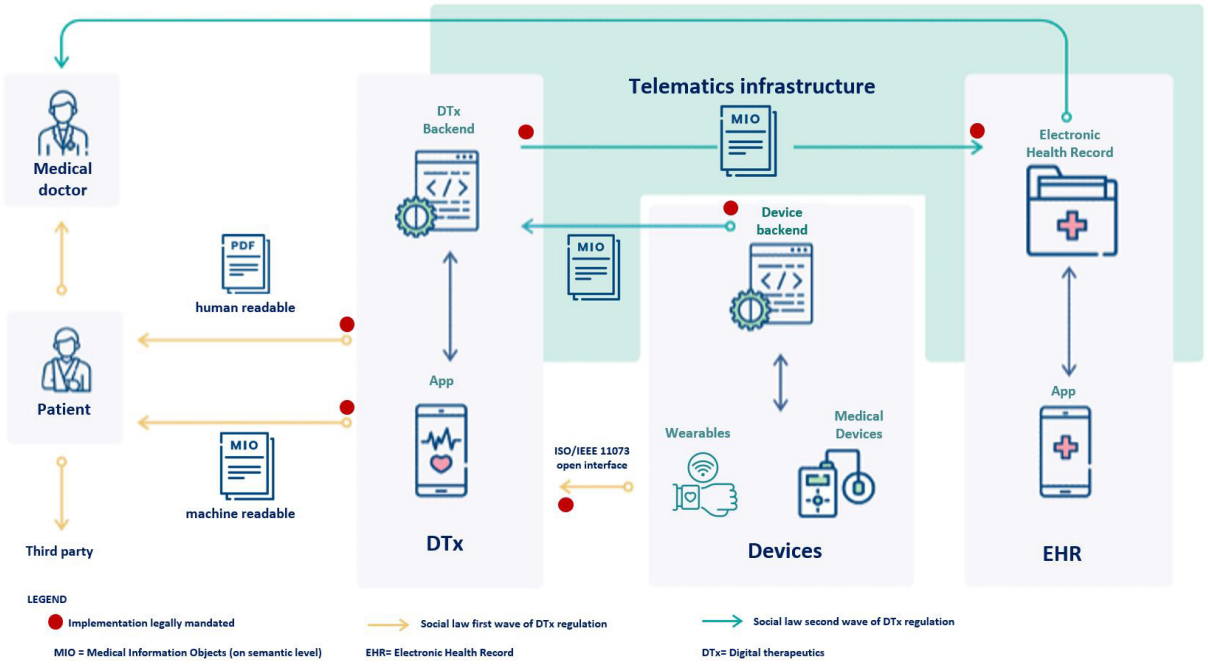

Figure 1. Landscape of DTx interoperability in Germany.

4.1 DTx and EHRs

The EHR, as a regulated central data hub for patient medical information, is one of the main interfaces for DTx data exchange along the care pathway. Our analysis was based on the regulatory measure that from 2023, the DTx regulation will enforce a mandatory machine-readable interface between DTx and EHRs, thus extending current human-readable (mostly PDF type) data export requirements. Consequently, there is a need for technical specifications from the DTx backend to the EHR, including syntactic and semantic interoperability considerations. Our analysis shows that there were several points of contention within the workshop that require further clarification and detailed regulation.

Firstly, the DTx-EHR interface is legally defined as **write-only**, meaning that DTx cannot use EHR data, leaving it in a delivery position. Although concerns have been raised about this regulation, there has been little complaint in workshops, possibly due to unrealized use cases. Secondly, the specified **technical exchange infrastructure** relies on outdated legacy infrastructure, requiring DTx manufacturers to purchase and install failure-prone card terminals to enable secure connections. This led to calls for longer transition periods and caused a disconnect between the legacy EHR world and the startup DTx domain. Additionally, experts criticized the outdated architectural choices in the EHR infrastructure, such as the use of IHE XDS profiles for folder-based data storage, which led to problems with **data reuse and analysis**. Experts recommend using a FHIR-based storage/server for subsequent usage by medical professionals and research. Thirdly, the specified semantic profiles for data exchange using the FHIR standard were appreciated, but specific country-related choices such as the degree of

free-text versus additional **semantic constraints** were contested. Fourthly, the responsibility for the **frontend display of DTx data** with physicians created debates about areas of responsibility between state agencies, DTx manufacturers, manufacturers of primary systems used with physicians, and doctors (and their associations). Fifthly, the potential for health insurances to use EHR data and integrate it with DTx into patient-specific care offerings was not yet fully realized. The study showed that the patient record, EHR app, and DTx apps were not yet fully aligned with each other.

