DOCTORAL THESIS

Interoperability and Governance in National Digital Health: A Framework-Based Argument for Integrative and Knowledge-Driven Approach

Janek Metsallik

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JANEK METSALLIK

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TALLINN UNIVERSITY OF TECHNOLOGY
School of Information Technologies
Department of Health Technologies
Curriculum: School of Engineering

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Supervisor: Peeter Ross, Tenured Associate Professor,
Centre for Digital Health
Department of Health Technologies, School of Information Technologies,
Tallinn University of Technology
Tallinn, Estonia

Co-supervisor: Dirk Draheim, Tenured Full Professor,
Information Systems Group
Department of Software Science, School of Information Technologies,
Tallinn University of Technology
Tallinn, Estonia

Opponents: Professor Yngve Lamo,
Department of Computer Science, Electrical Engineering and Mathematical Sciences,
Western Norway University of Applied Sciences, Norway

Associate Professor Laura-Maria Peltonen,
Department of Health and Social Management,
University of Eastern Finland, Finland

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Declaration:
Hereby I declare that this doctoral thesis, my original investigation and achievement, submitted for the doctoral degree at Tallinn University of Technology, has not been submitted for any academic degree elsewhere.

Janek Metsallik _____
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TALLINNA TEHNIKAÜLIKOOL
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Koosvõime ja valitsemine riiklikus digitaaltervises: raamistikupõhine käsitlus integreerituse ja teadmuspõhisuse toetuseks

JANEK METSALLIK

TAL TECH
KIRJASTUS

Contents

List of Publications

The present PhD thesis is formally based on four Scopus-indexed, peer-reviewed publications that are referred to in the text by Roman numerals I–IV and included as appendices.

I Janek Metsallik, Peeter Ross, Dirk Draheim, and Gunnar Piho. Ten Years of the e-Health System in Estonia. In *CEUR Workshop Proceedings*, volume 2336, pages 6–15, Bergen, Norway, 2018. CEUR Workshop Proceedings. URL https://www.academia.edu/download/76879592/MMHS2018_invited.pdf

II Janek Metsallik and Peeter Ross. Testing the Applicability of Digital Decision Support on a Nationwide EHR. In Rim Jallouli, Mohamed Anis Bach Tobji, Hamid Mcheick, and Gunnar Piho, editors, *Digital Economy. Emerging Technologies and Business Innovation*, Lecture Notes in Business Information Processing, pages 134–146, Cham, 2021. Springer International Publishing. ISBN 978-3-030-92909-1. doi: 10.1007/978-3-030-92909-1_9

III Markus Bertl, Janek Metsallik, and Peeter Ross. A systematic literature review of AI-based digital decision support systems for post-traumatic stress disorder. *Frontiers in Psychiatry*, 13, August 2022. ISSN 1664-0640. doi: 10.3389/fpsyt.2022.923613. URL https://www.frontiersin.org/journals/psychiatry/articles/10.3389/fpsyt.2022.923613/full

IV Janek Metsallik, Dirk Draheim, Zlatan Sabic, Thomas Novak, and Peeter Ross. Assessing Opportunities and Barriers to Improving the Secondary Use of Health Care Data at the National Level: Multicase Study in the Kingdom of Saudi Arabia and Estonia. *Journal of medical Internet research*, 26:e53369, August 2024. ISSN 1438-8871. doi: 10.2196/53369. URL https://www.jmir.org/2024/1/e53369

Author's Contributions to the Publications

I In Publication I, I was the main author. Drawing on experience gained from my earlier role as the chief architect of the national electronic health records system in Estonia, I contributed the core architectural content based on original system design documentation and earlier architectural presentations, reflecting the applied interoperability standards and architectural principles; the manuscript was prepared collaboratively with the co-authors.

II In Publication II, I was the main author. The testing of decision support algorithms on electronic health records data formed part of preparation for the national clinical decision support solution; drawing on detailed knowledge of the electronic health records technical architecture acquired through prior involvement as the chief architect of the national electronic health records system in Estonia, I proposed the testing approach, guided the preparation and execution of test scripts, and synthesised the results into design principles for a national decision support solution. The selection and clinical interpretation of specific algorithms were led by the co-author and involved clinical experts. I wrote the manuscript.

III In Publication III, I was the second author. My role corresponded to investigation, data curation, and writing of the original draft; together with the lead author, I screened and synthesised the literature, co-developed the analytical framework for evaluating results, contributed additional dimensions to this framework, proposed quantitative visualisations, and participated in drafting the manuscript.

IV In Publication IV, I was the main author. In both cases, my role focused on mapping the actual state of data standards and information systems and shaping systematic change; in the Estonian study, I additionally adapted the health information sharing maturity model and analysed the results. While the studies relied on colleagues' clinical and policy expertise, I synthesised a higher-level analytical framework to explain the tensions and discontinuities observed in the data flows and contributed to writing the manuscript.

Abbreviations

Abbreviation	Meaning
5P	Predictive, Preventive, Personalised, Participatory, Psycho-cognitive (medicine)
ACE	Angiotensin-Converting Enzyme
AI	Artificial Intelligence
AKM	Active Knowledge Modelling
API	Application Programming Interface
ATC	Anatomical Therapeutic Chemical (classification system)
BRCA1/2	Breast cancer susceptibility genes 1 and 2
C1-C4	Empirical clusters 1–4
CDA	Clinical Document Architecture
CDS	Clinical Decision Support
CIM	Computation-Independent Model
CIOMS	Council for International Organizations of Medical Sciences
ContSys	System of concepts to support continuity of care (ISO 13940)
CTS2	Common Terminology Services 2
DDSS	Digital Decision Support System
DESI	Digital Economy and Society Index
DHP	Digital Health Platform (World Health Organization/International Telecommunication Union term for a common digital health information infrastructure or infostructure; used here analytically for the platform function within national digital health)
DRG	Diagnosis-Related Group
DSS	Decision Support System
EBMeDS	Evidence-Based Medicine Electronic Decision Support (Duodecim)
eCRF	electronic Case Report Form
EGCUT	Estonian Genome Center, University of Tartu (biobank)
eGFR	Estimated Glomerular Filtration Rate
EHDS	European Health Data Space
EHDS2	European Health Data Space (secondary use of data; “EHDS2” usage in EU interoperability toolkit literature)
EHIF	Estonian Health Insurance Fund (Estonia)
EHIS	Estonian Health Information System (legal/institutional umbrella of Estonia’s health information infrastructure; related to, but not identical with, the functional national EHR/DHP layer analysed)
EHR	Electronic Health Record (shared longitudinal patient record; in this thesis, used for the Estonian national EHR as a central shared-service arrangement)
EMR	Electronic Medical Record
EPR	Electronic patient record
ESC	European Society of Cardiology
EU	European Union

Abbreviation	Meaning
EVS	Estonian Centre for Standardisation and Accreditation (national standards body)
FHIR	Fast Healthcare Interoperability Resources, a standard by HL7
GCM	Generic Component Model
GDPR	General Data Protection Regulation
GP	General practitioner
HbA1c	Glycated haemoglobin
HISMM	Health Information Sharing Maturity Model
HL7	Health Level Seven, a non-profit organisation for health information standards
HL7 CIMI	HL7 Clinical Information Modelling Initiative
ICD-10	International Classification of Diseases, 10th Revision
ID	Identification; national digital identity (e.g., ID-card, Mobile-ID)
IEC	International Electrotechnical Commission
IEL	Institute of the Estonian Language
IMM	Interoperability Maturity Model
ISO	International Organization for Standardization
IT	Information Technology
ITU	International Telecommunication Union
KBI	Knowledge-Based Interoperability
LCIM	Levels of Conceptual Interoperability Model
LOINC	Logical Observation Identifiers Names and Codes
M0–M3	Modelling abstraction levels as defined in MOF (instance to meta-metamodel)
MDA	Model-Driven Architecture
MMM	Macro–Meso–Micro (analytical perspective)
MOF	Meta-Object Facility
MUT	Mutation carrier cohort (cohort label in estPerMed breast/ovarian cancer pathway pilots)
NCSP	Nordic Classification of Surgical Procedures
NGHA	National Guard Health Affairs (Saudi Arabia)
NHS	National Health Service (UK)
NIHD	National Institute for Health Development (Estonia)
OCL	Object Constraint Language
OMG	Object Management Group
OMOP	Observational Medical Outcomes Partnership
OMOP CDM	Observational Medical Outcomes Partnership (Common Data Model)
openEHR	A non-profit organisation for EHR technical standards
PACS	Picture Archiving and Communication System
PHR	Personal health record
PIM	Platform-Independent Model

Abbreviation	Meaning
PRS	Polygenic risk score
PSM	Platform-Specific Model
PTSD	Post-Traumatic Stress Disorder
QA	Quality assurance
QVT	Query/View/Transformation (model transformation standard)
REDCap	Research Electronic Data Capture
RM-ODP	Reference Model for Open Distributed Processing
RQ	Research Question
SCI	Supply Chain Interoperability
SNOMED CT	Systematized Nomenclature of Medicine – Clinical Terminology
SoM	Ministry of Social Affairs (Estonia)
SQL	Structured Query Language (database query language)
TAI	National Institute for Health Development (Estonian abbreviation)
TalTech	Tallinn University of Technology
TEFCA	Trusted Exchange Framework and Common Agreement (United States nationwide health information exchange governance framework)
TEHIK	Centre for Health and Welfare Information Systems (Estonian abbreviation)
TQC	Terminology Quality Checklist
TS	Terminology Server
UML	Unified Modelling Language
US	United States (of America)
UT	University of Tartu
WHO	World Health Organization
XML	Extensible Markup Language

Terms and definitions

Term	Working definition in this dissertation
Conceptual interoperability	Interoperability grounded in shared conceptual models and purposes that link data meaning to institutional intent and coordinated action. *(See: Section 3.3)*
Digital health platform (DHP)	A common digital health information infrastructure (“infostructure”) on which digital health applications and systems are built. It consists of common and reusable components, including software, shared information resources, integration services, data definitions, and standards-based interfaces, through which applications such as electronic health records, insurance, supply-chain and patient-engagement systems can interoperate. In this dissertation, DHP is used as an analytical descriptor of this platform/infostructure function within national digital health. (See: [5], Section 1.2)
Governance (of interoperability)	The institutionalised allocation of roles, responsibilities, decision rights, and change-control mechanisms through which interoperability is legitimised, stabilised, and made accountable over time. *(See: Section 5.4, Chapter 6)*
Institutional logics	Relatively stable patterns of values, norms, and rationales that structure action and legitimacy across domains such as clinical care, administration, research, and policy. *(See: Section 3.6)*
Interoperability	An emergent, multi-level socio-technical coordination capability that depends on the explicit alignment of technical, semantic, conceptual, institutional, and governance arrangements. Interoperability is not treated as a cumulative system property or maturity stage. *(See: Section 1.3, Section 3.7)*
Interoperability capability	The qualitative profile of interoperability across abstraction levels and institutional domains, used analytically to characterise coordination conditions rather than to rank systems by maturity or performance. *(See: Section 3.4)*
Knowledge governance	The governance of semantic and knowledge artefacts across their lifecycle, including stewardship, validation, change management, and accountability for reuse. *(See: Section 3.5, Section 6.4)*
Knowledge-based interoperability	A form of interoperability in which domain knowledge, rules, constraints, and decision logic are explicitly formalised, governed, and reusable across systems and contexts, enabling decision-relevant reuse and learning. *(See: Section 3.5, Section 5.3)*
M0–M3 abstraction levels	Meta-modelling levels distinguishing institutional reality (M0), formalised knowledge artefacts (M1), modelling and alignment mechanisms (M2), and paradigmatic coordination principles (M3). *(See: Chapter 3, Chapter 4)*
Macro–meso–micro levels	Analytically distinct but interdependent coordination contexts used to examine how policy intent, institutional arrangements, and operational practice are aligned or decoupled in national digital health arrangements. *(See: Section 3.1)*

Term	Working definition in this dissertation
National digital health	Nationally coordinated socio-technical arrangements through which digital services, shared platforms, standards, legal mandates, data flows, knowledge-use practices and governance routines are organised for digitally mediated information work across healthcare and related administrative domains. In this dissertation, this is the primary analytical object. *(See: Section 1.2)*
National EHR / EHIS (Estonia)	Context-dependent labels for the Estonian empirical infrastructure through which national digital health interoperability is analysed. Estonian Health Information System (EHIS) denotes the legal and institutional umbrella of Estonia's health information infrastructure. The national electronic health record (EHR) denotes the central shared-service arrangement for aggregating, exchanging and providing access to longitudinal patient information across providers. This use follows the World Health Organization (WHO) distinction between facility-level electronic medical records and electronic health records as shared patient records compiled from local medical and other health-related records and supported through a central repository or shared access layer. (See: [5], Section 1.2)
Semantic interoperability	The ability to interpret exchanged data consistently based on shared terminologies, coding systems, and semantic models. Treated as a necessary but insufficient condition for knowledge-based interoperability. *(See: Section 5.5)*

1 Introduction

1.1 Background and motivation

Estonia's national digital health arrangements, comprising a broad portfolio of nationwide digital services, have long served as a reference point in international comparisons of digital health systems [6–9]. In the European Commission's Digital Decade indicator on access to electronic health records, reported through the Digital Economy and Society Index (DESI) visualisation tool under the title "Access to e-health records", Estonia and Belgium are the only European Union (EU) Member States shown with a composite score of 100 in the 2025 assessment based on 2024 data (Figure 1). The indicator is based on twelve equally weighted sub-indicators that operationalise citizens' online access to electronic health record data in terms of available data types, data suppliers, access modes, and access requirements. This positioning makes Estonia a demanding mature access-oriented case for examining what national digital health arrangements deliver in practice and where their limits become visible even under high-coverage conditions.

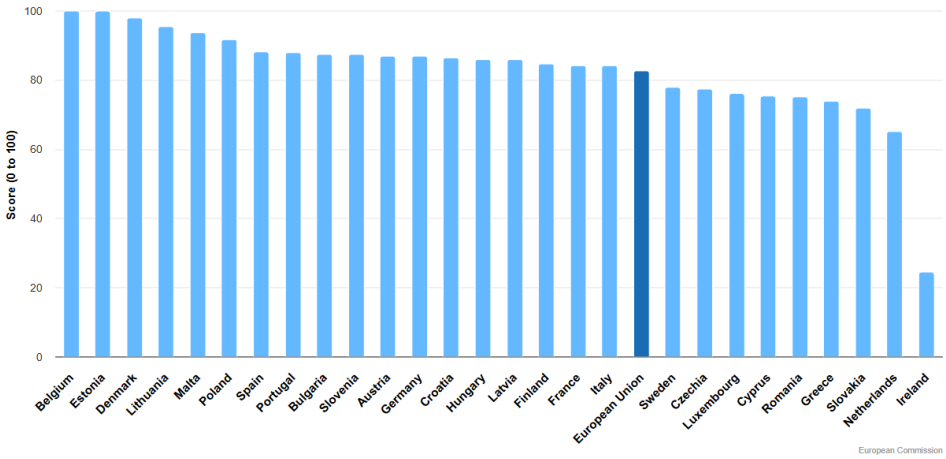

Figure 1: Estonia in the Digital Decade / Digital Economy and Society Index (DESI) 2025 indicator "Access to e-health records" (data from 2024). The 0-100 composite score reflects the maturity of citizen-oriented online access to electronic health record data, including portal or mobile access, population coverage, electronic identification, available data types, data suppliers and accessibility support. The figure positions Estonia as a mature access-oriented case of national-scale electronic health data access and data availability. (source: European Commission Digital Decade/DESI visualisation tool and Digital Decade indicator methodology [10]).

Behind these aggregate scores lies a socio-technical arrangement in which national services build on e-government infrastructure and integrate a heterogeneous landscape of provider systems, registers, central services and standardised data flows. Early economic expectations around Estonia's national-scale exchange and access trajectory were articulated in the 2008-2010 DIGIMPACT study, conducted in the context of the national EHR programme. The study estimated that the direct, indirect and intangible benefits of standardised document exchange and central access would outweigh their costs by a factor of 4-5, assuming that deeper workflow transformation would follow once national exchange and access had been implemented [11]. Subsequent empirical work has complicated this optimistic picture. Studies examining the usability and quality of health data made available through national exchange and access arrangements in Estonia have repeatedly identified constraints that limit cross-process use, secondary analysis and decision-oriented reuse [12–17]. These findings are relevant at the level of national digital health because they expose limits in how national access and exchange arrangements support reliable interpretation, cross-process

continuity, decision support and secondary use.

Almost two decades after the national EHR and related exchange and access services became core components of Estonia's digital health arrangements, Estonia's digital health strategy for 2025-2030 still prioritises person-centricity, multiple use, and process integration [18]. Read against early expectations that standardisation and central access would enable deeper workflow transformation, this continuity of ambition is analytically important. It suggests that national-scale access and exchange can be stabilised earlier than the semantic, organisational and institutional conditions required for integrated, knowledge-driven and person-centred care.

The author's direct experience as chief architect of Estonia's national EHR (2006-2011), followed by research and advisory work on country-level digital health initiatives elsewhere, shows that digital health development at this scale is never merely a technical activity. The Estonian EHR project itself already involved more than building a central repository: it connected provider systems, existing registers, e-government services, emerging central services and standardised data flows to make health information available across organisational boundaries. Later work on decision support, personalised medicine, secondary use and platform development broadened this perspective to settings where health-sector data needs are addressed by combining multiple systems, registers and data flows. This shifts attention from the EHR as an artefact - a repository, its services and the standards that shape its interfaces - to the wider operational and governance context in which roles, boundaries, meanings and responsibilities are negotiated and stabilised. The resulting question is not only about Estonia. It concerns whether the tensions visible in a high-coverage setting are specific to local implementation history or reflect more general limits of national digital health arrangements. If they are more general, what must change for coverage and access to translate into cross-process continuity, decision support and systematic secondary use?

This reading is consistent with prior analyses of the conditions that enabled Estonia's national-scale digital exchange and access to health data. These analyses emphasise that successful interoperability does not follow from technical integration alone, but from co-evolving technical, organisational, and institutional arrangements. Scale-up depends on enabling conditions that span mandate and governance, shared infrastructure and core services, including identity, standards with life-cycle change control, sustainable financing and capacity building, and trust-, security-, and privacy-related practices that make inter-organisational exchange dependable in day-to-day operations [19, 20].

This dissertation therefore treats Estonia's mature access-oriented setting as an empirical entry point for examining a broader coordination problem in national digital health. The following sections delimit the terminology, conceptual frame, aim, research questions, and publication corpus through which this problem is analysed.

1.2 Terminology and analytical scope

This dissertation uses *national digital health* as the primary analytical object. As defined in the opening Terms and definitions section, the term refers to nationally coordinated socio-technical arrangements through which digital services, shared platforms, standards, legal mandates, data flows, knowledge-use practices and governance routines are organised for digitally mediated information work across healthcare and related administrative domains. This section clarifies how this definition delimits the analytical scope of the thesis and how related system-level labels are used. The focus is therefore not on a single information system, database, portal or standard, but on the interoperability and governance conditions under which such arrangements support, or fail to support, integrated, knowledge-driven and person-centred care.

In the Estonian case, the national *electronic health record (EHR)*, the Estonian Health Information System (EHIS) and the *digital health platform (DHP)* are related but not synonymous terms. EHIS refers to the legal and institutional umbrella of Estonia's health information infrastructure. The national EHR refers to the central shared-service arrangement for aggregating, exchanging and pro-

viding access to longitudinal patient information across providers. This use follows the World Health Organization (WHO)/International Telecommunication Union (ITU) distinction between facility-level electronic medical records and electronic health records as shared patient records compiled from local medical and other health-related records [5].

Following the WHO/ITU DHP handbook, *digital health platform (DHP)* refers to a common digital health information infrastructure, or infostructure, on which digital health applications are built and integrated. Such an infostructure consists of common and reusable components, shared information resources, integration services, data definitions and standards-based interfaces that support interoperability [5]. In this dissertation, DHP is used as an analytical descriptor of this platform/infostructure function within national digital health. It is not used as a separate official Estonian system name or as a component-by-component architecture description.

Here, *national* denotes a governance and mandate boundary rather than a claim that the findings are specific only to Estonia. Analytically, the thesis addresses large-scale, multi-stakeholder digital health infrastructures that face comparable coordination problems across jurisdictions. The included reprints are reproduced in their original form and may use narrower or different labels for the same arrangements; in the integrative text, these labels are treated as context-dependent references rather than as distinct systems.

1.3 Conceptual framing of the thesis

The preceding sections establish the empirical puzzle that motivates the thesis: Estonia represents a mature access-oriented national digital health setting, while the expectations attached to national digital health extend beyond access itself. This section frames how that puzzle is turned into a researchable problem. The issue is not whether digital services, EHR access or document exchange exist, but how their relationship to broader healthcare aims can be understood after such arrangements have been implemented and used over time.

The author's earlier studies provide the starting material for this framing. They examined national EHR development, digital health requirements, governance questions, data-use opportunities, decision-support applicability and concrete digital health artefacts from different empirical and practical entry points. Across these orientations, they were directed towards a shared concern: how national digital health arrangements can better support health-sector data, knowledge-use and governance needs across care, decision support, reuse and policy contexts. In this dissertation, these works are therefore not treated only as separate publications, but as material for an integrative reading of national digital health interoperability [I], [21, 22], [IV], [23].

The significance of this material lies partly in its longitudinal character. Estonia's national digital health arrangements have moved beyond planning and piloting: they have been operated, adjusted and relied on for a long period. This makes it possible to examine what a mature access and exchange logic can demonstrably support, and where further coordination problems appear after infrastructure has become operational. The point is not to dismiss the achievements of national-scale exchange and access arrangements, but to clarify the analytical problem that emerges once technical operation and data availability are no longer the only central concerns.

The motivation is also not limited to Estonia. The author's international work with national digital health initiatives has repeatedly shown that similar questions arise in settings with different institutional maturity, technical baselines and policy expectations. This gives the thesis a reason to treat the Estonian experience as analytically informative rather than merely local: it provides a mature setting in which the relationship between digital health infrastructure and healthcare-oriented use can be examined in depth.

This framing therefore positions national digital health as an implemented and evolving coordination arrangement rather than only as a technological infrastructure. The issue is not only whether systems exchange information, but how the resulting arrangements connect access, interpretation,

reuse, responsibility and change over time. At this stage, this concern defines the problem space of the thesis rather than its contribution or final findings. This relationship is summarised in Figure 2.

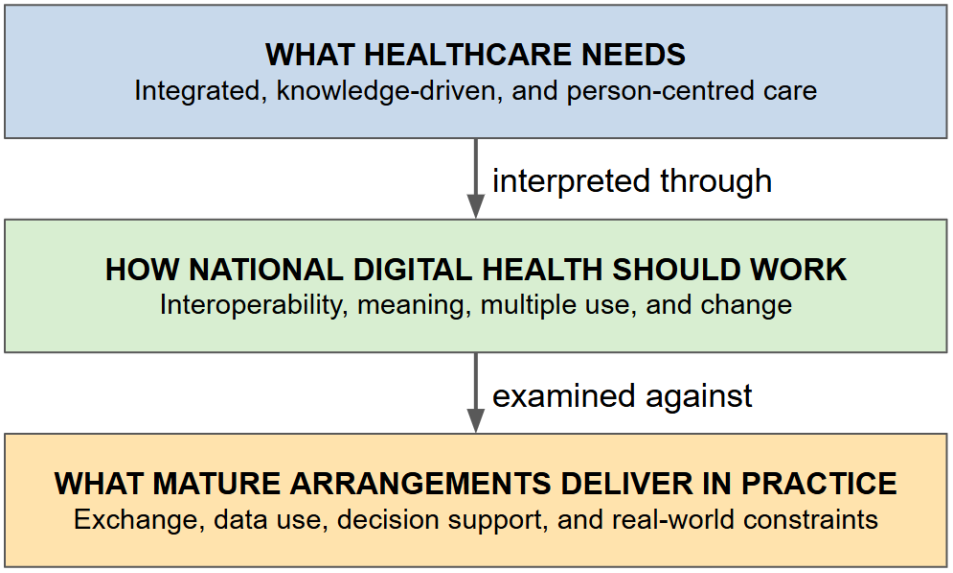

Figure 2: Conceptual problem frame of the thesis. The figure links the healthcare expectations placed on national digital health to the thesis's analytical view of how national digital health should work, and then to the empirical question of what mature arrangements deliver in practice. It frames the thesis as an inquiry into the relationship between access-oriented infrastructure and broader expectations of semantic continuity, knowledge-ready use, governed multiple use, and person-centred care. (source: author).

This frame narrows the thesis from a broad concern with digital health development to a more specific inquiry into what national digital health interoperability becomes once access and exchange have been substantially developed. It orients the following aim and research questions by identifying the empirical and conceptual tension that the dissertation addresses.

1.4 Contribution and novelty

This dissertation contributes to the study of national digital health interoperability by reframing it as a governed coordination capability rather than as a cumulative technical or organisational maturity trajectory. The central argument is that national digital health cannot be understood only through the expansion of exchange infrastructure, access services, standards adoption, or platform functionality. These elements are necessary, but they do not by themselves ensure that data become decision-relevant, semantically stable, reusable across contexts, or accountable as part of a learning health system.

The novelty of the dissertation lies in showing how the gap between technical exchange and knowledge-ready digital health emerges from weak coupling between architectures, semantic and conceptual formalisations, institutional responsibilities, and governance of change. The Estonian case is used as a longitudinal and empirically grounded setting in which high-coverage national exchange infrastructure has stabilised access to health information and document flows, while decision support, personalised medicine, and secondary use still expose constraints related to data meaning, temporal coherence, contextual completeness, accountability, and authorised reuse.

The dissertation therefore advances an integrated analytical framework for explaining why technically mature national digital health arrangements may still fall short of integrative, knowledge-

based, and person-centred digital health. It brings together institutional logics, macro-meso-micro coordination, M0-M3 abstraction levels, technological and modelling spaces, interoperability capability, knowledge-based interoperability, and governance of change and reuse. The contribution is not a new maturity model, reference architecture, or implementation blueprint. It is an explanatory framework for analysing how interoperability capability is realised, constrained, and negotiated across institutional domains, abstraction levels, and knowledge-use contexts.

In practical terms, the dissertation clarifies that the next stage of national digital health development depends less on adding further technical connectivity and more on governing the relationships between data production, semantic stabilisation, knowledge artefacts, reuse purposes, and institutional accountability. This makes interoperability a continuing coordination problem: one that requires explicit alignment between shared infrastructures, formalised meanings, modelling and knowledge artefacts, responsible actors, and authorised mechanisms of change.

1.5 Aim of the thesis

Building on this analytical scope, the thesis examines how infrastructures, standards, data practices, organisational responsibilities and governance mechanisms shape how health data are exchanged, interpreted, reused and changed at national scale.

The aim of this thesis is to develop a theoretically grounded and empirically supported argument for how national digital health can be designed and governed so that technical exchange infrastructure is coupled with the semantic and conceptual alignment, knowledge readiness, and governance capability needed for integrated, knowledge-based, and person-centred care.

This argument is developed through a synthesis and reinterpretation of the author's prior empirical and normative research on national digital health interoperability, decision support, personalised medicine, secondary and multiple use of health data, and standards-based semantic and conceptual coordination.

1.6 Research questions

To address this aim, the thesis is guided by four research questions (RQ).

RQ1. **Interpreting national interoperability.** How can the evolution and functioning of national digital health interoperability be interpreted as a socio-technical phenomenon beyond the scaling of access and exchange infrastructure?

RQ2. **Knowledge-ready reuse.** How do the technical, semantic, and organisational conditions under which data are produced, exchanged and accessed through national digital health arrangements enable or constrain knowledge-ready reuse for clinical decision support, personalised medicine, and other forms of computable knowledge use?

RQ3. **Governed multiple use.** How do institutional logics, governance arrangements, and accountability structures shape the trustworthy multiple use of health data across care delivery, management, research, and policy contexts?

RQ4. **Higher-order interoperability.** How can standards, semantic alignment, conceptual modelling, and governance of change be brought together to support higher-order interoperability in national digital health?

Together, these questions move from the interpretation of national interoperability as an evolving socio-technical phenomenon, through the conditions for knowledge-ready reuse and trustworthy multiple use of health data, towards a higher-order account of how technical, semantic, conceptual, and governance dimensions of interoperability need to be coordinated.

1.7 Publication corpus

This dissertation distinguishes between the formal publication basis of the thesis and a broader analytical source set used to support the integrative argument. The formal publication basis consists of four Scopus-indexed, peer-reviewed publications listed as Publications I, II, III, and IV and reproduced as appended publications. These publications constitute the official publication basis of the thesis and demonstrate the doctoral-level quality of central parts of the dissertation's argument.

The formal publication basis is selective. The four publications were chosen because they contribute directly to the thesis problem: how mature national access and exchange infrastructure relates to the semantic, organisational, knowledge-use and governance capabilities required for integrated, knowledge-based and person-centred care. They address national e-health development, interoperability architecture, clinical decision support, artificial intelligence (AI)-based decision-support research, and governance of secondary use of health data.

The broader analytical source set consists of selected author-involved publications, technical reports and documented project materials. These sources are cited through ordinary bibliographic references and used where they clarify implementation settings, policy development, architectural choices, pilot arrangements, data requirements, terminology work, standards-related developments or governance constraints relevant to the thesis argument.

Publication I concerns the development and interpretation of Estonia's national e-health system [I]. It establishes the mature access and exchange setting from which the thesis problem arises. Additional case-based and professional publications clarify Estonia's national digital health development, including the national EHR, architectural choices, standardisation efforts and longitudinal system coordination [21, 22]. These sources help explain why Estonia can be treated as a demanding case for examining what national-scale digital health infrastructure can and cannot deliver after prolonged operation.

Publications II and III address the move from data availability to knowledge-ready use. Publication II empirically tests whether Estonian EHR data can support computable clinical decision-support rules [II]. Publication III complements this by showing, through a systematic review, the wider gap between AI-based decision-support research and operational integration into real-world health data environments [III]. Personalised medicine feasibility and pilot materials are used as contextual sources for implementation expectations, data requirements, workflow constraints and institutional arrangements [24, 25].

Publication IV addresses governance, institutional alignment and secondary use of health data [IV]. It analyses how institutional logics, responsibility allocation, legal mandates, stewardship and trust-related barriers shape the reuse of health data in national settings. Additional standards-oriented and project-based materials, including work on standards-based approaches to health data reuse, clarify implementation responses to these challenges [23].

Semantic and conceptual alignment is treated as a cross-cutting analytical concern within the broader source set. Standards-oriented publications on conceptual models, semantic annotation and terminology quality document practical work aimed at operationalising conceptual interoperability in national digital health [26–28]. They show how conceptual interoperability depends on coordinated work on clinical concepts, information models, terminology resources, semantic annotation and implementation guidance across clinical, organisational, regulatory and technical domains.

The included reprints are reproduced in their original form and may therefore use historical or context-specific labels such as "EHIS platform", "EHR platform" or related terms. In the integrative text of this dissertation, such labels are interpreted according to their original publication context and are not treated as separate systems unless explicitly stated.

The methodology chapter explains how the formal publications and the broader analytical source set are used in the dissertation's analytical procedure.

1.8 Structure of the thesis

This dissertation is structured in six chapters that move from research problem and positioning to theoretical framing, methodology, empirical synthesis, and discussion. This introduction establishes the problem, aim, research questions, terminology, conceptual framing, and publication corpus of the dissertation.

Chapter 2 positions the thesis in relation to scholarship on national digital health interoperability, semantic and conceptual interoperability, knowledge readiness, and governance of health-data use. Its main function is to show that existing approaches explain important parts of national digital health, but often leave insufficiently connected the relationships between technical exchange, meaning, knowledge use, responsibility, and governed change.

Chapter 3 develops the integrated analytical framework used in the dissertation. Rather than treating information technology and healthcare as separate framing domains, the chapter brings together architectural, semantic, conceptual, institutional, and knowledge-based interoperability perspectives into one framework for interpreting national digital health interoperability as a governed capability.

Chapter 4 explains the publication-based and framework-guided research design. It describes the evidence hierarchy, the selection and role of the publication corpus, the formation of RQ-oriented empirical clusters, and the analytical procedure through which the empirical material is re-read abductively using the theoretical framework.

Chapter 5 presents the empirical and analytical findings. The chapter is organised around four empirical clusters introduced in the methodology chapter: architecture and exchange, decision support and knowledge readiness, governed multiple use of health data, and standards, semantics, and conceptual interoperability. Across these clusters, the results identify recurring coordination problems that explain why access and exchange do not automatically translate into integrated, knowledge-driven, and person-centred care.

Chapter 6 synthesises the findings in relation to the research questions and related work. It clarifies the dissertation's main contribution: interoperability in national digital health extends beyond technical and semantic achievement. The chapter also discusses implications for policy, architecture, and research, outlines the limitations of the work, and concludes the dissertation.

2 Related work

2.1 Scope and approach

This chapter reviews scholarly research that addresses interoperability and governance as *ecosystem-scale* problems in national digital health systems. Consistent with the dissertation's analytical scope, the unit of analysis is not a single application, database, platform, or repository, but a national digital health arrangement in which shared EHR-type record and repository capabilities and DHP-type platform functions enable cross-organisational exchange, access, and, where relevant, governed multiple use.

The review is deliberately selective and narrative rather than systematic. It does not provide a general review of digital health, nor does it repeat the empirical background of Estonia as a national case. Instead, it positions the dissertation in relation to four partially overlapping streams of literature: national systems as evolving arrangements; semantics and knowledge readiness; governance of secondary and multiple use; and conceptual integration across architecture, platforms, capability and infrastructure scholarship. The purpose is to clarify what these streams explain, what remains insufficiently coupled, and why an integrated analytical framework is needed to examine how access and exchange contribute to a knowledge-ready, accountable and adaptable national digital health capability.

2.2 National systems as evolving arrangements

This stream is needed to position national digital health systems as long-running socio-technical programmes rather than as bounded technical deployments. It explains how rollout, installed bases, shared services, access coverage, coordination mechanisms and implementation outcomes shape national exchange-and-access capability. For the dissertation, this literature is especially important because it helps position mature access-oriented cases without treating access coverage as evidence of comprehensive digital health performance.

Recent synthesis work treats national digital health programmes as long-running socio-technical transformations rather than bounded information technology (IT) deployments. In a scoping review of 86 articles published between 2000 and 2020, Scheibner et al. synthesise evidence across national and regional programmes and describe how "national" infrastructures combine shared components (identity, exchange services, registries, access control and audit) with heterogeneous local systems and workflows, producing persistent coordination work even where coverage is high [29].

Related work also frames interoperability as a multi-dimensional coordination capability rather than a singular technical property. In their systematic review of 36 full-text articles on heterogeneous health information systems, Torab-Miandoab et al. emphasise that interface-level connectivity and syntactic agreement do not resolve higher-order interoperability needs (e.g., longitudinal coordination, decision support, cross-context reuse), and therefore motivate attention to organisational alignment and semantic constraints [30].

Complementary empirical and conceptual work makes the "evolving arrangement" view more concrete by analysing coordination mechanisms during infrastructure formation and evolution. Elizondo Solano's doctoral thesis examines early orchestration of a large-scale regional interoperability infrastructure in the National Health Service (NHS) in England and develops the notion of orchestration spaces to describe how coordination work is organised across institutions [31]. A related national-programme perspective on the United Kingdom's NHS is provided by Currie and Guah, who analyse the National Programme for IT and interpret its trajectory through competing institutional logics and field-level governance tensions [32].

Stegemann's doctoral thesis analyses interoperability management in digital health platform ecosystems and provides a vocabulary for discussing how interoperability depends on ecosystem governance, boundary resources, and the wider actor configuration, not only on standards selection

[33]. In Norway, Linstad et al. analyse the development of an "inclusive" national digital health governance model (2012-2022), offering a longitudinal governance account of how national-scale coordination is negotiated and stabilised over time [34].

Implementation-oriented synthesis work highlights that ecosystem characteristics often become visible through observed implementation outcomes rather than through architectural descriptions alone. In a scoping review of 37 studies (2010-2023), Lum et al. examine how implementation outcomes are reported for health information exchange solutions and related interoperability technologies, showing why national-scale interoperability remains difficult to implement and evaluate consistently [35]. Li et al. complement this evidence base by synthesising 12 studies on how electronic health record interoperability affects patient safety and other quality dimensions in high-income settings, reporting heterogeneous evidence and mixed effects across outcome categories [36].

Taken together, these works motivate treating national digital health systems as evolving sociotechnical arrangements shaped by the co-development of shared services, heterogeneous installed bases, institutional mandates, and governance capacity [29, 33]. They also show that technical "maturity" is compatible with persistent coordination work, supporting an analytical focus on how change is governed and operationalised over time [35].

The remaining gap is that this literature explains infrastructural consolidation, standardised exchange, rollout and implementation difficulty better than it explains why these achievements do not automatically accumulate into semantic continuity, knowledge readiness, multiple use or person-centred integration. For this dissertation, exchange and access are therefore positioned as necessary infrastructural capabilities that are insufficient on their own; their higher-order effects depend on coupling with meaning, knowledge use, responsibility and governed change.

2.3 Semantics and knowledge readiness

This stream is needed because data availability does not equal knowledge readiness. Semantic interoperability literature explains how terminologies, standards, information models, ontologies, conceptual models and clinical data quality make data interpretable across organisations and use contexts. Computable knowledge and decision-support literature extend this question further by asking whether structured data can support rule-based, algorithmic or personalised knowledge use in practice.

A stable theme in recent synthesis work is that syntactic interoperability enables scalable transport and structural agreement, but does not by itself yield decision-relevant interoperability for advanced reuse. In a systematic review of 14 studies, Palojoki et al. review semantic interoperability research and report that reuse for analytics and clinical decision support depends on complementary semantic assets (terminologies, clinical information models, ontologies) and on governance processes that stabilise meaning across contexts and over time [37]. For this dissertation, this makes decision support a practical test of whether semantic interoperability has reached the level of knowledge readiness.

Alongside terminology- and model-centric semantic work, some platform-relevant studies explicitly mobilise International Organization for Standardization (ISO) 13940, System of Concepts to Support Continuity of Care (ContSys) as a cross-domain concept system for continuity of care, using it to structure meaning across health and social care settings. Pecoraro et al. apply ContSys to build a shared conceptual model harmonised with social care and assistive domotics concepts in the design of an interoperable open platform (Health@Home) [38]. RossiMori develops an extension of ContSys to support continuity of care across health and social care contexts, illustrating how a continuity-of-care concept system can be adapted to cross-sector coordination needs [39]. Das and Hussey provide a complementary semantic-interoperability pathway by formalising ContSys concepts in an ontology based on Fast Healthcare Interoperability Resources (FHIR), a standard

developed by Health Level Seven International (HL7), as a way to support continuity-of-care data interoperability across stakeholders [40].

Related work also provides concrete illustrations of how semantic and technical gaps surface in mature exchange-and-access arrangements. Van Laere et al. analyse discrepancies between electronic prescriptions and dispensing in Belgium several years after e-prescribing rollout, using a mixed-method approach to make end-to-end consistency problems observable across production and use settings [41]. While domain-specific, this study is useful as related work because it demonstrates how exchange-and-access capability can be constrained by alignment problems that sit between local workflow, semantics, and downstream use contexts.

Patient-facing access studies provide a complementary view by making the practical value of national exchange-and-access mechanisms visible at scale. Kujala et al. benchmark usability of national patient portals that provide access to EHR data in Estonia, Finland, Norway, and Sweden and report how differences in functionality and user experience coexist with shared policy ambitions of transparency and patient involvement [42]. These findings are relevant here not because portal usability is itself semantic interoperability, but because they illustrate how exchange-and-access mechanisms can remain uneven in their practical interpretability and perceived value even in otherwise mature settings.

Taken together, this literature explains why standards, terminologies, information models, conceptual models and structured data are necessary for interpretation, decision support and advanced reuse. The remaining gap concerns the conditions under which these semantic assets become knowledge-ready: meaning, temporality, clinical intent, validation, versioning and authorised change must be governed across abstraction levels. This dissertation therefore positions meaning and knowledge readiness as governed lifecycle capabilities, not as the mere availability of standards, terminologies, structured fields or algorithms.

2.4 Governance of multiple use

This stream is needed because national digital health infrastructures are expected to support more than direct care delivery. They are increasingly expected to support multiple forms of data use across clinical, policy, funding, management, research, innovation and personal health contexts. Governance literature explains how legitimacy, accountability, decision rights, access pathways and stewardship arrangements shape whether such reuse becomes trustworthy multiple use.

Governance-focused reviews and frameworks converge on the view that secondary use is constrained less by the absence of data flows than by institutional arrangements that allocate decision rights, responsibilities, and accountability. In a scoping review of 37 documents, Ghaffari Heshajin et al. propose a health information governance framework and synthesise governance dimensions (principles, roles, and procedures) used to structure trustworthy use [43]. Wieland-Jorna et al. develop a governance framework for secondary use of routine health data and operationalise governance through concrete categories such as role separation, access procedures, and accountability mechanisms [44]. These frameworks are used here to make governance design choices explicit and comparable across contexts, without claiming that any single framework is universally sufficient.

Institutional-theory work that explicitly draws on the institutional logics perspective provides complementary, platform-relevant accounts of how governance tensions emerge and persist in large-scale health information infrastructures. Currie and Guah analyse the United Kingdom's National Programme for IT in the National Health Service and show how competing institutional logics in the organisational field shape both governance arrangements and the practical possibility of aligning programme objectives across heterogeneous actors [32]. Hansen and Baroody analyse how enterprise-scale electronic health record use in the United States mediates the interplay of multiple institutional logics (including medical professionalism, managerialism, technical design, and regulatory oversight), thereby illustrating how platform-mediated practices can yield both com-

plementarity and conflict that matter for interoperability and reuse ambitions [45]. Linstad et al. provide a complementary governance case perspective by analysing the development of an "inclusive" national digital health governance model in Norway (2012-2022), thereby making governance arrangements visible as negotiated multi-stakeholder configurations over time [34].

Participation and legitimacy are recurrent governance concerns in both primary exchange-and-access and secondary use settings. Keuper et al. analyse determinants of patient consent in a Dutch opt-in exchange setting, which makes participation mechanics visible as an operational variable rather than a purely legal statement [46]. Holt et al. analyse factors associated with opting out of a national EHR programme in Australia, providing empirical material on legitimacy and participation dynamics in a mature programme setting [47].

Other studies anchor governance through concrete access pathways and stewardship arrangements for secondary use. Sandhu et al. document health data governance for research use in Alberta (Canada), describing custodianship, governance mechanisms, and access processes as institutionalised pathways for reuse [48]. Such access-pathway analyses are useful for tracing where formal authorisation is translated into operational practice and where accountability is practically located.

At the international level, the emergence of the European Health Data Space (EHDS) has stimulated peer-reviewed work that connects governance requirements to interoperability instruments for secondary use. In a rapid systematic review of 67 academic sources, Donia and Marelli synthesise ethical and social dimensions discussed in relation to EHDS (European Union policy context) and highlight that trustworthy secondary use requires explicit attention to legitimacy, rights, and public value considerations [49]. Hussein et al. develop an interactive toolkit intended to guide alignment with secondary-use interoperability requirements under the European Health Data Space, drawing on lessons from multiple European cancer data projects; the work is relevant here insofar as it treats governance and interoperability standards as coupled implementation challenges [50]. Zhang et al. provide a complementary national-scale anchor by mapping and evaluating electronic patient data flows across England and discussing transparency and privacy as governance conditions for legitimate large-scale reuse and infrastructural transformation [51].

US-related scholarship provides an additional contrast case for how governance frameworks can reshape participation in exchange networks in a market-shaped ecosystem. Everson et al. report a national survey of health information organisations and their plans to participate in the Trusted Exchange Framework and Common Agreement (TEFCA), offering empirical material on how participation, incentives and compliance mechanisms interact when exchange is mediated by networks and vendor ecosystems [52].

Together, these works show that secondary and multiple use depend on more than legal permission, institutional mandate or technical access. They require stewardship, role separation, legitimacy mechanisms, accountability arrangements and operational access pathways. The remaining gap is how these governance arrangements actively produce interoperability capability across clinical, policy, funding, management, research and personal contexts. For this dissertation, governance is therefore not treated only as a compliance layer or constraint on data access, but as one of the mechanisms through which trustworthy multiple use becomes possible.

2.5 Towards conceptual integration

This final stream positions the dissertation in relation to integrative approaches that seek to connect infrastructure, semantics, governance and normative goals. It brings together work on learning health systems, platform and infrastructure evolution, conceptual interoperability, architecture-level frameworks and model-driven approaches. For this dissertation, this literature is important because it shows both the need for integration and the difficulty of explaining how different interoperability conditions are coupled across levels.