4.2 DTx and Devices

Two mandatory interfaces between DTx and devices have been specified (as part of the DTx regulatory framework in social law), with different use cases and intentions. One is a frontend interface. It supports the direct exchange between devices (e.g., wearables and Personal Health Devices) and DTx (e.g., via Bluetooth, Wifi, or Ethernet). The other one is a backend interface. The backend interface connects server-sided data from devices to DTx. In contrast to the frontend interface, the backend interface requests medical device manufacturers (with assistive technology devices or implants which are available for reimbursement by statutory health insurances) to implement an interface that will provide its data for usage by the DTx within the DTx' defined medical purpose. The backend interface was especially highly contested, and several amendments have been made to the original regulatory proposal.

One of the primary arguments in the debate surrounding the integration of high-risk medical devices with DTx was related to risk classification. There were concerns about the appropriate connection of high-risk medical devices to DTx. Additionally, affected medical device manufacturers expressed concern over the potentially **high costs of recertification** according to the medical device regulation with newly mandated interfaces. Secondly, there was a lack of clarity regarding **responsibilities** in the implementation of the regulation. The envisioned frontend interface aimed to enable easy switching between different wearables and personal health devices within the same DTx, such as insulin pens from different manufacturers. However, there were **no strong example use cases** to illustrate the benefits of this integration. It was noted that much of the integration would likely occur in backend interfaces. Finally, the debate highlighted the issue of **closed or semi-closed data access models**, which posed a challenge for intermediaries between devices and DTx. While the regulation of data access was seen as necessary, there was a concern about the potential risks associated with national strategies without broader consensus at the European or international level.

4.3 DTx and Other Digital Health Innovations, Including Telemedicine

A final area of discussion revolved around other digital health innovations, including telemedicine. With upcoming regulations to reform telemedicine services and structured telemedicine programs for certain care pathways, such as cardiovascular care, it was clear that this area also needed to be revisited.

Firstly, the study revealed the existence of various types of **telemedicine programs**, with some having a commercial nature and others being more public, regional, or localized in their approach. While it was observed that machine-readable interfaces at the syntactic and semantic level could serve as a suitable basis for connecting DTx with telemedicine, there were no or inadequate specifications for EHR telemedicine interfaces. Secondly, tensions emerged as DTx primarily focuses on digital interventions, often driven by algorithms, and therefore, their integration with **blended care models** needs to be worked out. This integration involves the development of integrated portals that include telemedicine, DTx, and other interventions, such as prevention apps, as well as addressing questions related to reimbursement, data privacy, and security issues. Although these models have been conceptually developed for some time, they have not yet been incorporated into regulations. Additionally, it was unclear how DTx would **integrate with other types of care-related or medical apps**, such as triage apps, prevention apps, or apps that track patient-reported outcomes or satisfaction with care pathways. Although the current regulation did not intend to address these issues via DTx, it was evident that these apps would be necessary and would become a focus of future regulation.

4.4 Summary

The key findings, stakeholder perceptions, and derived issues are summarized in Table 1, along with summarized implications for regulators/government, standards-setting organizations (SSO), and manufacturers. The summary prepares our discussion that turns to the central role of the national patient record as a key interface with DTx in care management, and further turns to the role of DTx in generating real-world evidence in care and medical research from an IS in Healthcare perspective.

#	Issues	Implication	Audience
Topic area (1) DTx and EHR	Write only interface	To ensure a secure and beneficial interface between EHR and DTx, the design must incentivize innovation for DTx manufacturers while also mitigating risks. A bi-directional interface offers greater benefits, but commercial use should be regulated within the context of patient data use regulations to prevent unintended secondary uses of data. It is crucial to avoid any backdoors that could compromise the security and privacy of patient data.	Regulators/ Government
	Technical exchange infrastructure was outdated and missing digital identities	To balance the need for modern and innovative solutions with the constraints of outdated infrastructure, it is necessary to find intermediate solutions that maintain user-friendliness and enable data reuse and analysis.	SSO
	Problems with data reuse and analysis		
	Semantic constraints	Achieve semantic interoperability through unified implementation guidelines. Adherence to international best practices is vital to avoid overly national restrictions that can hamper innovations.	SSO
	Frontend display of DTx data	Clear rules and responsibilities for implementing interoperability requirements are needed. Positions must be discussed from a patient viewpoint to avoid economic logics and interests blocking solutions	Regulators/ Government
Topic area (2) DTX and Devices	Risk class-related considerations	Balancing the costs incurred by (interoperable) connection of highly regulated devices with DTx versus the benefits of access the to the data and the ecosystem. Health economic analysis should show the trade-off between lost lives and quality of life of not using reimbursable DTx in relation to high-class devices versus potential patient risks.	Manu-facturers
	Good example use cases were lacking	Development of convincing examples for manufacturers to use a new interface for direct data exchange with devices. Exemplary digital patient pathways should be developed for specific conditions.	SSO
	Closed or semi-closed data access models	There is a need for semantic data models that can be uniformly implemented by implementation guidelines. European legislation to prevent information blocking and metadata platforms that allow to access data	Regulators/ Government
Topic area (3) DTx and Innovations	Specifications for EHR telemedicine interfaces were missing	Enable patient data sovereignty by providing flexible interface connections for data exchange with innovative healthcare solutions. Conceptual developments in blended care models should also be reflected in legislation.	Regulators/ Government
	Integration with other types of care-related or medical apps	From a patient-centric point of view, there is a clear need to facilitate the linking of data from different services and, with the help of innovative services, to be able to take advantage of preventive health services based on their own health data.	Regulators/ Government

Table 1. Identified issues and their implications.

5 Discussion

This paper aims to analyze the issue of designing future-oriented and patient-centric care pathways related to DTx and their interoperability. This was achieved through an analysis of three main DTx-related interfaces, namely to EHRs, devices, and other digital health innovations, such as telemedicine. We outlined important regulatory and technological framework conditions for designing future-oriented, interoperable, and patient-centric care pathways, which considers the integration of patient-collected information into the care pathways. The analysis suggests that early DTx design choices established DTx as stand-alone applications. Current regulation seeks to open DTx to the digital health landscape and increase optionality from a user/patient perspective. However, these efforts face opposing interests and path dependencies. Our analysis revealed interest-driven positions in all the areas examined, highlighting the need for an overarching systemic perspective and approach to establish technical and regulatory conditions that enable the development of patient pathways in an open, user-friendly manner that is future-oriented. To this end, we put forward a DTx interoperability landscape as a modifiable conceptual tool for future research. We discuss our results, implications, and recommendations in two broad areas – (1) DTx as integral component of care pathways with EHRs as regulatory anchor points and hubs of care coordination and (2) DTx as treasures of data for data-driven research and real-world evidence.