A recurring observation across the related literature is that national programmes are analysed through partial integrative perspectives - implementation frameworks, governance models, or ecosystem management vocabularies - while the linkage between technical integration, semantic standardisation, governance mechanisms, and normative goals remains uneven across studies. A prominent normative framing in digital health scholarship is the ambition of national learning health and care systems, in which shared digital infrastructure is expected to support integrated, person-centred care and continuous learning across sectors [53]. This is visible in synthesis work that reports both positive associations and persistent limitations in comparability and interpretability across contexts [29, 35].

Platform- and infrastructure-oriented work contributes integrative language by treating interoperability as an emergent property of a socio-technical system of systems. Stegemann's ecosystem perspective and Elizondo Solano's orchestration-space concept both emphasise the role of coordination mechanisms and governance practices in shaping interoperability as infrastructures evolve [31, 33].

Semantic interoperability research provides a complementary integration direction by treating reusable meaning as a governed resource that must be stabilised across contexts to support knowledge reuse and decision support [37]. This complements governance scholarship by specifying what must be governed at the semantic and knowledge level if reuse is to remain interpretable across heterogeneous contexts.

Beyond the semantic interoperability stream, a small but relevant set of studies explicitly mobilises architecture-level frameworks and model-driven development concepts to interpret large-scale interoperability. El-Yafouri and Klieb use the Levels of Conceptual Interoperability Model (LCIM) as a framing device in a scoping review of electronic health record interoperability levels and approaches, thereby providing an example of LCIM-based interpretation without relying on the original LCIM authorship [54]. In the European Health Data Space implementation context, Gyrard et al. map standards adoption across multiple large-scale health data projects and position ISO 23903 as one of the architectural reference points for aligning interoperability instruments across domains and use cases [55].

Model-driven interoperability research offers a methodological bridge between conceptual models and implementable artefacts by treating standards and representations as distinct modelling spaces that can be aligned through metamodel-level mappings and transformations. In biomedical informatics, this is visible in work on dual-model clinical standards, HL7 metamodels, MOF/QVT-style transformation infrastructure and reusable open data models [56–59]. These works are relevant here not as implementation methods to be adopted directly, but because they make visible the need to coordinate conceptual, technical and representational levels of interoperability.

Related enterprise modelling scholarship also offers conceptual modelling perspectives for complex platform and ecosystem arrangements that include health contexts. Tsai et al. review modelling approaches for digital business ecosystems and explicitly include Active Knowledge Modeling among multi-perspective modelling approaches; as an illustrative case type, they describe digital health platform ecosystems involving public organisations, multiple providers, and citizens as users [60]. España et al. make a complementary methodological argument for enterprise modelling as a research method for studying complex socio-technical arrangements, positioning such modelling approaches as suitable for generating traceable explanations across organisational and technical concerns [61].

Capability and maturity perspectives are useful because they provide language for discussing levels, dimensions and comparative states of interoperability. However, they may also imply a more cumulative and linear progression than national digital health systems actually exhibit. A system may stabilise exchange, access and standards adoption while remaining weaker in semantic continuity, knowledge readiness, accountability for multiple use or governance of change. The

dissertation therefore does not aim to propose a new maturity model, scoring instrument, reference architecture or evaluative framework. Its contribution is a framework-based explanation of how higher-order interoperability capability emerges or breaks down when exchange, meaning, knowledge use, responsibility and authorised change are not coupled.

These strands become relevant here when they connect national arrangements' technical and semantic design choices to governance mechanisms and articulated goals such as integrated care, learning and personalised medicine. The cited works provide fragments of such integration, while also indicating that these elements are often analysed in isolation and are therefore difficult to interpret as a single interoperability capability. The remaining gap is a sufficiently explicit explanation of the coupling mechanisms that make access, exchange, semantic assets, responsibilities and authorised change coherent across levels.

2.6 Positioning gap and contribution

Taken together, the reviewed literature treats national digital health infrastructures not only as technical enablers, but also as socio-technical, semantic and governance arrangements expected to support integrated, person-centred and learning-oriented health systems. Evidence syntheses nevertheless show that realised effects remain heterogeneous and context-dependent. This cautions against treating exchange coverage, portal access or infrastructure maturity as sufficient evidence of comprehensive digital health performance.

The positioning gap addressed by this dissertation is that the literature explains important parts of national digital health interoperability through partially separated perspectives: infrastructural consolidation, rollout and access; semantic assets and knowledge readiness; legitimacy, decision rights and stewardship for secondary and multiple use; and conceptual or infrastructural accounts of interoperability across levels. These streams are necessary, but they do not fully explain how access and exchange become - or fail to become - a knowledge-ready, accountable and adaptable national digital health capability. The dissertation's positioning in relation to these streams is summarised in Table 1.

Table 1: Contribution of the dissertation in relation to the reviewed literature.

Literature stream	What the literature helps explain	What this dissertation adds or refines
National digital health infrastructures, rollout and access	How national digital health infrastructures are implemented, scaled and used to support exchange, access and service integration.	It interprets mature exchange and access infrastructure as a necessary but insufficient condition for higher-order interoperability, showing why national-scale operation may still leave semantic continuity, decision relevance and governed reuse fragile.
Semantic interoperability, standards and knowledge readiness	How terminologies, information models, standards and semantic resources support more consistent interpretation and reuse of health data.	It connects semantic formalisation to knowledge readiness by examining whether data, concepts, rules and decision logic are sufficiently aligned for computable reasoning and reusable knowledge artefacts.

Literature stream	What the literature helps explain	What this dissertation adds or refines
Governance, legitimacy and secondary use	How stewardship, decision rights, legal arrangements and institutional responsibilities shape access to and reuse of health data.	It extends the governance question from data access and reuse permissions to the coordinated governance of meaning, responsibility, change control and accountability across the data supply chain.
Conceptual and infrastructural accounts of interoperability	How interoperability can be described across technical, semantic, organisational and conceptual levels.	It treats interoperability not as a cumulative maturity trajectory, but as a governed coordination capability that depends on explicit coupling across institutional domains, abstraction levels, modelling spaces and governance arrangements.

As shown in Table 1, the dissertation does not position itself by adding another separate infrastructure, standards, governance or maturity perspective. Instead, it uses these streams as necessary but incomplete foundations for the integrated theoretical framework developed in the next chapter.

3 Theoretical framework

This chapter develops the integrated theoretical framework of this dissertation for analysing interoperability and governance in national digital health systems. Rather than adopting a single existing model, it brings together institutional theory, model-driven thinking, and architectural coordination perspectives into a common analytical approach. The resulting framework provides the conceptual basis for the dissertation's empirical analysis and is later operationalised through seven analytical attributes.

The central premise is that national digital health systems do not operate under a single coherent rationality. Rather, they emerge at the intersection of multiple institutional domains, each governed by its own normative, epistemic, and operational logic [62–64]. An integrated theoretical framework is therefore required because interoperability in such systems is shaped not only by technical connectivity, but also by the alignment - or misalignment - of institutional, semantic, organisational, and technological arrangements.

From this perspective, models, architectures, and interoperability standards are not neutral representations of reality. They are purposive coordination instruments that both reflect and shape institutional rationalities, decision-making practices, and power relations [65–67].

Consequently, interoperability is approached in this dissertation not as a static property of systems, but as an emergent coordination capability. It arises from the ability of actors to align, interpret, and operationalise shared models and standards across institutional, organisational, semantic, and technological boundaries. This stance provides the theoretical rationale for combining institutional analysis with model-driven and architectural frameworks in the study of digital health governance and transformation.

3.1 A cross-level macro-meso-micro perspective for digital health systems

As an orienting analytical frame, the dissertation adopts the widely used macro-meso-micro (MMM) perspective from integrated care and health systems research. Originating in public health, organisational studies, and integrated care theory, this perspective distinguishes between population-level structures and governance (macro), organisational and inter-organisational coordination (meso), and individual clinical interaction and decision-making (micro) [68–71]. In these traditions, macro structures enable system-wide direction-setting, meso arrangements coordinate actors and workflows, and micro practices deliver human-centred care. A similar cross-level vocabulary is also visible in national digital health strategy and impact analyses, including the DIGIMPACT study (2008-2010) [11] and the Estonian eHealth Strategy 2025-2030 [18].

In this dissertation, the macro-meso-micro model is introduced as an orienting analytical perspective to clarify how digital health operates across system levels. Digital health is not treated as a separate layer of the health system, but as a transversal enabler whose functions manifest differently at each level: at the macro level, it supports population-level analytics, surveillance, standardisation, and policy steering; at the meso level, it enables organisational and inter-organisational data flows, workflow integration, and data stewardship; and at the micro level, it enhances clinical decision support, data-driven personalisation, and real-time data capture in care delivery. This cross-level perspective allows digital health capabilities to be analysed in relation to governance, coordination, and practice without reifying levels as architectural components. Figure 3 illustrates how digital health functions as a transversal enabler across macro, meso, and micro levels rather than as a separate organisational layer or architectural component.

Throughout the theoretical framework, MMM is used as a cross-cutting analytical perspective rather than as a system decomposition. Institutional logics, modelling spaces, and architectural mechanisms are examined in terms of how they manifest and interact across macro, meso, and micro levels. Domain distinctions and architectural constructs are introduced separately through

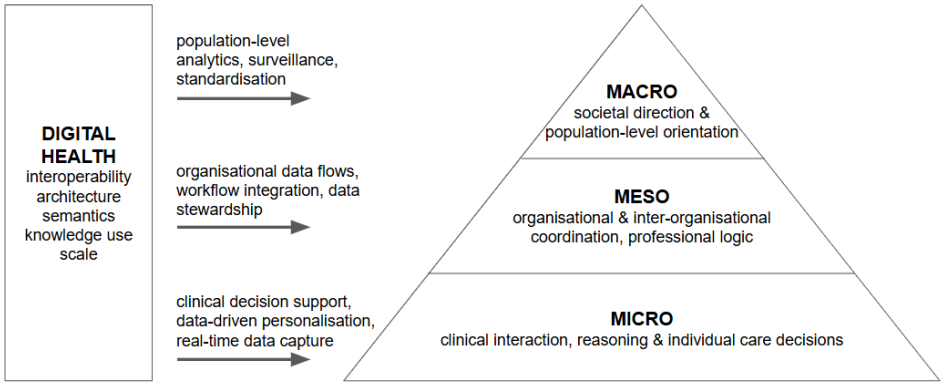

Figure 3: Digital health is depicted as a transversal enabler that connects clinical decision-making (micro), organisational coordination (meso), and population-level orientation (macro). Through interoperability, shared semantics, and computer-supported knowledge use, digital health links real-time clinical data capture and decision support with organisational data stewardship and, ultimately, with standardisation, surveillance, and population-level analytics. The figure highlights how digital health infrastructures mediate coordination across levels rather than functioning as an isolated technical layer (source: author).

the Generic Component Model (GCM) to avoid conflating organisational levels with epistemic, semantic, or institutional domains (see Section 3.3).

3.2 Modelling spaces and technological spaces

One important mechanism through which institutional logics are translated into technical systems is modelling. To make this mediation analytically explicit, the framework adopts the notions of modelling spaces and technological spaces as developed by Djurić, Bézivin, Ivanov, and colleagues [72, 73].

At the most general level, technological spaces are understood, in their original IT and model-engineering context, as relatively autonomous working contexts structured by specific bodies of knowledge, concepts, tools, languages, skills, and practices [72, 73]. In this dissertation, this notion is extended beyond software and modelling technologies to denote socio-technical knowledge-practice contexts such as clinical care, public health, research, health economics, and governance. This dissertation-specific extension is analytical: it is used to compare how different communities stabilise concepts, tools, validation criteria, and legitimate forms of action, without implying that all such communities are technological spaces in the original model-engineering sense.

Within such spaces, modelling is not an abstract or context-free activity but a situated practice. Actors employ modelling approaches, languages, and abstractions that are feasible, meaningful, and legitimate in their technological environment. Modelling spaces therefore operate within technological spaces as purpose-specific environments for formalising knowledge through explicit models. Depending on their purpose, they may be meaning-oriented or realisation-oriented and can include ontologies, conceptual models, information models, executable artefacts, mappings, and transformation specifications.

For analytical coordination between modelling spaces, the MOF-style M0-M3 abstraction logic is useful because it distinguishes between empirical or operational instances (M0), models (M1), metamodels (M2), and meta-metamodels (M3). Establishing a modelling space typically relies on metamodels that preserve meaning consistently across the models created within that space [74, 75]. When one modelling language is used, coherence can usually be maintained via its metamodel.

When multiple modelling languages or domain-specific metamodels must be related, an additional abstraction is needed to preserve meaning between metamodels. This role is fulfilled by a meta-metamodel that defines common concepts and relations enabling alignment across heterogeneous modelling languages and modelling spaces.

Such meta-level structures are not always explicitly articulated or formally documented. They may remain implicit, embodied in expert practice, shared professional habits, or long-term collaboration, corresponding to tacit knowledge that resists direct formalisation but guides competent action [76, 77]. In these cases, knowledge transfer depends heavily on specific individuals and accumulated human experience, which limits scalability and typically constrains interoperability to lower levels. From an interoperability capability perspective, the degree to which such metamodels and meta-level assumptions are made explicit, shared, and institutionally embedded is consequential for the scalability and robustness of interoperability.

Following Djurić and colleagues, relations between modelling spaces may be characterised as parallel or orthogonal. Parallel modelling spaces describe the same real-world phenomena using different formalisms and are therefore primarily related through translation and transformation. Orthogonal modelling spaces, by contrast, treat elements of another modelling space as their modelling objects, for example when conceptual models are represented, constrained, or operationalised using a different modelling language or platform. In complex socio-technical systems, both relations typically coexist: clinical or software-related modelling spaces often operate in parallel with respect to shared real-world situations, while orthogonal relations arise when one space selectively models, constrains, or operationalises abstractions originating in another space. While the use of multiple modelling approaches increases expressive power, it also significantly raises the cognitive burden on practitioners. Empirical and methodological studies note that developers working under time and resource constraints tend to focus on isolated modelling aspects rather than maintaining a comprehensive view across heterogeneous modelling approaches, making meta-level coordination an architectural rather than a purely local modelling concern [72].

In the analytically reconstructed clinical technological space, relevant knowledge can be interpreted as distributed across multiple abstraction levels, ranging from situated practice (M0) and case-specific reasoning (M1) to generalised medical knowledge and classificatory schemes (M2-M3). Software-based representations typically do not mirror this stratification in full, but operationalise selected abstractions - primarily those stabilised at the M1 level - while treating higher-level medical knowledge as external reference material and lower-level practical judgement as out of scope. This should be understood as an analytical generalisation reflecting dominant software engineering practices rather than an empirical universal; specific architectures, such as ontology-driven systems or advanced clinical decision support frameworks, may deliberately operationalise abstractions beyond M1 under additional governance and modelling constraints. Orthogonality therefore emerges not because the spaces describe different realities, but because one technological space models another through a partial, level-specific projection of its abstraction ladder.

To make this dissertation-specific analytical extension explicit, Figure 4 contrasts two illustrative technological spaces that relate to the same clinical situation through different, space-specific abstraction ladders and modelling layers.

As an explicit instance of a meta-metamodelling reference discussed above, the Meta-Object Facility (MOF), standardised in ISO/IEC 19502 and further developed in later OMG specifications, provides mechanisms for defining, relating, and transforming metamodels. In MOF 2, the M0-M3 layering is treated as a conventional organisational scheme rather than a strict requirement, with MOF functioning as a reflective kernel that supports semantic alignment and transformation across modelling environments [72, 74, 75].

The Unified Modelling Language (UML) exemplifies a MOF-grounded modelling space that provides a shared vocabulary for structure, behaviour, and information flows. In health informatics,

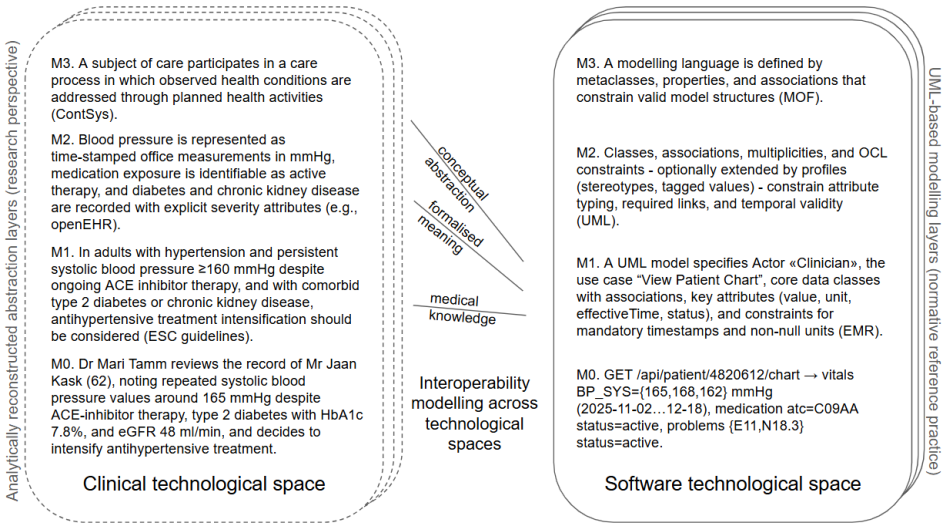

Figure 4: Analytically reconstructed modelling layers (M0-M3) in two relatively autonomous technological spaces related to the same clinical situation. The clinical space represents an analytical reconstruction of practice, medical knowledge, and formalised representations, without implying that these levels are explicitly used in everyday work. The software modelling space illustrates a normative UML/MOF-based modelling perspective. Both technological spaces are illustrative instances; in practice, multiple clinical and software spaces may coexist in parallel. The figure frames interoperability not as the existence of shared models, but as an open problem of aligning heterogeneous abstractions and formalised meanings across technological spaces. Abbreviations used in the figure: UML = Unified Modelling Language; MOF = Meta-Object Facility; M0-M3 - MOF-style modelling abstraction layers used here as an analytical reconstruction; OCL - Object Constraint Language; ESC - European Society of Cardiology; ACE - Angiotensin-Converting Enzyme; HbA1c - glycated haemoglobin; eGFR - estimated glomerular filtration rate; ATC - Anatomical Therapeutic Chemical classification; ICD-10 - International Classification of Diseases version 10 codes E11, N18 denote type 2 diabetes mellitus and chronic kidney disease, respectively (source: author).

comparable metamodel-based reasoning underpins several standards and modelling initiatives, including ISO 13940 (ContSys), HL7-related modelling work, openEHR archetypes, and the HL7 Clinical Information Modelling Initiative (HL7 CIMI) [58, 78–82].

This broader interpretation of technological spaces has a direct coordination implication. Technological spaces should be treated as operationally autonomous: participants act locally on the basis of situated knowledge, role-specific responsibilities, domain-specific validation criteria, and partial system visibility. Expecting any actor or community to maintain global awareness across all relevant technological spaces is unrealistic in complex socio-technical settings. This is consistent with research on autonomic computing, which frames autonomy as self-management under growing complexity and motivates engineering capabilities such as self-configuration, self-optimisation, self-healing, and self-protection [83, 84]. The analogy does not imply that institutional actors are equivalent to autonomic software systems; rather, it clarifies why coordination architectures must accommodate bounded self-management across heterogeneous knowledge-practice contexts. In this dissertation, autonomy therefore denotes the limited possibility of central control across such contexts, not merely organisational independence.

A concrete illustration can be found in the interaction between clinical, software, analytical, managerial, and governance spaces. Clinicians reason using pathophysiological concepts, guidelines, and experiential judgement; developers work with information models, application programming interfaces (API), and executable logic; analysts operate in statistical or machine-learning modelling spaces; managers rely on indicators, contracts, and policy instruments; and governance actors work with mandates, accountability structures, and legitimate procedures for change. Each group is fluent in only a limited subset of modelling languages and metamodels, while much coordination knowledge remains implicit. Without meta-level constructs that make these differences explicit and relatable, interoperability efforts tend to collapse into local translations and ad hoc assumptions, producing fragile integration and recurrent misunderstandings across domains.

Interoperability, therefore, depends on creating explicit bridges between technological spaces and, more specifically, between the modelling spaces through which their knowledge is formalised, without attempting to eliminate the autonomy of the participating actors. In the case of parallel modelling spaces, such bridges take the form of mappings, transformations, and mediating representations that relate alternative conceptualisations of the same underlying reality. These bridges are themselves models: they must represent the source space, the target space, and the transformation logic between them. Consequently, model exchange and translation introduce an additional orthogonal modelling space dedicated to the transformation technology itself, supported by approaches such as Model-Driven Architecture (MDA) and MOF Query/Views/Transformations (QVT) [72]. At the same time, this bridging work must respect a foundational constraint highlighted in interoperability maturity research: technical integration is necessary but not sufficient; conceptual solutions depend on a solid technical foundation, yet technical proposals alone cannot resolve conceptual problems [85].

In the specific context of this dissertation, a central question is whether such alignment can be achieved not only at technical and semantic levels, but also at the level of the business viewpoint, where institutional intent, value assumptions, and decision rationales must be made interoperable across autonomous technological spaces and institutional domains.

The following section introduces the Generic Component Model (GCM) as an architectural framework for analysing how such autonomous technological and modelling spaces can be coordinated across multiple viewpoints and system dimensions without collapsing their distinct logics.

3.3 Generic Component Model (GCM) as an architectural coordination framework

This section positions the Generic Component Model (GCM, ISO 23903) as a cross-domain architectural coordination framework for national digital health systems [86–88]. The focus is not on modelling techniques or implementation artefacts, but on GCM's capacity to structure and relate heterogeneous institutional, organisational, and technical concerns in a way that preserves their autonomy while enabling meaningful alignment.

Against the background of autonomous technological spaces and largely implicit meta-level coordination challenges discussed in the previous section, GCM is treated here as an architectural coordination space rather than a modelling method [89, 90]. It provides a stable frame for reasoning about interoperability across institutional domains while allowing domain-specific models, standards, and technologies to evolve independently. In this sense, GCM does not prescribe how systems should be modelled or implemented, but delineates the architectural conditions under which coordination between otherwise independent systems becomes possible. The analytical emphasis is on conceptual separation and alignment rather than on model transformations or platform-specific realisation paths.

Building on the notion of technological spaces introduced in the previous Section 3.2, GCM can be understood as offering a higher-level, multi-dimensional coordination space for relating distinct technological spaces. Each technological space is a bounded knowledge space, defined by its internal concepts, formalisms, tools, and practices, and constrained by the cognitive and organisational capacities of the actors operating within it (see Section 3.2). Interoperability challenges arise not only from technical incompatibilities, but from the limited ability of actors to reason across multiple such spaces simultaneously. GCM does not replace these technological spaces, but provides a structured architectural environment in which their relationships can be explored, compared, and aligned, enabling the identification of viable interoperability contact points without requiring full unification of underlying models or epistemic assumptions. This relationship between autonomous technological spaces and the GCM coordination space is illustrated in Figure 5.

The practical value of such a coordination space becomes visible when interoperability is traced across domains, technological realisations, and scale boundaries at once. For example, a cardiology referral carries clinical intent, urgency, episode context, and follow-up responsibility in one technological space, while radiology realises related work through modality-specific workflows, imaging artefacts, and PACS-centred infrastructures. As the same information is projected into hospital, national, or cross-jurisdictional exchange contexts, coordination problems rarely appear only as interface failures. They more often surface as semantic drift: request versus order, episode boundary versus billing period, local identifier versus national master identifier, or clinical intent versus administrative mandate. The Figure 5 therefore motivates GCM as a coordination space for making such cross-space projections explicit, governable, and changeable.

Within this coordination space, GCM distinguishes three orthogonal coordination dimensions: domain, component, and evolution [86, 88]. These dimensions do not represent alternative viewpoints, but complementary axes along which the same system can be analysed and aligned.

The domain dimension organises system concerns around institutional and functional domains as carriers of domain knowledge, each interpreting system structure, responsibilities, and change from its own normative, epistemic, and operational context. The component dimension addresses the same concerns through structural composition, modelling the system as interacting components and subsystems with defined responsibilities and interfaces across domains. The evolution dimension coordinates domain and component concerns over time by relating them to successive lifecycle stages and transformation phases.

Distinct viewpoints emerge within the evolution dimension, reflecting stage-specific concerns, modelling formalisms, expert roles, and decision criteria appropriate to a given phase of system evolution. These viewpoints are therefore treated as perspectives within the evolution dimension

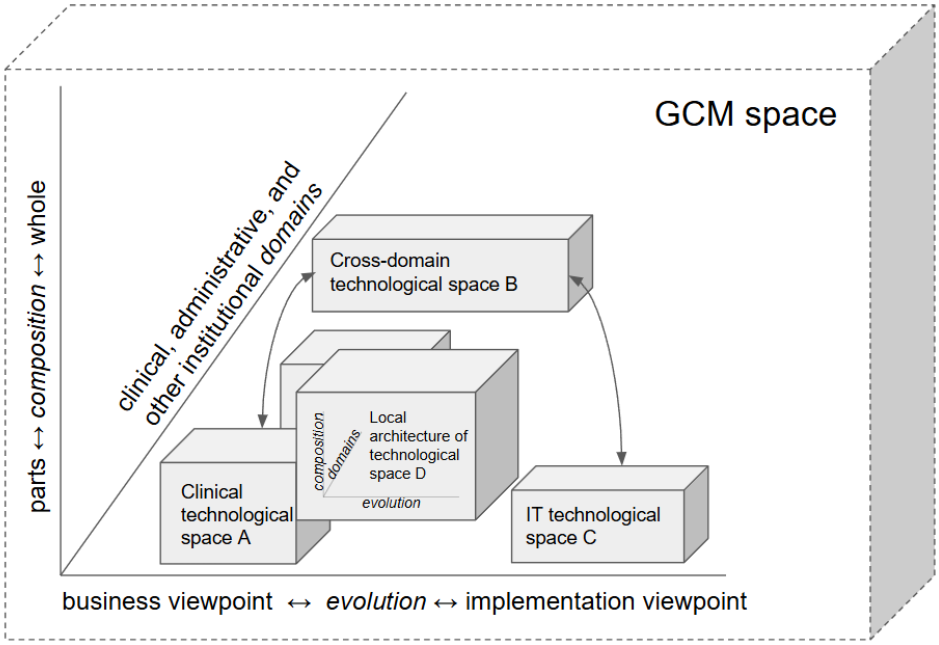

Figure 5: GCM as an architectural coordination space relating autonomous technological spaces across institutional domains, coordination dimensions, and lifecycle perspectives. The dashed boundary denotes the GCM coordination space; individual technological spaces retain autonomous local architectures while being analysed in relation to one another through domain, component, and evolution dimensions, anchored in the business or needs viewpoint (source: author).

rather than as independent dimensions of GCM.

A central anchoring role within the evolution dimension is played by the business or needs viewpoint [91, 92]. This is the locus where institutional intent, policy objectives, and legitimate purposes of data use are made explicit and rendered commensurable across domains. In national digital health systems, this viewpoint is where cross-institutional goals are articulated, constraints arising from law, ethics, and governance are formalised, and expectations regarding the depth and scope of interoperability are defined. Without such explicit formalisation at the needs level, lower-level interoperability efforts risk optimising technical alignment while reinforcing institutional fragmentation.

By providing an explicit architectural coordination space for such articulation, GCM enables alignment across institutional domains without collapsing their internal logics. Each domain retains autonomy over its internal models and processes, while GCM supplies a shared architectural language for coordination at agreed boundaries. This is particularly relevant in digital health, where clinical care, secondary data use, regulation, and innovation operate under partially incompatible institutional logics. GCM does not resolve these tensions; rather, it renders them explicit, comparable, and governable through deliberate architectural and governance decisions.

Within the broader theoretical framework of this dissertation, the macro-meso-micro perspective provides a cross-level analytical perspective for locating phenomena, while GCM functions as the architectural coordination space across these levels. The next section introduces the Levels of Conceptual Interoperability Model (LCIM) and related capability frameworks to qualify the depth of coordination that can be achieved within this space [93].

3.4 Interoperability capability across technological spaces

The purpose of this section is to elaborate interoperability capability as a means of assessing how coordination between technological spaces can be sustained in practice. Building on the preceding sections, which conceptualised technological spaces as operationally autonomous knowledge-practice contexts (Section 3.2) and positioned the Generic Component Model (GCM) as an architectural coordination space between them (Section 3.3), the focus now shifts from architectural possibility to capability: at what level, and with what depth, such coordination can actually be achieved.

Interoperability capability is used here to describe the depth at which autonomous technological spaces can sustain shared understanding and coordinated action. The issue is not only whether systems can exchange data, but whether participating actors can operate locally while still producing collectively meaningful and governable outcomes. This connects the technological-spaces argument to interoperability maturity research, where higher capability levels presuppose increasing semantic, pragmatic, and conceptual alignment rather than technical connectivity alone [84, 85, 93].

Interoperability capability is commonly articulated through staged maturity or capability models. The Levels of Conceptual Interoperability Model (LCIM) traces progression from technical connectivity toward semantic and conceptual interoperability, where actors achieve shared interpretation and coordinated action [93]. Interoperability Maturity Models (IMM) generalise this progression across organisational and technological contexts by framing interoperability as an evolving capability characterised by governance alignment and increasing decision autonomy [85]. Knowledge-based interoperability (KBI) further operationalises higher capability levels by modelling systems as autonomous decision centres supported by mediating middleware that encapsulates domain knowledge and enables coordination without relinquishing local control [84]. A closely aligned perspective appears in supply-chain interoperability research, where Supply Chain Interoperability (SCI) conceptualises interoperability as the capability of independently governed organisations to synchronise decisions and operations through shared information models and governance arrangements rather than centralised orchestration [94].

As discussed earlier (Section 3.2), interoperability capability increases when semantic and con-

ceptual structures are made explicit, shared, and institutionalised rather than remaining implicit or embedded in isolated implementations. Across LCIM, IMM, KBI, and SCI, a common requirement emerges: higher interoperability capability presupposes the explicit articulation of system needs, constraints, decision logics, and legitimate purposes as shared coordination artefacts. This convergence provides a direct rationale for the Generic Component Model's business or needs viewpoint (Section 3.3), because that viewpoint is where institutional intent and policy objectives must be made explicit before they can be consistently translated into semantic, organisational, and technical arrangements.

Table 2: Synthesis of interoperability capability levels across LCIM, IMM, and SCI (with KBI as an enabling cross-cutting concept; author's synthesis)

Capability zone	Interoperability focus	Reference (LCIM, IMM, SCI)	Typical characteristics
Concrete	Connectivity and message exchange	LCIM: Level 0-1 (No / Technical interoperability) IMM: Stand-alone, disjoint operations capability SCI: Communication level	Physical connectivity, point-to-point interfaces, one-time or ad hoc data exchange; no shared structure or intent
Concrete-structural	Shared structure and syntax	LCIM: Level 2 (Syntactic interoperability) IMM: De-conflicted operations capability SCI: Communication / early coordination level	Agreed message formats and data structures; reliable transmission of outcome data without shared interpretability; limited process awareness
Intermediate (semantic)	Shared meaning	LCIM: Level 3 (Semantic interoperability) IMM: Coordinated operations capability SCI: Coordination / early collaboration level	Common terminology and semantic coding; sustained information flows; consistent interpretation of exchanged data
Abstract-pragmatic	Shared intent and coordinated action	LCIM: Level 4-5 (Pragmatic, Dynamic interoperability) IMM: Collaborative / integrated operations capability SCI: Collaboration level	Exchange of state information; alignment of processes and timing; actors adapt actions based on others' behaviour
Abstract-conceptual	Shared conceptual models and purposes	LCIM: Level 6 (Conceptual interoperability) IMM: Coherent / transformed operations capability SCI: Cooperation / partnership level	Shared goals, decision logic, and conceptual frameworks; composable activities; high autonomy with collective coherence

The table (Table 2) should be read as an analytical synthesis rather than as a deterministic maturity path. Although LCIM, IMM, SCI, and KBI originate in different domains - military command and

control, systems interoperability theory, logistics and supply-chain management, and knowledge-based systems - they converge on the same structural insight: interoperability capability deepens as coordination moves from connectivity and syntax toward shared semantics, shared intent, and eventually shared conceptual models. This does not mean that higher-order interoperability accumulates automatically from lower levels. Rather, technical exchange is a necessary but insufficient condition for integrated digital health ecosystems; semantic and conceptual alignment must be explicitly governed if autonomous actors are expected to act coherently across institutional and technological boundaries [84, 85, 94].

This synthesis positions LCIM, IMM, SCI, and KBI as complementary analytical frameworks for assessing interoperability capability across technological spaces. Together, they provide a structured way to reason about how concrete technical interoperability, semantic mediation, pragmatic coordination, and abstract conceptual alignment jointly shape the achievable forms of coordination in complex, multi-institutional digital health systems.

While the present section has treated interoperability capability at an abstract, cross-domain level, it also establishes the criteria for analysing where such capability can realistically be scaled. In practice, interoperability does not evolve uniformly across all parts of a digital health ecosystem. Rather, it emerges within and between specific technological spaces - such as clinical care delivery, public health and population-level monitoring, health financing and administration, research infrastructures, and supporting IT ecosystems - each shaped by distinct institutional logics, evidentiary standards, and modes of knowledge validation. The following section therefore shifts the analytical focus from capability levels to scalability mechanisms, examining how interoperability can be expanded across these concrete technological spaces through shared or connected knowledge spaces, and under what institutional and modelling conditions such scaling remains coherent rather than producing only superficial or false interoperability.

3.5 Scaling interoperability through knowledge spaces

The preceding section examined interoperability capability in terms of the depth of shared understanding and coordinated action. This section turns to scalability: the conditions under which such capability can be preserved as participation, institutional diversity, and system dynamics increase. Interoperability does not scale simply by adding interfaces or adopting shared messaging formats. It scales only insofar as domain concepts, rules, constraints, and purposes are formalised sufficiently to travel across technological spaces without losing their institutional meaning or operational validity.

From this perspective, difficulties in achieving interoperability across technological spaces can be understood as a scalability problem rooted in abstraction and conceptual alignment. As participation expands, concepts, evidentiary standards, and organisational arrangements that are coherent within one space become increasingly difficult to transfer into another without distortion, unless they are supported by sufficiently expressive and shared conceptual models. Prior research has shown that the use of identical data or information models may result in false interoperability, where exchange is technically feasible but semantic intent and usage rules diverge [85, 88, 92]. General-purpose standards, such as Health Level Seven Fast Healthcare Interoperability Resources (HL7 FHIR) or the Observational Medical Outcomes Partnership (OMOP) Common Data Model (OMOP CDM), may therefore conceal rather than resolve underlying tensions when applied without explicit ontological alignment [88]. Comparable limitations have been observed in terminology harmonisation efforts in healthcare: terminologies yield stable benefits only when terms denote compatible concepts for the participating communities within their respective technological spaces [85, 95].

These observations motivate a distinction between two complementary classes of mechanisms that support interoperability at scale. The first concerns the coordination of meaning across institu-

tions and domains by providing shared conceptual structures. ISO 13940 (ContSys) exemplifies this role by offering a structured system of healthcare concepts and process relations oriented toward continuity of care, thereby supporting both vertical, or shared-care, and horizontal, or seamless-care, integration [78, 95]. In this dissertation, ContSys is treated as a meta-level conceptual reference rather than as a concrete system architecture. It provides a semantic orientation against which domain models, terminologies, and workflows from different technological spaces can be aligned [88, 92].

A shared conceptual bridge alone, however, is insufficient in ecosystems characterised by continuous change. Change affects not only interfaces, but also encoded knowledge, rules, constraints, and causal dependencies. A second class of mechanisms therefore concerns the controlled transfer and preservation of knowledge across system lifecycles and architectural layers. Model-Driven Architecture (MDA), standardised by the Object Management Group, provides a structuring principle for this purpose by distinguishing between a Computation Independent Model (CIM), capturing domain intent and causal assumptions; a Platform Independent Model (PIM), formalising this intent without commitment to specific technologies; and one or more Platform Specific Models (PSM), which bind the PIM to concrete implementation platforms [88, 96]. From this perspective, interoperability capability increases when modelling links domain intent expressed at the CIM level to its realisation at PIM and PSM levels while preserving semantic coherence across layers [84].

Knowledge-based interoperability further implies that domain experts must be able to manage and evolve knowledge as part of institutional practice, rather than relegating modelling to episodic activities performed exclusively by specialised analysts. Active Knowledge Modelling (AKM) conceptualises modelling as gradual elicitation and refinement of knowledge during everyday sense-making and operational work, enabling practitioners to manipulate and apply knowledge models as part of their routine activities [97]. Taken together, MDA and AKM articulate complementary mechanisms for scaling interoperability: MDA stabilises knowledge transfer across architectural layers, while AKM supports the continuous evolution of knowledge within institutional practice. As participation expands, ecosystem coherence increasingly depends on whether domain knowledge can be updated, governed, and propagated into operational artefacts without excessive latency or reliance on scarce programming resources.

Interoperability can therefore be scaled across heterogeneous technological and institutional spaces only if shared meaning and domain intent are made explicit and supported by mechanisms that preserve and evolve this knowledge over time. The frameworks discussed above - including conceptual references such as ISO 13940 (ContSys), architectural layering through MDA, and practice-oriented knowledge evolution through AKM - are best understood not as alternative solutions, but as complementary responses to different aspects of the same scaling problem. They explain why interoperability based only on interfaces, message formats, or static standards becomes increasingly fragile as participation and institutional diversity grow.

Figure 6 synthesises this argument by situating interoperability scalability within an analytical space defined by institutional scope and the depth of knowledge formalisation.

At this point, modelling methodology becomes part of interoperability scalability rather than a purely technical implementation concern. External modelling paradigms, which represent domains as black boxes with well-defined inputs and outputs, are useful for structuring development work but tend to under-represent domain causality and deep knowledge. In dynamic domains, this limits adjustability because cascading effects of domain change remain invisible at the level of externally specified interfaces and workflows [84]. Internal modelling approaches, by contrast, explicitly represent causal dependencies within the domain and are therefore better suited to assessing how changes in policy, knowledge, rules, or organisational responsibilities affect operational systems.

This argument is reinforced by the internal model principle from control theory and the good regulator theorem, according to which an effective regulator must embody a model of the system

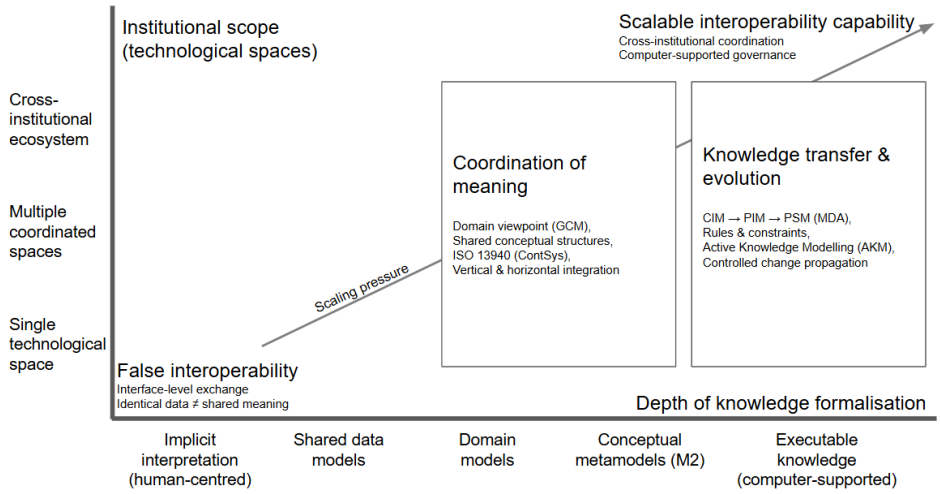

Figure 6: Scaling interoperability through explicit knowledge formalisation. The figure situates interoperability scalability within an analytical space defined by increasing institutional scope and depth of knowledge formalisation. It highlights how coordination across heterogeneous technological spaces becomes progressively constrained when relying on implicit, human-centred interpretation alone, and why additional mechanisms are required as institutional participation expands. Two complementary classes of mechanisms are distinguished: coordination of meaning through shared conceptual structures and metamodels (e.g. GCM and ISO 13940), and the preservation and evolution of domain intent across system lifecycles and architectural layers (e.g. MDA and AKM). The figure is analytical rather than prescriptive and does not represent a maturity model. Abbreviations used in the figure: GCM - Generic Component Model; ISO 13940 - System of concepts to support continuity of care (ContSys); MDA - Model-Driven Architecture; AKM - Active Knowledge Modelling; CIM - Computation-Independent Model; PIM - Platform-Independent Model; PSM - Platform-Specific Model; M2 - metamodel level in the MOF-style abstraction logic used in this dissertation (source: author).

it regulates [98–100]. When cross-institutional interoperability is interpreted as a coordination and change-management problem, the internal model becomes an analytical construct for scaling interoperability capability: it enables systematic assessment of change impacts beyond what is visible through external interfaces alone [84]. Research on model-driven process execution similarly shows why static redeployment cycles become limiting under institutional diversity and frequent change, while model-interpreting environments can reduce the latency between institutional change and system response [101–103].

The theoretical perspectives reviewed in this section converge on a bounded analytical proposition: interoperability scalability is increasingly associated with a shift from predominantly implicit, human-centred coordination toward more explicit and computer-supported forms of knowledge management [84, 85, 92]. This is not advanced as a prescriptive or evaluative claim. Rather, it provides a way to organise theoretical arguments concerning abstraction, modelling depth, and coordination mechanisms in large-scale digital health ecosystems.

To clarify the internal structure of this argument, Table 3 summarises a set of theory-informed analytical dimensions recurring across the reviewed literature. These dimensions are introduced as conceptual reference points for examining how explicitly domain knowledge, rules, constraints, and institutional obligations are represented and managed in digital health solutions, as opposed to treating interoperability as a purely interface-level or syntactic concern.

Table 3: Theory-informed indicators for examining knowledge-based interoperability scalability (author's synthesis)

Dimension	Theoretical basis	What is examined	Indicative states
Knowledge formalisation	Knowledge-based interoperability; internal modelling [84]	Explicit representation of domain concepts, rules, and constraints	Absent / partial / systematic
Conceptual alignment	Ontological interoperability; domain models [92, 95]	Use of shared domain or conceptual references, such as ContSys	None / implicit / explicit
Model layering	Model-Driven Architecture [96]	Separation of conceptual, logical, and technical layers, such as CIM-PIM-PSM	Collapsed / partial / explicit
Knowledge governance	Knowledge lifecycle; institutional coordination [104]	Roles, decision rights, and change control for knowledge models	Informal / ad hoc / formalised
Computational support	Executable knowledge; knowledge-based interoperability [84]	Degree of computer-supported reasoning or execution	Human-only / rule-based / adaptive
Change propagation	Internal model principle; adaptive systems [98, 99]	Propagation of domain and policy changes into operational systems	Manual / semi-automated / automated

Dimension	Theoretical basis	What is examined	Indicative states
Institutional embedding	Institutional logics [63]	Reflection of legal, professional, organisational, and accountability obligations	Implicit / partial / explicit

Taken together, these perspectives contribute a distinct theoretical component to the dissertation's integrated framework for reasoning about interoperability as a coordination problem shaped by abstraction, knowledge formalisation, and institutional conditions. They articulate how modelling approaches, conceptual references, lifecycle mechanisms, and governance arrangements relate within a coherent analytical space, without presupposing specific empirical methods or evaluation strategies.

This framing also foregrounds the role of institutional logics in conditioning interoperability outcomes. Different institutional arrangements privilege different forms of evidence, accountability, decision authority, and temporal coordination. These differences shape how domain models, standards, and modelling practices are adopted, constrained, or resisted. The feasibility and form of knowledge formalisation and computer-supported interoperability therefore do not arise in a vacuum; they depend on institutional expectations concerning legitimacy, accountability, decision authority, and acceptable forms of evidence. This necessitates a more explicit analytical treatment of institutional logics and their role in delineating domains for interoperability analysis.

3.6 From institutional logics to analytical domains

This concluding part specifies how the dissertation delineates analytical domains in national digital health. The purpose is not to describe all empirically observable organisations, infrastructures, or knowledge communities, but to define a limited set of theoretically justified domains through which interoperability and governance can be analysed. The distinction is important: analytical domains are grounded in institutional logics, whereas empirically observable technological and knowledge spaces reflect historically evolved practices, mandates, infrastructures, and modelling arrangements.

As established in the preceding sections, technological spaces are socio-technical knowledge-practice contexts, while modelling spaces are the more specific environments in which knowledge is formalised through models, metamodels, mappings, and transformation logic (Section 3.2, Section 3.4). Analytical domains are different. They are not derived directly from current data flows, organisational charts, system components, or technical architectures. Rather, they identify distinct sources of legitimacy, authority, accountability, and decision rationality that shape what interoperability is expected to achieve and how it can be governed.

This distinction also explains why bottom-up empirical mappings are useful but insufficient for domain delineation. Existing governance arrangements, legal mandates, organisational responsibilities, and technical infrastructures reveal how digital health has historically been assembled; for example, the map of data flows and governing bodies in Estonian digital health provides such contextual orientation (Appendix 1). However, such mappings cannot by themselves define the analytical domains of the framework. Contemporary infrastructures often encode historical compromise, implementation path-dependence, and suboptimal responses to future-oriented needs. Treating these arrangements as the primary basis for domain definition would risk reifying legacy constraints as conceptual necessities rather than making them objects of analysis.

The framework therefore adopts a reflexive approach. Institutional logics provide the theoretical basis for domain delineation, while the business or needs viewpoint of the Generic Component

Model (GCM) provides an architectural location at which institutional purposes, constraints, and interoperability expectations can be explicitly articulated [63, 64]. Standards, information models, and modelling frameworks then introduce secondary representational constraints: they shape what can be formally expressed, exchanged, computed, and governed across heterogeneous implementations. These representational constraints do not replace institutional domains, but mediate how clinical, administrative, public health, and research intents can be operationalised in interoperable systems (Section 3.3, Section 3.5).

Institutional logics are carried, reproduced, and contested by concrete institutions. Ministries and regulatory authorities stabilise public health and policy logics through legislation, reporting obligations, and strategic programmes. Health insurance funds and administrative agencies enact economic and managerial logics through reimbursement rules, contracts, and performance indicators. Professional bodies, healthcare providers, and clinical communities carry clinical-professional logics through standards of practice, ethical codes, and everyday decision-making. Universities, research institutes, registries, and biobanks institutionalise scientific and learning logics through methodological norms, ethics review, and data access governance. National digital health infrastructures operate at the intersection of these institutions and their logics; architectural choices therefore inevitably privilege some rationalities while constraining others.

Viewed through the macro-meso-micro perspective, institutional logics are predominantly stabilised at the meso level through governance arrangements, organisational coordination, and infrastructure, while macro-level visions and micro-level practices interact with these arrangements through policy direction, professional practice, and feedback from outcomes (Section 3.1). This does not mean that logics belong only to the meso level. Rather, the meso level is where institutional rationalities are most visibly translated into mandates, roles, rules, standards, and operational infrastructures.

At this point, the framework makes a further analytical distinction. Digital health is not treated as an additional institutional domain, nor as a functional layer alongside clinical care, administration, public health, or research. Instead, it is treated as a reflexive meta-level relative to institutional reality: a means through which institutional knowledge is formalised, aligned, and rendered actionable in interoperable systems. This meta-level can be differentiated according to whether digital artefacts and frameworks realise institutional knowledge in computable form, structure and align knowledge across domains, or define the paradigmatic and normative conditions under which such realisation and alignment are considered legitimate.

Table 4: Analytical levels of digital health coordination (M0-M3) (author's synthesis).

Level	Analytical role	Typical outcome	Typical coordinating competence
M3 - Paradigmatic coordination	Defines how digital health and interoperability are conceptualised and legitimised	Paradigms, grammars, assessment frameworks	Research, policy, and architecture coordination
M2 - Modelling and alignment	Structures and aligns heterogeneous knowledge spaces and viewpoints	Metamodels, viewpoints, transformation logics	System and enterprise architecture

Level	Analytical role	Typical outcome	Typical coordinating competence
M1 - Formalised digital knowledge	Realises institutional knowledge in computable and operational form	Models, rules, profiles, documents	Domain expertise, analysis, and development
M0 - Institutional reality	Actual policy, governance, clinical practice, and organisational action	Decisions, practices, outcomes	Institutions and professional communities

The Table 4 is used strictly as an analytical device. It adapts meta-modelling and architectural coordination logic to distinguish institutional reality from the formalisation, alignment, and paradigmatic framing of institutional knowledge in digital health. It is not a maturity model, evaluative hierarchy, or claim that all digital health artefacts can be neatly assigned to one level. Its purpose is to clarify the levels at which interoperability and governance problems may arise: in practice and outcomes (M0), in formalised digital knowledge (M1), in modelling and alignment mechanisms (M2), or in the paradigms and legitimacy assumptions that define what counts as appropriate coordination (M3).

The domain structure developed in this dissertation is therefore grounded in institutional logics rather than in functional decomposition or system architecture. Institutional logics theory posits that complex societal systems are constituted by multiple, coexisting rationalities that define legitimate actors, goals, decision criteria, and forms of accountability [62–64]. This interpretation aligns with Glouberman and Mintzberg's characterisation of healthcare as an inherently pluralistic system, in which clinical practice, managerial coordination, public policy, and knowledge production follow different organising principles that cannot be hierarchically subsumed without loss of meaning or effectiveness [105, 106].

On this basis, the framework identifies four analytically salient domains. These domains are not exhaustive taxonomies, organisational layers, or system components. They are theoretically grounded perspectives on the principal institutional rationalities that must be coordinated in national digital health systems:

- **Public health and policy domain** - oriented toward population-level stewardship, accountability, and policy steering, with legitimacy derived from public authority and collective value creation [63, 107].
- **Economic and administrative domain** - structuring financing, reimbursement, resource allocation, and organisational coordination, with legitimacy derived from contracts, budgets, purchasing arrangements, and performance indicators rather than clinical judgement alone [108–111].
- **Clinical-professional and empowerment domain** - governing individual care decisions, professional responsibility, and patient participation, grounded in specialised expertise, ethical accountability, trust, and shared decision-making [112–114].
- **Scientific research and learning domain** - organising the secondary use of health data for knowledge generation, validation, and system learning under conditions of methodological abstraction, uncertainty, and ethical governance [115–117].

Figure 7 summarises how institutional logics, analytical domains, and macro-meso-micro perspectives relate within the proposed framework. The figure should be read from right to left. The macro-meso-micro pyramid represents institutional reality at M0, while the digital health levels on the left represent a reflexive meta-level through which institutional intents are formalised at

M1, aligned at M2, and conceptually framed at M3. Digital health is therefore not depicted as an additional organisational domain, but as a coordination mechanism through which institutional knowledge is translated into interoperable technological realisation.

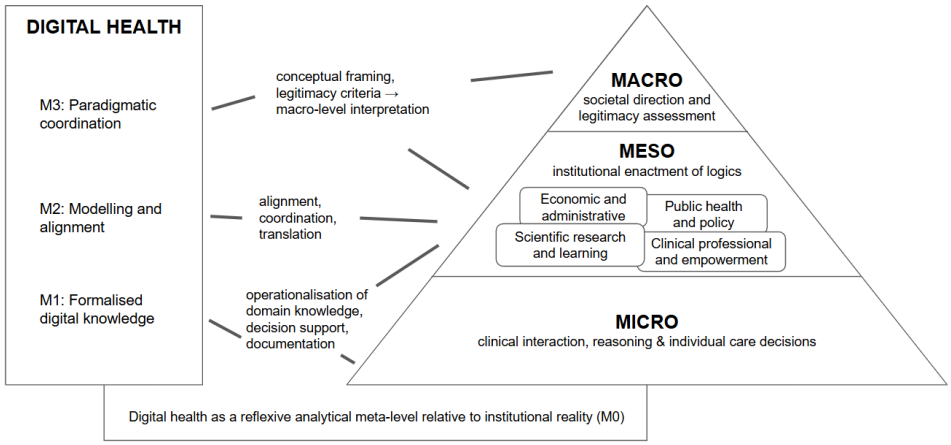

Figure 7: The figure illustrates how national digital health operates as a reflexive analytical meta-level that coordinates institutional reality across macro, meso, and micro levels. The pyramid on the right represents the health system structure: micro-level clinical interaction and individual care decisions; meso-level institutional enactment of multiple, partly overlapping logics, including clinical, public health, administrative-economic, and scientific logics; and macro-level societal direction and legitimacy assessment. The left-hand column depicts digital health across abstraction levels M1-M3, from formalised digital knowledge and decision support, through modelling and alignment mechanisms, to paradigmatic coordination and legitimacy framing. The connecting elements indicate how digital health mediates alignment, translation, and interpretation across institutional levels rather than merely implementing existing arrangements (source: author).

The Figure 7 clarifies the final position of the theoretical framework. Institutional logics give rise to analytical domains that cut across macro, meso, and micro levels. These domains are stabilised most visibly at the meso level through governance, coordination, and infrastructure, while macro-level visions and micro-level outcomes provide direction and feedback. Digital health operates as a reflexive meta-level: formalised digital knowledge (M1), modelling and alignment mechanisms (M2), and paradigmatic coordination principles (M3) shape how institutional intents are translated into interoperable technological realisation.

The four domains therefore stabilise the conceptual scope of the framework without claiming empirical exclusivity. Their empirical operationalisation and comparative use are developed in the analytical attributes and applied in the publication-cluster analysis that follows.

3.7 Bridging theory, analytical attributes and research questions

The preceding sections have developed the theoretical framework for analysing interoperability and governance in national digital health systems. The framework combines institutional logics, macro-meso-micro reasoning, modelling and technological spaces, GCM-based architectural coordination, interoperability capability, knowledge-based interoperability, and governance of change into one conceptual basis for the dissertation.

The central position is that national digital health interoperability is a governed coordination capability. It depends on whether technical exchange, semantic meaning, institutional responsibility, knowledge representation, and authorised change are sufficiently coupled across heterogeneous domains and levels. Technical connectivity and standards adoption are therefore necessary but

insufficient conditions for knowledge-ready, accountable, and adaptive national digital health.

The normative horizon of this framework is informed by predictive, preventive, personalised, participatory, and psycho-cognitive (5P) medicine. In this dissertation, 5P medicine does not function as a separate analytical attribute, maturity scale, or evaluation criterion. It clarifies why higher-order interoperability matters: advanced forms of care require digital health systems that can support knowledge-intensive, trust-sensitive, and learning-oriented coordination [118–122].

The theoretical novelty of the framework follows from the positioning gap identified in Section 2.6. Existing research offers important but partly separate accounts of digital health architectures, semantic standards, platforms, institutional governance, and knowledge reuse. This dissertation brings these strands together to explain why national systems may achieve broad exchange and access while still struggling with decision relevance, knowledge readiness, trustworthy reuse, and adaptive governance. The contribution is therefore an integrated explanatory framework, not an additional maturity model or reference architecture.

To make this theoretical position usable across the dissertation, the framework is expressed through seven analytical attributes. These attributes are not independent variables, indicators, or maturity stages. They identify the main kinds of coordination that must be considered when national digital health interoperability is analysed as a governed capability:

- **Institutional domains and logics** - captures the plurality of institutional rationalities and the need to make their responsibilities, values, and accountability claims governable.
- **Macro-meso-micro localisation** - locates interoperability problems and coordination mechanisms across policy direction, governance and infrastructure, and operational practice.
- **M0-M3 coordination levels** - distinguishes institutional reality, formalised digital knowledge, modelling and alignment mechanisms, and paradigmatic coordination.
- **Technological and modelling spaces** - makes visible the translation problems between heterogeneous systems, standards, knowledge-practice environments, and modelling traditions.
- **Interoperability capability** - qualifies the depth of coordination, from technical and syntactic exchange toward semantic, pragmatic, dynamic, and conceptual interoperability.
- **Knowledge-based interoperability** - concerns the explicit representation and governance of concepts, rules, computable knowledge, decision-support logic, and reusable knowledge artefacts.
- **Governance of change and reuse** - concerns authorised change, discrepancy resolution, accountability, reuse governance, and propagation of updated knowledge into operational settings.

Together, these attributes define the conceptual bridge between the theoretical framework and the dissertation's research questions. They do not correspond to the research questions one by one. Instead, each research question draws on a particular configuration of attributes.

RQ1 concerns national digital health as an evolving socio-technical arrangement. The framework supports this question by combining attributes that make institutional domains, system levels, architectural coordination, modelling spaces, and interoperability capability visible. This makes it possible to examine national digital health as more than a bounded technical infrastructure.

RQ2 concerns the transition from data exchange to knowledge-ready use. The framework supports this question by combining attributes that distinguish technical access from semantic continuity, computable knowledge, decision relevance, and governed change. This makes it possible to examine why data availability may still be insufficient for advanced reuse, decision support, and personalised care.

RQ3 concerns trustworthy secondary and multiple use of health data. The framework supports this question by combining attributes that make legitimacy, responsibility, authorisation, accountability, stewardship, and reuse governance visible as interoperability concerns. This makes it possible

to treat secondary use as an institutional and governance problem, not only as a data-access problem.

RQ4 concerns the conceptual revision of interoperability. The framework supports this question by bringing all seven attributes into an integrated view of interoperability as a governed coordination capability. This makes it possible to reconsider interoperability as more than a cumulative sequence of technical, semantic, and organisational maturity stages.

The research questions define what the dissertation investigates, while the analytical attributes specify which theoretical distinctions are needed to investigate it coherently. The framework's main claim is that national digital health interoperability does not accumulate automatically from technical exchange toward semantic, organisational, and governance maturity. It has to be produced through explicit coordination between meanings, models, responsibilities, knowledge structures, and mechanisms of authorised change.

This theoretical framework provides the conceptual basis for the methodological choices and empirical analysis developed in the following chapters.

4 Methodology

4.1 Scope and orientation

This chapter specifies the methodological approach used to examine national digital health interoperability. The dissertation adopts a critical realist orientation and an abductive logic of inquiry, implemented as an article-based and framework-guided qualitative multi-study design. The theoretical framework developed in Chapter 3 is operationalised through seven analytical attributes (see Section 3.7).

The methodological purpose is to identify conditions that enable, constrain or leave incomplete interoperability as a coordination capability. The analysis is therefore not designed as a performance evaluation, implementation assessment or maturity measurement. Its focus is on how source-based observations can be interpreted in relation to structural, semantic, institutional and governance-related boundary conditions.

The explanatory orientation follows Strevens' account of explanation as the identification of causally relevant unifying structures rather than the reconstruction of exhaustive causal mechanisms [123]. To maintain analytical clarity, the study draws on Archer's morphogenetic approach by distinguishing between structure, agency and culture, thereby avoiding the collapse of technological artefacts, institutional arrangements and human practices into a single explanatory layer [124]. This position supports the critical realist treatment of observable system behaviours as manifestations of deeper generative mechanisms and relatively enduring structural conditions [125].

Within this stance, abductive analysis provides the practical logic of inquiry. The analysis moves iteratively between source-based observations, analytical attributes and emerging cross-cluster patterns in order to formulate plausible explanatory interpretations. The methodological role of the chapter is therefore to define how empirical material is selected, interpreted, bounded and synthesised, while the substantive interpretation of the findings is developed in the Results and Discussion chapters.

4.2 Research design: qualitative multi-study design

The core research design of the dissertation is a qualitative multi-study design, implemented as an article-based and framework-guided synthesis. It is article-based because the empirical material is drawn from the published and contextual source set introduced in Section 1.7. It is framework-guided because the same analytical attributes are applied across empirically different materials to support comparison and synthesis.

The source materials are not aggregated into a single uniform dataset. They are organised as analytically differentiated empirical entry points into the dissertation's overarching research problem. Estonia's national digital health system provides the main longitudinal case, while selected comparative international materials are used where they clarify architectural, semantic or governance-related conditions beyond the Estonian setting.

Conceptual work and empirical analysis are used in a mutually reinforcing way. The theoretical resources reviewed in the preceding chapter provide the interpretive categories for the analysis. The empirical material provides concrete settings in which these categories can be examined under real-world constraints. This design makes it possible to trace where coordination is achieved, where it remains partial, and where progress in one area does not propagate into other required forms of alignment.

The qualitative multi-study design is therefore suited to the dissertation's aim because it allows national digital health interoperability to be examined across several empirically distinct but theoretically connected settings. It supports a framework-guided synthesis without converting heterogeneous source materials into a uniform measurement scheme or treating individual cases as exhaustive causal accounts of system behaviour.

4.3 The empirical corpus

The empirical corpus is drawn from the source set described in Section 1.7 and organised for framework-guided analysis into four thematic clusters. While the publication corpus section defines the status and role of the formal publications and the broader analytical source set, the present section explains how this material is arranged for empirical analysis.

The clusters follow the substantive progression of the empirical analysis: national interoperability as a socio-technical phenomenon; knowledge-ready reuse; governed multiple use of health data; and higher-order interoperability through standards, semantic alignment and conceptual modelling. Their relationship to the research questions is orienting rather than one-to-one. The clusters provide empirical vantage points that are later interpreted through the analytical attributes and brought together in the cross-cluster synthesis.

For compact reference in the dissertation, the empirical clusters are labelled Cluster 1-Cluster 4 and abbreviated after first definition as C1-C4: Cluster 1 (C1) covers national EHR architecture and longitudinal development; Cluster 2 (C2) covers decision support and personalised medicine; Cluster 3 (C3) covers governance and secondary data use; and Cluster 4 (C4) covers standards, semantics and conceptual interoperability. These labels are analytical shorthand for the empirical clusters. They do not denote publication numbers, maturity stages or a hierarchy of evidence.

Within the qualitative multi-study design, the clusters function as empirical entry points for analysing how architectural, semantic, clinical and institutional dimensions of national digital health interoperability interact. Each cluster contributes a distinct analytical role: establishing a longitudinal baseline, testing knowledge-ready reuse, examining governance conditions, or tracing semantic and conceptual stabilisation.

Table 5: Empirical material and its analytical role. This table specifies how the four analytical clusters organise the dissertation's empirical source material. It indicates the empirical focus and synthesis function of each cluster (source: author).

Empirical cluster	Empirical focus	Role in the synthesis
C1. National digital health architecture & longitudinal development	Long-term development of Estonia's national digital health exchange infrastructure, including architecture, standardisation and system-level coordination	Establishes the historical and architectural baseline for analysing what mature national access and exchange infrastructure can and cannot deliver after prolonged operation
C2. Decision support & personalised medicine	Conditions of data production, exchange, access and reuse as empirical stress tests for decision support, personalised medicine and knowledge-ready reuse.	Tests the move from data availability to knowledge-ready use, surfacing constraints in data quality, semantic structure, temporality and workflow integration
C3. Governance & secondary data use	Institutional, legal and governance arrangements shaping secondary or multiple use of health data in national and comparative settings	Shows how trust, responsibility, stewardship, legal mandates and institutional logics condition governed health data reuse
C4. Standards, semantics & conceptual interoperability	Standards-oriented, terminology-related and conceptual-modelling work aimed at stabilising meaning across contexts	Documents how conceptual interoperability is operationalised through clinical concepts, information models, terminology resources and implementation guidance

For analytical purposes, the source material is arranged across the clusters as follows. Cluster 1 centres on the longitudinal development and interpretation of Estonia's national e-health system, drawing on the formal publication on ten years of Estonian e-health development and supporting Estonia-focused case and professional materials [I], [21, 22]. Cluster 2 brings together the empirical testing of EHR data applicability for clinical decision support, the systematic review of AI-based decision-support research, and contextual personalised medicine feasibility and pilot materials [II], [III], [24, 25]. Cluster 3 focuses on governance and secondary or multiple use of health data, drawing on the formal governance publication and related standards-oriented or project-based material on health data reuse [IV], [23]. Cluster 4 groups standards-oriented, terminology-related and conceptual-modelling sources that support the analysis of semantic and conceptual interoperability [26–28].

This clustering does not redefine the formal publication basis of the dissertation. Rather, it provides the analytical structure through which the source material is interpreted in the Results chapter. Together, the clusters provide a longitudinal and multi-layered empirical basis for analysing national digital health interoperability as a coordination problem across architecture, semantics, clinical knowledge use and governance. Their role is summarised in Table 5 and operationalised in the analytical procedure below. A more detailed source-material mapping is provided in Appendix 2, which relates individual source materials to coordination scope, institutional logics and implications for interoperability and governance.

4.4 Analytical procedure and construction of results

This section explains how the empirical material described in Section 4.3 is transformed into the structured results presented in Chapter 5. The status of the source materials is defined in Section 1.7, while their cluster placement and analytical role are specified in Section 4.3. The present section specifies the procedure through which source-based observations are extracted, interpreted, represented, bounded and synthesised in order to support the construction of answers to the research questions.

The Results chapter is constructed as a cluster-based, framework-guided qualitative synthesis. The clusters provide differentiated empirical vantage points, while the seven analytical attributes developed in Section 3.7 provide the common interpretive structure. Comparison therefore takes place at the level of analytical attributes, boundary conditions and coordination patterns, while preserving the empirical specificity of each cluster.

The analytical attributes are used as linked interpretive categories rather than as separate measurement variables. The analysis records whether each attribute-level pattern is instantiated, implied or not instantiated within the source materials of a cluster. The resulting attribute patterns are then compared across clusters. This supports synthesis across heterogeneous source materials without converting the clusters into a uniform measurement scheme.

The construction of results follows six steps.

1. Empirical observation extraction. Within each cluster, the analysis identifies source-based observations, reported findings, artefacts, constraints and implementation conditions relevant to the cluster's analytical focus. This step establishes the traceable source basis for later abstraction.
2. Attribute-guided interpretation. Source-based observations are interpreted through the analytical attributes defined in the theoretical framework Section 3.7. The purpose is to determine which attribute-level claims can be supported within the empirical scope of the cluster and how they can be formulated.
3. Pattern abstraction and source-status marking. Empirical observations are abstracted into cluster-level patterns and represented in framework-aligned tables. Each table row links

an analytical attribute, an abstracted pattern and its empirical basis. The row prefix marks the relationship between the pattern and the source materials: [Instantiated] indicates that the pattern is directly represented in the cluster source materials; [Implied] indicates a pattern inferred from traceable source material; and [Not instantiated] indicates that the cluster source materials provide no defensible basis for formulating that attribute-level pattern within the scope of the cluster.

4. Cluster-level boundary-setting. Each cluster concludes with an interim conclusion that states what the cluster establishes and what remains outside its empirical scope. These interim conclusions separate cluster-specific findings from claims that require cross-cluster synthesis.
5. Cross-cluster synthesis. After the cluster-level analysis, the same analytical attributes are used as common reference points for cross-cluster synthesis in Section 5.6. The synthesis is constructed in two moves. First, cluster-level patterns are consolidated into *as-is* observations that describe source-grounded conditions, limitations and partial achievements. Second, these *as-is* observations are contrasted with *to-be* coordination requirements derived from the theoretical framework. This contrast separates empirically grounded findings from theoretically derived coordination requirements and is used to identify recurring boundary conditions, coordination gaps and cross-cluster implications.
6. Research-question-level consolidation. The final analytical step consolidates the cluster-level and cross-cluster patterns into research-question-level findings by using the RQ-attribute alignment developed in Section 3.7. This alignment specifies which analytical attributes are most relevant for each research question and what type of analytical outcome the Results chapter is expected to support. The step brings together attribute-level patterns across the empirical corpus, identifies supporting, limiting or contrasting evidence, and distinguishes what the empirical material establishes, what it only implies, and what remains outside the supported scope. The resulting research-question-level answers are formulated in Chapter 6.

Within this procedure, tables function as the primary analytical artefacts. They make explicit how empirical observations are transformed into attribute-mediated patterns and how those patterns remain linked to their source basis. Figures support interpretation where visual representation clarifies relations that are difficult to express in prose alone. Together, this procedure keeps the Results chapter traceable to the empirical corpus and establishes how cluster-level findings and cross-cluster synthesis support the formulation of research-question-level answers in the Discussion (see Chapter 6).

4.5 Use of generative text production

Generative text production tools (including large language models) were used in this dissertation in a limited and transparent manner as supportive instruments within the research process. Their use was confined to linguistic editing, structural refinement, consistency checking (including terminological harmonisation), and the translation of the author's research notes, working drafts, and methodological instructions from Estonian into English. These tools were not used to generate empirical material, conduct data analysis, produce analytical results, or formulate theoretical claims. All translated and revised content was manually reviewed and validated by the author. Responsibility for all conceptual decisions, interpretations, and normative conclusions presented in the dissertation rests solely with the author. In this sense, generative text production functioned as language and editing support within an explicitly reflexive and author-driven research process.

4.6 Ethical considerations

The dissertation adopts an ethics-by-design perspective in which ethical considerations are treated not only as procedural safeguards for individual studies, but also as methodological conditions for

analysing digital health governance and interoperability architecture. In this dissertation, ethical issues are especially relevant at the M1-M3 levels, where normative orientations, institutional responsibilities, data access conditions, and architectural constraints are defined and aligned across heterogeneous technological and organisational spaces.

The empirical sources and studies used in the dissertation involved different levels of ethical sensitivity. Some relied primarily on published materials, technical documentation, standards, policy texts, and architectural analysis. Others involved expert knowledge, organisational insight, or patient-related and patient-derived data. Across these source types, the research followed established principles of research ethics, data protection, and research integrity. Sensitive health-related information was handled in accordance with applicable legal and institutional requirements; informed consent was obtained where primary empirical work involved human participants; and the secondary use of documents, policy materials, and datasets followed recognised standards of responsible research conduct.

Several studies relied on expert knowledge, technical documentation, and organisational insights provided by system architects, clinicians, policy-makers, and institutional stakeholders. Although such contributions did not involve personal health data, they could still reflect sensitive organisational arrangements, strategic decisions, or system-level constraints. To address these risks, the analysis followed principles of contextual confidentiality and role-based anonymisation. Individual experts and organisations were not made identifiable unless their role and contribution were already part of the public record. Interview material and expert input were analysed at an abstracted thematic level, focusing on structural patterns, governance mechanisms, and architectural properties rather than on attributable opinions or institution-specific vulnerabilities.

A smaller subset of the empirical material involved patient-related or patient-derived data, including EHR data readiness testing [II], the HealthSense project [23], and the estPerMed clinical pilot study [25]. These cases required explicit attention to ethical oversight, data protection, access control, purpose limitation, and accountable roles. They are important for the dissertation not as clinical intervention studies, but as cases showing how ethical requirements are operationalised through governance arrangements, data flows, consent procedures, and institutional responsibility.

The estPerMed pilot study is a particularly relevant example. At the project level, it involved direct contact with patients, including clinical consultations and counselling related to breast cancer and cardiovascular risk, as well as the communication of genetic and polygenic risk information by qualified healthcare professionals. These activities were conducted within routine clinical care frameworks, under formal ethical approval, with explicit informed consent and controlled handling of sensitive health and genetic data [25]. The primary ethical concerns at the project level therefore concerned confidentiality, informed consent, responsible communication of high-sensitivity information, and governed use of derived outputs.

The author's role in estPerMed, and in the dissertation more broadly, was not situated at the level of clinical intervention, patient recruitment, consent procedures, counselling, clinical decision-making, or operational processing of identifiable personal health or genetic data. The author's contribution was located at the level of architectural, conceptual, and governance-oriented coordination: the design of interoperable digital solutions, the specification of secure and governed data flows between systems, and the analytical use of aggregated or otherwise non-identifying outputs.

Accordingly, the ethical risks most directly relevant to the author's research activities concern data governance, secondary use, institutional responsibility, expert confidentiality, and the protection of both patient-related and organisationally sensitive information. This positioning is consistent with the dissertation's methodological orientation: empirical material is analysed to identify structural, semantic, institutional, and governance-related conditions, not to evaluate individual patients, clinicians, experts, or organisations.

From this perspective, ethics is treated as part of the governance conditions that constrain and

enable interoperability. It shapes who may access which data, under what conditions, for which purposes, and with what accountability. Ethical principles are therefore relevant to the dissertation not only as compliance requirements, but also as architectural and governance constraints that must be considered when analysing trustworthy, knowledge-based, and person-centred national digital health.

4.7 Limitations and positionality

The author occupies a dual position as both a long-term practitioner involved in the design and implementation of the Estonian digital health system and as a researcher analysing its conceptual, architectural and governance foundations. This insider position provides access to institutional knowledge, longitudinal insight into design rationales, and practical understanding of how interoperability frameworks operate under real-world constraints. At the same time, it introduces risks of analytical bias, path dependency and over-familiarity with the national context. The dissertation addresses these risks through an explicit reflexive stance: the author's positionality is made transparent, and insider experience is treated as an analytical resource only when anchored in traceable source material, including peer-reviewed publications, technical and policy documents, international standards and established conceptual frameworks.

The empirical core of the dissertation is anchored in the Estonian digital health system. This focus enables an in-depth examination of interoperability, governance and semantic alignment over an unusually long temporal horizon, but it also limits the scope of empirical generalisation. The dissertation therefore supports analytical rather than statistical generalisation. Its findings are transferable at the level of conceptual distinctions, analytical attributes, boundary conditions and coordination patterns, while their practical application depends on local institutional arrangements, legal frameworks, health system structures and implementation histories.

The author has also contributed to national digital health architecture and interoperability projects in several other countries, including Ukraine, Finland, Mongolia, Uzbekistan and Romania (see CV). These experiences inform the author's analytical sensitivity to recurrent coordination problems across different national settings. They are, however, not treated as primary empirical material in this dissertation. Academic publication of the respective project results has not been possible to date due to contractual and confidentiality constraints, which limits the extent to which those experiences can be used as traceable evidence within the dissertation.

Methodologically, the dissertation prioritises conceptual, architectural and governance-oriented analysis over exhaustive empirical measurement. It does not seek to quantify system performance, population-level outcomes, implementation efficiency or causal effects. Instead, the qualitative multi-study design is used to identify structural, semantic, institutional and governance-related boundary conditions that shape interoperability as a coordination capability. The resulting claims are therefore explanatory and interpretive, rather than predictive, evaluative or statistically generalisable.

The integrative theoretical framework also entails a methodological trade-off. It prioritises explanatory breadth and cross-level conceptual coherence over parsimony, benchmarking or the construction of a prescriptive architecture blueprint. This creates a risk of conceptual overlap across theoretical traditions, which is mitigated through the explicit use of seven analytical attributes, abstraction levels, source-status marking and cluster-level boundary-setting. These devices help discipline the synthesis, but they do not eliminate the interpretive judgement required when heterogeneous empirical materials are brought into a common analytical frame.

The empirical depth is uneven across the areas examined. The dissertation foregrounds system-level architecture, semantic coordination, governance arrangements, knowledge-readiness conditions and authorised change more strongly than micro-level professional practice, patient experience, economic outcomes, usability or organisational change management. These aspects are rele-

vant to national digital health, but they fall outside the primary analytical scope of this framework-guided synthesis.

The work also adopts an explicit normative orientation toward integrated, knowledge-based and person-centred national digital health. This orientation is consistent with the dissertation's research problem and theoretical framework, but it means that the analysis is guided by a particular understanding of what national digital health systems should be able to support. Alternative normative priorities, such as administrative efficiency, market innovation, local autonomy or short-term implementation scalability, may lead to different interpretations of the same empirical material. These boundaries are treated as part of the dissertation's methodological positioning rather than as unintended shortcomings.

Taken together, these limitations define how the results should be interpreted. The dissertation offers a theoretically grounded and empirically supported synthesis of coordination conditions in national digital health, not a comprehensive evaluation of the Estonian system or a universal implementation model. The Results chapter should therefore be read as a cluster-based and framework-guided analysis of how architectural, semantic, knowledge-related and governance conditions become visible across the empirical material. The contribution lies in clarifying why technically mature digital health infrastructures may still require stronger semantic, institutional, knowledge-related and governance coordination in order to support trustworthy, knowledge-based and person-centred care.

5 Results

5.1 Empirical scope and structure of results

This chapter presents the empirical findings in relation to the research object defined in the methodology: national digital health as a socio-technical and institutional coordination problem in which architectures, semantic formalisations, and governance arrangements jointly shape interoperability capability across macro, meso, and micro levels.

The Results chapter follows the four empirical clusters introduced in the methodology: national EHR development; decision support and personalised medicine; governance and secondary data use; and standards, terminology, and semantic formalisation. These cluster-specific findings are then consolidated in a cross-cluster synthesis structured by the seven analytical attributes developed in the theoretical framework (Chapter 3).

Before the cluster-specific results, Table 6 provides a compact orientation to the empirical source base used in the chapter. The table is intended as a reader aid: it summarises the temporal scope, empirical scale, methodological orientation, and principal outputs of the studies and source materials that underpin the results. It does not define the analytical clusters anew and does not replace the methodological account provided in Chapter 4.

Table 6: Overview of the empirical source base used in the Results chapter. The table summarises the temporal scope, methodological orientation, empirical scale, and principal outputs of the studies and source materials underpinning the dissertation's results. The term "publication" in this table is used descriptively for the written source in which the empirical material, method, or analytical output is documented. It does not by itself denote an official thesis core publication; the table therefore also includes supporting scientific publications, reports, and analytical subsets where they provide source material for the results. Where several closely related publications document the same empirical strand, they are treated together. Selected sources may appear in more than one row when the same empirical material supports distinct analytical perspectives. (New abbreviations in this table: SQL - Structured Query Language; HISMM - Health Information Sharing Maturity Model; DDSS - Digital Decision Support System.)

Cluster & empirical strand (related publication/source)	Period (data; publication)	Methodological approach	Participants & data (condensed)	Key outputs
C1 - Longitudinal development of the Estonian Health Information System *(related publications: [I], [21, 22])*	Data: 2006-2011; Publications: 2018-2020	Longitudinal case study; architectural and institutional analysis	National-scale programme; core public authorities, healthcare providers, vendors; documentary sources and insider project material	Empirical reconstruction of national EHR architecture, governance arrangements, and early interoperability decisions
C2 - EHR data readiness for computable decision support *(related publication: [II])*	Data: 2012-2017; Publication: 2021	Design-oriented empirical testing; secondary EHR data analysis	System-level study; 9 algorithms; 41 parameters → 172 EHIS elements (24 document sections); 40 SQL queries; ~0.75M records	Empirical validation of CDS feasibility on national EHR data; data readiness metrics

Cluster & empirical strand (related publication/source)	Period (data; publication)	Methodological approach	Participants & data (condensed)	Key outputs
C2 - Personalised medicine / DDSS framing *(related source: [24])*	Data: 2015; Publication: 2015	Conceptual and design-oriented analysis	Conceptual study; scope refinement (3 → 2 disease domains)	National roadmap for personalised medicine decision support
C2 - Systematic literature review of DDSS for PTSD *(related publication: [III])*	Data: 2001-2019; Publication: 2022	Systematic literature review	30 studies (75 + 13 screened); sample sizes 10-89,840	Evidence base on DDSS effectiveness and design patterns
C4 - Terminology validation methodology - TermX *(related publication: [28])*	Data: 2005-2024; Publication: 2025	Method construction via targeted literature review	38 + 20 papers reviewed; 3 rule blocks	Formal checklist for terminology governance and validation
C4 - ContSys-based semantic annotation of clinical content *(related publication: [27])*	Data: 2019-2023; Publication: 2025	Semantic annotation and model application	17 ContSys concepts assessed; 15 identified	Quantitative indicator of conceptual coverage and limits
C2 - Personalised medicine data-infrastructure pilot, Estonia *(related source: [25])*	Data: 2020-2021; Publication: 2021	Pilot implementation; mixed-methods evaluation	69 physicians (67 responses); 3-component IT solution	Usability and feasibility evidence for personalised medicine infrastructure
C3 - Secondary use of health data - multicase assessment (Saudi Arabia, Estonia) *(related publication: [IV])*	Data: 2019-2020; Publication: 2024	Exploratory multicase study; qualitative analysis	Estonia: 9 organisations (4-5 participants/session); Saudi Arabia: national-level bodies	Governance recommendations; national master-plan inputs
C3 - Governance and maturity assessment of data sharing, Estonia *(related publication: [IV], analytical subset)*	Data: 2020; Publication: 2024	Capability maturity assessment (HISMM)	9 organisations (4-5 participants/session); 11 capability characteristics × 6 stakeholder purposes; maturity levels 2-4	Identified governance and interoperability bottlenecks

Cluster & empirical strand (related publication/source)	Period (data; publication)	Methodological approach	Participants & data (condensed)	Key outputs
C4 - ISO 13940 (ContSys) national-language standardisation *(related publication: [26])*	Data: 2021-2023; Publication: 2025	Design-oriented standardisation project	4 partner organisations; 5 work packages	Operational semantic standard supporting governance
C3 - Health Sense: universal data model and continuity-of-care standard *(related publication: [23])*	Data: 2021-2023; Publication: 2023	Design-oriented modelling; standard and data-model development	Multiorganisational expert consortium; iterative model development and validation	Universal data model and continuity-of-care standard aligned with next-generation health information systems

As shown in Table 6, the empirical source base is heterogeneous in period, scale, and output type. This reflects the longitudinal and integrative character of the dissertation: some empirical material was collected or operationally relevant before it was later analysed, validated, or published. Where the same publication or source material appears in more than one row, this indicates a distinct analytical use of the material rather than duplication of evidence.

The Health Sense study is the most explicit cross-cutting case in the source base [23]. It combines architectural coordination principles, assessments of data suitability and reuse, terminology development, semantic alignment, application of ISO 13940 (ContSys) concepts, and governance-oriented data-management criteria. In the present Results structure, it is positioned under Cluster 3 because the author's primary contribution to this study concerns institutional coordination, governance mechanisms, and the conditions enabling or constraining secondary use of health data. Its standards- and semantics-related implications are taken up again where relevant in the cluster-specific analysis and in the cross-cluster synthesis.

5.2 Cluster 1 - National EHR architecture & longitudinal development

5.2.1 Overview of cluster source material

This cluster brings together source material that describes the design, implementation and long-term evolution of Estonia's nationally mandated Health Information System (EHIS). The material is used in this cluster to establish the empirical basis for analysing national-scale access and exchange infrastructure, architectural coordination, institutional embedding, platform-enabled services and the limits of document-centric interoperability. EHIS is discussed in this dissertation as a national EHR when the emphasis is on its role as a nationwide coordinating infrastructure for health data exchange.

Metsallik et al. describe EHIS as a nationwide health information infrastructure operational since the end of 2008. Their account emphasises the enabling conditions of implementation, including governance arrangements, legal clarity, Estonia's mature e-state environment, agreement on access rights, and standardisation of medical data and data exchange rules. The paper presents EHIS as a federated set of integrated services rather than a single centralised database. Its architecture is described through three main layers: repositories for documents and images, a secure data

exchange layer, and an application layer. The account also situates EHIS within the wider national digital infrastructure, especially secure data exchange, digital identity, digital signing and auditability [I].

In the same source, EHIS is characterised primarily as a document-centric health information exchange environment. It supports continuity of care through routine cross-institutional access to clinical documents and image references, and includes patient-facing access through a portal. The paper reports national-scale adoption and routine use, and identifies recurring challenges related to semantic interoperability, data quality, secondary use, and change management in clinical documentation and sharing practices. It also describes legally mandated document submission, access-control arrangements, strong authentication, digital signing and audit logging as part of the operating model [I].

The high-level architecture used in this cluster is reproduced in Figure 8.

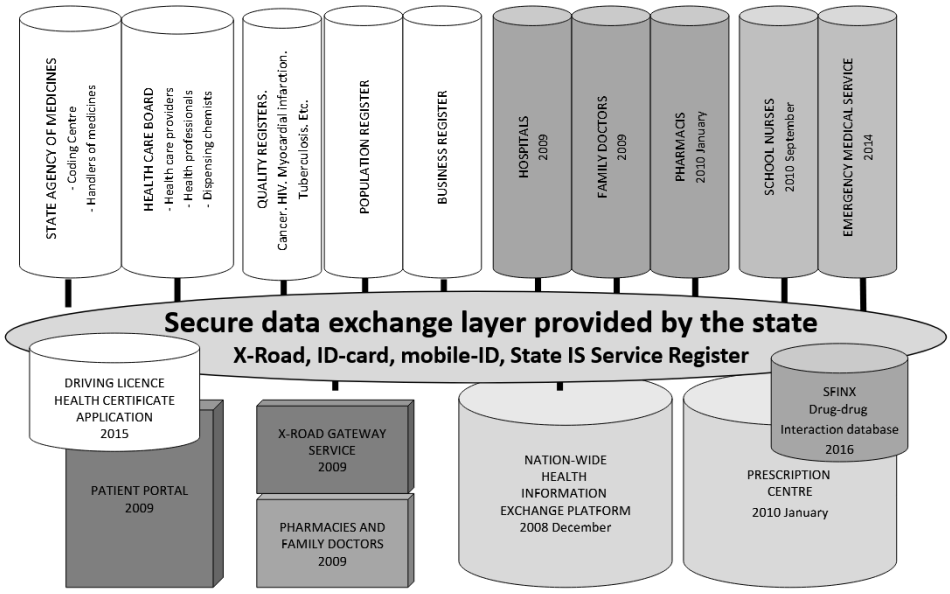

Figure 8: High-level architecture of Estonia's health data exchange and service ecosystem integrated with the national digital public infrastructure. The figure depicts secure cross-institutional health data exchange, connecting health sector applications and registries with shared infrastructure services such as secure data exchange and digital identity. The years shown on components denote initial deployment periods (source: [I]).

Metsallik and Ross provide a post-launch implementation experience report that describes EHIS through its architectural layering, e-state dependencies, programme-level governance and funding arrangements, and routine service use. In this account, EHIS integrates data from healthcare providers through repositories for medical documents and images, the state-provided secure internet-based exchange layer X-Road, national digital identity and signature services, and an application layer providing role-specific services, including the Patient Portal. The chapter reports routine professional use of the Electronic Health Record, e-prescription and national PACS through local information systems, and gives national-scale activity indicators for early 2017, including 1,163 healthcare institutions sending and retrieving data, physician query volume close to 50,000 queries per day, population coverage of 1.5 million people, and large volumes of outpatient summaries, inpatient summaries and diagnostic examination reports [21].

The implementation account also reports that internal institutional processes were kept unchanged as much as possible, with the main implementation task framed as integrating local in-

formation systems with central repositories. It describes the phased implementation of EHIS from 2005 through four initial programmes and the establishment of a multi-stakeholder coordinating organisation for ongoing standardisation and central system maintenance. The same source identifies implementation lessons and limitations, including that early data-quality targets and measures could have been stronger and that usability was not a primary design priority at the outset. It also describes a nationally shared drug-drug interaction checking service as a service-specific decision-support capability linked to e-prescription workflows [21].

The WHO and ITU handbook case presents Estonia through the vocabulary of a digital health platform and reference architecture. This source is therefore used here as an external handbook framing of the Estonian case, not as a domestic system specification. It situates the Estonian case within a wider digital public infrastructure context and describes a staged national programme launched in 2005 through four initial projects: Electronic Health Records, Digital Images, Digital Registration and Digital Prescriptions. The case describes the platform's main components, including the national Health Information System, prescription centre, patient portal and registries, and presents an explicit catalogue of cross-institutional business processes supported by the Estonian platform [22].

The handbook case frames interoperability through schema specifications, shared reference data and classifications, and interaction specifications that connect process events, message structures and participating systems. It also describes governance and standardisation responsibilities of a coordinating organisation, including maintenance of shared classifications and national care guidelines, and identifies enforcement mechanisms such as licensing and audit-related controls, including personal access to audit logs [22].

The cross-institutional business processes catalogued in the handbook case are reproduced in Table 7.

Table 7: Business processes supported by the Estonian platform, presented in the WHO and ITU handbook as an illustrative national example rather than as an exhaustive or evaluative process model (source: [22]).

Health service delivery processes	Administrative processes
Health records process: enables clinicians to share patient data with one another and with a person related to the patient.	*Consents process:* states a patient's request about health care or records, including restricting clinicians' or trustees' access to records.
Critical report process: enables ambulances and emergency care clinicians to receive a quick summary of a patient's health records.	*Demographics process:* gathers personal demographic data into shared records from sources such as a population registry, patient portal, or health provider.
Ambulance process: enables ambulance units to issue communications to a patient's subsequent care providers via shared health records.	*Usage audit process:* allows patient access to the health records access log.
Prescriptions process: connects clinician, pharmacist, insurer, and patient in one digital workflow.	*Professional digital licensing process:* registers an individual as a licensed health professional, enabling access to shared health records.
Laboratory diagnostics process: requires all medical labs to report diagnostic results to shared health records, enabling patient-centric viewing of results.	*Institution digital licensing process:* registers an institution, allowing network access to the health records system.

Health service delivery processes	Administrative processes
Imaging diagnostics process: regulates information sharing of diagnostic images and updates health records with radiology reports.	*Institution digital certification process:* allows digital authentication for institutions via cooperation with public authorities.
Epidemiology process: updates medical registries automatically from shared health records.	*Personal digital certification process:* allows digital authentication for individuals.
Health certificates process: delivers specific health condition data to outside parties.	*Reimbursement process:* connects the health service provider with the insurer.
Referrals process: supports the transfer of patients from one provider to another.	
Consultation process: allows patients to receive medical advice via digital health channels.	
Research process: allows scientific researchers to view certain data in shared health records, following approval from an ethical committee.	

Taken together, the source material establishes the empirical starting point for Cluster 1. Metsallik et al. provide the retrospective account of EHIS as a mature national health information infrastructure; Metsallik and Ross add implementation-oriented detail on architecture, programme governance, operational scale and post-launch lessons; and the WHO/ITU handbook case reframes the Estonian example through digital health platform and reference-architecture vocabulary. The cluster therefore provides evidence of mature national access and exchange infrastructure while also surfacing limitations related to semantic interoperability, data quality, usability, secondary use and the governance of change. These source-based observations are mapped to the seven analytical attributes in the following section.