5.1 DTx as Integral Component of Care Processes and Role of Public EHR

Our main finding was that DTx are currently conceptualized mostly as stand-alone applications, and that DTx are not yet fully integrated into the digital health landscape. While previous commentaries have noted the importance of coordinated care, especially for chronic conditions (e.g., Dadgar and Joshi, 2018; Bardhan et al., 2020), our analysis suggested a structural mismatch between different components in the care continuum responsible for the siloed position of DTx. We, importantly, noted a *coordination vacuum* regarding responsibilities for creating integrated apps/platform portals for users/patients with multiple, recurring and chronic conditions. While health insurances building integrated platform portals on top of the nationwide EHR could in principle take this role (e.g., Stegemann and Gersch, 2021), the analysis suggested that the payer role of health insurances created opposition with patient representatives and medical professionals for them to take the lead, and health insurances themselves were unsecure on how bold and fast they should move in such direction. While other health care systems such as the NHS, through their centralized approach, have created such entry points into integrated care, these potentials remained largely unrealized today in our context[2]. If not tackled appropriately, the void may soon be filled by private firms such as Amazon, as noted by Gleiss et al. (2021) and Rowe and Markus (2022), providing easy-to-use and integrated platform offerings including telemedicine, DTx, and ambulatory and clinical health services. While, in the German context, some regional care coordinators set a worldwide example for good care for some patient groups, including Healthy Kinzigtal for a regional care network (e.g., Schubert et al., 2021) and APST for ALS patients (e.g., Fürstenau et al., 2021), a nationwide EHR which offers the potential to build services on top of it had been lacking for a long time. Our analysis suggested that even now, key infrastructural components in the current EHR/DTx interface environment are based on legacy architectures, thus creating path dependencies for the coming years, which will make further development at the interface between DTx, EHR and devices difficult. Specific problem areas concern the basic architecture of the EHR (XDS, file-based storage), the interfaces of the EHR via IHE-XDS, and the interface of the EHR with DTx via card connectors (also virtual), which from the beginning should be consistently future-oriented.

Following evidence on conflicting logics of care in other contexts (e.g., Hansen and Baroody, 2020), our recommendation to practice overall would be to clarify and carefully monitor the responsibilities for who provides the entry point into patient care pathways and to build the EHR consequently on the basis of established technologies (such as RESTful Architectures and the FHIR standard), which is also based

[2] Clemons et al. (2022) have used the term life control interfaces, which indicates the comprehensive and holistic claim of such solutions, and have pointed to a cooperation paradox in regard to creating such a solution on the European level.

on this as the foundation for a (re-)development of the EHR and its interfaces. To address the diverse challenges associated with interoperability, including the differing perspectives of various stakeholders, the need for international connectivity to scale innovative solutions, and the emphasis on patient-centric principles, it is essential to manage interoperability in an iterative process that considers highly relevant design options in the short-term, medium-term, and long-term. This has been recognized by the regulator with the establishment of a permanent interoperability board (Interop Council) that will moderate and shape this iterative process in the future (Gematik, 2022). In our view, the EHR carries a great data treasure for the reuse of the data: for individual patients, the EHR creates a seamless digital history; in care delivery, inefficiencies due to unavailable information could be reduced; such a treasure trove of data offers health research and care management - together with the tools already available for existing tools of modern data utilization such as data analytics, artificial intelligence (e.g., Lehne et al., 2019) an immense added value, which has not yet been tapped in Germany. However, this requires a transformation of the EHR that is open for the future.

5.2 DTx as Treasure for Data-Driven Research and Real-World Evidence

To this date, the data collected by DTx can only be (further) used to a very limited extent, although these data can provide an important basis for adaptive further development and adjustment of the quality of care. On the one hand, this concerns the dimension of *evidence generation on the efficacy of DTx in the form of real-world evidence.* Through its real-world usage, DTx will create behavioral data that should be made available for effectiveness studies that could extend approval-related controlled trials. This data can be used for price determination and pay-for-performance models. Following the call for patient-centricity, DTx can be used as a tool for Patient Reported Outcome Measures (PROM). Data on patient-reported outcomes can be generated and continuously monitored via DTx. Additionally, DTx can incorporate patient-collected data from wearable devices, smartphones, biomarkers, and process flow-related capacity management, which could prove beneficial for early disease detection, targeted treatments, and improved management of the care pathway. Although individual data can be transmitted through interfaces from devices in DTx to be used for their standalone purpose, it can be challenging to subsequently use this data for care management and research under the investigated regulatory regime. In addition, there are no defined corresponding responsibilities or infrastructural foundations, such as in the EHR, for this purpose.