5.2.2 Interoperability and knowledge characteristics

This section summarises the reported results of the Cluster 1 publications in relation to the analytical dimensions introduced in the theoretical framework (see Chapter 3). The synthesis is presented as a structured table to make the relationship between architectural description and framework attributes explicit (Table 8).

Table 8: Framework-aligned summary of Cluster 1 findings (author's synthesis based on reported results).

Analytical attribute	Abstracted pattern	Empirical basis
[Instantiated] Institutional domains and logics	National EHR architecture is characterized by institutionally embedded coordination that aligns healthcare delivery and public administration obligations through legally mandated information exchange.	*Metsallik et al. (2018)* - governance and legal clarity framed as success factors; mandated information exchange and security posture described. *Metsallik & Ross (2018)* describe mandated document sets, access entitlements, and institutional arrangements for standardisation and maintenance. *WHO/ITU (2020)* - national EHR described as digital public infrastructure with institutional enabling conditions.
[Instantiated] Macro-meso-micro localisation	Reported coordination effects concentrate on inter-organisational coupling (meso level) through shared services and mandates, while local clinical workflows are described as largely unchanged.	*Metsallik et al. (2018)* - shared infrastructure connects autonomous institutions and supports routine professional and citizen access. *Metsallik & Ross (2018)* - local systems integrated with central repositories; internal processes kept unchanged as much as possible. *WHO/ITU (2020)* - cross-institutional processes catalogued as platform-supported capabilities.
[Instantiated] M0-M3 coordination levels	The publications report extensive operational and infrastructural coordination (M0-M1), while semantic and knowledge-level coordination is described as limited or uneven within the document-centric exchange model.	*Metsallik et al. (2018)* - document-centric exchange at national scale; semantic interoperability and data quality challenges stated. *Metsallik & Ross (2018)* - uptake of services and exchange; usability and data quality limitations reported as affecting advanced use and secondary use.
[Instantiated] Technological and modelling spaces	A shared technological space (secure exchange, identity, registries, standardised document formats) connects heterogeneous local systems without imposing uniform internal data models.	*Metsallik et al. (2018)* - three-layer architecture; X-Road and e-identity as shared infrastructure; federated services rather than a single central database. *Metsallik & Ross (2018)* describe a three-layer architecture and integration with public infrastructure. *WHO/ITU (2020)* - platform component groupings and interoperability specifications described (platform zones and standards framing).

Analytical attribute	Abstracted pattern	Empirical basis
[Instantiated] Interoperability capability	Interoperability is described as primarily technical and syntactic, supported by nationally defined document sets and exchange services, with partial and uneven semantic alignment noted as a persistent characteristic.	*Metsallik et al. (2018)* - standards-based document exchange and mandated document sets described; semantic interoperability difficulty stated. *Metsallik & Ross (2018)* - standardisation of exchange rules described; data quality targets and measures described as having been weaker than needed for advanced use.
[Implied] Knowledge-based interoperability	Knowledge-based services are referenced mainly through boundary statements: the system supports informational continuity and access to distributed clinical information, while decision-ready knowledge representations and adaptive decision support are not reported as achieved outcomes in this cluster corpus.	*Metsallik et al. (2018)* - platform positioned as EHR with emphasis on service enablement; limits for semantic deepening and secondary use discussed. *Metsallik & Ross (2018)* - service-specific decision support via drug-drug interaction checking described; no general-purpose knowledge-based decision support claimed.
[Implied] Governance of change and reuse	Change is described as coordinated through phased programmes and a dedicated national coordinating organisation for standardisation and central maintenance, while governance mechanisms for systematic reuse (e.g., reusable semantic artefacts with explicit lifecycle control) are not made explicit in the cluster publications.	*Metsallik et al. (2018)* - governance and legal embedding described as enabling conditions; continued evolution of mandated exchange and services described in a longitudinal trajectory. *Metsallik & Ross (2018)* - coordinating organisation established for ongoing standardisation and central maintenance; stakeholder governance forums described as supporting coordination. *WHO/ITU (2020)* - coordinating organisation responsibilities described for platform management, registry maintenance, and ongoing standardisation, including shared classifications and national care guidelines; enforcement mechanisms include licensing and audit-related controls and personal access to audit logs.

Taken together, the table characterises EHIS primarily as a legally embedded, service-oriented coordination infrastructure whose reported strengths lie in national-scale connectivity and routine information exchange, while semantic deepening and systematic reuse governance remain only

partially evidenced within this cluster corpus.

5.2.3 Interim conclusion

Empirically, this cluster establishes how institutional embedding and meso-level coordination (institutional domains and logics; macro-meso-micro localisation) are realised through a shared national technological space and document-centric interoperability capability in the longitudinal development of Estonia's national EHR. It does not address knowledge-based interoperability beyond boundary statements and only implies governance of change and reuse. The corpus reports phased implementation and coordination arrangements but does not make reuse-oriented change-control mechanisms explicit. These limitations are taken up in Cluster 5.3 (applied data use and decision-support readiness), Cluster 5.4 (governance and stewardship of secondary or multiple data use), and Cluster 5.5 (semantic and conceptual instruments for durable coordination).

5.3 Cluster 2 - Decision support & personalised medicine

5.3.1 Overview of cluster source material

This cluster brings together source material that examines digital decision support and personalised medicine in relation to national digital health data infrastructures. The cluster is used to analyse the move from data availability toward knowledge-ready use: whether algorithmic rules, personalised risk models and clinical decision-support workflows can be operationalised on the basis of available EHR data, documentation practices, semantic structures, data flows and institutional arrangements. The materials are treated together because they describe different empirical positions within the same problem space: AI-based decision-support research, national EHR data applicability testing, scenario-based personalised medicine planning, and pilot-phase implementation of risk-based personalised prevention.

Bertl et al. analyse 30 peer-reviewed publications on AI-based digital decision support systems for post-traumatic stress disorder published between 2001 and 2019. The review classifies the studies by decision-support function, data source, maturity level, interaction modality and validation characteristics. Prediction-oriented systems form the largest group, followed by screening, treatment recommendation, monitoring, diagnosis and assessment. The review reports that questionnaires and structured clinical assessments are the most frequently used inputs, while electronic health record data are used in only 3 of the 30 studies. Most systems are described as proof-of-concept or prototype implementations evaluated retrospectively on secondary datasets, rather than as workflow-embedded clinical services. The median reported sample size is 151 patients, and validation is concentrated on algorithmic accuracy, while user acceptance, clinical effectiveness, legal compliance, security and long-term organisational impact are rarely or not systematically evaluated [III].

The same review reports that only one system had progressed beyond experimental use toward an operational product, and none of the reviewed systems were described as deployed nationwide or embedded in routine care through production-grade EHR infrastructures. Interoperability with existing EHR systems, semantic harmonisation of clinical concepts, modelling of longitudinal patient state and alignment with routine clinical workflows are reported as weakly specified. For this cluster, the review therefore provides a comparative research baseline: AI-based decision-support research is shown to be dominated by algorithm development and performance evaluation, with limited attention to the infrastructural, organisational and governance conditions required for scalable clinical use [III].

Figure 9 visualises the reported distribution of DDSS maturity levels across the reviewed studies.

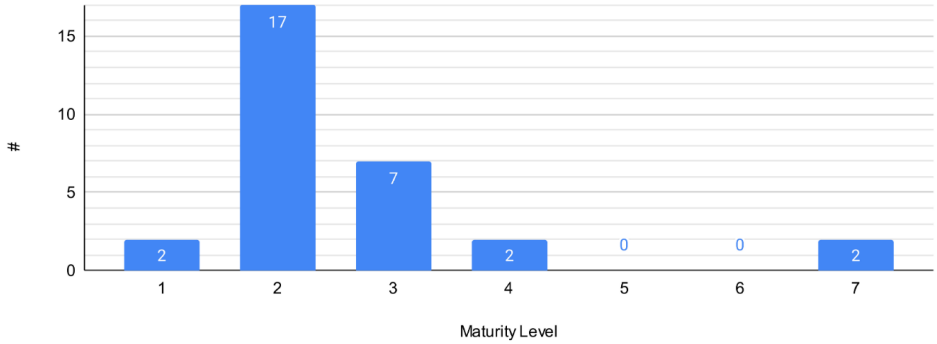

Figure 9: Capability spectrum of digital decision support systems (DDSS) based on the maturity framework adopted by Bertl et al. (2022). The horizontal axis represents DDSS maturity levels (1-7) as defined in the systematic review, ranging from conceptual ideas without implementation (Level 1), through algorithmic implementations using secondary data (Level 2), to progressively more integrated prototypes and operational products with real-world clinical interaction and adoption (Levels 3-7). The vertical axis shows the number of reviewed studies (#) per maturity level in the literature. The distribution shows a strong concentration of research at lower maturity levels, reflecting a predominance of algorithm-focused studies with limited clinical integration. The figure is descriptive of the reviewed literature and does not imply a normative development path or required progression sequence (source: [III]).

Metsallik and Ross test whether historical data from the Estonian National Health Information System can support automated clinical decision support. The study applies nine established clinical decision-support algorithms from the Evidence-Based Medicine Electronic Decision Support rule base to national EHR data, with a data window from January 2012 to May 2017. The algorithms cover mainly cardiovascular decision scenarios, including both phenotype- and genotype-dependent logic. Data processing and query execution were performed in a controlled environment within the national e-health infrastructure operator because of data protection and access constraints. The study therefore examines decision-support applicability under real-world national EHR data conditions rather than under a purpose-built research dataset [II].

Across the nine algorithms, the study identifies 41 distinct input parameters grouped into six parameter classes: diagnosis or condition, observation, medication, procedure, patient demographics and adverse events. These parameters are mapped to 172 structured data fields across 24 HL7 Clinical Document Architecture document sections. The mapping uses several terminologies and classifications, including ICD-10, ATC, LOINC, DRG, Estonian Health Insurance Fund service codes, SNOMED CT and NCSP. In total, 40 SQL queries are implemented and executed to simulate algorithm behaviour on population-scale historical data. From a technical perspective, all mappings and query executions are reported as successful on both the national EHR and a hospital electronic medical record comparator. Empirically, however, only one of the nine algorithms produced any matching cases in the national EHR, and no patient records in EHIS simultaneously fulfilled all required input parameters for any of the tested algorithms [II].

The study reports a particularly important negative result for the congestive heart failure diuretics algorithm. Although the EHIS dataset contained 751,251 patients with a heart failure diagnosis, 1,717,634 diagnosis entries and 640,774 recorded body weight observations, zero cases satisfied the algorithm's requirement for repeated body weight measurements within a three-week window. Comparative execution on the hospital electronic medical record (EMR) showed higher local data density, with two algorithms fully applicable and three partially applicable, but still insufficient longitudinal continuity and integration for population-scale decision support. The reported limitations

concern not only missing data, but also document-centric event models, inconsistent temporal granularity, limited structured representation of key parameters such as smoking status, left ventricular ejection fraction and genetic test results, and limited integration with complementary national data sources such as e-prescription and biobank infrastructure [II].

Figure 10 summarises the four-phase mapping and applicability-testing method applied in the nationwide EHIS experiment.

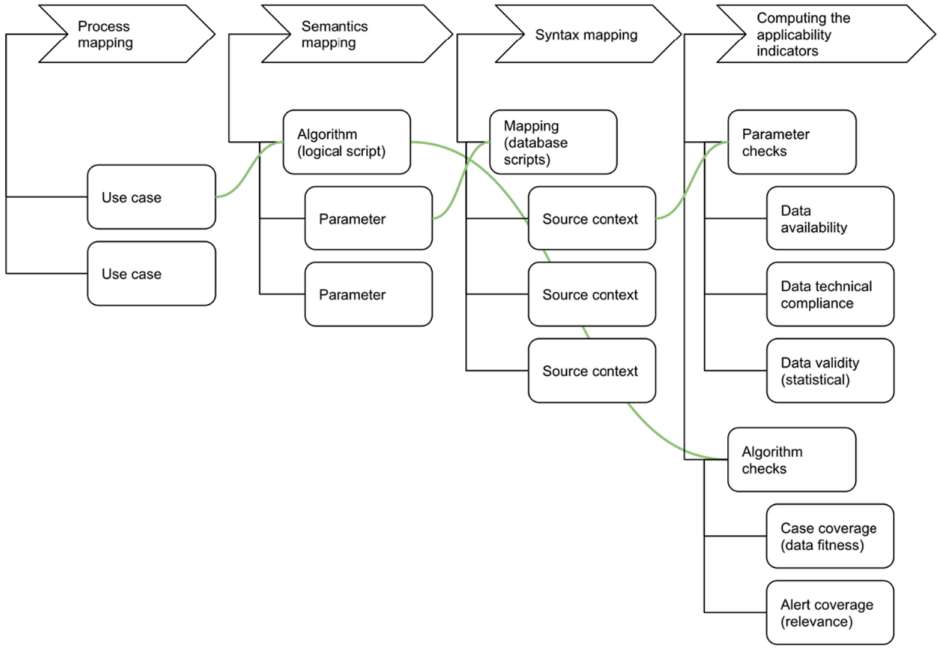

Figure 10: Overview of the decision-support algorithm applicability testing process, as defined and applied in the nationwide Estonian EHR experiment. The figure schematically represents the four successive phases of the method: (1) process and use-case mapping, where clinical decision scenarios are selected and aligned with guideline-based decision support algorithms; (2) semantic mapping, in which algorithm logic and parameter definitions are mapped to clinical concepts, terminologies, and parameter classes such as conditions, observations, medications, procedures and demographics; (3) syntactic mapping, where abstract parameters are operationalised through database-level scripts linking them to concrete document sections, data fields and source contexts in the EHR; and (4) computation of applicability indicators, where query results are aggregated to assess parameter availability, technical compliance and statistical validity, as well as algorithm-level properties such as case coverage and alert relevance. The figure emphasises that DDSS applicability is evaluated as a multi-dimensional property emerging from data availability, structure, semantics and event dynamics, rather than as a binary outcome of algorithm correctness. The workflow is analytical and evaluative in nature and is intended to identify structural limitations of national EHR data models for automated decision support, not to prescribe an implementation architecture. Abbreviations: EHR = Electronic Health Records. (source: [II]).

The national personalised medicine feasibility study specifies how digital decision support for personalised medicine could be implemented on top of Estonia's national health data landscape. The study combines mapping of existing national information systems and standards, scenario-based modelling of decision-support use in selected disease areas, and requirements elicitation for a functional prototype. It develops two exemplary end-to-end scenarios: a personalised prevention plan for genetic breast cancer risk and chronic patient monitoring with personalised treatment for cardiovascular disease and type II diabetes. The scenarios include prototype views for patient-facing and professional use, including genetic risk reporting, professional access to sequencing results,

patient-portal notifications, professional notifications and treatment suggestions [24].

The feasibility study positions the required decision-support inputs as distributed across multiple institutional sources, including EHIS, the Estonian Health Insurance Fund and the Estonian Genome Centre or biobank. It treats document-centric exchange as insufficient for algorithmic decision support, because decision-support logic requires structured data elements and clinically meaningful timelines to be reconstructed from clinical documents. The report highlights that secondary use may involve transforming structured entries into Health Level Seven Clinical Document Architecture (HL7 CDA) narratives for exchange and then parsing them back into computable data elements. It therefore frames digital decision-support readiness as a progression from technical and syntactic interoperability toward semantic, pragmatic, dynamic and conceptual interoperability requirements. It also identifies informed-consent handling and organisational coordination as prerequisites for cross-source linkage and reuse of genotype and phenotype inputs in clinical contexts [24].

The personalised medicine pilot material reports the implementation of personalised prevention and risk-based decision support in two domains: cardiovascular disease prevention in primary care and personalised early detection and prevention pathways for breast and ovarian cancer. For the cardiovascular disease prevention study, the reported sampling frame draws on the University of Tartu biobank, which included 52,274 donors as of 1 January 2018. From this frame, 2,000 high-inherited-risk candidates were selected to achieve a target enrolment of approximately 1,000 participants. Participants were randomised into intervention and control groups, and the intervention group completed three general-practitioner visits. The pilot used the Kardiokompass / CardioCompass tool with 72 family doctors, combining polygenic risk score with established risk factors to compute and visualise overall cardiovascular risk [25, 126].

For the breast and ovarian cancer pathway pilots, the pilot material specifies several cohorts and operational steps, including high-risk single-gene variants such as breast cancer susceptibility genes 1 and 2 (BRCA1/2) and a polygenic risk score (PRS) approach. One reported invitation-based cohort includes 905 consented participants, of whom 890 remained after excluding prior breast cancer cases, and a separate mutation cohort is reported as 265 subjects. These pilots relied on biobank-linked risk information and required operational coordination with screening and specialist services [25].

Across both pilot domains, the material documents limited end-to-end interoperability. Informed consent was collected manually on paper; clinical and study data were captured in Research Electronic Data Capture (REDCap) electronic forms that were not integrated with the national e-health network; and clinicians therefore performed double data entry across research, decision-support and routine-care systems [25, 127, 128]. The report also describes operational frictions in everyday clinical work, including the burden of working with separate REDCap and Kardiokompass tools and usability issues in data-capture workflows. Decision support was implemented through stand-alone tooling and project-specific data flows rather than persistently stored as structured outputs in longitudinal routine records. The pilots therefore provide evidence of feasibility under controlled project conditions, while also showing that personalised decision support had not yet been embedded as an end-to-end national service capability [25].

Figure 11 depicts the pilot-phase data-flow configuration across biobank, research data capture, decision-support tooling and routine care systems.

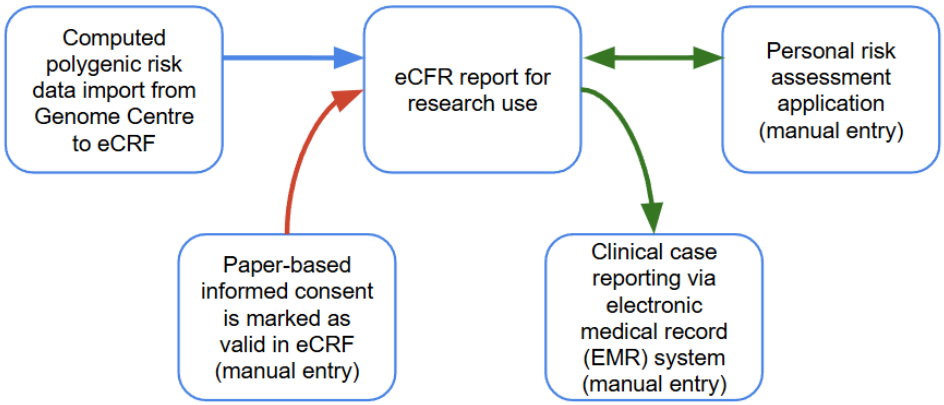

Figure 11: Data flow and system interaction model from Estonian personalised medicine pilot studies, illustrating the interim handling of polygenic risk score data, informed consent and clinical information across research and healthcare systems. Genomic risk data are transferred digitally from the Genome Centre into a research electronic Case Report Form, while informed consent and clinical case information are recorded manually. Relevant data are re-entered into a standalone personal risk assessment application and into routine Electronic Medical Record systems, reflecting the absence of end-to-end integration between research, decision support and clinical information infrastructures during the pilot phase. The figure depicts a transitional configuration adopted in the absence of a national decision-support platform. Abbreviations: eCRF = electronic Case Report Form; EMR = electronic medical record. (source: [25]).

Taken together, the source material establishes the empirical starting point for Cluster 2. Bertl et al. show that AI-based decision-support research is mostly algorithm-centred and weakly integrated with routine EHR infrastructures. Metsallik and Ross test decision-support applicability directly against national EHR data and show that successful technical mapping does not imply knowledge-ready data use. The feasibility study specifies the cross-source data, scenario and interoperability requirements expected from personalised medicine. The pilot material shows how personalised risk-based decision support was implemented through project-specific data flows and stand-alone tooling rather than as an end-to-end national service. These source-based observations are mapped to the seven analytical attributes in the following section.

5.3.2 Interoperability and knowledge characteristics

This section describes cross-publication regularities observed in Cluster 2 regarding interoperability and knowledge-related properties, using the analytical attributes introduced in the theoretical framework (see Chapter 3). It does not introduce new empirical material; instead, it abstracts recurring constraints and enabling conditions already reported in the reviewed publications into a framework-consistent, evidence-traceable summary. The table below, therefore, operationalises the cluster's synthesis boundary by stating (i) an abstracted pattern per analytical attribute and (ii) the compact *Author (Year)* basis that supports it (see Table 9).

Table 9: Framework-aligned summary of Cluster 2 findings (author's synthesis based on reported results).

Analytical attribute	Abstracted pattern	Empirical basis
[Instantiated] Institutional domains and logics	Decision support and personalised medicine are treated as supplementary capabilities organised through research, pilot, and policy programmes, rather than as routine-care functions embedded in production EHR services.	*Bertl et al. (2022)* report an algorithm-development-dominated DDSS literature with limited workflow embedding and rare EHR integration, as assessed using structured evidence extraction and maturity/validation dimensions. *The National personalised medicine feasibility study (2015)* frames personalised medicine as a national capability that requires cross-institutional coordination beyond routine documentation practices. *Clinical personalised medicine pilot projects (2021)* implement decision support through time-bounded pilots and stand-alone tooling rather than through national services.
[Instantiated] Macro-meso-micro localisation	Empirical effects and operational feasibility are demonstrated at the micro level (patient-level parameter availability) and meso level (local pilots), while macro-level (national) stabilisation as an operational service remains unachieved in the reported material.	*Metsallik & Ross (2021)* report that only 1/9 algorithms find any matching records in EHIS, and none can be executed end-to-end from national EHR data alone, despite large diagnosis-linked cohorts. They note that execution is conducted in a controlled environment within the national e-health infrastructure operator due to data protection/access constraints. *Clinical personalised medicine pilot projects (2021)* report meso-level feasibility via controlled studies (e.g., 1,000-participant cardiovascular disease trial; multiple cancer-risk cohorts) implemented through stand-alone tooling and parallel data capture rather than national embedding. *National personalised medicine feasibility study (2015)* specifies scenario-based prototypes that require cross-source linkage beyond routine EHR flows.

Analytical attribute	Abstracted pattern	Empirical basis
[Instantiated] M0-M3 coordination levels	Technical executability (M0-M1) is demonstrated through mappings and query execution, but semantic and knowledge-level coordination (M2-M3) remains insufficient to produce complete, decision-ready inputs across longitudinal timelines and institutional boundaries.	*Metsallik & Ross (2021)* report successful technical execution (CDA mapping and SQL query runs) while complete input sets are not jointly satisfied in EHIS. *National personalised medicine feasibility study (2015)* identifies missing temporal/semantic coherence across required inputs distributed across sources.
[Instantiated] Technological and modelling spaces	Document-oriented representations and fragmented event documentation remain misaligned with the state-, timeline-, and parameter-stability assumptions embedded in guideline-based decision logic and risk models.	*Metsallik & Ross (2021)* report document-centric event models, inconsistent temporal granularity, and dispersed parameter representations across CDA sections that hinder the construction of a coherent longitudinal patient state. *National personalised medicine feasibility study (2015)* reports that several required elements are not available in computable form and require cross-source assembly.
[Instantiated] Interoperability capability	Interoperability is achieved primarily as technical access and partial semantic codification, but not as pragmatic interoperability that preserves decision relevance, temporal context, and cross-source coherence required for automated decision support.	*Bertl et al. (2022)* report limited specification of interoperability and integration conditions in the DDSS literature (EHR data used in 3/30 studies; integration rarely detailed). *Metsallik & Ross (2021)* show that syntactically accessible data do not support end-to-end decision logic due to missing and temporally discontinuous inputs. *The National personalised medicine feasibility study (2015)* frames DDSS readiness as a progression beyond technical/syntactic interoperability toward semantic, pragmatic, dynamic, and conceptual interoperability requirements, and highlights the need to reconstruct computable data and timelines from document exchanges. *Clinical personalised medicine pilot projects (2021)* report parallel systems and manual reconciliation due to limited integration (e.g., REDCap + stand-alone tool).

Analytical attribute	Abstracted pattern	Empirical basis
[Instantiated] Knowledge-based interoperability	National EHR infrastructures and adjacent datasets support retrospective access, but do not (in the reported studies) yield longitudinal, decision-ready knowledge representations that satisfy complete algorithm or scenario input requirements without manual supplementation.	*Metsallik & Ross (2021)* report that no patient records simultaneously meet all the parameter requirements of the tested algorithms in EHIS. *National personalised medicine feasibility study (2015)* reports that none of the analysed decision scenarios can be executed end-to-end without manual supplementation and cross-source combination, and notes that secondary use may require converting structured entries into CDA narratives and parsing them back into computable elements. *Clinical personalised medicine pilot projects (2021)* rely on stand-alone applications and research databases with double data entry, rather than on persistent, structured decision outputs in routine records.
[Implied] Governance of change and reuse	Governance needs (e.g., consent management and organisational coordination for cross-source assembly and reuse of decision inputs/outputs) are articulated as prerequisites, but the cluster corpus does not specify durable change-control and accountability mechanisms for reuse of shared artefacts.	*National personalised medicine feasibility study (2015)* reports the need for consent management and organisational coordination to support decision-ready representations. *Clinical personalised medicine pilot projects (2021)* report reliance on bespoke data flows and manual coordination, implying unresolved governance arrangements for routine reuse.

5.3.3 Interim conclusion

Empirically, this cluster shows that decision support and personalised medicine remain only partially coupled to national digital health infrastructure. The materials analysed in this cluster point to two related patterns. First, decision support is still largely organised through algorithm-centric research, experimental validation, and time-bounded pilots rather than as a routinely embedded national capability [III], [24, 25]. Second, the Estonian EHR data tested for guideline-based decision support did not provide the longitudinal, decision-ready inputs needed for end-to-end execution of the selected algorithms, despite the existence of national-scale exchange infrastructure and structured document elements [II]. This cluster-level finding is consistent with broader studies of Estonian EHR data usability discussed in the Introduction, which identify data-quality, completeness, temporality, and cross-process reuse constraints that limit secondary analysis and decision-support use [12–17].

The cluster therefore demonstrates a gap between data availability and knowledge readiness. National EHR data can be technically accessible and partially structured while still lacking the semantic consistency, temporal coherence, contextual completeness, and lifecycle governance required for computable clinical reasoning and personalised medicine at scale.

Governance of change and reuse appears in this cluster mainly as a prerequisite for decision support and personalised medicine, rather than as the primary object of analysis. Issues such as binding accountability, change-control mechanisms for cross-source data assembly, consent management, and persistence of decision-support outputs are addressed in the feasibility and pilot materials as enabling conditions, but not yet as fully institutionalised governance arrangements.

These limitations are taken up in Cluster 3, which examines governance and secondary data use, and Cluster 4, which analyses semantic and conceptual interoperability instruments. Together, these subsequent clusters address the institutional arrangements and meaning-coordination mechanisms required for durable reuse at scale.

5.4 Cluster 3 - Governance & secondary data use: institutional logics in tension

5.4.1 Overview of cluster source material

This cluster brings together source material concerned with governance arrangements and the conditions for secondary, multiple and learning-oriented use of health data. The cluster is used to analyse how health data reuse depends on institutional responsibilities, data flows, stewardship arrangements, access conditions, semantic alignment and reusable governance artefacts. The materials are treated together because they describe complementary aspects of the same problem space: comparative national conditions for secondary use of health data, and Estonia-specific design work aimed at strengthening governance, semantic alignment and reuse readiness.

Metsallik et al. report two exploratory national case assessments, covering Saudi Arabia and Estonia. The study is designed as purposively sampled evaluation research using semistructured interviews and documentation review, followed by qualitative content analysis coded against a predefined framework organised around data purpose, data flow and data sharing. The Estonian case also uses the Health Information Sharing Maturity Model (HISMM) as an additional coding and assessment instrument, whereas the Saudi Arabian case does not include HISMM because it preceded the model's introduction into the research programme [IV].

The comparative study describes multiple-use governance through functionally distinct role groupings. These include policy and regulatory actors defining reuse purposes and access conditions; national operators coordinating platforms, registries and exchange services; healthcare providers responsible for the production and custodianship of data; data users such as research, public health and planning actors requesting access for defined purposes; and oversight bodies authorising and monitoring reuse. The study uses this role differentiation to describe where responsibilities and handovers occur. It reports fragmentation across these groupings, especially unclear stewardship allocation and weak mechanisms linking primary data capture to reuse requirements, as a source of case-by-case negotiation and uneven reuse performance [IV].

For Saudi Arabia, the study reports a national population of 35 million and a structurally plural provider landscape. The Ministry of Health is described as operating 287 hospitals with 45,180 beds, alongside primary care centres and specialised facilities, with additional parallel governmental and private subsystems. The Saudi Arabian sub-study reflects an earlier stage of national digital health consolidation. It frames multiple-use constraints primarily as cross-system alignment and governance formation challenges in a plural institutional landscape, and reports reuse initiatives as relying on ad hoc, case-by-case agreements across parallel subsystems rather than on a stable end-to-end reuse pathway at the time of the study [IV].

For Estonia, the same study reports a legally unified national infrastructure and a 2019 service landscape of 1428 health care institutions, including 52 hospitals with 6788 beds. The empirical basis consists of nine interviewed stakeholder groups, with sessions lasting 1.5-2 hours and typically involving 4-5 participants. The interview guide was structured into 11 HISMM capability categories. The Estonian sub-study examines multiple use in a technically mature national digital health environment. It positions TEHIK as the national health information system operator and the Estonian

Health Insurance Fund as a major administrative and analytic user. HISMM is used to relate stakeholder data-use purposes, 11 capability characteristics grouped into technology, use and governance, and capability maturity levels. Reported maturity falls mainly between levels 2 and 4, while policy-oriented decision flows are reported as the lowest-maturity reuse pathway. In this source, multiple-use limitations in Estonia are therefore reported primarily in relation to stewardship and governance constraints rather than missing technical exchange infrastructure [IV].

As part of the Estonian sub-study reported by Metsallik et al. (2024), Figure 12 summarises the HISMM-based capability assessment.

		1 Empowering	2 Clinical	3 Management	4 Research	5 Policy	6 Funding
Technical	01 Data quality	2	2	2	3	2	3
	02 Data transport	2	3	2	2	2	3
	03 Data security	4	4	4	4	4	4
	04 Interoperability	3	3	3	2	2	3
Process	05 Usability	3	3	3	3	2	3
	06 Alignment	2	3	3	3	2	2
	07 Participation	4	3	4	3	3	2
	08 Consent	3	3	3	3	2	2
Governance	09 Data governance	3	3	2	2	2	2
	10 Stakeholder governance	2	3	3	2	2	2
	11 Sustainability	4	2	2	4	3	4

Figure 12: HISMM-based capability assessment for multiple use of health data in Estonia. The matrix maps 11 information-sharing capability characteristics, grouped into technology, use and governance, against six stakeholder data-use purposes: patient engagement, clinical decision-making, healthcare management, research, policy and funding. Each cell indicates the assessed capability maturity level (1-5), where lower levels reflect project- or expert-based practices and higher levels indicate standardised and performance-driven information sharing. The figure is descriptive of the HISMM-based assessment reported for the Estonian case. Abbreviations: HISMM = Health Information Sharing Maturity Model. (source: [IV]).

Ross et al. report Estonia-specific assessment and design work carried out in the Health Sense project between 2021 and 2023. The project addresses governance, semantic alignment and data readiness for multiple use of health data. The report frames its outputs as practical coordination instruments rather than as benchmarking results. It states three headline design targets: a transferable next-generation data model, a continuity-of-care or care-pathway continuity standard, and a terminology database structure. It also reports programme-level deliverables, including three completed data-mining or AI pilots and ten trained specialists [23].

The Health Sense report positions ISO 23903, ISO 13940 (ContSys) and ISO 19502 (MOF) as reference frames for relating data-use requirements, workflows and semantic structures. It reports several reuse-enabling activities, including inventorying datasets and registries, analysing data-quality and timeliness constraints, piloting metadata descriptions for dataset discovery and comparability, exploring HL7 FHIR profiling, including TEHIK's EEBase profiles, and testing semantic alignment approaches such as mapping local clinical concepts to SNOMED CT. Concrete outputs include a continuity-of-care-oriented conceptual data model, governance indicators and checklists for reuse readiness, and prototype metadata and governance tools [23].

The same report describes how reuse requirements were elicited and translated into semantic and governance artefacts. In early mapping work, three semistructured interviews were used to articulate a patient-oriented view of data collection for WHO stroke indicators, followed by mapping of data, terminologies, roles and activities. A public health and research view was developed

through discussions with National Institute for Health Development units. The report also describes systematic inventory and mapping work across datasets, registries and standards, and differentiates responsibilities for data production, stewardship, custodianship and reuse [23].

On the semantic and modelling side, the Health Sense report describes operational steps for aligning local data compositions with international semantic artefacts. Care-pathway data compositions were mapped to SNOMED CT concepts using the SNOMED CT browser; national HL7 FHIR profiling policy and TEHIK's EEBase profiles were reviewed; and profiling and mapping work was used as a basis for creating or extending FHIR profiles. The report uses ISO 23903, ISO 13940 and ISO 19502 to relate requirements, workflows and semantics. It also reports continuity-of-interoperability principles covering data, concepts and terminology. Practical challenges identified in the report include the cognitive burden on domain experts when reasoning across abstraction layers and the effort required to maintain coherence as requirements, standards and operational systems evolve [23].

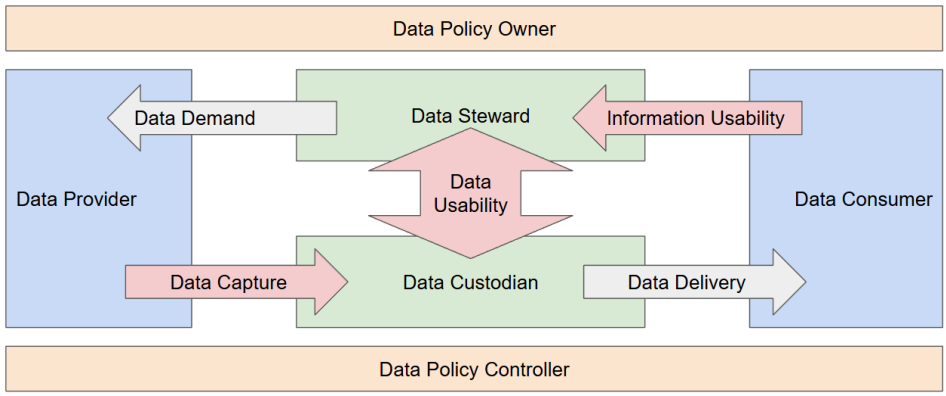

Figure 13: Conceptual governance cycle for multiple data use. The figure illustrates a cyclical governance logic for coordinating primary and secondary use of health data, focusing on how data demand, data capture, stewardship, custodianship and delivery are linked across organisational boundaries. It depicts governance as a coordination process connecting data demand and data supply over time (source: [IV]; [23]).

The governance cycle shown in Figure 13 is complemented by an explicit role-based breakdown of responsibilities reported in the Health Sense governance model. This role model distinguishes policy setting, compliance oversight, data production, data use, semantic and standards coordination, and operation of data services as separate responsibilities in multiple health data use.

Table 10: Summary of governance roles and responsibilities in multiple health data use, adapted from the Health Sense governance model (source: [23]).

Role	Core responsibility in data reuse
Data policymaker	Defines data policy, legal mandates and governance indicators
Data controller	Oversees compliance with data policy and monitors governance performance
Data producer	Generates primary data and aligns data capture with defined requirements
Data consumer	Specifies information needs and applies data in decision-making
Data steward	Harmonises requirements, standards and semantic models
Data manager	Operates data services and ensures conformity with standards

Taken together, the source material establishes the empirical starting point for Cluster 3. Metsallik et al. provide comparative evidence on how secondary-use governance is shaped by insti-

tutional structure, role allocation, stewardship and maturity of information-sharing capabilities in Saudi Arabia and Estonia. Ross et al. provide Estonia-specific design material showing how governance roles, semantic alignment, metadata, terminology work and standards-based modelling can be operationalised as coordination instruments for multiple use of health data. These source-based observations are mapped to the seven analytical attributes in the following section.

5.4.2 Interoperability and knowledge characteristics

This section aligns what the two Cluster 3 publications *report* with the seven analytical attributes defined in the theoretical framework (Chapter 3). The purpose is to state evidence-traceable patterns without extending into cross-paper interpretation beyond what can be justified by the publications.

Table 11: Framework-aligned summary of Cluster 3 findings.

Analytical attribute	Abstracted pattern	Empirical basis
[Instantiated] Institutional domains and logics	Multiple use of health data is governed through distinct institutional roles and value logics (policy/regulation, service provision, financing/administration, research/public health) whose misalignment becomes a primary barrier to reuse.	*Metsallik et al. (2024)*: reports fragmented stewardship and case-by-case access negotiation across policy authorities, national operators, providers, secondary users, and oversight bodies in both Estonia and Saudi Arabia. *Ross et al. (2023)*: formalises a role model and a governance cycle to allocate responsibilities for reuse.
[Implied] Macro-meso-micro localisation	Reported constraints concentrate primarily at meso-level interfaces (organisational roles, access procedures, stewardship arrangements) rather than at micro-level data capture alone or macro-level policy intent alone.	*Metsallik et al. (2024)*: Estonia reuse requests traverse sequential approval and coordination steps (ethics review, registry holders, central operator), while Saudi Arabia highlights cross-organisational interfaces between parallel provider subsystems and emerging national platforms. *Ross et al. (2023)*: governance cycle frames reuse as a recurring cross-organisational coordination loop.
[Implied] M0-M3 coordination levels	The publications report stronger operational/technical coordination than higher-order alignment and governance coordination, but do not explicitly position findings in M0-M3 terms.	*Metsallik et al. (2024)*: HISMM differentiates higher maturity in exchange/reporting from lower maturity in stewardship and anticipatory reuse planning, implying higher-order coordination gaps. *Ross et al. (2023)*: uses ISO 23903/ISO 13940/ISO 19502 as design frames to relate requirements, workflows, and semantics, implying M2/M3-type alignment work without naming it.

Analytical attribute	Abstracted pattern	Empirical basis
[Instantiated] Technological and modelling spaces	Technical integration is necessary but insufficient; reuse requires sustained semantic mediation across heterogeneous representations (terminologies, episodic vs longitudinal views, metadata descriptions) and across modelling artefacts.	*Metsallik et al. (2024)*: Estonia - despite a unified national infrastructure - still requires interpretation and transformation for reuse; Saudi Arabia requires bespoke integration across parallel subsystems. *Ross et al. (2023)*: reports concept alignment (SNOMED CT mapping), metadata/profiling work (HL7 FHIR/EEBase), and continuity-of-care-oriented modelling as concrete semantic and modelling-space activities supporting reuse.
[Instantiated] Interoperability capability	Capability maturity is uneven: exchange- and reporting-oriented capabilities are reported as more mature than stewardship-, governance-, and learning-oriented reuse capabilities.	*Metsallik et al. (2024)*: HISMM-based assessment indicates higher maturity in secure exchange/standardised reporting than in cross-organisational stewardship, reuse governance, and anticipatory planning; qualitative material attributes reuse delays to governance and coordination rather than missing infrastructure.
[Instantiated] Knowledge-based interoperability	Durable multiple use depends on making reuse purposes, provenance, and meaning explicit and maintainable across contexts through shared semantic artefacts (terminology alignment, structured metadata, longitudinal constructs) and practices that translate information needs into reusable representations.	*Ross et al. (2023)*: reports needs elicitation leading to mapping of data, roles, activities, and terminologies (e.g., WHO stroke indicator view); documents concept/model alignment (SNOMED CT mapping; continuity-of-care modelling using ContSys) and prototype tooling supporting reuse. *Metsallik et al. (2024)*: links reuse barriers to missing mechanisms that translate reuse needs into capture and stewardship practices.

[Instantiated] Governance of change and reuse	Governance for multiple use is reported as a cyclical coordination problem that requires explicit role allocation, defined reuse purposes, stewardship/accountability mechanisms, and monitoring instruments rather than ad hoc project-based agreements.	*Ross et al. (2023)*: governance cycle plus role model; reports governance indicators/checklists for monitoring reuse readiness and the work required to maintain coherence as requirements and artefacts evolve. *Metsallik et al. (2024)*: reports unclear stewardship allocation and fragmented reuse pathways, including ad hoc agreements in the Saudi case and governance gaps layered on mature infrastructure in Estonia.

The Table 11 enforces the seven-attribute schema and restores traceability by keeping each abstracted pattern tied to the empirical material and design artefacts explicitly reported in the two Cluster 3 publications.

5.4.3 Interim conclusion

Empirically, this cluster establishes that barriers to multiple use of health data persist in both mature and rapidly developing digital health systems when stewardship responsibilities, reuse purposes, and accountability/oversight arrangements are fragmented or misaligned, even where technical exchange capabilities are comparatively strong. [IV] [23]

It does not address, with direct evidence in this cluster corpus, how these governance and meaning-alignment challenges can be stabilised at higher-order coordination levels (e.g., explicit M0-M3 mechanisms) or through formalised semantic/conceptual interoperability artefacts beyond the design and exploratory outputs reported in Health Sense, and therefore several attributes remain implied rather than instantiated.

These limitations are taken up in Cluster 4, which examines how standards, semantic models, and conceptual interoperability frameworks can be mobilised as durable coordination mechanisms for governing change and reuse across contexts. Section 5.5

5.5 Cluster 4 - Standards, semantics & conceptual interoperability

5.5.1 Overview of cluster source material

This cluster reviews source material on standards-based semantic alignment, conceptual interoperability and terminology quality. The included materials address three connected but empirically distinct lines of work: the translation and national introduction of ISO 13940 (ContSys) in Estonia, the use of ContSys for semantic annotation of healthcare legislation, and the design of a terminology quality assurance methodology for national terminology infrastructure. The ContSys-related work is adjacent to the Health Sense programme discussed in Section 5.4, but the materials reviewed here are used for their reported semantic, terminological and conceptual-modelling contributions rather than as evidence of governance or reuse outcomes.

Kankainen et al. (2025a) examine the translation and national introduction of ISO 13940 (ContSys) in Estonia. The paper treats translation as a prerequisite for cross-stakeholder process connectability and concept harmonisation. It reports a translation project launched in October 2021, submitted for standardisation in May 2022, and published as a national standard in February 2023. The organisational set-up assigns the leading translation role to a terminology workgroup at the National Institute for Health Development (NIHD), with Tallinn University of Technology's Center for Digital Health contributing mapping to local terminologies and legislation and expert verification. The national eHealth system operator TEHIK explored architectural integration, but this strand was

not completed due to resource constraints. The Institute of the Estonian Language contributed as a consultant, and the Estonian Centre for Standardisation and Accreditation managed publication and public commentary.

The reported workflow consists of five tasks: translation of the concept system; translation of the remaining text; mapping to local terminologies and legislation; two rounds of proofreading; and submission with public commentary. The paper describes concrete artefacts supporting this work, including a shared spreadsheet with concept anchors and bilingual term and definition fields, a synonym and brainstorming field, and a separate artefact for concept associations, which was later moved from a spreadsheet to a web visualisation. Reported translation decisions include the use of country-specific notes to preserve the ContSys concept system while supporting local intelligibility, the exclusion of English deprecated terms, and the inclusion of English terms in parentheses in Estonian concept titles.

The paper also reports several semantic and terminological difficulties encountered during the translation and mapping process. These include "familiar label" ambiguities, such as *episode of care* being initially interpreted through an insurance-claim meaning, and a mapping-driven discrepancy concerning *referral* and *request*. In the latter case, ContSys differentiates mandate movement, while Estonian legislation collapses the labels but still encodes a traceable distinction in activity descriptions; national health data model documentation is reported to encode another distribution. The paper also notes early reuse of the translated concept system in other ongoing projects as an uptake indicator, without claiming downstream interoperability effects [26].

A representative structure of a translated ContSys concept entry, based on the entry "subject of care" / *patsient*, is shown in Table 12. The example illustrates how the Estonian publication records the preferred local term, synonyms, definition, ISO note, country-specific notes, examples and associations while preserving the underlying ContSys concept structure.

Table 12: Structure of a translated ContSys concept entry, illustrating the standardised elements reported in the Estonian ContSys publication. The example is based on the ContSys entry "subject of care" / patsient *(source: [26]).*

Concept element	Example content (English gloss for the Estonian publication)
Concept domain	Healthcare actor
Preferred term	*patsient* (subject of care)
Synonyms	*abisaaja* (beneficiary); *ravialune* (person under treatment); *andmesubjekt* (data subject)
Definition	A healthcare actor in the role of a person; someone who wants to receive, receives, or has received care in a healthcare system.
Notes (ISO NOTE)	A foetus may be considered a subject of care if it receives or has received treatment.
Notes (EE NOTE)	EE NOTE 1: Although Estonian law defines a patient as a natural person who has expressed the wish to receive, or is receiving, a healthcare service, the Estonian publication uses *patsient* also for a person who has received care in the healthcare system. EE NOTE 2: In some contexts other labels are used instead of *patsient*, such as a medical certificate applicant; in personal data processing the patient is referred to as a data subject.
Examples	Treated patient; physiotherapy client; a person selected for a population screening; a member of a diabetes group participating in health education; a person seeking health advice.

Concept element	Example content (English gloss for the Estonian publication)
Associations	Linked to treatment; health state; health need; personal health record; self-care; next of kin; consent capacity; subject of care desire; informed consent; refusal of assistance; healthcare contact; proxy decision rights; preference delay; and to the fact that healthcare activities, healthcare processes, authorisations, healthcare matters and health records are defined for, or concerning, the subject of care.

The example shows how country-specific notes and synonym mapping are used to make local terminological and legal mismatches explicit while retaining the ContSys concept system. In this case, the publication documents scope differences and contextual legal usage instead of smoothing them into a single local definition.

Kankainen et al. (2025b) propose a method for ContSys-based semantic annotation of legal texts, using the chapter of the Estonian Law of Obligations Act that defines the healthcare service provision contract as the empirical corpus. Semantic annotation is operationalised as a two-step manual procedure. First, relevant excerpts are identified and mapped to ContSys concepts, allowing multiple parallel concept assignments for the same excerpt. Second, relation annotation is used to disambiguate concept choices by applying ContSys relations, notes and examples as contextual constraints. The contract text is inserted into a semantic annotation platform configured with the full ContSys concept and relation inventory. The procedure is performed by one annotator and reviewed by a medical terminology expert with in-depth ContSys knowledge.

The study reports coverage of 15 out of 17 responsibility-related ContSys concepts in the analysed contract and presents the resulting concept-relation coverage diagram in Figure 14. The two missing concepts are treated as scope-boundary conditions, because they are defined in other legal instruments. In ContSys terms, the contract is represented as a *healthcare mandate* requiring *healthcare commitment* by the *healthcare provider* and either *informed consent* or *authorisation by law* when *consent competence* is missing. The mandate is assignable implicitly at the start of a *mandated period of care* or explicitly by accepting a *referral*. The paper reports a linguistically supported distinction between *referral* and *request* that is consistent with ContSys, because mandate movement differs. It also reports a divergence where the contract allows both *next of kin* and a legal *subject of care proxy* to express *informed consent*, while ContSys constrains this to proxies; this motivates a proposed relation adjustment in the diagram. Reported limitations include the expansion tendency of relation-based annotation, described as a difficulty in determining when annotation should stop, and the conclusion that automating the method with generative AI was not feasible at the time because proof-checking automated annotations requires even more elaborate ContSys knowledge [27].

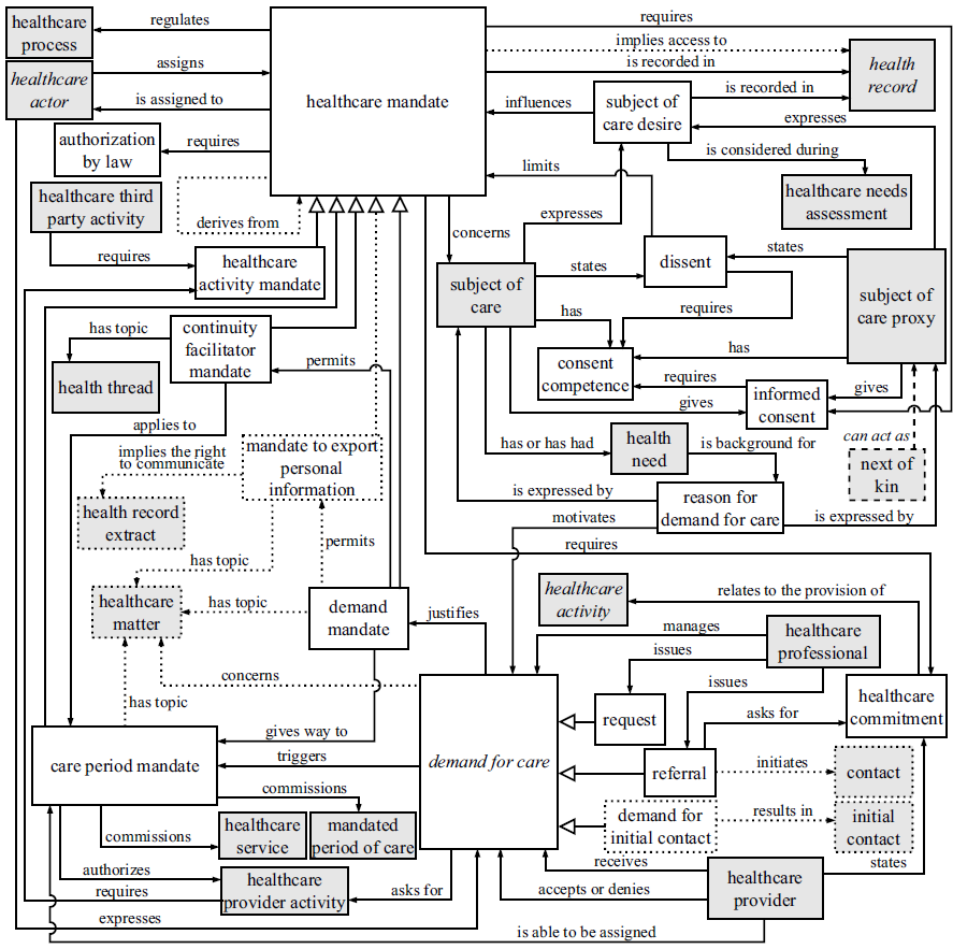

Figure 14: Coverage of ContSys responsibility-related concepts in the Estonian Law of Obligations. The figure shows a ContSys-based coverage map of the healthcare service provision contract in the Estonian Law of Obligations Act. Nodes denote ISO 13940 (ContSys) responsibility-related concepts and edges denote ContSys relations used to represent mandates, consent/authorisation, care periods, and role responsibilities. Solid lines indicate concepts/relations annotated in the contract; dotted lines indicate responsibility-related ContSys concepts not covered in the analysed legal scope; dashed lines indicate divergences or proposed relation adjustments reported by the authors. Abbreviations: ContSys = System of Concepts to Support Continuity of Care. (source: [27]).

Bossenko et al. (2025) design and validate a terminology quality assurance methodology intended to be operationalised within a terminology server. The paper frames semantic interoperability as dependent on consistent and machine-processable terminology evolution. It reports Cimino's desiderata as the primary quality basis and complements these with concept-model literature. The authors review 38 papers retrieved through a "concept model" AND "controlled medical vocabulary" query to select Oliver's GOLDMINE conceptual model and the SNOMED CT concept model. They also review the first 20 results of a "terminology work" AND "concept" AND "designation" query to select Suonuuti's *Guide to Terminology* as an additional source of criteria.

The paper defines a generic concept model in which a uniquely identified concept is linked to exactly one code, may have properties to formalise meaning, and is expressed through one or more designations characterised by language, acceptability, use and technical parameters. The model is shown in Figure 15. On this basis, the Terminology Quality Checklist specifies rules with acceptance criteria and a stated verification mode, distinguishing software-verifiable and human-verifiable checks across three lifecycle stages.

At the design-time code-system level, the checklist includes criteria such as explicit methodology for content discovery and expansion, non-semantic identifiers, formal definitions through properties and associations, and evolution mechanisms such as inactivation, replacement concepts and reactivation support. At the per-concept-version level, it includes criteria such as at least one designation, exactly one preferred term per language, preferred-term uniqueness checks per language, and human judgement for non-ambiguity where strict automation is not possible. At the per-release level, it includes uniqueness of formal definitions, treatment of "Not Elsewhere Classified" concepts through warnings or blacklists plus human evaluation, context-independent concept creation requirements, and consistency constraints such as avoiding active relationships to inactivated components.

For operationalisation, the software-verifiable rules are implemented in the TermX terminology server and verified in the context of the Health and Welfare Information Systems Centre. The paper further reports configurable rule sets by terminology type and exception-aware validation, such as handling homographs with error and warning notification levels. It also reports that the migration of hundreds of terminologies from multiple sources into TermX revealed frequent lack of graceful evolution support [28].

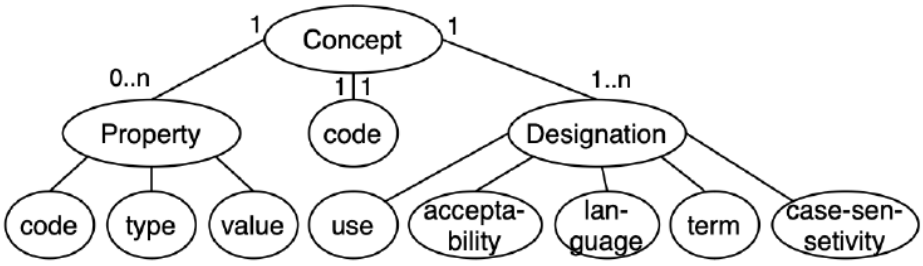

Figure 15: Generic concept model underlying the Terminology Quality Checklist (TQC). A concept, as a unit of meaning, is linked to exactly one code, may have properties that formalise its meaning, and is expressed through one or more designations characterised by language, acceptability and use (source: [28]).

Together, the reviewed source materials establish the cluster's empirical basis for analysing how semantic alignment is operationalised through standard translation, concept mapping, legal annotation, terminology modelling and terminology-quality controls. The following analytical section maps these reported materials to the seven analytical attributes used across the Results chapter.

5.5.2 Interoperability and knowledge characteristics

This section presents the reported results of the Cluster 4 publications in relation to the analytical dimensions introduced in the theoretical framework (see Chapter 3), with a focus on how the reported activities contribute to the *conditions* for knowledge-based interoperability rather than to interoperability outcomes. In line with the framework introduced earlier, knowledge-based interoperability is treated here as a capability emerging from coordinated semantic, conceptual, and governance arrangements, not as a property of individual systems or datasets. The alignment is summarised in a structured, framework-aligned table (Table 13).

Table 13: Framework-aligned summary of Cluster 4 findings (author's synthesis based on reported results).

Analytical attribute	Abstracted pattern	Empirical basis
[Instantiated] Institutional domains and logics	ContSys-based translation and annotation are reported as mechanisms for aligning meaning across legal, clinical, and technical domains without collapsing domain-specific mandates into a single "master" logic.	*Kankainen et al. (2025a)*: translation discussions and mapping surfaced concept-term divergences across legislation, professional usage, and national data model documentation; country-specific notes were introduced to clarify meaning without adapting the concept system. *Kankainen et al. (2025b)*: legal obligations in the healthcare service provision contract are represented using responsibility-related ContSys concepts and relations.
[Implied] Macro-meso-micro localisation	The reported semantic work is situated primarily at meso-level (stakeholder communities, professional interpretation, institutional terminology programmes), with micro-level disambiguation handled through concept-relation annotation practices.	*Kankainen et al. (2025a)*: multi-stakeholder translation set-up and workshops exposed interpretation differences (e.g., 'episode of care' readings) and required expert-mediated resolution. *Kankainen et al. (2025b)*: the two-step annotation method operationalises micro-level disambiguation through relation constraints while tolerating residual ambiguity where phrases express multiple synchronous aspects.
[Implied] M0-M3 coordination levels	The publications position conceptual standards and quality rules as meta-level coordination instruments (M2-M3) that require operational artefacts (e.g., servers, annotation platforms, rule execution) to be enacted at M1.	*Kankainen et al. (2025a)*: ContSys is treated as a generic concept system to support mutual understanding across stakeholders and to underpin further modelling strands. *Bossenko et al. (2025)*: Checklist rules are specified with acceptance criteria and verification modes and are implemented as executable validation within a terminology server.

Analytical attribute	Abstracted pattern	Empirical basis
[Instantiated] Technological and modelling spaces	Formal concept models and semantic annotation are reported as mediating structures connecting heterogeneous modelling spaces (concept systems, legal text, terminology services) and enabling computable validation and traceability of meaning.	*Bossenko et al. (2025)*: generic concept model (code, properties, designations) underpins rule formulation; rules reference Common Terminology Services 2 (CTS2)/FHIR terminology module structures and are operationalised in TermX. *Kankainen et al. (2025a)*: translation produced spreadsheet-based concept artefacts and association visualisations. *Kankainen et al. (2025b)*: annotation inserts legal text into an annotation platform and uses ContSys relations for disambiguation.
[Implied] Interoperability capability	The cluster reports semantic and quality assurance work as enabling conditions for interoperability (shared meaning, stable terminology evolution), but does not evaluate interoperability performance or downstream data-exchange outcomes.	*Kankainen et al. (2025a)*: translation is framed as a prerequisite for inter-connectable processes and concept harmonisation, while explicitly not claiming that translation changes existing policies or terminologies. *Bossenko et al. (2025)*: Checklist is framed as reducing design/publication errors and supporting machine-processable terminologies, without claiming guaranteed “high quality” outcomes.
[Instantiated] Knowledge-based interoperability	The publications specify mechanisms for durable meaning and reuse: concept harmonisation (meaning over labels), relation-based disambiguation for integrating legal knowledge, and rule-based quality control enabling terminology evolution over time.	*Kankainen et al. (2025a)*: shift from term harmonisation to concept harmonisation is stated; country-specific notes support local intelligibility without adapting the concept system. *Kankainen et al. (2025b)*: high coverage of responsibility concepts and relation-based disambiguation supports integration of legal obligations into process collaboration modelling. *Bossenko et al. (2025)*: lifecycle-staged rules with acceptance criteria support consistent terminology development and evolution.

Analytical attribute	Abstracted pattern	Empirical basis
[Instantiated] Governance of change and reuse	Change control is treated as an explicit design requirement, operationalised through standardisation processes (public commentary and publication) and through configurable, exception-aware validation rules embedded in terminology services.	*Kankainen et al. (2025a)*: translation project governance includes defined partner roles, two proofreading rounds, a public commentary process, and standards-body publication procedures; deliberate avoidance of concept-system adaptation via country-specific notes. *Bossenko et al. (2025)*: rules explicitly address evolution mechanisms (inactivation, replacement, reactivation), configurable rule sets per terminology type, and exception/notification management (warning/error levels; homograph exceptions) implemented and verified in a national terminology server context.

5.5.3 Interim conclusion

Empirically, this cluster establishes that standards translation, ContSys-based semantic annotation, and rule-based terminology quality assurance can be executed as concrete semantic artefacts and processes that stabilise meaning across legal, clinical, and technical domains and support durable terminology evolution (key [Instantiated] rows: Institutional domains and logics; Technological and modelling spaces; Knowledge-based interoperability; Governance of change and reuse).

It does not address measured interoperability performance, clinical outcomes, or realised secondary data use, and it only implies macro-meso-micro localisation and M0-M3 coordination levels because these are discussed as enabling conditions and implementation mechanisms rather than evaluated system-level effects ([Implied] rows: Macro-meso-micro localisation; M0-M3 coordination levels; Interoperability capability).

These limitations are taken up in Cluster 3 with respect to institutional governance, stewardship, and reuse readiness, and in Cluster 2 with respect to applied data use and decision support outcomes, while Cluster 1 provides the infrastructural and architectural baseline against which semantic instruments can be interpreted in the overall Results narrative.

5.6 Cross-cluster synthesis: framework attributes across empirical clusters

This section consolidates the four empirical clusters through the seven analytical attributes developed in the theoretical framework (Chapter 3). The synthesis contrasts observed *as-is* patterns with framework-implied *to-be* coordination requirements. It makes visible where national digital health capability is already stabilised, where it remains partial, and what forms of coordination would be required for progression toward more knowledge-ready, accountable, and adaptive interoperability. The strategic and normative implications of these requirements are developed in Chapter 6.

Table 14: Cross-cluster synthesis of framework attributes. The table contrasts empirically observed as-is patterns with framework-implied to-be coordination requirements across the four empirical clusters. The to-be column identifies coordination requirements derived from the theoretical framework; these requirements function as analytical bridges to the Discussion rather than as a standalone implementation model.

Analytical attribute	As-is: cross-cluster analytical pattern	To-be: framework-implied coordination requirement
Institutional domains and logics	Interoperability is realised under persistent institutional plurality; coordination stabilises interaction without resolving divergent clinical, administrative, technical, legal, and research logics.	Mediate explicitly between institutional domains, preserving legitimate plurality while coordinating interaction across domains rather than enforcing a single system rationality.
Macro-meso-micro localisation	Interoperability capability is unevenly distributed across levels; macro- and meso-level coordination dominate, while micro-level practices remain weakly aligned with national coordination intent.	Coordinate explicitly across levels by linking macro-level policy intent and meso-level governance arrangements to micro-level operational, organisational, and clinical practice.
M0-M3 coordination levels	Coordination is concentrated at infrastructural and formalisation levels (M0-M1), with fragmented advancement toward conceptual and paradigmatic coordination (M2-M3).	Model and govern M2-M3 coordination explicitly, linking conceptual intent, modelling alignment, and shared assumptions to operational artefacts and institutional reality.
Technological and modelling spaces	Interoperability is achieved between heterogeneous systems, but transitions between modelling spaces remain weakly articulated and unevenly governed across the ecosystem.	Manage transitions between technological and modelling spaces systematically through shared conceptual metamodels, transformation logic, and governance of semantic change.
Interoperability capability	Capability is strongest at the technical and syntactic levels, while semantic, conceptual, pragmatic, and institutional coordination remain partial and uneven.	Treat interoperability as a multi-level coordination capability in which semantic and conceptual alignment are governed alongside technical connectivity and organisational arrangements.
Knowledge-based interoperability	Knowledge artefacts and semantic instruments are demonstrably constructible, for example terminology quality rules, conceptual models, and pilot decision logic, but remain weakly coupled to routine data production and reusable decision-ready representations at scale.	Formalise, govern, and maintain reusable knowledge artefacts that support computer-assisted reasoning, decision support, learning, and reuse across contexts.

Analytical attribute	As-is: cross-cluster analytical pattern	To-be: framework-implied coordination requirement
Governance of change and reuse	Change control exists for selected shared semantic artefacts and is articulated in governance models, yet end-to-end change propagation and accountability for reuse across the data supply chain remain largely case-specific and resource-intensive.	Institutionalise mechanisms for governing change, reuse purposes, data-supply responsibilities, and accountability across organisational and system boundaries.

As shown in Table 14, the principal cross-cluster pattern is not a simple absence of interoperability, but an uneven distribution of interoperability capability. National exchange, access, and formal standardisation can be stabilised while decision relevance, semantic reuse, knowledge lifecycle management, and accountability for secondary use remain fragile. The framework-implied requirements therefore point to a need for explicit coordination across institutional domains, macro-meso-micro levels, M0-M3 abstraction levels, technological and modelling spaces, and knowledge-governance arrangements.

Taken together, the synthesis indicates that the observed limits are largely structural rather than narrowly technological. They reflect coordination gaps between exchange infrastructure, stabilised meaning, reusable knowledge artefacts, authorised change, and institutional responsibility. In capability terms, the prevailing *as-is* position corresponds to an *intermediate interoperability capability level*: stable technical and organisational coordination, partial semantic alignment, and weak institutionalisation of knowledge reuse (see Table 2).

These contrasts provide the analytical bridge to Chapter 6, where the framework-implied requirements are interpreted as part of the dissertation's normative argument for next-generation national digital health interoperability.

6 Discussion

This chapter interprets the results of the four empirical clusters through the theoretical framework and methodological stance developed earlier. It explains why mature national exchange-and-access infrastructures can coexist with fragile decision relevance, weak knowledge readiness, and project-bound reuse that does not yet amount to durable multiple use.

The chapter's central argument is that higher-order interoperability cannot be inferred from technical exchange, portal access, standards compliance, or infrastructure maturity alone. It depends on whether meaning, responsibility, reusable knowledge artefacts, and authorised change are governed together across institutional domains, abstraction levels, modelling spaces, and operational settings. Interoperability is therefore treated here as a governed coordination capability rather than as a cumulative maturity trajectory.

A central distinction is maintained between reuse and multiple use. Reuse denotes data use within a bounded functional or organisational scope, whereas multiple use denotes the capability of the same data to support heterogeneous decision contexts without loss of meaning, legitimacy, or accountability. Secondary use is treated primarily as a legal and policy category governing access and authorisation, not as evidence that multiple use capability has been achieved.

The chapter first makes the dissertation's answers to the research questions explicit (see Section 6.1). It then consolidates the cross-cluster interpretation, positions the theoretical contribution, derives implications for policy and system design, discusses limitations and future research, and closes with a concise synthesis of the explanatory argument.

6.1 Answers to research questions

This section makes the dissertation's answers to research questions explicit for traceability. Because the Results chapter is organised by empirical clusters and analytical attributes rather than by research questions (see Section 3.7), the answers below consolidate the cluster-level findings, the cross-cluster synthesis, and the Discussion's core interpretation into research question-level statements. These answers are not maturity-style scores; they specify how the dissertation's conclusions follow from the preceding chapters and from the clustered empirical corpus.

RQ1. Interoperability and architectural frameworks support an analytical interpretation of Estonia's national digital health system by making its layered structure, installed-base evolution, and coordination dependencies explicit. They are particularly useful for interpreting national-scale exchange-and-access, the stabilisation of shared infrastructure, and programme-level governance coordination (see Section 5.2). The cross-layer capability reading used in this answer is developed in the technological-spaces synthesis (see Section 3.4). Empirically, this interpretation is anchored in the longitudinal architectural baseline and system evolution reported in [I], [21], and [22]. However, the cross-cluster findings show that such frameworks become explanatorily limited when they are read as implying upward propagation from technical exchange to decision-relevant meaning, reusable knowledge, and accountable change. The dissertation therefore refines their use by treating interoperability as a non-accumulative coordination capability rather than as a linear maturity trajectory. This boundary condition is consistent with implementation-outcome syntheses that emphasise persistent coordination work beyond initial roll-out, while the dissertation specifies non-accumulativity as a structural property rather than as a contingent implementation deficit [29, 35]. Evidence pointer: see Table 8.

RQ2. Estonia's national shared-service arrangement enables robust exchange and bounded reuse, but it does not reliably enable decision-ready reuse, scalable clinical decision support, or personalised medicine beyond controlled pilots. The scaling argument is developed through the knowledge-space framing (see Section 3.5) and empirically tested in the decision-support and personalised-medicine cluster (see Section 5.3). The empirical stress tests reported in [II],

supported by the national feasibility framing [24] and pilot evidence [25], show that data availability does not translate into decision relevance when required variables are missing, temporally misaligned, embedded in narrative structures, or weakly coupled to decision logic and knowledge artefact governance. The limitation is therefore interpreted as a structural ceiling produced by misalignment between abstraction levels, modelling spaces, semantic commitments, and responsibility allocation, not primarily as an algorithmic or analytical-technique deficit. This is compatible with semantic interoperability scholarship that emphasises governed semantic assets as prerequisites for advanced reuse and decision support, while the dissertation strengthens the claim by making lifecycle coupling and authorised change explicit [37]. Evidence pointer: see Table 9.

RQ3. Trustworthy secondary use is shaped primarily by institutional logics and governance arrangements that allocate decision rights, stewardship responsibilities, accountability, and authorisation across actors and contexts. Exchange mechanisms and legal access permissions are necessary, but they do not by themselves create trustworthy multiple use (see Section 5.4). The institutional-logics framing that grounds this claim is set out in Section 3.6. Empirically, the argument is anchored in the comparative governance analysis [IV] and the Health Sense governance-and-standards case [23], which treat standards, data models, and access arrangements as governance-relevant coordination resources rather than as purely technical artefacts. The discussion therefore maintains a functional distinction between secondary use as a legal and policy category governing access and authorisation, and multiple use as an achieved capability in which the same data supports heterogeneous decision contexts without loss of meaning, legitimacy, or accountability. This aligns with governance frameworks emphasising legitimacy, accountability, decision rights, and operational access pathways, while the dissertation refines the mechanism by framing governance as part of the production of interoperability capability rather than as an external constraint on reuse [43, 44]. Evidence pointer: see Table 11.

RQ4. The cross-cluster synthesis supports a revised conceptual model of interoperability as a governed, non-accumulative coordination capability. Rather than extending maturity models or adding new interoperability levels, the dissertation specifies the boundary conditions under which higher-order, decision-relevant interoperability can be sustained at national scale (see Section 5.6). In this model, progress at lower abstraction levels does not propagate by default to decision relevance, knowledge reuse, or trustworthy multiple use. These higher-order effects depend on coupling mechanisms that institutionalise alignment between intent, meaning, knowledge artefacts, responsibility, and authorised change. This revised stance is empirically anchored in the architectural baseline (C1), the decision-reuse stress tests (C2), the governance analyses (C3), and the semantic and conceptual instrumentation work (C4), including standards translation, semantic annotation, and terminology lifecycle governance (e.g., [26–28]). Relative to related work, the model is compatible with ecosystem and orchestration accounts, but makes their dependency on governed semantic and knowledge resources explicit [31, 33]. Evidence pointer: see Table 14.

6.2 Core message and cross-cluster interpretation

This section consolidates what the four empirical clusters jointly establish about the nature and limits of interoperability in mature national digital health systems. For traceability, the consolidated cross-cluster configuration is summarised in Table 14. The purpose is not to restate cluster-level findings, but to identify the common configuration that explains why technically mature exchange-and-access arrangements can coexist with fragile decision relevance, weak knowledge readiness, and project-bound multiple use.

The clusters form a deliberate analytical progression rather than a maturity trajectory. Cluster 1 provides the architectural and historical baseline for national exchange-and-access. Cluster 2 functions as a stress test, showing that infrastructural robustness does not translate into decision-ready data or scalable clinical reuse. Cluster 3 adds an institutional and governance perspective,

demonstrating how legal ambiguity, fragmented responsibilities, and competing institutional logics constrain secondary and multiple use even where technical prerequisites exist. Cluster 4 examines the semantic and conceptual instruments intended to stabilise meaning, showing both their enabling role and the limits that follow when lifecycle coupling and stewardship remain weak.

Across these perspectives, a consistent pattern emerges: progress at lower interoperability levels does not reliably propagate to higher-order effects. Technical connectivity and procedural coordination can stabilise exchange, while semantic coherence, decision relevance, and accountable knowledge reuse remain fragile because coupling mechanisms between intent, meaning, knowledge artefacts, responsibility, and authorised change are insufficiently institutionalised. The limiting factors are therefore structural rather than primarily technological. They arise from gaps between abstraction levels, modelling spaces, and institutional domains, not from a simple absence of technical infrastructure.

This pattern clarifies the core explanatory mechanism used in the Discussion. Interoperability does not accumulate linearly from technical exchange toward semantic, knowledge-based, and decision-oriented capability. Decision relevance requires semantic and conceptual alignment that remains connected to actual decision needs. Knowledge-based interoperability requires formalised and governed knowledge artefacts across abstraction levels. Durable multiple use requires governance arrangements that authorise interpretation, allocate responsibility, and coordinate change. The cross-cluster configuration therefore points to weak coupling between data availability, meaning, knowledge, accountability, and authorised adaptation.

The observed configuration is best interpreted as an intermediate interoperability capability state relative to the capability conceptualisation developed in the theoretical framework. It combines stable technical connectivity and organisational coordination with partial semantic alignment and weak institutionalisation of knowledge reuse and change governance. It enables large-scale exchange and procedural coordination, but does not reliably support decision-relevant reuse, learning across cases, or adaptation to heterogeneous clinical and organisational contexts (See Section 3.4).

This intermediate capability state should not be read as an immaturity score or as a stage in a linear maturity model. It is an attribute profile: robust exchange-and-access and procedural coordination coexist with semantic alignment that remains weakly lifecycle-coupled to data production, and with governance arrangements that do not yet institutionalise knowledge stewardship, authorised change, and accountability chains for decision-relevant reuse. The profile is intermediate because the required coordination conditions are present only partially and unevenly. The limiting condition is not any single missing layer, but the absence of durable coupling among layers.

A central implication concerns autonomy and the human-centred ambitions often used to justify interoperability investments. In this dissertation, autonomy refers to legitimate decision authority and accountability within shared interoperability arrangements, not freedom from coordination. The empirical material shows a persistent gap between the promise of decision-relevant, person-centred, learning-oriented use and the operational realities of national infrastructures. Data may circulate at scale, yet the capacity to support contextual clinical judgement, shared decision-making, and learning across cases remains fragile.

This pattern is visible across the clusters. Decision-support experiments show that data availability does not yield locally adaptable decision support without reconstructive work and expert mediation. Semantic instrumentation work shows that meanings can be stabilised locally, but remain weakly coupled to operational capture and lifecycle governance. Governance studies show how responsibility and change-control arrangements drift upward without corresponding mechanisms for legitimate local adaptation and feedback.

More broadly, the material reveals a recurring tension between local autonomy and central coordination. Many interoperability arrangements stabilise exchange by privileging standard compliance, central processing, or procedural control. This can support access and exchange, but it

may also narrow actors' capacity to adapt data production, interpretation, and reuse to heterogeneous decision contexts. This loss of autonomy is not incidental: it is one mechanism through which exchange-and-access can be stabilised while decision-relevant, learning-oriented multiple use remains structurally constrained (see Table 14; Table 11).

When interoperability is operationalised primarily through centrally defined rules, compliance-driven semantics, or standardised processing layers, local actors increasingly encounter meaning and decision logic as fixed outputs rather than as governable coordination resources. Contextual meaning-work then shifts from legitimate adaptation into exception handling, while accountability for interpretation and change drifts upward without corresponding authorisation to adjust capture practices, semantic definitions, or knowledge artefacts at the point of production (see Table 13).

The cross-cluster synthesis also clarifies the longer-term shift in the interoperability problem observed across the dissertation's empirical material. In the earlier national EHR phase, the dominant challenge was document exchange, access, and transaction-level integration. As these capabilities became more established, the central problem shifted toward semantic readiness, computable knowledge, responsibility allocation, and governed change. Interoperability therefore appears less as a capability finally achieved once infrastructure and standards are in place, and more as a continuing process of aligning shared purposes, meanings, responsibilities, knowledge artefacts, and authorised adaptations across changing institutional and clinical contexts.

Governance is therefore not a downstream constraint added after technical and semantic interoperability have been achieved. It is part of the mechanism through which higher-order interoperability is produced. By allocating responsibility, legitimising use, maintaining knowledge artefacts, and authorising change, governance determines whether shared data remains confined to exchange and bounded reuse or becomes usable for decision-relevant, knowledge-based, and trustworthy multiple use.

Read together, the cross-cluster findings reinforce the core claim advanced in the theoretical framework: interoperability is an emergent, multi-layer coordination capability rather than an attribute of interfaces or individual systems. Higher-order effects do not arise automatically from lower-level progress; they depend on explicit coupling mechanisms that align intent, meaning, responsibility, knowledge artefacts, and authorised change across contexts. This provides an integrated analytical response to research questions and establishes the basis for the theoretical and policy implications developed in the following sections.

6.3 Contribution to interoperability theory

The preceding synthesis specifies the theoretical role of the dissertation's central reframing. Interoperability in national digital health is best analysed as a governed, non-accumulative coordination capability: progress in exchange infrastructure, access services, or standards compliance may be locally effective without necessarily producing decision relevance, knowledge readiness, or trustworthy multiple use at national scale.

The theoretical contribution has three connected elements. First, the dissertation treats higher-order interoperability as an emergent capability produced through explicit coupling between intent, meaning, knowledge artefacts, responsibility and authorised change across abstraction levels, institutional domains and technological spaces. In this view, interoperability is not a property of systems, interfaces or standards alone, but a capability sustained through relations between operational practice, semantic formalisation, knowledge artefacts and governance arrangements (see Section 3.2; Section 3.4).

Second, the dissertation specifies why mature interoperability arrangements may encounter a structural ceiling. Stable exchange and procedural coordination can coexist with weak semantic continuity and project-bound knowledge reuse when decision needs, data capture, conceptual models, knowledge artefacts and accountability arrangements are not linked through durable feed-

back and change-control mechanisms. This explains the intermediate capability state identified in the cross-cluster interpretation: the limitation is not lack of infrastructure, but insufficient cross-level coupling between data production, semantic and conceptual alignment, knowledge lifecycle governance and institutional responsibility.

Third, the dissertation clarifies the theoretical role of coherence, composability and governed autonomy. Coherence denotes the stability of meaning, responsibility and decision logic across contexts. Composability denotes the capacity of actors, data, models and knowledge artefacts to be combined across changing decision situations without loss of interpretability or legitimacy. Governed autonomy denotes legitimate local capacity to interpret, adapt and extend shared resources within explicit accountability and authorisation arrangements. Together, these concepts shift interoperability theory away from cumulative maturity narratives and toward a capability-oriented account of how national digital health systems can support decision-relevant, knowledge-based and human-centred use.

This reframing also clarifies the role of semantic and conceptual coordination. Semantic models, terminologies, data quality rules and decision logic are not merely technical resources; they function as coordination artefacts that make decisions, meanings and responsibilities comparable across organisational and institutional boundaries. Their theoretical significance depends on lifecycle governance. Semantic interoperability is insufficient unless linked to knowledge lifecycle management and authorised change: without stewardship, validation, versioning and accountable revision, semantic instruments may improve local consistency while remaining too fragile to support scalable reuse or learning (see Section 3.3; Section 3.5).

The macro-meso-micro perspective further specifies where this coordination work occurs. Macro-level policy intent must be translated into meso-level governance arrangements that make micro-level decision demand actionable for data capture, semantic maintenance and knowledge artefact revision (see Section 3.1). Advanced interoperability therefore depends less on central control than on governable feedback loops through which autonomous actors can contribute to shared information and knowledge spaces without fragmenting meaning or accountability.

This theoretical stance makes data-sharing paradigms analytically relevant. Document-centric exchange, registry-based sharing and more event-driven or feedback-enabled arrangements should not be treated only as implementation options; they represent different coordination regimes. They differ in how visible decision demand becomes, how quickly missing or unreliable information can affect data production, and how change is authorised. From this perspective, knowledge-based interoperability is constrained not only by semantic expressiveness, but by the ability of the sharing regime to institutionalise feedback between decision-making, data production and knowledge governance (see Section 5.3).

Taken together, the dissertation extends interoperability theory by showing that the decisive question is not whether technical, semantic, organisational and governance layers are present, but whether they are coupled in ways that sustain coherence, composability and governed autonomy over time. This provides a theoretical explanation for why digitally mature national systems may achieve stable access and exchange while remaining structurally constrained with respect to decision support, learning health systems, trustworthy multiple use and person-centred care.

6.3.1 Artificial intelligence as a boundary case for interoperability theory

Artificial intelligence functions in this dissertation as a boundary case for the proposed interoperability concept. AI is sometimes presented as a way to compensate for semantic heterogeneity, weak standard adoption or fragmented data landscapes by learning from data and automating harmonisation work. For example, machine-learning approaches have been used to map heterogeneous laboratory test representations to standard codes such as LOINC, explicitly in response to inconsistent standard use as a barrier to interoperability and reuse [129].

Viewed through the capability perspective developed here, AI does not remove the need for interoperability governance. It can accelerate reasoning, classification, mapping and prediction where data, meaning and purpose are sufficiently explicit, but it cannot substitute for conceptual boundary-setting, responsibility allocation, data quality, provenance, validation or authorised change. Governance-oriented guidance on trustworthy AI similarly frames accountability, oversight and institutional control as necessary conditions rather than optional safeguards [130]. The dependence of medical AI on data quality further reinforces this point: model reliability remains bounded by the integrity, completeness and interpretability of the underlying datasets [131].

The empirical material supports this interpretation. The decision-support and personalised-medicine cases show that algorithmic or AI-enabled functionality remains dependent on pre-existing semantic alignment, decision-ready data, explicit conceptualisation and governed responsibility structures (see Section 5.3; Table 9). Where such conditions are absent, decision support tends to rely on stand-alone tools, parallel data capture and manual coordination rather than on persistent, longitudinal knowledge representations embedded in routine services [II] [24, 25].

AI therefore changes the tempo and scale of interoperability challenges, not their underlying conditions. Where meaning, responsibility and authorised change are well governed, AI may shorten the latency between emerging decision needs, knowledge formalisation and information provision. Where these couplings remain weak, AI may amplify the consequences of poorly governed semantics, fragile data quality and contested legitimacy rather than resolving them.

For this reason, AI is treated here as a scaling pressure on knowledge-based interoperability, not as a separate empirical object or as an alternative to interoperability governance. Its theoretical relevance lies in making the dissertation's core claim more visible: higher-order digital health capability depends on governed relations between data, meaning, knowledge, responsibility and authorised change, even when advanced analytical techniques are available.

6.4 Implications for policy and system design

Many components required for advanced interoperability already exist or are emerging in national digital health systems, including shared infrastructure, standards, terminologies, semantic models, data quality rules and decision-support artefacts. Their systemic impact remains limited, however, when these assets are governed as isolated technical, semantic or project-specific components rather than as shared coordination resources for integrated, knowledge-driven and human-centred care. The core policy challenge is therefore not only to extend infrastructure, but to create institutional conditions under which existing assets can be maintained, trusted, adapted and reused across heterogeneous decision contexts.

The preceding discussion also clarifies the role of AI and advanced analytics. AI may accelerate mapping, interpretation, prediction and decision support, but it does not remove the need for semantic readiness, data quality, provenance, accountability and authorised change. Without these conditions, AI-based solutions are likely to amplify fragmentation, opacity or contested legitimacy rather than compensate for weak interoperability governance.

Read as analytically derived boundary conditions rather than as a prescriptive blueprint, the findings imply a minimal governance stack for national digital health interoperability:

- Needs-and-intent articulation: legitimate clinical, regulatory, research, innovation and patient-centred decision needs must be explicitly articulated as a reference point for data capture, semantic design and knowledge governance. This corresponds to the business view as an articulation space rather than as a managerial control layer (see Section 3.3).
- Stewardship of semantic and knowledge artefacts: terminologies, information models, data quality rules, decision logic and other knowledge artefacts require accountable roles, mandates and maintenance processes. Without such stewardship, semantic instruments may

remain analytically sound but operationally fragile (see Section 5.5).

- Lifecycle governance across abstraction levels: versioning, validation and authorised change management must link operational data production, semantic formalisation and evolving knowledge claims across M0-M3. This is necessary if meanings, responsibilities and decision contexts are to remain aligned over time (see Section 3.5).
- Legitimised decision support as an institutional function: clinical decision support and personalised medicine require more than local technical deployment. Policy frameworks must specify who is authorised to define, maintain, revise and audit decision logic and its evidential basis beyond project settings (see Section 5.3).
- Accountability and authorisation chains for reuse: trustworthy multiple use requires clear allocation of responsibility for interpretation, reuse and downstream consequences across institutional boundaries. This shifts governance from procedural access control toward accountable reuse, contestability and legitimate adaptation (see Section 5.4).
- Actionable feedback loops from decision practice: gaps observed in practice, such as missingness, semantic misalignment or unreliable information, must become institutionally actionable for revising capture practices, event definitions, semantic commitments and knowledge artefacts. This is particularly important where decision-support use exposes the limits of routine data production (see Section 5.3).

Together, these elements specify the conditions under which legally permitted secondary use can develop into trustworthy multiple use. Access rights and technical availability are necessary but insufficient: the same data can support heterogeneous clinical, regulatory, research, innovation and patient-centred contexts only when meaning, responsibility, evidence requirements and authorised change remain aligned across those contexts.

These implications also suggest that national digital health policy should treat interoperability as a capacity for institutional and technical responsiveness, not as a fixed end state achieved through infrastructure deployment or standards compliance. Governance arrangements must stabilise shared artefacts while also enabling them to evolve as clinical evidence, technologies, care practices and institutional purposes change. Responsiveness is therefore not a deviation from strategic control, but a condition for sustaining legitimacy and coherence in a continuously developing health information environment.

A further implication concerns the operationalisation of ethical and legal principles. Transparency, accountability, consent, purpose limitation and fairness cannot be secured only through procedural safeguards or access-control mechanisms. They also have to be embedded at the level of meaning, knowledge and responsibility: in how data categories are defined, how decision logic is validated, how provenance is maintained, how reuse is authorised, and how contested interpretations can be challenged. Ethics-by-design therefore concerns not only restricting access, but governing the conditions under which data and knowledge artefacts remain interpretable, legitimate and accountable across contexts.

Finally, the findings have implications for autonomy-enabling participation. From the perspective of knowledge-based interoperability, autonomy does not mean reduced coordination or weaker governance. It means that healthcare providers, researchers, innovators, patients and other actors are legitimately able to contribute to, reinterpret and extend shared data and knowledge resources within explicit accountability and authorisation arrangements. Without an articulated business view and lifecycle governance, distributed adaptation risks becoming fragmentation. Under appropriate governance, however, such conditioned autonomy expands the space for innovation, learning and participation while preserving systemic trust and coherence.

Taken together, effective policy and system design for national digital health interoperability must prioritise governance capability, institutional clarity and knowledge stewardship alongside technical and organisational investments. These conditions are necessary for translating existing

interoperability assets into durable support for decision-making, learning, trustworthy multiple use and human-centred care, rather than assuming that such outcomes will emerge automatically from continued technical integration.

6.5 Limitations and directions for future research

The limitations outlined below delimit the scope of the dissertation's claims and indicate directions for future research. They follow from the dissertation's theoretical framing and methodological design. The study examines national digital health as a long-term socio-technical and institutional coordination problem, and therefore prioritises explanatory depth, cross-level interpretation and analytical transferability over benchmarking, prediction or direct performance evaluation.

The theoretical framework developed in Chapter 3 is intentionally integrative. It brings together layered interoperability models, institutional governance perspectives, model-driven and abstraction-level reasoning, and knowledge-based conceptions of coordination. This makes it possible to interpret interoperability as an emergent coordination capability and to identify failures of coupling between technical infrastructure, semantic alignment, knowledge artefacts, institutional responsibility and authorised change. The trade-off is that the framework does not produce a maturity score, evaluative taxonomy or parsimonious causal model. It is therefore most useful for strategic governance analysis and theoretical explanation rather than for short-term implementation benchmarking.

The methodological design follows this analytical ambition. The dissertation adopts a qualitative, integrative multi-study design combining longitudinal case analysis, comparative institutional examination and design-oriented empirical work. The empirical material consists of peer-reviewed publications, project artefacts, policy documents and documented system-level practices, complemented by expert knowledge embedded in the research process. This design enables analysis of institutional path dependencies, design rationales and coordination tensions that unfold over extended time horizons and across organisational domains. Its findings are therefore analytically rather than statistically generalisable.

First, the empirical material is strongly anchored in the Estonian national digital health context, complemented by selected comparative and project-based cases. This focus supports longitudinal analysis of a digitally mature national system and allows the dissertation to examine how early architectural and governance choices continue to shape later interoperability capability. However, contextual specificity limits direct transfer to settings with different legal traditions, institutional capacities, financing arrangements or levels of digital maturity. The analytical framework is conceptually transferable, but concrete manifestations of governance capability, semantic stewardship and authorised change may differ substantially. Future research should therefore test the framework across contrasting national and institutional contexts.

Second, the dissertation examines interoperability as a structural and institutional coordination capability rather than as a directly measured performance outcome. This enables analysis of why robust exchange-and-access arrangements may coexist with fragile decision relevance, weak knowledge readiness and project-bound multiple use. However, it does not support numerical assessment, ranking or probabilistic claims about system performance. Future research could complement this approach through mixed-method designs that operationalise selected attributes of governance, semantic readiness, knowledge stewardship or feedback-enabled interoperability while retaining sensitivity to institutional context.

Third, although the dissertation foregrounds governance and knowledge stewardship as central to higher-order interoperability capability, it does not empirically test alternative governance models or policy instruments in controlled or experimental settings. The conclusions are therefore primarily diagnostic and explanatory rather than evaluative. Design-oriented research, pilot interventions and longitudinal policy experiments are needed to examine how different steward-

ship arrangements, accountability structures, lifecycle governance mechanisms and authorisation models affect decision support, multiple use of health data and autonomy-enabling participation in practice.

Fourth, researcher involvement in several empirical contexts introduces interpretive risk. This risk is mitigated through the use of documented artefacts, publication-level anchoring, explicit analytical attributes and a separation between empirical reporting and cross-cluster interpretation. Nevertheless, the analysis reflects the perspective of a researcher-practitioner working close to the development and governance of national digital health systems. Future studies could strengthen this line of work through independent replication, broader stakeholder interviews and comparative analyses involving clinicians, patients, policymakers, technology providers and governance bodies.

Fifth, human-centred and 5P-oriented care is addressed indirectly through infrastructural, semantic and institutional preconditions rather than through measured clinical, experiential or participatory outcomes. The dissertation does not analyse patient-reported outcomes, professional experience, shared decision-making practices or care-process effects at the point of service delivery. Future research should connect interoperability arrangements to variations in clinical practice, patient participation, professional autonomy and learning-oriented care, thereby empirically testing the relationship between interoperability capability and human-centred digital health.