Our practice recommendation involves the establishment of an official body dedicated to data-based health care research, which includes DTx and beyond. This body should have the capability to securely store aggregated and anonymized data for research purposes in a trust fund, similar to the Danish model (DHDA, 2022). To facilitate this, a suitable technical data infrastructure in the form of public data spaces (Beverungen et al., 2022) needs to be established. In this regard, existing solution proposals from patient-oriented entities (Slosarek et al., 2020) and ongoing conceptualization efforts by European Health Data Space projects (Shabani, 2022) can serve as valuable guides.

6 Conclusion and Outlook

This paper noted the importance of integrating DTx into iteratively developed digital health landscapes. It assumed that such integration is widely assumed to be necessary. However, integration is by no means easy to achieve in practice. In the introduction, a VR-based DTx solution for the treatment of anxiety patients was used as an example to demonstrate both the relevance and the limitations of the current approach. One of the main implications for research is to view DTx from a patient-centric inter-operability perspective, which can be refined by future studies. The analysis suggests that the way forward will require finding new approaches to foundational architectures of core systems (e.g., nationwide EHRs), overcoming historical path dependencies regarding care coordination, and tackling challenging questions of how to build public data spaces (e.g., Beverungen, et al., 2022), including DTx data to draw systematic insights on many patient histories over long periods of time. We contribute to the discussion of considering interoperability in a patient-centric and multidimensional way. We see interoperability requirements regarding both the (vertical) levels of interoperability – e.g., technical,

syntactic, and semantic – and the (horizontal) integration between domains (e.g., Hodapp and Hanelt, 2022). The patient-centric view of interoperability along care pathways enabled us to identify future friction points for a future-oriented health care system.

The results of the study have to be considered under certain limitations. Our analysis considered a limited period and considered DTx as a digital innovation recently introduced into the healthcare systems of many countries, and thereupon explored key interfaces to EHRs, devices, and other healthcare innovations, including telemedicine. The findings were generated in the context of the German health care system; the generalizability of these findings would have to be investigated through studies in other contexts. Further work is needed to deepen our understanding of these issues. This work could provide additional analysis of single interfaces and solution options that provide requisite variety and value for patients using multiple DTx, devices, and other digital health innovations. This research could adopt a longitudinal perspective of several episodes of technical, organizational, and regulatory innovation, taking into account the complex, partly competing logics and stakeholder dynamics and how to reconfigure them to maximize patient value, considering the interests of the public and private entities.

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Appendix

A1: List of workshops Oct 2021 – April 2022

WS	Contents	Part.
1	The future of DTx and landscape of DTx interoperability*	30
2	Standards and Medical Information Objects for DTx†	36
3	Interface DTx and EHR†	63
4	DTx and device connection (Frontend, §5 DiGAV, Annex 2-4a) †	62
5	DTx & device connection / implants & assistive technology devices (Backend, §374a SGB) †	50
6	DTx panel on DTx patient-centric interoperability & data spaces**	25

Notes. #Part … number of participants, * on-site, † online ** hybrid # for WS6 includes only on-site participants without additional streaming participants

A2: Perspective of interviewees

#	Topic	Illustrative quote
Topic area (1) DTx and EHRs	Write-online interface	"At the moment, the EHR is rather uni-directional … that should be changed" (Industry expert, Jan. 2022). "Data such as from the EHR could make a digital-based "therapy companion" (e.g. DTx) better and more accurate" (DTx Manufacturer, Jan. 2022).
	Technical exchange infrastructure outdated	"The EHR is useful for everything that is scanned and archived" (IOP Expert, Jan. 2022). "One has apps/folders with read/write permissions, but is signed, locked within itself." (International Standards Expert, Mar. 2022). "It is too complex for the DTx manufacturers" (Industry expert, Jan. 2022). "Understanding is necessary and not SMC-B and plastic cards" (IOP Lead, Jan. 2022).
	Semantic constraints	"Which specification to choose is often unclear and subject to very wide discussion" (IOP expert, Jan. 2022). "Deep semantic processing is much of a way still " (IOP consultant, Dez. 2021). "There [guidance for semantic constraints] we need to become stronger" (FHIR manager, Dez. 2021). "[There is] a narrow measurement selection for specific measurement points." (Manufacturer Associate, Mar. 2022)
	Problems with data reuse and analysis	"What is being exchanged ... we fear lots of data garbage in the EHR" (Health Insurance Representative, Jan. 2022). "Transferring raw data to a registry would not be difficult technically, to be seen as untapped potential" (Physician, Nov. 2021). "Reusability of data must be improved" (Health Insurance Manager, Dec. 2021)