Taken together, these limitations delimit the dissertation's claims and outline a coherent research agenda. The next step is to move from diagnosing structural interoperability ceilings toward empirically grounded strategies for building knowledge-based, autonomy-enabling and human-centred national digital health systems. Such research should examine not only whether data can be exchanged or reused, but whether meanings, responsibilities, knowledge artefacts and authorised change mechanisms remain coherent as clinical evidence, technologies, care practices and institutional purposes evolve.

6.5.1 Scope of normative claims

The normative implications developed in this chapter should be read as analytically derived boundary conditions, not as a policy blueprint, target architecture or implementation roadmap. The dissertation specifies coordination requirements and failure modes that any viable national digital health design must address if decision support, learning-oriented reuse, trustworthy multiple use and autonomy-enabling participation are to be realised without undermining legitimacy, trust or contextual meaning.

6.6 Concluding synthesis

This dissertation concludes that national digital health interoperability is best understood as more than the cumulative outcome of technical exchange, access provision, standards compliance, or isolated governance arrangements. Across research questions, the analysis shows that mature national infrastructures can successfully stabilise exchange, access, and document flow, while their capacity to support decision relevance, knowledge readiness, trustworthy multiple use, and person-centred care depends on further coordination conditions. The decisive transition is from infrastructure availability toward durable coupling between meaning, responsibility, knowledge artefacts, decision logic, and authorised change.

Returning to the conceptual framing introduced in the opening chapter (see Section 1.3), the dissertation clarifies what is needed for access and exchange to develop into semantic continuity, reusable knowledge, and ethically governed digital health. Higher-order interoperability requires coherence, composability, and governed autonomy. Coherence refers to the stability of meaning, responsibility, and decision logic across contexts; composability refers to the capacity to combine data, models, actors, and knowledge artefacts across changing decision situations without loss of interpretability or legitimacy; and governed autonomy refers to the capacity of actors to adapt and

use shared resources within explicit accountability and authorisation arrangements. These conditions define interoperability as a socio-technical and institutional capability rather than as a technical state (see Section 3.4).

The empirical synthesis identifies the structural and institutional conditions through which this capability can be strengthened. Decision-support and personalised-medicine cases show that technically available and partly structured data require semantic, temporal, and contextual alignment before they can support computable clinical reasoning. Governance and secondary-use cases show that legal access and reuse permissions become trustworthy multiple use when they are complemented by responsibility allocation, interpretive accountability, and authorised change. Standards and semantic instruments show that formalised meaning becomes scalable when linked to stewardship, lifecycle management, validation, and change control. Together, these findings support the cross-cluster interpretation developed earlier in the Discussion (see Section 6.2).

The practical implication is that next-generation national digital health should build on existing exchange infrastructure by adding explicit and durable mechanisms for aligning clinical and policy intent, semantic and conceptual models, knowledge artefacts, institutional responsibilities, and feedback from practice to data production and system change. Through such mechanisms, operationally mature national digital health systems can become more capable of supporting integrated, knowledge-driven, trustworthy, and person-centred care.

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Abstract

Interoperability and Governance in National Digital Health: A Framework-Based Argument for Integrative and Knowledge-Driven Approach

National digital health is increasingly expected to support integrated, knowledge-driven, and person-centred care. This expectation goes beyond reliable data exchange and includes clinical decision support, learning health system functions, secondary and multiple use of health data, personalised medicine, and cross-domain coordination. However, empirical experience from large-scale digital health infrastructures shows that mature access and exchange capabilities do not by themselves ensure the consistent interpretation of health data, their responsible reuse, or their transformation into decision-relevant knowledge.

This dissertation investigates interoperability and governance in national digital health, using Estonia's national electronic health record infrastructure as the central empirical anchor and complementing it with comparative insights from international digital health initiatives. The empirical material is organised into four clusters: national electronic health record architecture and longitudinal development; decision support and personalised medicine; governance of secondary and multiple use of health data; and standards, semantics, and conceptual interoperability.

The analysis is based on an integrated theoretical framework that combines a macro–meso–micro coordination perspective with Tolk's Levels of Conceptual Interoperability Model (LCIM), Blobel's Generic Component Model (GCM) and its standardised expression in ISO 23903, ISO 13940 (ContSys), and a knowledge-based interoperability perspective. Together, these frameworks make it possible to analyse interoperability not merely as technical data exchange, but as a problem of coordinating meaning, knowledge models, decision contexts, and governance.

Through a framework-based and abductive synthesis, the dissertation shows that national digital health infrastructures may institutionalise access to data and data exchange while leaving meaning, knowledge use, responsibility, and governance of change weakly coupled. These gaps become especially visible when the same data are expected to support different clinical, research, administrative, and policy decision contexts.

The dissertation contributes to conceptualising interoperability as a governed capability of national digital health: the capacity to coordinate technical infrastructure, shared meaning, knowledge use, and authorised and accountable institutional change in support of integrated, knowledge-driven, and person-centred care.

Kokkuvõte

Koosvõime ja valitsemine riiklikus digitaaltervises: raamistikupõhine käsitlus integreerituse ja teadmuspõhisuse toetuseks

Riiklikult koordineeritud digiterviselt oodatakse üha enam integreeritud, teadmuspõhise ja inimkeskse tervishoiu toetamist. See ootus ei piirdu töökindla andmevahetusega, vaid hõlmab ka kliinilist otsustustuge, õppiva tervisesüsteemi funktsioone, terviseandmete teisest ja mitmekordset kasutust, personaalmeditsiini ning valdkondadeülest koordineerimist. Suuremahuliste digitervise taristute empiiriline kogemus näitab siiski, et küps ligipääsu- ja andmevahetusvõimekus ei taga iseenesest terviseandmete järjepidevat tõlgendamist, vastutustundlikku taaskasutust ega nende muutumist otsustusrelevantseks teadmuseks.

Käesolev väitekiri uurib koosvõimet ja valitsemist riiklikus digitervises, kasutades Eesti riikliku elektroonilise terviseloo infrastruktuuri keskse empiirilise ankruna ning täiendades seda võrdlevate tähelepanekutega rahvusvahelistest digitervise algatustest. Empiiriline materjal on koondatud nelja klastrisse: riikliku elektroonilise terviseloo arhitektuur ja pikaajaline areng; otsustustugi ja personaalmeditsiin; terviseandmete teisese ja mitmekordse kasutuse valitsemine; ning standardid, semantika ja kontseptuaalne koosvõime.

Analüüs põhineb integreeritud teoreetilisel raamistikul, mis ühendab makro–meso–mikrotasandi koordineerimise vaate Tolk'i Levels of Conceptual Interoperability Model'i (LCIM), Blobel'i osiste üldmudeli (GCM) ja selle ISO 23903-s standarditud väljenduse, ISO 13940 ehk ContSys'i ning teadmuspõhise koosvõime käsitlusega. Need raamistikud võimaldavad käsitleda koosvõimet mitte üksnes tehnilise andmevahetuse, vaid tähenduse, teadmusmudelite, otsustuskontekstide ja valitsemise koordineerimise probleemina.

Raamistikupõhise ja abduktiivse sünteesi tulemusena näitab väitekiri, et riiklikud digitervise taristud võivad institutsionaliseerida andmetele ligipääsu ja andmevahetuse, jättes samal ajal tähenduse, teadmuskasutuse, vastutuse ja muutuste valitsemise nõrgalt seotuks. Need lüngad muutuvad eriti nähtavaks olukordades, kus samu andmeid eeldatakse toetavat erinevaid kliinilisi, teaduslikke, administratiivseid ja poliitikakujunduslikke otsustuskontekste.

Väitekiri panustab koosvõime käsitamisse riikliku digitervise valitsetud võimekusena: suutlikkusena koordineerida tehnilist taristut, jagatud tähendust, teadmuskasutust ning volitatud ja vastutustundlikku institutsionaalset muutust integreeritud, teadmuspõhise ja inimkeskse tervishoiu toetamiseks.

Appendix 1. Map of data flows in Estonia

Data Flow	Source	Steward	Consumer	Governor
Distribution of personal health status data				
Clinical summaries	Patient records maintained by medical professionals	TEHIK Digilugu	Medical professionals, home users	ETIS*
Emergency service data	Emergency call center, Ambulance services	TerK eAmbulance	Ambulance services	TerK
Laboratory data	Laboratory information systems	Medipost, Digilugu	Medical professionals, home users	Medisoft, ETIS*
Imaging studies	Radiology information systems	National Image Bank	Radiologists, Medical professionals	ETIS*
Medical certificates	Patient records	TEHIK Digilugu	Home user, Road Administration, Social Insurance Board	ETIS*
Health declarations	Home user	TEHIK Digilugu	Medical professional	ETIS*
Changing rights related to healthcare services				
Prescriptions	Patient records	TerK ePre-scription	Pharmacies, medical professionals, home users	TerK
Laboratory orders	Patient records	Medipost	Laboratories	Medisoft
Referrals	Patient records	TEHIK Digilugu	Medical professionals	ETIS*
Consultations	Patient records	TEHIK Digilugu	Medical professionals	ETIS*
Cancer screening invitations	Digilugu, Healthcare providers, NIHD	TEHIK Cancer Screening Registry	Healthcare providers, home users	NIHD

Data Flow	Source	Steward	Consumer	Governor
Registration as a healthcare professional	Healthcare provider, Health Board	TEHIK Medre	Healthcare providers, Digilugu	Health Board
Issuance of operating license	Healthcare provider, Health Board	TEHIK Medre	Healthcare providers, Digilugu	Health Board
Authorization of medicines, special foods, and medical devices	Medicines Agency	TEHIK Medicines Register	Healthcare providers, home users	Medicines Agency
Patient listing with a family doctor	Family doctor service providers	TerK Health Insurance Information System	Healthcare providers	TerK
Changing rights related to health data				
Consent for data use in Digilugu	Individual	TEHIK Digilugu	Healthcare providers	ETIS*
Consent for use of data in national registries	Individual	RIA Consent Service	Third parties	In development – Data Protection Act, Public Information Act
Audit log of Digilugu data use	Digilugu	TEHIK Digilugu	Individual	ETIS*
Assisted access to Digilugu	Social worker	TEHIK Digilugu	Medical professional, home user	ETIS*
Decision support based on health data				
Time-critical data	Digilugu	TEHIK Digilugu	Medical professionals	ETIS*
Data viewer	Digilugu	TEHIK Data Viewer	Medical professionals	ETIS*
Drug interaction decision support	ePrescription	Synbase	Medical professionals	TerK

Data Flow	Source	Steward	Consumer	Governor
Clinical decision support	Digilugu, Patient record	TEHIK Health Insurance Fund Decision Support	Medical professionals	TerK
Research data based on health data				
Epidemiological data	Patient records	NIHD Medical Registries	Researchers	NIHD
Genetic and health data	Patient records, Digilugu, Medical registries, genetic studies, medical bills	Biobank	Researchers	University of Tartu
Decisions on health service financing				
Treatment bill data	Healthcare provider	TerK Health Insurance System	TerK, Researchers	TerK
Health service price list	TerK	TerK Service List	Healthcare providers	Ministry of Social Affairs
Family doctor lists	TerK	TEHIK Medre	Healthcare providers, home users	TerK
Basic registries				
Population registry	Local governments	SMIT Population Register	Healthcare providers, Researchers	Ministry of the Interior
Legal entities register	Legal entity	RIK Business Register	X-road, Digilugu, Healthcare providers, home users	Tartu County Court
Address registry	Local governments	KMIT ADS	Digilugu, Healthcare providers	Land Board
Standards for health data and their dissemination				

Data Flow	Source	Steward	Consumer	Governor
Digilugu data structures, formats, and lists	TEHIK	TEHIK Information Center	Digilugu, Software developers	ETIS*
Disease classification	Ministry of Social Affairs	MoSA ICD web	Digilugu, Healthcare providers	Ministry of Social Affairs
Laboratory services classification	Medical labs, ELMÜ	TEHIK e-Lab Admin Tool	Digilugu, Healthcare providers	ETIS*
Services of the secure electronic data exchange platform				
Trust services for digital identity	Legal entity, individual	SK ID Solutions, GuardTime	X-road, Digilugu, Healthcare providers, home users	RIA
Secure messaging platform (X-road) and portals (MISP)	Legal entity, individual	RIA	Digilugu, Healthcare providers	Government of Estonia

*According to its statute, ETIS has two responsible authorities — the Ministry of Social Affairs (MoSA) and the Health and Welfare Information Systems Center (TerK).

Appendix 2. Cross-source analytical mapping

Explanatory note.
This appendix provides a consolidated, theory-aligned overview of how the source material included in the dissertation relate to the core analytical dimensions introduced in the theoretical framework. Unlike the Results chapter, where empirical findings are presented through detailed, attribute-specific tables at cluster level, this table operates as a cross-source synthesis. It maps each paper to its primary coordination scope (macro–meso–micro), dominant institutional logics, and key implications for interoperability and governance, using established framework abbreviations (e.g. LCIM, GCM/ISO 23903, KBI) to maintain conceptual consistency while reducing descriptive redundancy.

Publication	Coordination scope (macro–meso–micro)	Institutional logic / governance tension	Implications for interoperability & governance (LCIM / GCM / KBI)
Kankainen et al. (ContSys annotation)	Aligns macro-level legal intent with an M3-level conceptual standard; establishes meso-level semantic–conceptual coordination shaping micro-level documentation.	Mediation between legal–administrative and professional logics via explicit conceptualisation.	Reduces recurring legal–semantic reconciliation costs; provides an M3 reference model (GCM) enabling LCIM-3→6 progression and a shared conceptual space (KBI).
Kankainen et al. (ContSys experience)	Tests macro policy-backed modelling in meso-level organisations; exposes micro-level workflow and cognitive frictions.	Tension between professional autonomy and standard-driven rationalisation; uneven readiness.	Shifts costs from downstream reconciliation to upfront modelling/training; shows practice-constrained LCIM-3 interoperability and limits of shared conceptual modelling.
Bossenko et al. (Terminology control)	Positions terminology governance as macro-level infrastructure supporting meso-level consistency and micro-level interpretation.	Reinforces professional logic through shared language authority and explicit quality rules.	Lowers misinterpretation and rework costs; stabilises LCIM-3 semantic interoperability and strengthens the semantic layer of KBI.

Publication	Coordination scope (macro–meso–micro)	Institutional logic / governance tension	Implications for interoperability & governance (LCIM / GCM / KBI)
Metsallik et al. (Secondary data use)	Makes macro-level privacy and legitimacy constraints explicit; identifies meso-level reuse bottlenecks affecting micro-level scenarios.	Conflict between data-protection, public-value, and innovation logics; legitimacy dominates.	Reveals hidden transaction costs of fragmented governance; exposes gap between LCIM-2/3 exchange and legitimate multiple use; absence of governed KBI for secondary use.
Ross et al. (Health Sense)	Contributes to macro-level data standardisation; bridges meso-level institutional practice and micro-level clinical sense-making.	Partial alignment of managerial optimisation and professional judgement.	Reduces costs of heterogeneous interpretations; strengthens structural and semantic foundations (LCIM-2/3) and provides scaffolding for analytic KBI reuse.
Bertl et al. (Decision support in PTSD)	Demonstrates micro-level DDSS feasibility on national EHR data; tests meso-level readiness for algorithmic mediation.	Tension between professional, technical, and epistemic logics; trust and accountability issues.	Reduces diagnostic error but introduces validation and governance costs; requires LCIM-4/5 interoperability and executable KBI artefacts.
Personalised medicine pilot projects	Signals macro-level strategic intent; reveals meso-level fragmentation across research, diagnostics, and care; affects micro-level risk prevention.	Conflict between innovation, ethics, and patient-empowerment logics.	High coordination costs due to immature governance; demands cross-domain LCIM-4/6 interoperability; risk models function as weakly governed KBI artefacts.
EHR / WHO case studies	Provide macro-level comparative strategies; show meso-level organisational integration patterns influencing micro-level care pathways.	Long-term layering and evolution of institutional logics.	Persistent transaction costs despite technical maturity; gaps between LCIM-2 exchange and LCIM-4/6 coordination; baseline conditions for national KBI emerge

Appendix 3. Publication I

I

Janek Metsallik, Peeter Ross, Dirk Draheim, and Gunnar Piho. Ten Years of the e-Health System in Estonia. In *CEUR Workshop Proceedings*, volume 2336, pages 6–15, Bergen, Norway, 2018. CEUR Workshop Proceedings. URL `https://www.academia.edu/download/76879592/MMHS2018_invited.pdf`

Ten Years of the e-Health System in Estonia

Janek Metsallik[1], Peeter Ross[1], Dirk Draheim[2], and Gunnar Piho[2]

[1] Department of Health Technologies
Tallinn University of Technology
Akadeemia tee 15a, 12618 Tallinn, Estonia
{janek.metsallik,peeter.ross}@taltech.ee
[2] Information Systems Group
Tallinn University of Technology
Akadeemia tee 15a, 12618 Tallinn, Estonia
{dirk.draheim,gunnar.piho}@taltech.ee

Abstract. The e-health system in Estonia, called the Estonian nationwide Health Information System (EHIS) has been operational since the end of 2008. The main success factors for the e-health system in Estonia are clear governance, legal clarity, a mature ecosystem, agreement about access rights, and standardization of medical data and data exchange rules. We present a short history, outline the general business and technical architecture and discuss the lessons learned.

Keywords: e-Health system, e-state system, Estonian nationwide Health Information System (EHIS).

1 Introduction

There are 1.3 million citizens in Estonia and every citizen and every resident has a unique ID-number. In Estonia, 88% of households have a broadband connection (2015), 82% of households use a mobile Internet connection (2016), 96% of income tax declarations are made via the e-tax board (2016), 32% of votes were cast over the Internet (2017), and 99% of bank transfers are carried out electronically. The NATO Cooperative Cyber Defense Centre is in Estonia and Skype, Transferwise and Taxify have been developed there.

The healthcare system in Estonia is based on health insurance, paid by employers. Healthcare providers in Estonia can be private, municipal or governmental. Most hospitals are publicly owned, and most general practitioners are private entrepreneurs. Healthcare costs make up to 6% of the GDP (9.5% in the OECD area). The e-health system in Estonia, called Estonian nationwide Health Information System (EHIS), has been operational since the end of 2008. EHIS, by containing the health data of every Estonian resident virtually from birth to death, integrates different healthcare databases and services and makes it possible to access medical data, prescriptions and medical images online in a secure and trusted way. The goal of the Estonian e-health system is to develop patient-friendly, efficient and high-quality healthcare services. In addition,

it aims to make time-critical medical information accessible for physicians and to decrease the level of bureaucracy in the daily routine of physicians.

The three main layers of the EHIS are the data layer, the data transfer layer and the application layer. The data layer consists of the data repositories for storing the medical documents and images. The data transfer layer provides a secure Internet-based infrastructure for data exchange both for citizens and healthcare providers. The developing and open-ended application layer is to provide services for different parties (citizens, healthcare providers, government authorities, policy makers, etc.) according to their demands now and in the future. Ten years of experience has shown that both the citizens and healthcare professionals, as well as politicians and government authorities, have accepted the e-health system.

In Sect. 2, we present a short history of the e-health system in Estonia. Next, in Sect. 3, we describe the services and the architecture of the Estonian e-health system. In Sect. 4 we present the e-state infrastructure, including the security and legal infrastructure, that is used in the e-health system. Finally, in Sect. 5 we conclude by discussing some lessons learned from the Estonian e-health system operation.

2 Historical Overview

The story of the Estonian e-health system states back to the first years of independence of Estonia and is closely related to the activities and influence of the first Prime Minister, Mr. Mart Laar, and his team. Mr. Laar served as Prime Minister of Estonia from 1992-1994 and 1999-2002. In those years, information technology was seen as an opportunity to develop the economy and politics in Estonia – a small and developing country. Firm foundations were built for many of the initiatives that today form the e-state of Estonia[3], including e-banking, e-health, e-documents [1–4], e-school, e-taxation, e-voting, etc.

As Estonia lacked legacy software at that time, and information technology was underdeveloped in the Soviet period, the utilization and deployment of information technology began to evolve rapidly during the first years of independence. Society believed in information technology and started using information technology in all domains, including healthcare. Fig. 1 illustrates the history of the e-health system in Estonia. Between 1990 and 2000, hospitals, general practitioners and other health providers started developing their own information systems and introducing the use of electronic health records. Several small and medium sized software companies, focusing on the development of healthcare systems, were founded at that time. In the same decade, the informal planning and the first ideas of the development of a nationwide e-health system were initiated.

The active preparation of the Estonian e-health project by the government authorities and proponents of e-health system took place between 2003 and 2005, however some important events took place earlier. In 2001, the digital invoicing

[3] https://e-estonia.com/

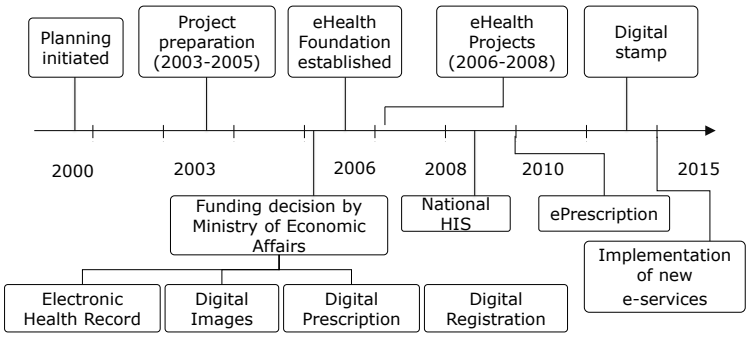

Fig. 1. The history of the EHIS platform.

system for electronic transfer of reimbursement claims, called Estonian Health Insurance Fund (EHIF), was launched. In 2002, all pharmacies were obliged by law to transmit the prescription information for reimbursement to the EHIF electronically. Over 75% of healthcare providers and 45% of all pharmacies had signed data transmission contracts. In 2005 all the reimbursement claims and prescription data in Estonia were submitted electronically.

The foundation for EHIS was established in 2005, when the Ministry of Social Affairs launched a concept for the e-health system. This concept postulated four main projects, i.e., electronic health records, digital images, digital registration and digital prescription. Soon after that, the official body for the development of EHIS, called the e-Health Foundation, was established. The e-Health Foundation was responsible for the development, financing and management of the the system. EHIS was funded by the EU (€ 1,196,206) and Estonia (€ 398,735) and was launched at the end of 2008.

EHIS continues to develop and add new functionalities and services. E-prescription, digital stamps, a driver's license health certificate application, drug-drug interaction services and e-registration are examples of such e-services. Today, EHIS is operated and developed by TEHIK[4], a government-owned private company. The system contains the health records of all the residents in Estonia and more than 10,000 healthcare professionals use the system on a daily basis[5]. In September 2017, the actual number of medical documents in the system was more than 30 million.

Although Estonia has about 1.32 million citizens, EHIS contains health information for 1.54 million people. Overall, 14 different medical document types are in use, covering more than 17 million out-patient case summaries, around 2 million stationary case summaries, and more than 8 million different medical

[4] https://www.tehik.ee/
[5] https://e-estonia.com/e-health-estonian-digital-solutions-for-europe/

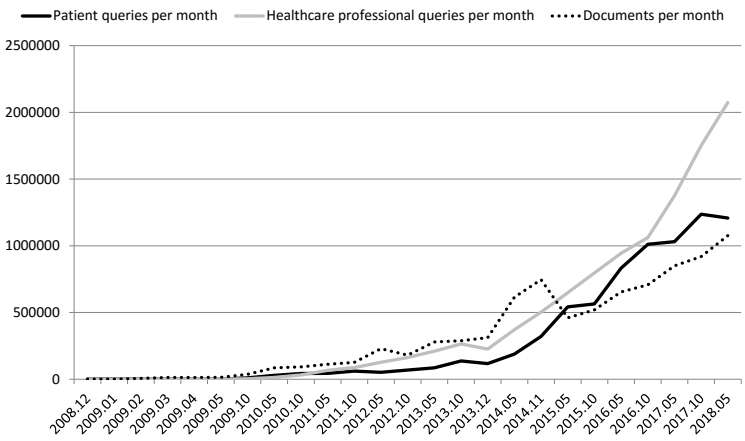

Fig. 2. The use of digital health data in EHIS platform.

diagnostic examination reports, including radiology reports and laboratory results [5]. Fig. 2 illustrates the growth in the number of the queries in EHIS per month. It was close to zero when the system started in 2008 and now more than 1.2 million queries per month are made by patients (black line) and more than 1.6 million by the healthcare professionals (gray line). In these queries, about 800,000 different healthcare documents per month (dotted line), are utilized.

3 Services and Architecture

EHIS is not a big centralized database but a federated system of mutually independent yet integrated healthcare-related software services [6]. Fig. 3 illustrates the main elements of the system.

The most widely implemented e-health project in Estonia is a nationwide health information exchange platform, which is called the nationwide Electronic Health Record (EHR) system. The EHR platform, which is based on widely accepted international standards such HL7 CDA (HL7 Clinical Document Architecture)[6], DICOM (Digital Imaging and Communications in Medicine)[7], LOINC (Logical Observation Identifiers Names and Codes)[8], etc., enables exchange of digital health documents in a standardized way. The EHR project began the ongoing standardization of digital health data artifacts in Estonia. By the beginning of 2017, a number of 1,163 healthcare institutions were sending and

[6] http://www.hl7.org/
[7] https://www.dicomstandard.org/
[8] https://loinc.org/

retrieving medical data using the EHR platform. The average number of queries was close to 50,000 queries per day. It is important to note that all medical data entered is digitally signed either by the physicians or healthcare institutions. Digital signing is also discussed in Sect. 4.

The other widely used healthcare service provided by EHIS is e-prescription. Physicians upload prescriptions, in electronic form, to the prescription center database, from where any pharmacist can request currently valid or previously dispensed prescriptions. The e-prescription system, that has been launched at the beginning of 2010, was very quickly accepted by all parties and today approximately 99% of medical prescriptions in Estonia are issued electronically. For more information about the e-prescription experience in Estonia, see [7].

The Picture Archiving and Communication System (PACS) is for sharing medical images between health institutions. Today all radiology facilities in Estonia have the duty to send, achieve and retrieve radiology images using the central PACS. Radiologists and all referring physicians have web-based access to PACS once they have signed the necessary contract with the Estonian Health Image Archive Foundation, the responsible authority of PACS.

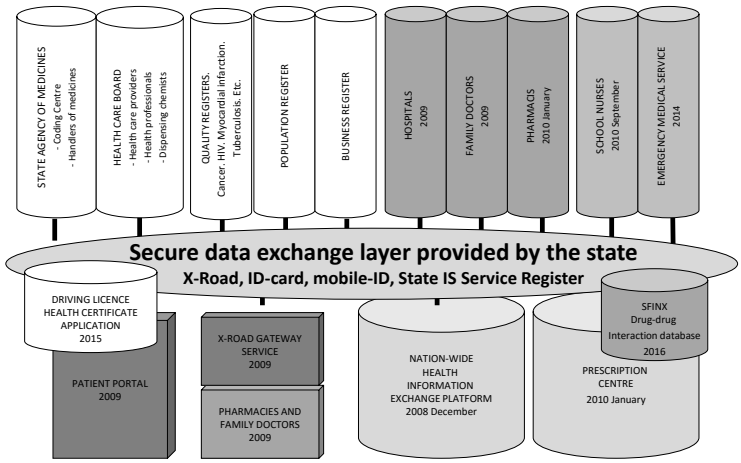

Fig. 3. Main elements of the Estonian nationwide Health Information System (EHIS).

EHIS also hosts many central registers and databases such as of hospitals, family doctors (general practitioners), pharmacies, school nurses, medicine interactions, and different quality registers (cancer, HIV, tuberculosis, etc.). Furthermore, it utilizes several nationwide registers such as the population and the business register.

One of the crucial parts of EHIS is the patient portal [8–11]. Using the patient portal, the user can:

- log in with ID card or mobile ID;
- view and update personal data and add contact data of close relatives;
- view his/her medical data from healthcare providers;
- view electronic referral letters and electronic prescriptions;
- add representatives for him/herself for actions such as collecting e-prescriptions;
- make declarations of intent (e.g. donation of organs);
- access health insurance data;
- hide sensitive health data from doctors and representatives;
- complete a health declaration form before an appointment;
- view the log of who has accessed his/her data.

Feedback from the healthcare providers' and the Estonian e-Health Foundation's helpdesks shows that, when patients do not have access to their health data (for example during system upgrade), they immediately contact the helpdesk. They are periodically interested in their data and want to view their test results before appointments. This information supports the idea that making health data easily accessible to patients will encourage them to take a more active role in monitoring their health.

4 The Infrastructure

EHIS is not a separate system but an integrated part of the Estonian e-state system used by the public and the private sector. The e-state system, by secure data exchange and authentication methods, provides a mature ecosystem for the e-services in Estonia. E-banking, e-school, e-taxation, e-voting and other e-services are all using this ecosystem. The most important parts of this ecosystem are the X-Road [12–14] (governmental service bus) and the e-identity [15] PKI (Public Key Infrastructure). X-Road (or X-Tee in Estonian) [9] is a data exchange layer for enabling a secure Internet-based data exchange between information systems. To ensure secure transfers, all outgoing data from X-Road is digitally signed and encrypted, and all incoming data is authenticated and logged. X-Road is based on the protocols and patterns of the standard SOA (Service-Oriented Architecture) stack [16, 17], i.e., SOAP (Simple Object Access Protocol) messages and WSDL (Web-Service Description Language) and utilizes the following principles:

- it enables the information systems of X-Road members to communicate with the information systems of data service providers across any software platforms;
- X-Road members are able to request access to any data services provided through X-Road;

[9] Both X-Road and X-Tee are registered trademarks.

- in X-Road, international standards and protocols are used wherever possible;
- exchanging data through X-Road does not affect the integrity, availability or confidentiality of the data.

Since 2002, in Estonia, every resident has had a digital identity. This identity is based on the unique identifier (personal ID number), digital certification organizations (police, certification center), and physical security devices like smart card (ID card), mobile SIM card (mobile ID) and smart ID. The digital identity has two functions: authentication and digital signature. The digital signature is available also for companies in the form of digital stamping.

Besides X-Road and e-identity, the important infrastructure for e-health is a legal environment initiated by the Estonian government and implemented by the Parliament. The first idea was to create separate legislation for the e-health system. However, due to the natural relationship between the e-health system and the healthcare system, and also due to the desire to direct healthcare professionals to accept and to use the e-health system, the relevant legislation was made part of the healthcare legislation.

The Health Services Organization Act, which regulates the healthcare service provision, was extended by a new chapter for EHIS. This chapter lays down the responsibilities of patients, health service providers, and provides requirements for document standards, etc. For example, all healthcare providers must send certain health data to EHIS. The set of documents is defined by the law. The Act also states that access to patient data is available only to licensed medical professionals, legal representatives or patients trustees. In the Estonian e-health system, the concept of the attending doctor has been introduced. This means that the physician or a nurse must prove the treatment relation to the patient, when accessing the patient's data in EHIS. The Act also states (and this is realized in the patient portal), that the patient has the right to hide their data so that healthcare professionals are no longer able to view them. This could be done either by hiding a single document or by hiding all their personal data in EHIS. All attempts to view healthcare data in EHIS are monitored by the government authorities and reported to the patients in the patient portal. In case of suspicions of unlawful access to the data, necessary actions are taken immediately. According to the Act, the ethical committee was created to lead the discussions on patients rights and to select the proper system for the EHIS. Citizens can access their own data, declare intentions and preferences, and monitor logs.

5 Discussion and Conclusion

The Estonian e-health system is unique as it is nationwide, integrates defined healthcare data of all healthcare providers and provides an overview of the health condition of every resident from birth to death. Such a comprehensive data system requires a robust security system. The security of the Estonian e-health system is ensured by the following six techniques:

- A secure authentication and authorization of all users with ID card, mobile ID or smart ID;

- Digital signing (by individuals) or digital stamping (by institutions) of all medical documents;
- Accountability and transparency provided by an untamperable and unremovable secure log (audit trail) containing all actions;
- Coding of personal data ensures separation of personal data from medical data;
- Encrypted database records allow a minimal confidentiality risk from the technical administrators of the system;
- Monitoring of all actions together with the corresponding countermeasures (both organizational and technical) allows identification of fraud and misuse quickly and definitely.

Huge change management issues that digitalization brings to healthcare is always a challenge. The observations and difficulties that were related to the Estonian e-health system were (and are) as follows:

- Physicians and other professionals must change the way they fill out medical files to some extent – the trend is towards more uniform language;
- Semantic interoperability of medical data is hard to achieve;
- Data quality and secondary usage of data is still challenging;
- General acceptance of hospital personnel to share medical data in patient portal with patient is problematic;
- Much attention must be paid to the security and electronic authentication of the users;
- User interface development must not be underestimated;
- Medical data is not what people are looking for – they are interested in services.

As an example, related to the last claim in the list above, e-health services that are crossing institutional and/or sectoral borders such as e-referral, e-consultation, e-prescription or filling in health declarations for a driving license application are the most popular services among the users. These types of services make healthcare processes more effective and save time for both healthcare professionals and individuals. The exchange of data and digital documents between institutions also puts high demands for data quality [18, 19] and has a clear potential to increase healthcare quality in general.

The aim of the Estonian e-health system was to develop a platform for health information exchange. However the solution had to provide some tangible services as well. During the first phase of the system, the scope to provide certain standardization and applications for most valuable documents and data was set, including outpatient summary notes, inpatient discharge letters, demographics, time-critical health data reports, and diagnostic image references.

Even though Estonia is considered an IT-mature society, it is important to understand that, similar to other European countries, Estonian society has members whose computer skills do not allow them to use e-services comfortably. This means that the digital society ecosystem should be accompanied by activities to

educate society members and to decrease the digital divide. New e-services must not replace ordinary services but should complement them to make processes more efficient and affordable for the whole society. This is the leading concept in the implementation of EHIS in Estonia, meaning that patients still have the right and the opportunity to receive services in conventional ways.

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Appendix 4. Publication II

II

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Testing the Applicability of Digital Decision Support on a Nationwide EHR

Janek Metsallik(✉) and Peeter Ross

Tallinn University of Technology, Tallinn, Estonia
{janek.metsallik,peeter.ross}@taltech.ee

Abstract. The rapid increase in digitisation is driving demand for better utilisation of health data. Personalised medicine promises a more predictive, preventive, and tailored approach to every person's health. An automated digital decision support system (DDSS), one of the main elements of personalised medicine, is also a cornerstone of Estonia's ambitious Personalised Medicine Programme, which builds on nationwide health information exchange success. This paper describes a method of testing the applicability of digital decision support algorithms on national electronic health records (EHR) by using Estonian National EHR (Estonian Health Information System, EHIS) as an example. The experiment aimed to enable better preparation for the nationwide DDSS implementation project and elicit possible issues with the present model of health data exchange. The investigation included choosing the decision algorithms, mapping the algorithms with the available data, and simulating the DDSS execution on the past health records. To better understand the peculiarities of a national EHR, the study runs the same algorithm testing process on both the National EHR and on a hospital electronic medical records (EMR). The study revealed several discrepancies between the expectations of the decision-makers and the current design of the EHR. The paper suggests paying closer attention to the discovered issues during the future developments of e-health systems and also adopt the demonstrated model of algorithm applicability testing as a standard procedure for a national DDSS implementation.

Keywords: Digital decision support system · Personalised medicine · Electronic health records · Health data interoperability

1 Introduction

The information age has increased the urge to transform healthcare from a reactive and disease-based model to a model where all the data available would allow a more predictive, preventive, and personalised approach [1]. The Estonian government has strategised implementing person-centric and personalised medicine-based healthcare as part of the healthcare innovation strategy [2] and e-health vision and strategy [3]. The established frame defines personalised medicine to "help determine as individually as possible the prevention or treatment plan for each person by analysing genetic data of the person in combination with the environment, health behaviour and health data of the person" [4, 5]. This view aligns well with the approach that personalised medicine is

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applying tools, facilitating individualised healthcare predictions, decisions, and therapies [1]. Hong and Oh suggest that personalised medicine requires health risk assessment, family health history, human genome sequence variation, and digital decision support systems (DDSS) [6]. The nationwide Health Information System in Estonia (EHIS) enables the efficient and secure exchange of health data to any required location of decision-making, which should cover the need for accessing health data in a person-centric way [7]. Advanced genomic research and decades of experience from Estonian Biobank are looking for opportunities for bringing the findings into medical practice [8].

The Estonian government conducted a comprehensive feasibility study of personalised medicine in 2015, including clinical approach, information architecture and data management, digital decision support systems (DDSS), and business and organisational evaluation methodology [4]. From the perspective of decision support, the study developed scenarios of health data and medical history use for decision making throughout a lifespan of hypothetical individuals with three types of clinical conditions (cardiovascular diseases (CVD), diabetes, cancer). One of the conclusions from the study was a suggestion that there is a need for "audit and analysis of data existing in nationwide and organisational (e.g., healthcare providers) medical and public health databases to agree about the sources of different data necessary for DDSS algorithms" [9].

Anyone trying to implement a digital decision support system faces a multi-dimensional challenge. Data sources must support adequate interoperability, quality, and availability. There is a need for useful formalised knowledge sources. Implementer has to be able to apply inference methods and possess mature architecture and technology. There shall be decent change management capability for DDSS implementation and clinical workflow integration. Users of the DDSS must be ready for sophisticated tools and work environments [10]. The type of intelligence encapsulated into a DDSS varies between or often combines information management, knowledge management, and analytical data modelling [11]. Artificial intelligence (AI) promises to transform the DDSS to be more autonomous in knowledge acquisition and go beyond the previously formulated algorithms. For AI to work, the implementation must constantly monitor the inputs and outputs for the quality of data [12].

Estonia implemented EHIS in 2008 [7, 13]. Sharing of health data through EHIS is mandated by the law for all healthcare providers. In addition to the EHIS and local information systems in healthcare facilities, the landscape of e-health in Estonia includes other potentially complementary sources of data for DDSS. Potential additional sources include the central database of e-prescriptions, the public health insurance reimbursement database, the genetic research database, and the registries at the National Institute for Health Development (NIHD) (including cancer registry, pregnancy registry, cancer screening registry, and others). These databases can improve the quality of decision support for mainly two reasons. First, they often collect data independently of EHIS, which may help find and fill in the gaps of EHIS data. Second, the data collection organisations apply domain-specific data quality checks on their records, which would support the increase of source data quality. However, the utilisation of EHIS as the primary data source for DDSS has been strategised in the national e-health strategy in Estonia [2].

The core functionality of EHRs is an improvement of access to the health care process and outcomes data [14]. The use of the EHR data for purposes other than

delivering records between human users has often faced issues with the data quality. A study of 10 year EHR data from Columbia University Medical Center identified 3068 patients with ICD9-CM code for pancreatic malignancies, where 48% of the patients missed the corresponding pathology report; and 52% of the records of the remaining 1589 patients missed some other essential variable for the study [15]. Another study in Estonia aimed to use referrals and case reports from EHIS for calculating waiting times to specialist appointments. The study found that out of 93 985 pairs of documents (referral + response, all specialist referrals from the second half of 2016), only 9% of documents included all required dates for calculation [16]. Estonian National Institute for Health Development found that in EHIS, there was only 85% of inpatient care and 62% of daycare data available compared to the records collected directly by the institute. The research showed an 11% increase in coverage of inpatient cases in EHIS during 2013–2016; the growth has not been sufficient for the quality level required [17].

The studies of EHR and DDSS implementations have not consistently confirmed the achievement of a better quality of care either [18–20]. Romano and Stafford studied the effect of EHR and DDSS on clinical quality by reviewing 255 402 ambulatory patient visits. The statistically significant improvement due to EHR was noted only in diet counselling in high-risk adults, just one parameter out of 20. Also, the DDSS contributed to only one measure, avoiding unnecessary ECGs during routine examinations [21]. The limited impact of DDSS may not always indicate the lack of data quality but missing function or wrong context for the data [22–24]. A study of the effect of nationwide DDSS integrated with the Estonian ePrescription System did not identify a decrease of clinically significant drug-drug interactions during the first year of its introduction regardless of the alerts displayed during the decision making. The prescription and dispensation data is very reliable but does not represent the actual use of drugs well enough for decision support [25].

This article presents a method for testing the applicability of DDSS algorithms on collecting standardised digital clinical documents from EHIS. The technique was designed and tested during a preparatory study of the nationwide DDSS implementation in Estonia. In the broader context of the Personalised Medicine Programme, we tested the feasibility of connecting a DDSS to the EHIS. We completed the experimental part of the study in 2017.

2 The Methods

This study aims to test if the data in the EHIS fit for automated decision support. The approach validates if the current model of the health data exchange is ready for personalised medicine.

Following the pilot scope of the governmental Personalised Medicine Programme, the study focuses on cardiovascular disease. The clinical consultants of the study selected a set of decision support algorithms that align with the needs of the medical domain and fit with the clinical guideline in Estonia.

The utilisation of the EHIS data for decision support is the main architectural scenario of the decision support implementation. Alternative strategies would include integrating decision support functions into local software systems used by hospitals, clinics, and

solo practices. To validate the main scenario, we have chosen to explore an alternative approach too. We run the same tests on a hospital database for comparison (Pärnu Hospital).

Healthcare providers report patient cases to EHIS in the form of HL7 CDA based XML documents (including discharge letter, consultation note, laboratory report, and others). These documents are securely piled up in the EHIS document repository and indexed for various use cases in the EHIS document registry (including patient diagnoses, patient encounters, chronic patient conditions, and others). In addition to the document repository and registry, EHIS includes a separate subsystem for analytical data use (data warehouse). The study completed an initial informal mapping of the decision algorithm to the EHIS data. This initial mapping revealed that neither of the query optimised options - EHIS registry nor EHIS warehouse - would satisfy the need for input data, which left us the only option to use the clinical documents in the EHIS repository.

The design of the method evolved into steps of.

- choosing the decision algorithms,
- logical mapping the parameters of the algorithms to the content model,
- technical mapping to the source records/documents,
- computing the indicators of the applicability (running the database queries) (Fig. 1).

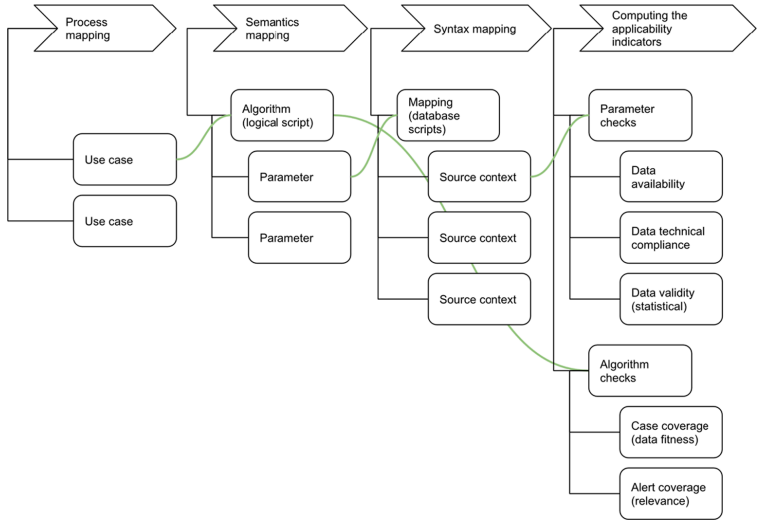

Fig. 1. The schematic overview of the phases of mapping and computation

The study has got approval from the Research Ethics Committee of the University of Tartu. Due to data protection requirements, the state agency responsible for EHIS operations (Health and Welfare Informatics Center, TEHIK) implemented all the data processing in their premises.

The clinical consultants of the study chose the decision algorithms from the library of an existing DDSS, the EBMEDS by Duodecim [25]. The selection aims to cover both

phenotype and genotype data. According to the experts, the selected nine algorithms have an excellent fit for the health care documentation in Estonia. The list of algorithms maintains a reference to the original library of scripts.

- Algorithm 1. Alerting on genetically determined high risk for statin-induced myopathy (scr01718)
- Algorithm 2. ACE inhibitors, angiotensin-receptor blockers, and beta-blockers in patients with congestive heart failure (scr00272)
- Algorithm 3. Avoiding the combination of aspirin and clopidogrel in patients without specific indications (scr01576)
- Algorithm 4. Glucose tests for patients with hypertension, dyslipidemia, or cardiovascular disease (EBMPracticeNet) (scr01371)
- Algorithm 5. Smoking cessation for secondary prevention in atherosclerotic disease (EBMPracticeNet) (scr01464)
- Algorithm 6. Statins for the secondary prevention of cardiovascular disease (scr01069)
- Algorithm 7. Adding or increasing diuretics in patients with congestive heart failure and fluid retention (scr00274)
- Algorithm 8. Alerting on genetically determined high risk for familial hypercholesterolemia (scr01719)
- Algorithm 9. Diagnosing hemochromatosis by genetic testing (scr01715)

We identified 41 parameters for the algorithms. The parameters fall into six classes. The classes included condition (diagnosis), observation (vital sign, measurement, examination), medication, procedure, patient (demographics), and adverse event (medication incompatibility). We also mapped the concepts referenced by the parameters to the clinical terminologies of the EHIS. For example, the condition of congestive heart failure maps to a set of ICD-10[1] codes, and medication history of statins maps to a group of ATC[2] codes. The list of referenced terminologies consists of ICD-10, ATC, LOINC[3], EHIF[4], DRG[5], and NCSP[6] codes.

The mapping of the parameters to EHIS data structures ended up as a list of computational statements (queries), which link to 172 data fields that are part of 24 document sections. 40 SQL statements were implemented and run in total. The technical team at Pärnu hospital did a similar mapping of the parameters to the hospital data structures.

[1] ICD-10, International Statistical Classification of Diseases and Related Health Problems, https://www.who.int/standards/classifications/classification-of-diseases.

[2] ATC, Anatomical Therapeutic Chemical (ATC) Classification, https://www.who.int/tools/atc-ddd-toolkit/atc-classification.

[3] LOINC, The international standard for identifying health measurements, observations, and documents, https://loinc.org/.

[4] EHIF, Estonian Health Insurance Fund services nomenclature, https://www.haigekassa.ee/en/partner/list-health-care-services.

[5] DRG, Diagnosis Related Groups, http://www.norddrg.net/norddrgmanual/NordDRG_2012_EST/index.htm.

[6] NCSP, Nomesco Classification of Surgical Procedures, http://nowbase.org/publications/ncsp-classification-surgical-procedures.

We expected that the quality of the recorded cases wouldn't allow applying the algorithms in every possible clinical case. The study developed a hypothesis that there may be problems with a single parameter reporting quality and issues with the availability of the parameters in the configuration required by the algorithm. To better understand the quality and availability of the required parameters in the actual content, we developed a set of supportive query scripts (Table 1).

Table 1. Overview of the query scripts developed for algorithm 7.

Algorithm 7. Adding or increasing diuretics in patients with congestive heart failure and fluid retention (scr00274)			
Parameter applicability checks			
Parameter	**Template scripts**	**Format scripts**	**Values scripts**
Congestive heart failure	Count the number of patients having the diagnosis reported as part of a template/document type combination		Count the number matching records grouped by the specific diagnosis code in use
Body weight	Count the number of patients having body weight reported as part of a template/document type combination	Count the number of patients having body weight value and unit reported in the form as required by standards	
Furosemide	Count the number of patients having furosemide medication reported as part of a template/document type combination		Count the number matching records grouped by the specific ingredient code in use
Algorithm applicability checks			
	One parameter left out	**All parameters available**	**Alert frequency**
Alert 1 Add Furosemide **Alert 2** Increase Furosemide	Count the number of patients having two out of the three parameters available in the configuration required by the algorithm	Count the number of patients having all of the three parameters available in the configuration required by the algorithm	Count the number of cases when the algorithm would have been alerted the user

3 Main Findings

3.1 Summary of the Applicability of the Algorithms

The experiment was successful from a technical perspective. We managed to run all the queries on both databases. We use time-bounded subsets of data from both databases; the algorithms accessed the records from Jan 2012 to May 2017.

The total number of alert matches in the data was low. Only one out of nine algorithms found any matching records from EHIS. The results from Pärnu Hospital present two fully and three partially applicable and four non-applicable algorithms. The main reasons for the unmatch were:

- The data is not available in the structured form - it does not follow a structured data standard, or no standard is defined.
- The data does is not collected with the required frequency.
- The data is not shared, or integrations do not work (Table 2).

3.2 Limitations of EHIS Data Model

The algorithms required several parameters, which are not available at the present model of EHIS. One example of such a parameter is the smoking status of a patient. The medical recording tools of primary care in Estonia support registration if a patient is a smoker; however, there is no standard available to share this data through EHIS. Another example of a missing parameter is the left ventricular ejection fraction (LVEF). The structured parts of EHIS do not include detailed echocardiography protocol; hence the LVEF outcome cannot be automatically accessed by the DDSS. Currently, it is possible only to check whether the LVEF examination has taken place. And finally, registration of genetic test results is still minimal; neither familial hypercholesterolemia nor SLCO1B1[7] gene status is available in code in the records.

3.3 Limitations of the EHIS Event Model

Algorithm 7 depends on parameters of patient diagnosis (heart failure), bodyweight dynamics (3-week change), and use of drugs (diuretics). The 5-year data set included 751 251 patients with 1 717 634 heart failure diagnosis and 471 339 patients with 640 774 bodyweight measurements in the records. However, the query could not identify any patients with body weight recorded multiple times during three weeks. This finding shows the limits of EHR data, which is built only from the case summaries.

We identified the same issue with bodyweight records also in the hospital information system. A single EMR is not able to provide a patient-centric view of health conditions.

[7] SLCO1B1 Polymorphism, https://www.sciencedirect.com/topics/biochemistry-genetics-and-molecular-biology/slco1b1.

Table 2. Aggregated results of the algorithms applicability testing

Algorithm	Pärnu hospital	EHIS
1. Alerting on genetically determined high risk for statin-induced myopathy	**Not applicable**. Genetic test results are not available	**Not applicable**. Genetic test results are not available
2. ACE inhibitors, angiotensin-receptor blockers, and beta-blockers in patients with congestive heart failure	**Partial**. Echocardiography (ECG) results are not structured. In total found 9634 records for the suggestion to order ECG	**Partial**. Echocardiography (ECG) results are not structured. In total found 43 matches for the suggestion to order ECG
3. Avoiding the combination of aspirin and clopidogrel in patients without specific indications	**Partial**. Aspirin is an over-the-counter drug, which is often not recorded. In total found 12 matches for the algorithm	**Not applicable**. Aspirin is an over-the-counter drug, which is not available as prescription data. In total found 0 matches
4. Glucose tests for patients with hypertension, dyslipidemia, or cardiovascular disease	**Partial**. Body mass index data is unstructured for adults (561 structured records were available). In total found 26 matches for the algorithm	**Not applicable.** Structured body mass index data not available. In total found 0 matches
5. Smoking cessation for secondary prevention in atherosclerotic disease	**Not applicable**. Structured data about smoking is not available. In total found 0 matches	**Not applicable**. Structured data about smoking is available as part of the health declaration, but the statement has a limited validity period. In total found 0 matches
6. Statins for the secondary prevention of cardiovascular disease	**Applicable**. In total found 8024 matches for the algorithm	**Not applicable**. Prescription data is not available without additional integration. In total found 0 matches
7. Adding or increasing diuretics in patients with congestive heart failure and fluid retention	**Not Applicable**. The structured data is available (16811 patients with the diagnosis), but the query did not match any records. In total found 0 matches	**Not Applicable**. The structured data is available (751 251 patients with the diagnosis), but the query did not match any records. Prescription data is not available without additional integration. In total found 0 matches
8. Alerting on genetically determined high risk for familial hypercholesterolemia	**Not applicable**. Genetic test results are not available. The hospital does not perform particular genetic tests	**Not applicable**. Genetic test results are not available

(*continued*)

Table 2. (*continued*)

Algorithm	Pärnu hospital	EHIS
9. Diagnosing hemochromatosis by genetic testing	**Applicable**. In total found 631 matches for the algorithm	**Not applicable**. The genetic test results were not available as structured data at the time of the experiment

3.4 Limitations of the EHIS Integrations

This study focused on the applicability of DDSS algorithms to the EHIS database. For certain classes of parameters, the e-health system in Estonia provides better alternatives to EHIS. In regards to prescription data, E-Prescription Center provides for better coverage of medication data. Also, the public health insurance claims management system maintains a database of reimbursed cases with a good range of diagnosis and service/procedure data. A comprehensive source for gene test data is the Estonian Genome Center, which could provide a data source of decision support.

4 Discussion

Kawamoto and McDonald recommend DDSS projects to ensure that EHR data is available, the decision algorithms are consistent with local care processes, and the algorithms are adequately tested [23]. The current study tests the applicability of decision support on a national-level health information exchange system. We mapped a set of decision algorithms to the EHIS data model and tried to emulate the work of DDSS on the past data. The testing revealed several obstacles in the way of successful DDSS implementation.

The logical and technical mappings demonstrate that most of the required decision support parameters are available in the EHIS data structures. Alternative data sources are available for some missing parameters (e.g., E-prescription Centre, Genome Center). Former studies have identified possible issues with data quality in EHIS; especially problematic dimensions seem to be coverage and use of free text instead of standardised structured fields [16, 17]. Some cases of missing data can be related to the misplacement of content in the data structures in our experiment (e.g., bodyweight in free text rather than in a particular structured field). However, the investigation indicates that in addition to the EHIS data quality, the event model or data dynamics and the lack of integration of various data sources may limit the applicability of DDSS.

The design of EHIS has its roots in the ongoing digitalisation of the health information exchange, which itself has been evolving for a long time (for centuries) in its paper-based forms – documents. Document-based thinking leads to a separation of primary and secondary use of data. The first iterations of digitalisation prioritise the data transfer between a data provider and data consumer; a document is a data transfer unit. Other uses of the same data are considered secondary (e.g., research, statistics) [26]. Secondary use of data is a separate effort with many risks for low reward, which may trigger a mental permit for an additional data capture for the new needs. In turn, it only increases the

primary use with more and more data structures conveying information about the same real-life events. The study's technical mapping, where a person's diagnosis maps to 8 data structures (templates - document fragments) and the transfer of diagnosis data is possible through 13 document types, clearly shows the consequence of denormalised primary data capture.

Algorithm 7 tested the availability of information about the gain of weight during 21 days. The total number of bodyweight records was 640 774, but the weight gain during 21 days was available in 0 cases. There are many possible explanations for this result. The current paradigm of document-based exchange influences the dynamics and content of the data. It is not essential to share the detailed timing and sequence of the observations (vital signs, measurements) after the case. In the example of case summaries, it seems enough to report only the data required for the rational argumentation of the main conclusion (the primary diagnosis). A physician could record the bodyweight with the interval necessary; however, the data is not shared timely or is not shared at all. The testing of the alternative data source, the hospital information system at Pärnu hospital, demonstrated that an EMR might have better data in some cases but lacks integrated patient-centric access to data.

Tolk et al. propose to look at the problem of interoperability as a spectrum of concerns. The range starts from the technology-related interoperability issues (integrability). It ends with putting the data correctly into the context of decision-making (composability) [27, 28]. Similarly, our experiment elicits a whole spectrum of issues. The lack of prescribed medication data in the EHIS is an integrability problem - making the prescription data available for the algorithm is an additional technical effort. The integrability issues also surface when an EMR of a healthcare pathway participant cannot support patient-centric continuity of data flow. In this experiment, we put a relatively great effort into mapping the various data structures and fields for the algorithm parameters. The mapping process is similar in every single case of decision support software development. The high cost of mapping shows the issues with semantic and syntactic interoperability - the data is not organised to make it easy to consume for the algorithms. The lack of usable bodyweight data in the EHIS (and the same in the hospital EMR) demonstrates issues with composability - the need for such data is not acknowledged. The dynamics of data sharing do not fit with the event model assumed by the decision algorithm.

The introduction of DDSS or any other automated secondary use on a national level e-health system reveals many new issues. The issues hidden in document-based health data exchange become suddenly urgent when we start introducing personalised medicine. Some of the problems are relatively easy to solve; the IT solutions and competencies are there already. It is also relatively easy to address technical integration and interoperability concerns. EHIS is one example of such a platform, where healthcare system stakeholders share structured semantically mapped data on a nationwide scale. However, composability is harder to get right. It requires a diverse mix of expertise, governance, and workflows. Healthcare system stakeholders need to revise the organisation of healthcare processes to achieve better composability. It may not be enough to digitise; one also needs to digitalise.

The study demonstrated that perfectly valid decision algorithms are useless because of data quality and interoperability weaknesses. DDSS aims to accelerate and raise the accuracy of decision-making. A well-working DDSS reduces the need to process data manually by a decision-maker (e.g., a patient, a clinician, a manager, a researcher, a policymaker). It is crucial to understand the trustworthiness of a DDSS. DDSS suggestions must be fully trusted or well-aligned with the context of decision-making. Otherwise, the users shall (manually) verify the basis for such a suggestion and apply additional safeguards for protecting against the lousy advice of DDSS. Low-quality DDSS makes users spend even more effort for decision-making than they would without a DDSS.

The DDSS implemented on top of EHIS is a huge step forward in advancing the value of e-health for the healthcare system. However, as the study has demonstrated, the objective cannot be achieved automatically by a simple IT project integrating DDSS and EHIS. Each of the algorithms proposed by the domain experts needs to a carefully testing. Any algorithm that fails to compute consistent and valid results on the data available shall stay in the premature, draft, or risky status.

5 Conclusions

This paper applied a formal approach for testing the applicability of specific decision support algorithms on EHIS data. The experiment results revealed several areas of mismatch between the expectation of the decision-makers and the current design of the EHIS. A clear outcome of this experiment is that EHIS needs a combined multilevel redesign of its interoperability model, enabling the correct context for the personalised medicine decision algorithms.

The study concludes with a suggestion to establish a straightforward procedure of testing the reliability of any DDSS before the full deployment into clinical use. We also suggest improving the capability of mapping the issues of data sharing to specific areas of development. The latter would enable efficiently targeted (intelligent) intervention by the e-health improvements, thus reducing the risk of misspending attention, time, and finance on redundant IT developments.

Future research should look into the systematic methods of mapping the interoperability issues into the right approach to addressing the problems. The further acceleration of the adoption of personalised medicine needs a more intelligent intervention by e-health.

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Appendix 5. Publication III

III

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EDITED BY
Oswald David Kothgassner,
Medical University of Vienna, Austria

REVIEWED BY
Weihui Li,
Central South University, China
Karin Waldherr,
Ferdinand Porsche FernFH – Distance Learning University of Applied Sciences, Austria

*CORRESPONDENCE
Markus Bertl
mbertl@taltech.ee

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A systematic literature review of AI-based digital decision support systems for post-traumatic stress disorder

Markus Bertl*, Janek Metsallik and Peeter Ross

Department of Health Technologies, School of Information Technologies, Tallinn University of Technology, Tallinn, Estonia

Objective: Over the last decade, an increase in research on medical decision support systems has been observed. However, compared to other disciplines, decision support systems in mental health are still in the minority, especially for rare diseases like post-traumatic stress disorder (PTSD). We aim to provide a comprehensive analysis of state-of-the-art digital decision support systems (DDSSs) for PTSD.

Methods: Based on our systematic literature review of DDSSs for PTSD, we created an analytical framework using thematic analysis for feature extraction and quantitative analysis for the literature. Based on this framework, we extracted information around the medical domain of DDSSs, the data used, the technology used for data collection, user interaction, decision-making, user groups, validation, decision type and maturity level. Extracting data for all of these framework dimensions ensures consistency in our analysis and gives a holistic overview of DDSSs.

Results: Research on DDSSs for PTSD is rare and primarily deals with the algorithmic part of DDSSs (n = 17). Only one DDSS was found to be a usable product. From a data perspective, mostly checklists or questionnaires were used (n = 9). While the median sample size of 151 was rather low, the average accuracy was 82%. Validation, excluding algorithmic accuracy (like user acceptance), was mostly neglected, as was an analysis concerning possible user groups.

Conclusion: Based on a systematic literature review, we developed a framework covering all parts (medical domain, data used, technology used for data collection, user interaction, decision-making, user groups, validation, decision type and maturity level) of DDSSs. Our framework was then used to analyze DDSSs for post-traumatic stress disorder. We found that DDSSs are not ready-to-use products but are mostly algorithms based on secondary datasets. This shows that there is still a gap between technical possibilities and real-world clinical work.

KEYWORDS

decision support systems (DSS), post-traumatic stress disorder (PTSD), artificial intelligence (AI), machine learning (ML), systematic literature review (SLR), clinical decision support (CDS), psychiatry, mental health

Introduction

According to Sauter, Digital Decision Support Systems (DDSSs) are computer-based systems that bring together information from various sources, assist in the organization and analysis of information and facilitate the evaluation of assumptions underlying the use of specific models (1). The concept of decision support systems originated in the 1960s (2) when researchers began to study computerized methods to assist in decision-making (3–5). Since then, the idea has extended throughout a broad spectrum of domains, one of which is healthcare. This work focuses on decision support systems in mental health, more precisely on decision support systems for PTSD. The American Psychiatric Association defines PTSD as "a psychiatric disorder that can occur in people who have experienced or witnessed a traumatic event such as a natural disaster, a serious accident, a terrorist act, war/combat, rape or other violent personal assault" (6). People with PTSD experience recurrent thoughts about their traumatic experience that influence their daily life. The lifetime prevalence of PTSD is around 12.5% (7). However, people suffering from PTSD are often undiagnosed or misdiagnosed, resulting in incorrect, incomplete or missing treatment (8). To investigate whether DDSSs could be a solution to this problem, we aim to review available decision support systems for PTSD and map their technological approaches in order to understand possible research gaps and obstacles in introducing decision support systems to clinical processes. Since no available reference architecture for decision support systems is applicable to our research, we contribute by introducing a novel framework for decision support systems that can be used to analyze existing systems. Ultimately, this also accelerates the development of new systems by highlighting essential dimensions.

Designers of earlier DDSSs have applied multiple alternative approaches for converting real-world data into something that stimulates better decisions. Information-management-based DDSSs try to organize data into usable presentations; modeling-(or data-analytics)-based DDSSs attempt to apply statistical (learning) methods for finding patterns or calculating indicators; and knowledge-management-based systems apply externally prepared algorithms (expert rules) to find matching data or derive new facts (9). While AI has been an essential element of DDSSs throughout its history, only recently has a new generation of decision support been facilitated by the availability of powerful computing tools to properly manage big data and to analyze and generate new knowledge. The evaluation of AI's earlier implementations was limited to the design and development phase; machine learning-based algorithms often do not generalize beyond the training data set (10). However, studies have still shown the benefits of machine learning algorithms in DDSSs (11–13). Current studies that test the application of healthcare AI algorithms often omit details of DDSS tools that apply AI models. A well-designed DDSS is likely to enable the real-world application of AI technology (14).

This review aims to contribute by introducing a framework for the features of DDSS implementation in mental health. We aim to identify the prevalent features of the current state of research on DDSS. Often, the development of information systems involves the continuous introduction of new features and quality improvements. We hypothesized that each available article presents only a selection of features, a selection which is dependent on the maturity of the DDSS. Maturity models are increasingly used as a means of benchmarking or self-assessment of development (15). In healthcare informatics, many maturity models are available [e.g., Hospital Information System Maturity Model (16)], but none of these models strictly provides an informed approach for the assessment of research on decision support systems (17). The available maturity models instead tend to look at the level of organizational adoption of specific technologies (e.g., how much an organization values data analytics technology) and provide little support for deciding on the readiness of DDSS tools in their early phases of development. As AI is often an essential element of a DDSS, we also explored AI maturity models. AI maturity models mostly look into the level of AI adoption in an organization rather than the maturity of the AI technology itself (18–20).

A DDSS is not a single technology but rather a set of integrated technologies (21–25). Sauser et al. (26) suggested a measure of System Readiness Level (SRL), which expresses the level of maturity of a system consisting of a set of integrated technologies (26). Exploring AI technology readiness or maturity, we encountered suggestions to look separately into the AI system's capacities of integrating existing data sources (machine-machine intelligence), interacting with human users (human-computer intelligence) and applying intelligent reasoning (core cognitive intelligence) (27).

Methods

To have a transparent and objective approach for this literature review, we decided to apply the five stages suggested by Kitchenham's "Guidelines for performing Systematic Literature Reviews in Software Engineering" (28):

(1) Search Strategy
(2) Study Selection
(3) Study Quality Assessment
(4) Data Extraction
(5) Data Synthesis

Research questions

Since our aim is to understand current research on decision support systems for PTSD, this paper is based on two research questions. First, we look for state-of-the-art decision support systems for post-traumatic stress disorder (RQ1). Second, we investigate the component elements of current decision support systems for PTSD (RQ2).

Search strategy

We built a search string based on the research questions identified and applied it to the Scopus abstract and citation database. Scopus was chosen as the primary source because it is the largest abstract and citation database of research literature with 100% MEDLINE coverage (29). The initial search string consisted of the disease to investigate – post-traumatic stress disorder – its abbreviation PTSD as well as the term "decision support." To find papers that covered the prediction and classification of PTSD, we also added Artificial Intelligence. In Scopus, we applied the search string to the title, abstract and tags of the research papers. We restricted our search to only include journal articles or conference proceedings in English. We also conducted a manual search using Google Scholar and the web to find additional research; however, this did not bring up any new articles not already covered by our database search and our reference screening process. We formed our search criteria as ("decision support" OR "Artificial Intelligence") AND [PTSD OR (post AND traumatic AND stress AND disorder)].

We conducted the search in Scopus on 3 March 2021. It resulted in 75 papers; reference screening of the included literature brought up an additional 13 papers. Our search process is visualized in **Figure 1**.

Study selection

The titles and abstracts of the queried articles were analyzed to identify relevant articles from the results of the search string queries. Articles fitting the research questions and meeting the inclusion criteria (see section "inclusion criteria") as well as the quality criteria (see section "study quality assessment") were included. Since the goal of this research is to give an overview of the state of the art, we did not put any constraints on study types and designs. To reduce bias in the study selection process, the task was done by two researchers independently. The two result sets were then merged and deviations were discussed among the authors. This resulted in a total set of 17 research papers.

We then repeated this process step to extract relevant studies from the reference lists of the selected articles. This resulted in 13 new research papers.

Inclusion criteria

Table 1 presents the inclusion criteria applied to the articles in our review (Inclusion criteria).

Study quality assessment

Table 2 presents the inclusion criteria applied to the articles in our review (Quality criteria).

Data extraction and synthesis

Data extraction and synthesis were based on an inductive approach. We applied thematic analysis (30) to answer our research questions. First, clear, scoped questions for data extraction were formed. Two researchers read through all the articles and iteratively clustered all of the information available on decision support systems into the extraction parameters. These extraction parameters describe how decision support systems work. This process is shown in **Figure 2**.

The answers extracted from the EQs (see **Table 3**) were then combined upon the agreement of the authors to create a feature matrix. The extracted features were then further clustered to create a common terminology that allows further analysis and the possibility to compare results. In the end, we combined the developed extraction questions and the clustered scales of each question into a novel framework for decision support systems in mental health.

Results

The selected 30 research articles (31–60) were published between 2001 and 2019. Three articles were published in journals about medical informatics, 10 in computer science journals or proceedings and 17 in medical journals. The following table shows how often each extraction parameter was present and indicates the terminology used in the selected studies. The terminology shown in **Table 4** was developed by manual, iterative clustering of the extracted features until the authors were satisfied with the granularity.

A framework for digital decision support systems

Based on our aim to find all relevant features of decision support systems in the PTSD area and our systematic literature review results, we propose a multidimensional framework that covers the different areas of DDSS. Each dimension represents one of our extraction parameters. **Figure 3** illustrates our framework with the different dimensions of DDSSs. Based on the extracted data, we clustered the terminology

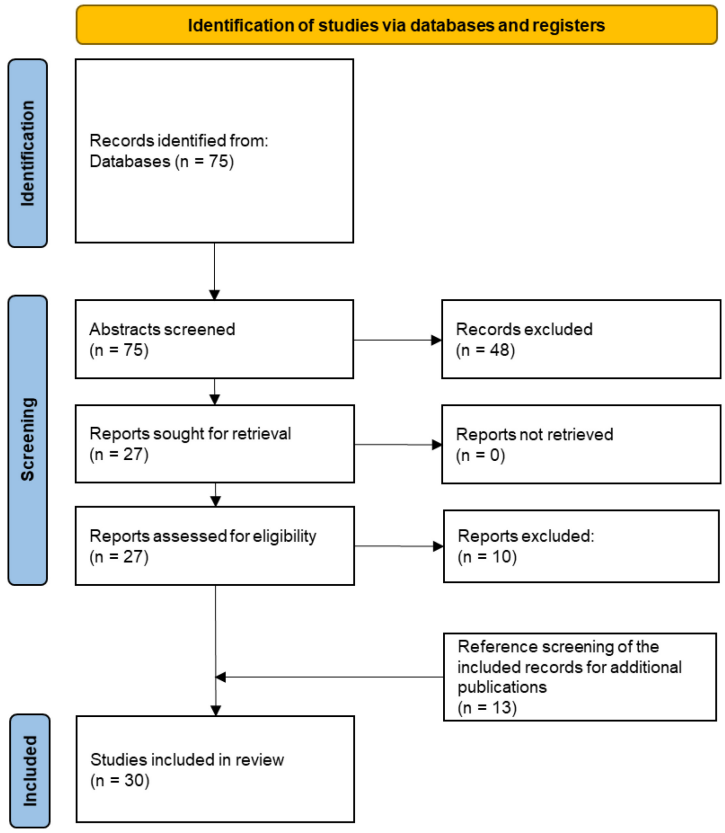

FIGURE 1
Search strategy.

to develop scales for dimensions in order to make results better analyzable.

Input Data: The input data dimension defines the information needed by a decision support system in order to function. Possible data could be structured like socio-demographic information or coded data [for example, with the International Statistical Classification of Diseases and Related Health Problems (ICD) (61) or the Diagnostic and Statistical Manual of Mental Disorders (DSM) (62)] as well as semi-structured information like patient records or unstructured information like free text or medical images. A combination of different structured, semi-structured and/or unstructured data is also possible.

TABLE 1 Inclusion criteria.

#	Inclusion criteria
IC1	Does the study deal with decision support systems (e.g., systems that help diagnose, screen, predict or treat)
IC2	Does this study apply a computerized algorithm?
IC3	Does this article deal with PTSD?
IC4	Is the article related to at least one of our research questions?

TABLE 2 Quality criteria.

#	Quality criteria
QC1	Is the research a journal article or conference proceeding?
QC2	Is the research peer-reviewed?
QC3	Does the study have a well-defined structure?
QC4	Does the study bring evidence for the proposed approach (either by citing relevant literature or validating the results)?
QC5	Does the study have ethics approval (if required by the study design)?

Technology: The technology dimension describes how the decision support system is implemented. This involves three sub-dimensions:

Decision technology: The decision technology explains the intelligence of the cognition of the system. This is the algorithm that powers the decision-making. Examples are different machine learning algorithms such as support vector machines or other statistical methods as well as rule-based approaches.

Interaction technology: This sub-dimension describes the technology needed to interact with other systems or user groups in the clinical process. Interaction technology can be API-based interfaces to systems, graphical user interfaces (websites, mobile apps) or sensory input like conversational interfaces (chatbots).

Data collection technology: The data collection technology sub-dimension defines how the data described in the input data dimension are collected. Examples are instance sensors, questionnaires or chatbots.

Validation: Validation describes how the success of decision support systems is measured.

Accuracy: The decision support system is evaluated by how many right or wrong decisions it makes. Examples are accuracy, recall (sensitivity), precision, specificity, area under the curve (AUC) values and F1 scores (harmonic mean of recall and precision).

User acceptance: End-users are involved in the evaluation of the DDSS.

Efficacy: The impact of the decision support system is evaluated based on potential benefits.

Security: The DDSS is evaluated against security regulations.

Legal: The legal compliance of the DDSS is evaluated.

User group: This dimension captures the different user groups interacting with the decision support system in the clinical process.

TABLE 3 Extraction questions (EQ).

#	Extraction parameters
EQ1	On the basis of which input data do existing decision support systems in mental health operate?
EQ1.2	What was the data sample size?
EQ2	What is the implementation technology of the DDSS?
EQ2.1	Decision technology
EQ2.2	User Interaction/Interface/Application
EQ2.3	Data collection technology
EQ3	What feature was validated?
EQ4	Which user groups are involved in the use of DDSS in mental health?
EQ5	What diseases are currently targeted by DDSS in mental health?
EQ6	What decisions are supported by the system?
EQ7	What maturity level does the DDSS have?

Medical domain: The medical domain dimension describes the disease for which the decision support system can be applied.

Decision: The following scale defines the decisions a digital decision support system can support:

Prediction: The system outputs a risk score based on the likelihood that someone gets a disease.

Assessment: The patient is already sick (knowingly or unknowingly).

Diagnosis: Testing individuals with symptoms and/or suspicion of illness

Screening: Testing for individuals without specific symptoms

Monitoring: Decision support that evaluates symptom severity or treatment progress

Treatment: Recommendation or intervention concerning care or therapy

Maturity: As none of the existing maturity models fits our research, we designed a DDSS maturity model based on the SLR scale (26), but with adaptions specific to healthcare. It introduces additional gradation for noticing the moment where human interaction is added to the core AI algorithm. Our maturity

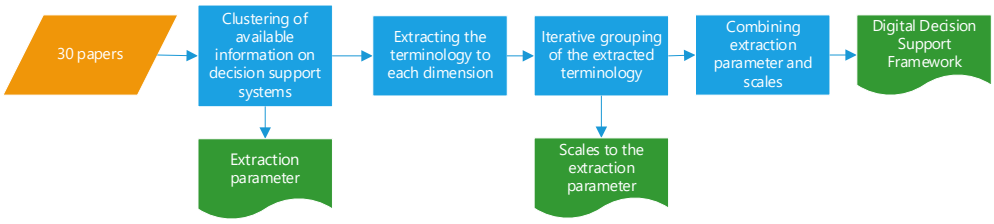

FIGURE 2
Extraction process.

levels describe on a scale from one to seven how advanced the DDSS is. Not all of the abovementioned dimensions are necessarily present in each of the maturity levels. As the maturity level gets higher, more dimensions are described.

1. Idea without implementation
2. Implementation without real-world interaction (algorithm development)
3. Implementation with real-world interaction but without patient intervention
4. Fully functioning prototype, system triggers real-world action, e.g., clinical trial
5. Operational product (at least one adopter, certified if required)
6. Locally adopted product
7. World-wide adopted product (transformational).

Data synthesis input data (EQ1)

The data used by digital decision support systems in the context of PTSD is diverse. Voice data (35, 45, 46, 55), text data (38, 48, 50), checklists and questionnaires (32, 33, 37, 41–43, 52, 53, 59), bio signals (32, 33, 36, 44, 45, 51, 57) and electronic medical records (34, 47, 56) as well as secondary data from other clinical studies (31, 40, 49, 54) are used. One article used the choices made by a virtual avatar in a role-playing game as input data (39). Of the 30 publications included in this review, 28 mentioned the sample size of the data they used to develop and test their decision support system. The minimum sample size was 10, and the maximum was 89,840 with a median (IQR) m = 151.5 (54.25 to 656.25). The violin plots (**Figures 4**, **5**) below show the distribution of the sample size. The top three outliers (89,840; 89,840; 5,972) were neglected in **Figure 5** for better visibility.

Figure 6 shows the data dimension of the studies in our review and indicates how the data used correlate with the average maturity levels of the DDSS. It visualizes the frequency and maturity of DDSSs based on the different data sources.

Data synthesis implementation (EQ2)

The majority (n = 15) of the investigated research uses a neural network approach (including support vector machines) in their systems. In 11 cases, support vector machines (SVM) were used. Other algorithms used were regressions, decision trees, random forest and rule-based approaches. We observed that 20 research papers did not have or mention any user interaction but worked solely on secondary data. The others used questionnaires or surveys, virtual humans or virtual reality. McWorther et al. proposed using temperature control, aromatherapy and auditory therapy capabilities for user interaction (36). Concerning maturity levels, AI algorithms are still mostly on maturity level two. Most advanced in terms of maturity were statistical methods and text mining methods, as indicated in **Figure 7**. The categories "statistics" and "machine learning" (ML) arose because some studies mentioned only these broad categories without further specifics.

Data synthesis validation (EQ3)

The majority (n = 23) of articles validated the accuracy of the DDSS studied. Three articles validated user acceptance, two validated efficacy and three did not mention validation. Comparing algorithmic validation among research papers was difficult since a variety of scores, such as F1 scores, area under the receiver operating curve (63) or overall accuracy, were used and they cannot be converted. To be able to provide an estimation of how well current DDSSs perform, we extracted all accuracy measurements present in each paper and aggregated each scale individually. The mean accuracy (n = 11) of the DDSSs is μ = 82.2% with a median of η = 82% and a standard deviation of σ = 0.095. The mean area under the curve value (n = 8) is μ = 0.845 with a median of η = 0.84 and a standard deviation of σ = 0.064.

Data synthesis user groups (EQ4)

The user groups mentioned were patients, clinicians and supporters of patients; however, the majority of papers did not explicitly mention specific user groups for their systems. Research covering decision support systems with higher maturity levels (four and above) included this information. Research dealing with decision support systems with lower maturity often lacked a clear user group since the process of using the proposed systems was not defined at that stage.

Data synthesis medical domain (EQ5)

In addition to PTSD, which was tackled by all 30 research papers, four investigated depression (46–48, 55), two anxiety (34, 48) and one paranoia (58).

Data synthesis decisions supported (EQ6)

Research focusing on predicting PTSD or its symptoms was most common (n = 11). Six papers focused on screening (35, 38, 45, 46, 50, 55) and six on treatment (32, 36, 43, 51, 53, 56). Four

TABLE 4 Terminology extraction.

EQ	Number of mentions	Terminology (frequency)
1 – Data	30	Jerusalem Trauma Outreach and Prevention Study (3); checklist (5); questionnaire (4); speech data (4); text data (3); electronic health records (3); sensor data (6); reactions in VR (2)
1.1 – Sample size	28	Not applicable (quantitative features)
2.1 – Decision technology	27	Machine learning algorithm; feed forward neural network; support vector machines, random forest; decision tree; sequential minimal optimization (SMO); Naïve Bayes; logistic regression; text mining; (LIWC); rule based
2.2 – Interaction technology	24	Questions (3); temperature control (1); aromatherapy (1); auditory therapy (1); virtual human (2); online survey (1); role-play-game (1); virtual reality (2)
2.3 – Data collection technology	22	Mobile app (4); web portal (3); skin conductance sensor (1); heart rate (1); accelerometer (1); IoT devices (1); microphone (1); webcam (1); Kinect (1); VR headset (1)
3 – Validation	29	Accuracy (23); user acceptance (3); efficacy (2)
4 – User groups	12	Patients (10); supporters (1); clinicians (6)
5 – Disease	30	PTSD (30); depression (4); anxiety (1); PTSD comorbidities (1); paranoia (1)
6 – Decisions	29	Prediction (11); assessment (1); diagnosis (4); screening (6); monitoring (5); treatment (6)
7 – Maturity level	30	Not applicable (quantitative features)

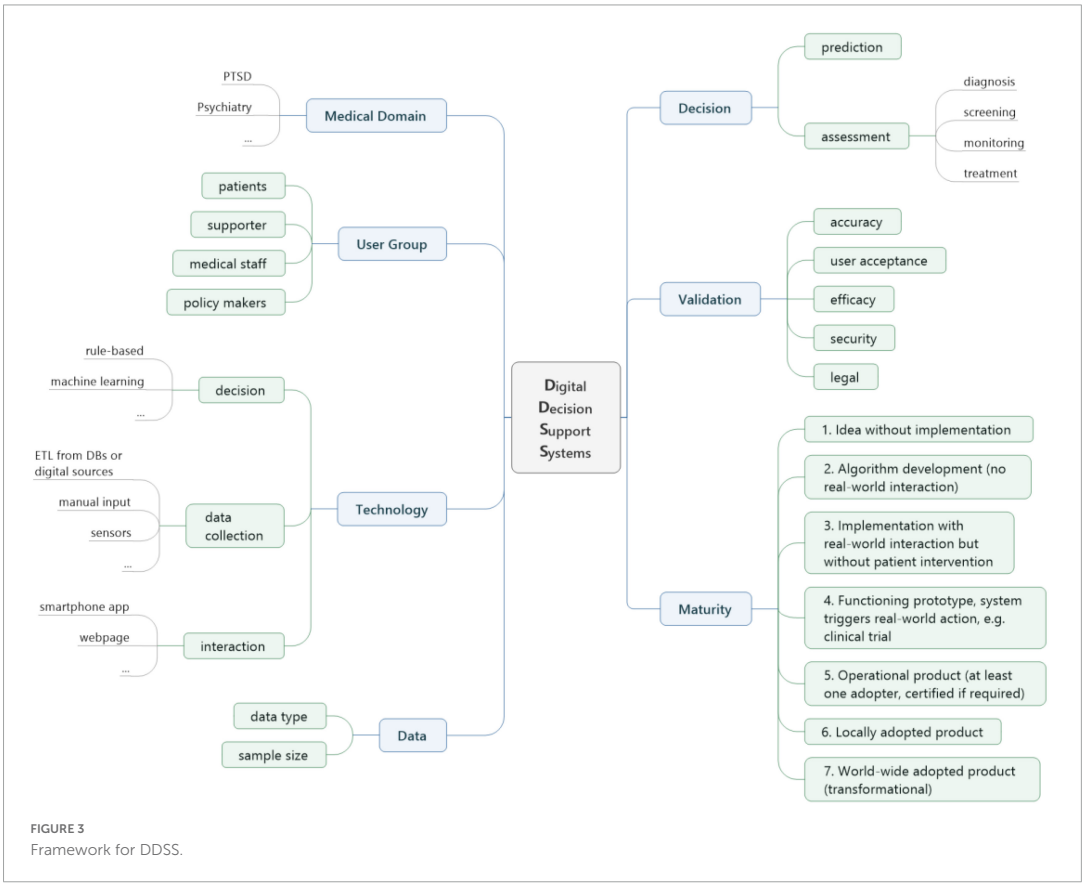

FIGURE 3
Framework for DDSS.

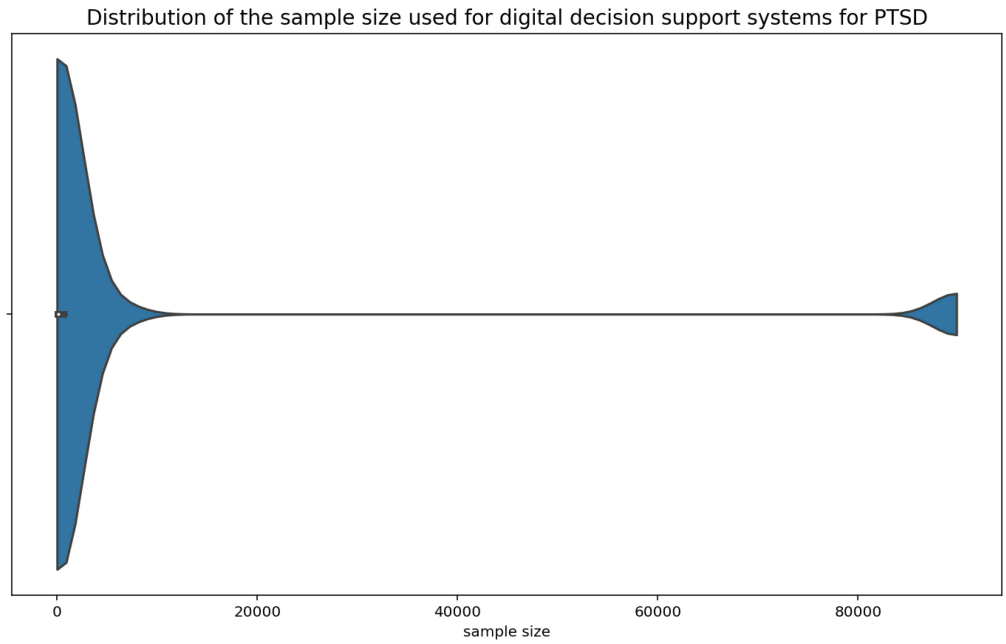

FIGURE 4
Sample size distribution.

papers investigated the diagnosis of PTSD (37, 41, 52, 60) and five focused on monitoring PTSD (33, 35, 56, 58, 59).

Data synthesis maturity level (EQ7)

The decision support systems were ranked according to the maturity scale described in see section "a framework for digital decision support systems." As stated by answering research question two, the majority of papers work with secondary data. This is supported by the high volume of research with a maturity level of two. **Figure 8** shows the number of articles grouped by maturity level.

Discussion

This research highlights the state of the art in digital decision support systems for PTSD based on our proposed framework. We developed the framework to ensure a holistic overview of all features of a DDSS. The dimensions of the framework represent the topics of interest and the choice of features is based on the conceptualization of the terminology extracted from the included articles dimension by dimension.

Concerning the data dimension, we noticed that questionnaires and checklists are still the most common and most mature (see **Figure 6**) input for decision support systems. When examining clinical guidelines like NICE (64) for diagnosing PTSD, questionnaires and checklists are still the only approach mentioned for diagnostics. Even though some new technologies, such as virtual or augmented reality, were investigated in the research found in this review, we noticed an absence of input parameters based on smartphones or wearables like GPS sensors or accelerometers. We hypothesize that this is due to the short life cycle of modern technologies, making it difficult to offer clinical evidence of their benefits. Questionnaires and checklists, however, have been around for many years and the methodology for administering them has not changed, therefore there is more scientific evidence of their use. Researchers and medical professionals are more likely to research, invest and adopt technology with strong evidence. This could be another reason why DDSSs using new technology are not widely included in clinical processes.

The data dimension also showed that the sample size is on average small and the statistical significance of the results was not proven by the majority of the research articles. Several reasons contribute to this. In general, medical data are hard to obtain for research because secondary use is still not easy with

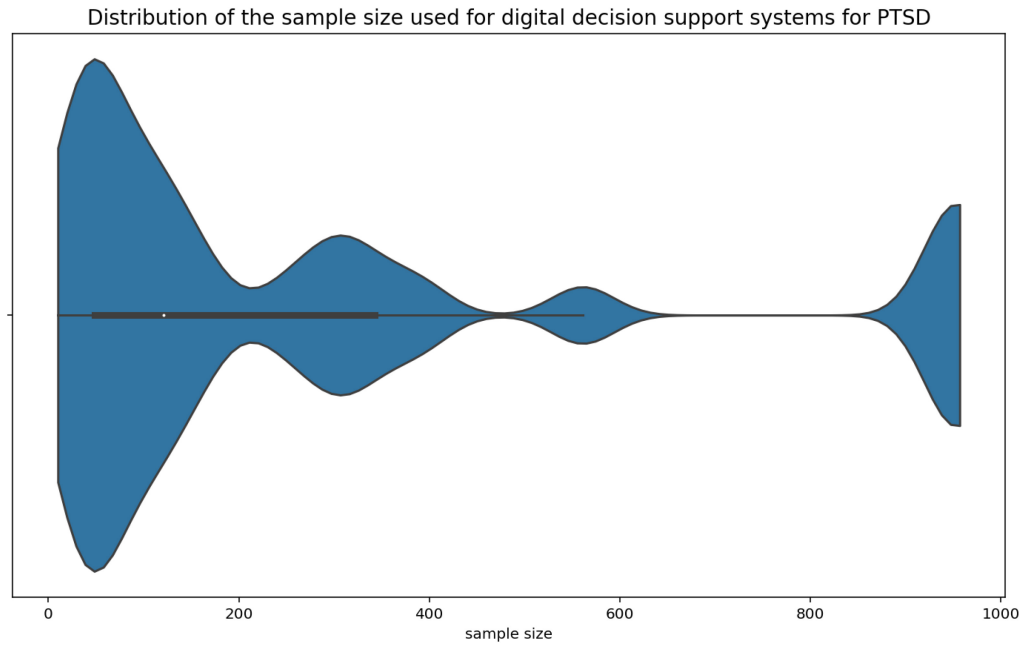

FIGURE 5
Sample size distribution excluding outliers.

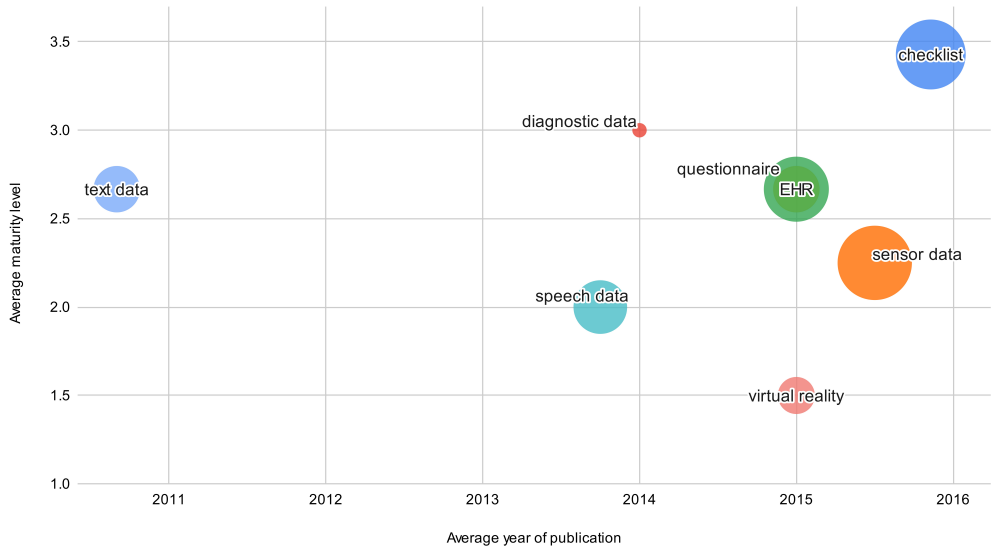

FIGURE 6
Data dimension concepts.