	Frontend display of DTx data	"As long as the physician has to 'swipe' on the patient's screen, this can't work" (Physician, Nov. 2021). "If digital apps are used: to what extent can the primary systems display the data so that there is a high degree of overlap with the previous preparation of the data" (Medical Association Rep, Feb. 2022).
Topic area (2) DTx and Devices	Risk class-related considerations	"They do not fit together right now … DTx must be opened to higher risk classes" (Industry Associate, Mar. 2022). "Implants and devices are in higher risk classes, which use completely different data than those considered in the current … profiles" (Manufacturer Associate, Mar. 2022).
	High possible costs for recertification	"The industry needs more lead time" (Technical Lead of Global Device Manufacturer, Mar. 2022). "Everything is major change, which is an interface" (DTx and Device Expert & Scientist, Mar. 2022).
	Insular nature of the regulation	"Primary systems are not subject to gematik or telematics regulations, but are crucial for the acceptance and possibility to work satisfactorily with DTx." (Medical Association Rep, 2/22). "Many different regulatory requirements have to be implemented, e.g. ISO 27007 and guidelines from the Federal Office for Information Security as well as for the data protection certificate from the Federal Institute for Drugs and Medical Devices and gematik (EHR)" (DTx Manufacturer, Feb. 2022).
	Unclear responsibilities	"I see a power vacuum, actually the National Drug Agency should control which medical devices are relevant for certification. The Association of Ambulant Physicians has only written the specification and made it available to the manufacturers." (IOP Consultant, Mar. 2022). "Who actually builds the interface for the data exchange between manufacturer and the DTx backend ... Mandate in the law is missing." (Industry Associate, Mar. 2022).
	Good examples were lacking	"There are no good examples [for the backend device interface]" (FHIR Manager, Feb. 2022). "We don't know how the data will be transferred concretely, and there are no user stories to mention" (Medical technology representative, Feb. 2022).
	Closed or semi-closed data access models	"Not every manufacturer… gives access" (CEO Middleware Manufacturer, Feb. 2022). "Certain manufacturers no longer release certain data types … [they provide] poor access due to incomprehensible restrictions" (Tech Lead Middleware manufacturer, Feb. 2022). "If an American company alone receives the data of our patients, that cannot be the solution." (DTx manufacturer, Feb. 2022)
	Broader European or international consensus	"No manufacturer listens to a single country or its own country-specific standard" (International IOP Expert, Mar. 2022). "No manufacturer would implement national mandates even with a high monetary incentive. There is no reason to make a country-specific or even a Europe-specific version." (IoT Architect, Mar. 2022).
Topic area (3) DTx and Digital Health Innovations	Heterogeneity of telemedicine programs	"Telemonitoring islands have formed: it is not okay that one physician has to serve 5 different processes. The lack of interoperability plays a role there" (Telemonitoring Scientist & Physician, Mar. 2022).
	EHR telemedi-cine interface specifications were missing	"This interface [EHR – telemedicine] is not prioritized" (Product Manager Telemedicine Solution, Mar. 2022). "At some point, we made a decision in the team not to wait for any structures" (Telemedicine Implementation Scientist, Mar. 2022).
	Integration with other care-related or medical apps, such as triage, prevention, etc.	"I wish the data could follow the patient" (Patient Representative, Nov. 2021). "[mentioning of non-DTx prevention solution for EGC measurement via smartphone] Again parallel strands potentially in question" (Medical Association Rep, Feb. 2022).

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