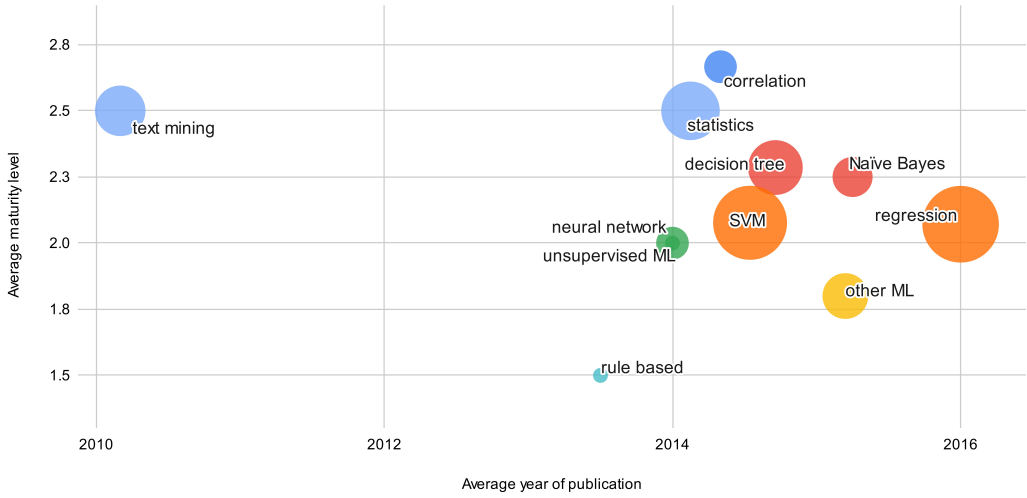

FIGURE 7
Decision technology concepts.

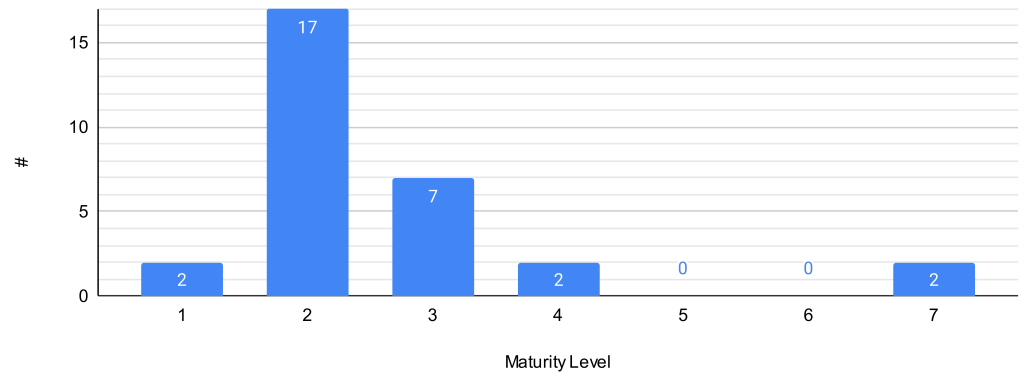

FIGURE 8
Bar chart – maturity levels.

many digital healthcare records and/or applications. Even if data can be obtained, they need to include the right parameters and have a structure that is usable for AI algorithms. Unstructured and text-based information is especially challenging to use for an AI. Further, most available datasets like the Jerusalem Trauma Outreach and Prevention Study do not include data on modern sensors (65).

The most common AI algorithm found during this literature review was support vector machines. Over the last few years, they have been developed to a *de facto* standard because they are easy to use, have good library support for programming and have low assumptions on the training data. We also observed that the number of research items resulting in usable products (maturity level $\geq$ 4) was low in three articles. Clinical studies with patient intervention (maturity level $\geq$ 3) were relatively low in nine papers out of 30. One reason for this could be that the small sample size of the research items does not provide sufficient evidence for clinical use.

All articles with a maturity level of 4 or more had, as one focus, validation of user acceptance and clearly defined user groups. Most articles with lower maturity levels did not have defined user groups. This could indicate a lack of strategic development and difficulties in bringing the research to a clinical setting. Our hypothesis is that interaction with

users or integration into clinical processes is often much more challenging to solve than intelligence of cognition. Still, most papers focus on cognition, not user interaction; our framework's validation dimension is evidence of this. We found 23 papers evaluating accuracy, which is an evaluation of AI technology, and five papers evaluating user acceptance or efficacy, meaning that they attempted to improve the current clinical process. Since most papers in our review are of maturity levels 1, 2 or 3 (meaning algorithm research), they do not include the clinical component necessary for user acceptance and efficacy evaluation. This shows a research gap when it comes to the enrichment of clinical processes with IT. The same goes for evaluating legal and IT-security constraints, which were not mentioned by any paper in our review. Since eHealth systems are getting increasingly focused by cyber attacks (66), IT and data security need to be a vital part of the evaluation to allow a safe DDSS adoption.

Further research has to be conducted on how the clinical process needs to be adapted for DDSSs to work, also in the context of the supported decisions. Most DDSS designers do not really understand the medical decision process but provide decisions in an "IT way." One limitation of this general hypothesis is that our research focuses solely on DDSS for PTSD. However, the narrow approach to include only PTSD shows that even in a very well-scoped area, a DDSS is hard to implement.

Since we used an inductive research approach to design our framework based on currently available literature, some important framework dimensions might be missing. One example is that the framework includes many technical aspects of the implementations and fewer organizational and financial perspectives. We encourage further research to include dimensions that describe the adoption of DDSSs in clinical processes.

Introducing our novel framework for DDSS, we provide a guide for decision support system evaluation. The framework is complementary to other healthcare technology evaluation methods (clinical, organizational, financial) and thus supports the design of comprehensive evaluation systems for DDSSs. Applying the maturity dimension helped us to examine what features of a DDSS are present, thereby indicating the steps to take in order to move up in maturity when developing decision support systems. Since the framework was developed out of general considerations, it can be applied to decision support systems outside of PTSD or mental health. However, it should be further evaluated to examine whether the terminology suits other domains. Higher maturity scales in particular need additional verification, since only two papers in our review had a maturity level above 4.

Conclusion

Our research aimed to analyze existing decision support systems for PTSD. Based on this goal, we developed a generic framework covering all dimensions of digital decision support systems. Our framework not only accelerates the development and benchmarking of DDSSs, but also acts as the foundation for our systematic literature review. Extracting data for all framework dimensions ensures consistency in our analysis and gives a holistic overview of DDSSs. During our review, we found working DDSS prototypes for PTSD and described their components. However, most of the systems are not evaluated in production use; they are only algorithmic models based on secondary datasets. This shows that there is still a gap between technical possibilities and actual clinical work. We proposed some possible explanations: small sample size, missing domain expertise, lack of focus to bring research to production. However, this gap should be analyzed further by testing our hypothesis and examining it with data from research on DDSSs for other mental diseases. For now, we conclude that only a few rare DDSSs for PTSD are ready for large-scale adoption in healthcare. The long-promised revolution of AI and ML for diagnosis in psychiatry, at least for PTSD, is yet to come.

Data availability statement

The original contributions presented in this study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Author contributions

MB: conceptualization, methodology, investigation, resources, data curation, and writing – original draft. JM: investigation, data curation, and writing – original draft. PR: writing, review, editing, and supervision. All authors contributed to the article and approved the submitted version.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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Appendix 6. Publication IV

IV

Janek Metsallik, Dirk Draheim, Zlatan Sabic, Thomas Novak, and Peeter Ross. Assessing Opportunities and Barriers to Improving the Secondary Use of Health Care Data at the National Level: Multicase Study in the Kingdom of Saudi Arabia and Estonia. *Journal of medical Internet research*, 26:e53369, August 2024. ISSN 1438-8871. doi: 10.2196/53369. URL https://www.jmir.org/2024/1/e53369

Original Paper

Assessing Opportunities and Barriers to Improving the Secondary Use of Health Care Data at the National Level: Multicase Study in the Kingdom of Saudi Arabia and Estonia

Janek Metsallik[1], MSc; Dirk Draheim[2], PhD; Zlatan Sabic[3], PhD; Thomas Novak[4], BA; Peeter Ross[1,5], MD, PhD

[1]E-Medicine Centre, Department of Health Technologies, School of Information Technologies, Tallinn University of Technology, Tallinn, Estonia

[2]Information Systems Group, School of Information Technologies, Tallinn University of Technology, Tallinn, Estonia

[3]Health, Nutrition and Population Global, The World Bank Group, Washington, DC, United States

[4]Office of the National Coordinator for Health Information Technology, Department of Health and Human Services, Washington, DC, United States

[5]Research Department, East Tallinn Central Hospital, Tallinn, Estonia

Corresponding Author:
Janek Metsallik, MSc
E-Medicine Centre, Department of Health Technologies
School of Information Technologies
Tallinn University of Technology
Akadeemia 15a
Tallinn, 12616
Estonia
Phone: 372 56485978
Email: janek.metsallik@taltech.ee

Abstract

Background: Digitization shall improve the secondary use of health care data. The Government of the Kingdom of Saudi Arabia ordered a project to compile the National Master Plan for Health Data Analytics, while the Government of Estonia ordered a project to compile the Person-Centered Integrated Hospital Master Plan.

Objective: This study aims to map these 2 distinct projects' problems, approaches, and outcomes to find the matching elements for reuse in similar cases.

Methods: We assessed both health care systems' abilities for secondary use of health data by exploratory case studies with purposive sampling and data collection via semistructured interviews and documentation review. The collected content was analyzed qualitatively and coded according to a predefined framework. The analytical framework consisted of data purpose, flow, and sharing. The Estonian project used the Health Information Sharing Maturity Model from the Mitre Corporation as an additional analytical framework. The data collection and analysis in the Kingdom of Saudi Arabia took place in 2019 and covered health care facilities, public health institutions, and health care policy. The project in Estonia collected its inputs in 2020 and covered health care facilities, patient engagement, public health institutions, health care financing, health care policy, and health technology innovations.

Results: In both cases, the assessments resulted in a set of recommendations focusing on the governance of health care data. In the Kingdom of Saudi Arabia, the health care system consists of multiple isolated sectors, and there is a need for an overarching body coordinating data sets, indicators, and reports at the national level. The National Master Plan of Health Data Analytics proposed a set of organizational agreements for proper stewardship. Despite Estonia's national Digital Health Platform, the requirements remain uncoordinated between various data consumers. We recommended reconfiguring the stewardship of the national health data to include multipurpose data use into the scope of interoperability standardization.

Conclusions: Proper data governance is the key to improving the secondary use of health data at the national level. The data flows from data providers to data consumers shall be coordinated by overarching stewardship structures and supported by interoperable data custodians.

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KEYWORDS

health data governance; secondary use; health information sharing maturity; large-scale interoperability; health data stewardship; health data custodianship; health information purpose; health data policy

Introduction

Background

Governments seek guidance and strategic directions for deploying effective, efficient, and reliable mechanisms for the secondary use of data collected in health care provision. While the primary use of digital data in health care institutions has developed well during the last decades, health care systems look to improve their practice for secondary use. The secondary use of data controls the burden of data capture by enabling the reuse of already collected data for alternative purposes. Among others, the categories of secondary data use include improving the patient experience, health care facility management, service planning and benchmarking, policy development, public health, health care financing, research, and business support [1]. The categories above exploit data traditionally collected in separate data streams and silos. For instance, public health registries or health insurance claims are managed in most countries by dedicated organizations within their databases using specific data collection processes. The siloed approach has led to the duplication of data collection and the waste of health care resources. A report by the Open Data Institute from 2021 concludes that initiatives for health data ecosystems for data reuse are still fragmented in Europe [2].

Digital data and digitalized processes allow for a change in these practices, making data capture universal and allowing digital health care data sharing for different purposes.

From 2019 to 2021, we conducted projects in the Kingdom of Saudi Arabia and Estonia, assessing health and health care data analytics and developing context-specific recommendations. The governments of both countries were looking to advance their decision-making capabilities due to the digitalization of the flow of health data.

The Project in the Kingdom of Saudi Arabia

The Saudi Health Council (SHC), in cooperation with the World Bank, developed the National Master Plan for Health Data Analytics to guide and provide strategic direction for the deployment of effective, efficient, and reliable mechanisms to share data from the health sector for policy and decision-making [3].

The government sought to boost the regulatory, institutional, and technical infrastructure, allowing for efficient data collection from health care systems to process and provide appropriate data analytics and business intelligence for policy and decision makers. The project assessed the existing situation and conceptualized the harmonized national health data analytics operational model and the logical architecture, including core elements such as the Health Data Analytics Framework, actors and their roles, and critical processes.

The initial driver for the development was perceived inefficiency and observable delays in producing analytical data products about the country's health care system. Indirectly, the existing data flow was limiting the ability to produce accurate and timely information for decision-making on many levels of the health care system. The project focused on the requirements of the significant national-level decision makers, including the SHC and management of the health care sectors, namely, Ministry of Health (MoH) Medical Services, National Guard Medical Services, Ministry of Interior Medical Services, and King Faisal Specialist Hospital & Research Center.

The Project in Estonia

The analysis of health and health care data management was part of the Structural Reform Support Service mission of the European Commission, to provide support for the preparation and implementation of growth-enhancing administrative and structural reforms by mobilizing European Union funds and technical expertise. Estonia requested support from the European Commission under Regulation (EU) 2017/825 on the establishment of the Structural Reform Support Program ("SRSP Regulation") to prepare the Person-Centered Integrated Hospital Master Plan [4].

The master plan targeted to (1) provide a map of the current hospital system, its ability to supply health care in different specialties, distribution of its physical and human resources, its financial flows, and its mechanisms of governance and information sharing; (2) provide evidence-based estimates of the population needs and the supply of health workforce and health care services and infrastructures; and (3) propose a hospital master plan of sound reforms in the hospital sector in the midterm.

The planning included an assessment of the data sharing mechanisms and governance. Current and future organizations delivering the data for decision-making throughout the hospital network were analyzed. The scope of the analysis included data for the national-level health care management and policy (Ministry of Social Affairs [MoSA]), public health (National Institute for Health Development [NIHD]), health care financing (Estonian Health Insurance Fund [EHIF]), and health care service management and clinical decision-making (hospitals and family health centers).

The Tension Between Demand and Supply of Information

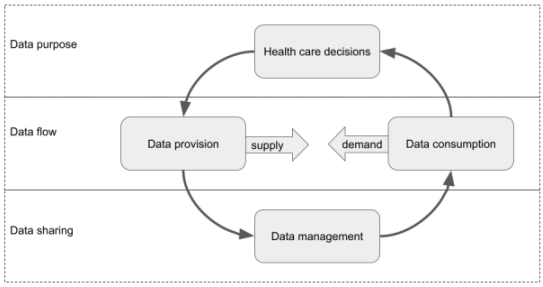
In both cases, the digitalization of the health and medical data flows should improve the quality of the decisions. Data in health care are often produced and consumed by different stakeholders. They need to cross the boundaries of specialties, institutions, regions, and sectors to deliver informational value to data consumers so that they can make decisions. From the point of view of decision makers, the place of capture has a surplus, and the place of decision-making has a shortage of information. The tension of disbalance generates the need for data flow: data consumers need data from data producers to extract information for decision-making.

The stakeholders in health care that need data for decision-making, such as governmental organizations, payers, policy makers, and others, feel the tension and try to resolve it. They request data providers to collect and deliver data for each type of consumption. As the providers cannot always align the requirements, they often capture the same information multiple times. The uncoordinated design of data flows has manifested in duplication, gaps, and delays.

The projects analyzed health care data supply and demand for data for different health care decisions. The analysis aimed to provide a better basis for planning data management organization and infrastructure.

In both cases, the client saw issues producing proper analytical data products. In the Kingdom of Saudi Arabia case, the focus was on the reports on public health and health care system indicators. The Estonian terms underlined person centricity and efficacy, which introduced the requirement to study data sharing for clinical decision-making, patient engagement, hospital management, health care system planning, health care policy, and health care funding. To assess the situation and plan for better data sharing, we found it essential to map the providers and consumers and evaluate the usability and use of data for decision-making. The assessment of health care data systems focused on the data purpose, flow, and sharing (Figure 1).

Figure 1. Health care decisions are the purpose of data consumption. Health care decisions also provide new data. Often, the source location of the provided data does not match the desired location of the consumed data. This disbalance between supply and demand creates tension that forces data to flow. Data management resolves the tension by sharing data to required locations.



The Aim of the Study

This study aimed to report problems and outcomes from the 2 distinct projects that assess the potential of secondary use of health care data and support of governmental decisions and to map the common thread of thought to apply in similar circumstances. We looked for the matching elements of the problems and the results of the 2 assessments.

Methods

Overview

The respective terms of the projects regulated the work conducted in the Kingdom of Saudi Arabia and Estonia. In general, both projects had to deliver an initial assessment and recommendations for improvement. In the Kingdom of Saudi Arabia, the project concluded with the National Master Plan for Health Data Analytics [3]. In Estonia, the results were integrated into the Person-Centered Integrated Hospital Master Plan [4].

This section describes the framework of definitions and research methods that we developed for the projects.

Mapping Data Sharing Purposes

Digitalization shall enable gains in the effectiveness of decision-making (better inputs, better decisions) and increase the efficiency of data processing (timely and cost-effective delivery of data), resiliency against missing or erratic data, and sustainability of the data management (agility of the data models and infrastructure). One can assess digital health effectiveness by its ability to generate data (inputs) for decision-making. The World Health Organization (WHO) lists various health care performance indicators for management and policy decisions. The WHO has divided the core health indicators into 4 domains: health status, risk factors, service coverage, and health systems [5]. The system of indicators supports rationalized alignment of priorities and harmonization of investments for various levels of health care systems. We used the system of indicators to model health data completeness. The indicators allowed us to cross-check if the needs of the decision makers were fully met. We analyzed the ability of a health care system to coordinate the data required for the indicators.

The purpose of the collected data is to support health care activities (Figure 1). The activities depend on input data and generate new data, including clinical, managerial, financial, and others. The organizational or human actors of studied ecosystems perform these activities. For example, a hospital manager preparing the financial plans consumes data about the average cost per patient case. On the basis of the WHO indicator domains, the studies searched for evidence of data consumption in public health status and risks, health care activity, resources, funding, and clinical decision-making and research. In the Kingdom of Saudi Arabia case, we paid less attention to the clinical side, mainly focusing on the national public health indicators and the health care system. In the Estonian case, in addition to clinical decision-making, we investigated patient-side decision-making, and patient engagement was considered a separate health care activity.

Mapping Data Flow

Digital health ecosystems facilitate data flows to resolve data provision and consumption tension. The projects in Kingdom

of Saudi Arabia and Estonia mapped the roles, procedures, structures, terminologies, and master data involved in coordinating the flow. We built catalogs of organizations that capture health care data (data providers) and organizations that receive health care data (data consumers). The interoperability between the sources and targets may be organized in many ways, either via bilateral point-to-point agreements or multilateral standards-based agreements. The parties share registries of identifiable objects, such as persons, legal entities, locations, services, and others. We checked the availability of data standards and master data registries. For greater secondary use, multilateral data-sharing agreements shall be in place. If we identified standards-based data sharing, we also examined the governing organization around the standards. Depending on the data governance setup, 1 or more entities would coordinate the data requirements between data consumers and providers, govern information assets, design and enforce data standards, and monitor the continuity of the data flow. The responsibility for the coordination is called data stewardship. The data policy's task is to regulate the distribution of data governance responsibilities and enable control over them. For example, a data policy may state that licensed health care institutions shall follow the data collection standards set by a single stewardship organization; this may enforce a data flow that makes a log of activities and resources spent on those activities available to health care management and funding stakeholders.

Mapping Data Sharing

Data sharing is based on the organizational and technical capability that transports data between decision-making locations. We gathered information about the data management platforms, the organizations running the platforms, and the standards supporting data exchange. A data manager or custodian is responsible for maintaining a technical environment and a database structure for data sharing. Regardless of the topology of a data sharing system, centralized or distributed, the data shall be delivered to the correct location at the right time for decision-making. For example, a public registry of laboratory results may transport data between the laboratories, health care providers, and researchers.

The discipline of enterprise information management defines the elements of data flow and sharing. Data governance roles, namely, data policy, data stewardship, and data custodianship, have been used for structuring enterprise information management [6,7]. In the case of the studied projects, we looked for the data governance structures in the national-level health care data organizations.

Assessing the Maturity of Capability

Various capability maturity models support assessing health care information systems [8]. Many maturity models focus on a specialty; a type of organization; or an area of function (hospital management, diagnostic images, and more). Some models focus on the digital health system's ability to connect sources and targets of data sharing. The Health Information Sharing Maturity Model (HISMM) from the Mitre Corporation suggests assessing a digital health system from the perspective of 11 capability areas, which cover technology, use, and governance perspectives [9].

The HISMM model has 2 dimensions: 11 characteristics and 5 maturity levels. The maturity level reflects the level of development or goal achievement regarding a capability. If each launch of a data flow requires the creation of a new organization, the flow has a project-based (1) capability level. At the expert-based (2) capability level, existing organizations (experts) can process a data flow. At the standard-based (3) capability level, data flow can be initiated by involving several organizations providing the same level of service. The data flow at the performance-based (4) level constantly produces indicators of the success of its activities. The data flow is at the learning-based or optimizing (5) level if the performance indicators trigger continuous improvement [9]. For the assessment, we enhanced the HISMM levels with the maturity criteria from ISO 33020 and Capability Maturity Model Integration (CMMI), which guide the assessment of capability maturity of processes related to information systems [10,11]. For example, when level 3 of ISO 33020 requires that "a standard process, including appropriate tailoring guidelines, is established and maintained," we looked for such evidence in our desktop research and in the interview notes.

The characteristics dimension of the HISMM model contains 11 characteristics. The 11 characteristics form a checklist for developing data flows. According to these 11 characteristics, analyzing which additions must be added to the use, technology, or governance organization to increase capacity is possible.

On the basis of our experience with the Kingdom of Saudi Arabia, we introduced the HISMM as an additional tool for assessment in Estonia. Despite our interest, it was economically unreachable for us to redo the assessment in the Kingdom of Saudi Arabia only to compare the HISMM assessment results.

In Estonia, we structured maturity evidence based on the stakeholders' purpose. The structuring allowed the study to analyze the variation in the inputs collected from different decision makers. For example, we were looking for the differences in the maturity of health care management, clinical decision-making, and patient engagement, where all stakeholders may need data about health care resources.

The Framework of the Assessments

The complete framework provides categories for mapping the capabilities and assessing the maturity of those capabilities. Textbox 1 below provides a summary of the categories.

The framework drove the capture and analysis of the findings in both projects. We asked the interviewees about the purposes of using health data and the means they used to manage the data. Together with the interview participants, we investigated the stakeholders, information systems, standards, technologies, and platforms on which their data flows were based. For example, we asked the hospitals' management about the indicators they used in decision-making. Then, we asked the statisticians and IT specialists to describe the sources of the data and the data processing activities.

Textbox 1. The assessment framework includes categories for mapping capabilities from the data and stakeholder purpose perspectives. The purpose is satisfied via data flow and sharing capabilities, which indicate details of the implementation's maturity level.

Data purpose

- Public health status
- Public health risks
- Health care activity
- Health care resources
- Health care funding
- Clinical decision-making
- Clinical research

Data flow

- Data providers
- Data consumers
- Data stewardship
- Data standards
- Data policy
- Master data

Data sharing

- Data platforms
- Data custodianship
- Data exchange standards

Stakeholder purpose

- Patient engagement
- Clinical decisions
- Health care management
- Research and monitoring
- Health care policy
- Health care funding

Capability maturity

- Level 5. Optimizing
- Level 4. Performance
- Level 3. Standards
- Level 2. Experts
- Level 1. Projects

Capability characteristic

- Technology

1. Data quality
2. Data transport
3. Data security
4. Interoperability

- Use

5. Usability
6. Alignment
7. Participation
8. Consent
- Governance

9. Data governance
10. Stakeholder governance
11. Sustainability

Project Activity in the Kingdom of Saudi Arabia

For the situational analysis in the Kingdom of Saudi Arabia, we completed a comprehensive institutional review of the current data systems in the health sector, with an emphasis on how these data were collected and could be routinely made available to the responsible authorities.

We assessed the processes at the institutional, operational, and technical levels. To understand the architectural options for integrated data management, we analyzed the current development plans and statuses, including a rapid assessment of existing computerized information systems, services, and tools. Specifically, we assessed the critical processes for data management and use, system architectures, database architectures, key relevant data sets, data exchange capabilities, geospatial tools, and system platforms available in the health system. The assessment identified the health system's critical information systems, data sets, and exchange capabilities.

The assessment methodology included primary and secondary sources, including interviews with stakeholders. The research team interviewed policy makers and stakeholders during a sequence of missions in 2019. The stakeholders included the national-level health care coordination (SHC) and management of the sectors, namely, MoH Medical Services, National Guard Medical Services, Ministry of Interior Medical Services, and King Faisal Specialist Hospital & Research Center. The project included an in-depth web search of written information and web-based resources on digital health tools and systems for data exchange and analytics. To improve the primary stakeholders' capacity and achieve a common understanding of master plan goals, a seminar about global experiences and examples of technical solutions took place during the first technical mission.

Project Activity in Estonia

The team evaluated Estonian hospitals' health data and information exchange levels. The method combined interviews and desk research. The aim was to understand the value of health and medical information sharing capabilities to stakeholders, identify gaps in funding, and relate governmental activities to strategies and frameworks.

This rapid assessment used semistructured interviews. Institutional, operational, and technical experts described their view on Estonian digital health care data governance; health data flows; information security; and existing computerized information systems, services, and tools. The analysis considered the hospitals part of a more comprehensive data sharing network. Hence, participants provided inputs about both internal and external data sharing. Specifically, interviews with the stakeholders touched on the critical processes for data management and use, system architectures, database architectures, key relevant data sets, data exchange capabilities, and system platforms available in the health system, considering the current use of the EHIF, the Estonian Health Information System (EHIS), and the NIHD databases.

The data sharing network under discussion included health care institutions, public authorities, and other data users, for example, researchers and patients (from the point of view of hospitals). As the interviews covered the involved participants in both data provider and data consumer roles, the captured evidence also touches on the existing and potential use of data for primary and secondary purposes. On multiple occasions, the interviewed stakeholders were able to share insights into the integration of health data exchange and services with social and labor market services. The assessment covered vital information systems, data sets, and data exchange capabilities of the Estonian health care system.

Altogether 9 stakeholders were interviewed, including hospitals (North Estonia Medical Centre, Tartu University Clinic, Pärnu Hospital, Viljandi Hospital, Põlva Hospital, and East Viru Central Hospital) and specialists from the NIHD, the EHIF, and the Estonian Society of Cardiology. Before the interview, we provided the interviewees with a comprehensive set of questions divided into 11 categories according to the capability attributes of the HISMM. The length of the interviews ranged from 1.5 to 2 hours. Usually, the group consisted of 4 to 5 persons, including the head or vice-head of the institution; chief specialists of clinical, IT, service development departments; health accounting; and statistics.

Ethical Considerations

This study compiled the framework, methods, and findings from the past project deliverables, which were available publicly or per request from the respective owners. The projects in the Kingdom of Saudi Arabia and Estonia assessed material available from public sources and interviews. The included organizations-appointed interview participants. The projects did not compensate for the participation. We informed the participants about the purpose of the assessment and used the interview results anonymously. The study team never recorded any health data during the interviews or site visits. This study

includes statements on the possible limitations of the conclusions.

Summary of the Methodology

Table 1 summarizes the methods used by the projects in the Kingdom of Saudi Arabia and Estonia.

Table 1. Methodology of the case projects.

Methodology element	The Kingdom of Saudi Arabia	Estonia
Research type	Evaluation research	Evaluation research
Research design	Exploratory case study	Exploratory case study
Sampling method	Purposive sampling	Purposive sampling
Data collection method 1	Personal semistructured interviews	Personal semistructured interviews
Data collection method 2	Documentation review	Documentation review
Data analysis method	Qualitative content analysis	Qualitative content analysis
Data coding 1	Data purpose, flow, and sharing	Data purpose, flow, and sharing
Data coding 2	—[a]	Health Information Sharing Maturity Model
Target application	National Master Plan for Health Data Analytics	Person-Centered Integrated Hospital Master Plan, and Information-Sharing Capability Maturity Assessment
Research question	What are the gaps and critical elements for the national-level improvement of the secondary use of health care data?	What are the gaps and critical elements for the national-level improvement of the secondary use of health care data?

[a]Not applicable.

Results

Digital Health Landscape in the Kingdom of Saudi Arabia

The Kingdom of Saudi Arabia health care information system encompasses several stakeholders, including primary health care (PHC), hospitals under different jurisdictions, the SHC, the MoH, public health research, quality management, and others. The project looked at the health care system as a whole.

The Kingdom of Saudi Arabia has a population of 35 million, divided between 21.4 million Saudis and 13.6 million non-Saudis. The annual population growth rate was 2.38 in 2020, which dropped slightly from 3.19 in 2010. Part of it can be accounted for by the lowered fertility rate of 1.9 in 2018 and 2.98 in 2010 [12]. The population aged >65 years was 3.4% in 2019, and it is expected to grow to 6% by 2030, which makes it a country with a relatively young population compared with its neighbors in West Asia [13].

The health care system in the Kingdom of Saudi Arabia is mainly funded via the MoH of the Kingdom of Saudi Arabia, which covers 287 hospitals with 45,180 beds, 2257 PHC centers, and 973 specialized medical facilities. In addition to MoH, the governmental health care sector includes providers under the Armed Forces Medical Services, National Guard Medical Services, Ministry of Interior Medical Services, King Faisal Specialist Hospital & Research Center, Royal Commission Hospitals, ARAMCO Hospitals, and Ministry of Education. The total number of hospital beds in other government sectors is 13,989, divided among 50 hospitals. The private sector in the Kingdom of Saudi Arabia runs 167 hospitals with 19,427 beds [14].

In 2000, the Kingdom of Saudi Arabia institutionalized the development of electronic health care as a governmental committee. In 2005, the government established the Saudi Association for Health Informatics, which focused on the growing awareness of electronic health among health care professionals [15]. The effort put into awareness and education has supported the adoption of health IT. Still, the adoption could have been more cohesive, and the use of electronic health systems has been limited [16]. A multiple-case study based on a survey (conducted in 2010) of 6 of the seemingly most advanced medical cities of the Kingdom of Saudi Arabia concluded that inadequate data management policies and procedures, resistance to change, the low analysis of data, and lack of accreditation impact the health IT adoption. The study revealed a need to introduce a national regulator and establish a data exchange plan through a national health information network [17]. The MoH of the Kingdom of Saudi Arabia has invested in the growth of health information exchange on all health care levels. Some researchers have found that the MoH's focus on information exchange between the health care system participants supports the greater adoption of electronic health records. The sharing adds more value to the data and increases the motivation for quality data capture and improvement of health IT tooling [18].

The SHC, established in 2014, is a successor to the Health Services Council, established in 2002. The role of the SHC is to coordinate and integrate health care stakeholders regardless of the type of ownership or the sector of governance. At the time of the project, the SHC included 16 representatives from several ministries, national health care agencies, education institutions, and health care institutions. The SHC governs some national health centers, including the National Center for Health Information [19].

The National Health Information Center (NHIC) was established in 2013, with the mission to organize health information exchange among all health sectors and related parties, to develop and customize terminology and data exchange standards, to create and supervise telehealth networks, to create national disease registries, and to provide health information to the beneficiaries [20].

Digital Health Landscape in Estonia

Estonia has a population of 1.3 million, which has declined since 1990. The annual population growth rate has been approaching 0 (from the negative side) in the past years. However, the growth rate has been lifted by migration as the fertility rate of 1.6 per woman is less than that required for reproduction [21]. The population aged >65 years was 20% in 2019 and is expected to grow to 23.5% by 2030, slightly above the average of 18.8% and 21.8% in the region of Northern Europe [22].

All health care institutions operate under private law in Estonia. General practitioners are private entrepreneurs or limited companies. At the same time, hospitals are joint-stock companies or not-for-profit foundations licensed by the Health Board and provide various inpatient or outpatient medical or nursing care. In total, 1428 health care institutions were covered by the National Institute of Health Development statistics in 2019. There are 52 hospitals with 6788 beds, 436 family health centers, 490 dental care providers, 317 specialized outpatient medical care, and others [23]. The health care system in Estonia is governed by the MoSA. The system's structure includes agencies of the MoSA (eg, State Agency of Medicines, Health Board, NIHD, and Center of Health and Welfare Information Systems); independent public bodies (EHIF); (mainly publicly owned) hospitals under private regulation; private PHC units; and various nongovernmental organizations and professional associations. The financing is organized chiefly through an independent single public-payer EHIF, including ambulance services [24]. The government regulation establishes a list of regional, central, general, local, and rehabilitation hospitals, a total of 19 hospitals, to ensure uniform access to health care services. These hospitals are entitled to receive the necessary construction, renovation, and reprofiling investments from the government budget. With the hospitals mentioned in the list, EHIF concludes treatment financing contracts for at least 5 years based on the type of hospital listed and the corresponding operating license.

The MoSA of Estonia covers public health from the state budget. Private, primarily out-of-the-pocket spending was 22.7% in 2016 [21].

Health care data are divided between 14 primary national-level sources, in-house sources of health care service providers, and databases of research institutions. In addition to inherent health care data sources, the e-government platform enables the secondary use of public registers for health care needs. For example, the Population Register, managed by the Estonian Police and Border Guard Board, is the source of personal data for patient management. The Health Board manages public registers of health care professionals and health care institutions. The State Agency of Medicines manages registers of drugs, medicinal products, and pharmacies. The EHIF collects reimbursement-related health data, registers the status of insured persons, and manages digital prescriptions. The Center of Health and Welfare Information Systems maintains a significant platform for health data sharing, the EHIS [25] that encompasses the whole country, registers all residents' health history from birth to death, and is based on the e-government infrastructure.

Since 2008, the Digital Health Platform (DHP) has been operating in Estonia, which shares the health care data of the entire country's residents in a secure e-government environment, both between authorized health care workers and between a health care worker and a natural person. The DHP, whose official name is the EHIS, aims, among other things, to process the data related to the area of health care for entry into and performance of contracts for the provision of health services; for ensuring the quality of health services and the rights of patients; and for the protection of public health, including for the upkeep of registers and the organization of health statistics and the management of health care [24].

Assessment Results in the Kingdom of Saudi Arabia

In the case of the Kingdom of Saudi Arabia, the project delivered 2 consecutive components that led to the recommendations for decision makers to boost the regulatory, institutional, and technical infrastructure within the country's health care system, thereby allowing for the efficient collection of health care data.

First, we performed the situational analysis of health and health care data management. The delivered assessment report provided a brief institutional review of the Kingdom of Saudi Arabia health care system's data management and identified vital information systems, analytical data sets, and data exchange capabilities.

The assessment report revealed that data reporting and analytics procedures, standards, and forms in health care should be coordinated and coherent across the ministries with health care institutions under their jurisdiction and with the MoH and SHC.

On the basis of the review, the report gave recommendations for the long-term institutional, organizational, architectural, and technical redesign of health care data analytics to move from static, fragmented, and incomplete data sets to rapid, reliable, and dynamic data processing, exchange, extraction, and consolidation. We used these recommendations as the basis for the development of the second deliverable, the Master Plan for National Health Data Analytics; it is a policy document that describes the regulatory, institutional, and technical infrastructure that allows the efficient collection of digital health and health care data from health care systems to process and provide appropriate data analytics and business intelligence for policy and decision makers. The SHC of the Kingdom of Saudi Arabia approved the Master Plan in 2020.

The Master Plan outlines a framework for data, roles, and processes. The framework considers analytical data sets, health care indicators, reports, metadata, and catalogs as parts of the data dimension. The framework of roles supports the governance of the data and information flows and endorses the strategic value of the analytical data. The Master Plan defines the specific

organizations that shall fulfill the defined roles. The process dimension outlined a set of workstreams for analytical data. It described a path to produce needed policies, objectives, data definitions, analytical product definitions, and standards.

The Master Plan evaluated multiple options for assigning the data governance roles. The final recommendation was to share the responsibilities between the units of the SHC: the policy and strategy management to the SHC Board, data stewardship and analytics to the National Health Analytics Department, data custodianship to the National Health Observatory at the NHIC, and standardization to the Data Standardization Unit at the NHIC.

To operationalize the framework, the Master Plan proposes 3 years to transition responsibilities and develop institutional capacity on all levels. After that, all actors at the national and subnational levels shall adapt to the general and national data analytics frameworks.

Assessment Results in Estonia

In Estonia, the study used interviews to collect inputs for the assessment. The researchers adopted the HISMM and reorganized the notes using capability attributes and stakeholder purpose. The purpose dimension aimed to summarize the capabilities or flows that the interviews covered. The interview content covered the purpose, flow, and sharing. We asked the interviewees to cover the topics for all the data governance roles of their institutions. For example, depending on a specific capability discussed, a hospital can be a data provider, consumer, custodian, and steward. The notes were analyzed for evidence of maturity and labeled accordingly. The method resulted in a 3D matrix with dimensions for stakeholder purpose, capability attributes, and maturity level (Figure 2).

The researchers estimated the maturity of the information sharing to be on levels 2 to 4. Level 2 represents a situation where the information flow stands on the existing expertise, and the flow outcomes are repeatable. Level 3 indicates the existence of standards and procedures that allow new providers to enter the market. On level 4, the assessed ecosystem shall demonstrate an ability to measure the achievement of the information sharing goals.

The assessment suggests, also visualized in Figure 3, that the improvement focus should be on data quality, transport, and stakeholder governance. From the perspective of stakeholder purpose, the flows that feed decisions on health care policy show the lowest maturity. The maturity matrix indicates that the data and information may circulate in silos of governance; experts are needed (level 2) to support the data to reach the policy makers. The below-average estimates on data and stakeholder governance hint that the coordination of the data flows is mostly implicit. The interviewees missed the explicit rules and coordination of the secondary use of data. The above-average estimates on data for clinical purposes indicate the success of standardizing patient data flows via the EHIS.

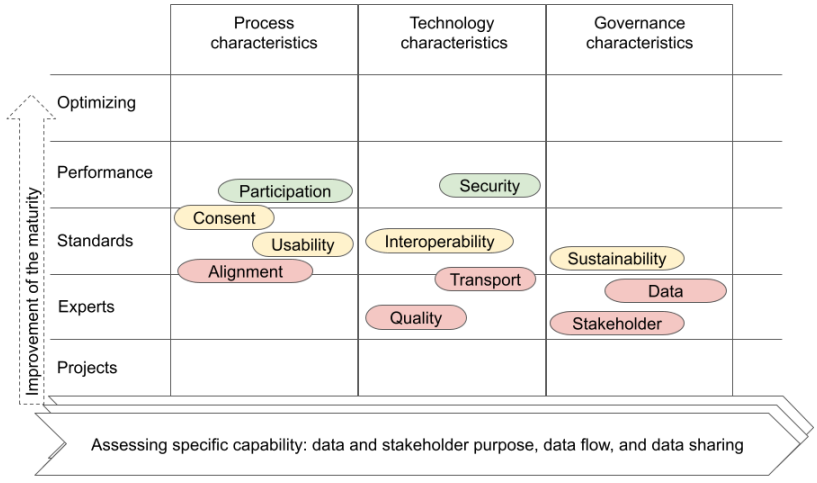
The project in Estonia combined the HISMM into the framework of analytics. The role of the HISMM was to provide insight into the improvement potential of the established flow of data. The findings of the maturity assessment allowed the stakeholders' viewpoints to be drawn to and the specific characteristics of the flows to be analyzed. The HISMM is a valuable tool for cases where the primary data policy, governance structure, and platform are already in place. Analysis of the specific characteristics provides a basis for targeted improvements. When a data flow misses expectations, an assessment may reveal a specific characteristic that limits the flow. The summary of the HISMM results in Estonia shows the need to improve the focus on data quality, data transport, data and stakeholder governance, and process alignment (Figure 3).

The study in Estonia concluded with a recommendation to align the roles of data providers, consumers, stewards, and custodians for the expanded multipurpose data flows. The current document-based health information sharing model shall transform into a shared space of Integrated Care Records. We reported the assessment results as part of the Person-Centered Integrated Hospital Master Plan, which also included reports of teams of other specialists.

Figure 2. The figure summarizes the Health Information Sharing Maturity Model assessment findings from Estonia. The matrix's cells depict the maturity levels grouped by the 11 capability characteristics in the vertical dimension and by the 6 stakeholder purposes in the horizontal dimension. The number in the cell shows the corresponding level of maturity, colored red for level 2, yellow for level 3, and green for level 4.

Perspective	Capability characteristic	Stakeholder purpose					
		1. Engagement	2. Clinical	3. Management	4. Research	5. Policy	6. Funding
Technology	1. Data quality	2	2	2	3	2	3
	2. Data transport	2	3	2	2	2	3
	3. Data security	4	4	4	4	4	4
	4. Interoperability	3	3	3	2	2	3
Use	5. Usability	3	3	3	3	2	3
	6. Alignment	2	3	3	3	2	2
	7. Participation	4	3	4	3	3	2
	8. Consent	3	3	3	3	2	2
Governance	9. Data governance	3	3	2	2	2	2
	10. Stakeholder governance	2	3	3	2	2	2
	11. Sustainability	4	2	2	4	3	4

Figure 3. The figure visualizes the maturity levels of Health Information Sharing Maturity Model characteristics in aggregation. It shows that data quality and transport, data and stakeholder governance, and process alignment maturity are lower than other characteristics.



Comparison of the Assessments

We conducted the assessments according to the framework discussed earlier in this study. To map the elements of data sharing, we interviewed stakeholders using the shared data for the purposes defined by the scope of the projects. We also captured the evidence of the stakeholders interacting with specific data sharing platforms.

The data collection in the Kingdom of Saudi Arabia took place 1 year before the project in Estonia. We mostly replicated the methodological experience from the Kingdom of Saudi Arabia in Estonia, except that we introduced an additional assessment tool, the HISMM (Table 2).

The analysis of the projects in the Kingdom of Saudi Arabia and Estonia demonstrates the challenges of coordinating data flows on a distributed data sharing system. Even if the health care systems in the 2 countries are coordinated differently, in both cases, the conclusions focus on the need to strengthen data flow stewardship (Table 3).

The conclusions advised the governments to introduce governance policies, which would clarify the responsibilities of the stakeholders. Proper management of the responsibilities of data stewards would increase the value of data providers' contributions and the value of the custodians' data. Figure 4 illustrates our conceptual understanding of the data governance roles and their relationships, which we used as a tool to map the roles of the existing or future organizations in our recommendation.

Current data governance in the studied countries follows the vertical model of stewardship, where the data consumers coordinate the information flows for their own needs. Most

consumers have also established their own data management or custodian organizations. Notable exceptions are the national databases and message exchange platforms, which support data consumption by multiple institutions. For example, the EHIS manages data consumed by the network of health care providers, patients, and health care registries. A pervasive stewardship function shall increase the secondary use of data.

Table 2. The assessments share comparable attributes of scope. The only exception is that the project in Estonia conducted a maturity assessment, which was not part of the project's scope in the Kingdom of Saudi Arabia.

Attributes of scope	The Kingdom of Saudi Arabia	Estonia
Assessed stakeholder purposes	• Clinical, population health, and health care management	• Clinical, population health, patient engagement, health care funding, health care management, and health care policy
Assessed data sharing platforms	• Hospital EMRs[a] and analytical data sets	• Hospital EMRs, the national EHR[b], disease registries, and insurance claims registry
Assessed capability maturity characteristics	—[c]	• HISMM[d] technology, use, and governance
Stakeholders interviewed	• National-level health care coordination (Saudi Health Council) • Management of the sectors (MoH[e] Medical Services, National Guard Medical Services, Ministry of Interior Medical Services, and King Faisal Specialist Hospital & Research Center)	• National-level health care management and policy (Ministry of Social Affairs, North Estonia Medical Centre, Tartu University Clinic, Pärnu Hospital, Viljandi Hospital, Põlva Hospital, East Viru Central Hospital, the National Institute of Health Development, the Estonian Health Insurance Fund, and the Estonian Society of Cardiology)

[a]EMR: electronic medical record.

[b]EHR: electronic health record.

[c]Not applicable.

[d]HISMM: Health Information Sharing Maturity Model.

[e]MoH: Ministry of Health.

Table 3. The findings from the 2 countries demonstrate similarities in the expected achievements, identified barriers, opportunities, and principal conclusions. Regardless of the digitization of workplaces in both cases and sophisticated data integration solutions in the Estonian case, siloed data stewardship limits the multiuse of health data.

Attributes of findings	The Kingdom of Saudi Arabia	Estonia
Expected achievement	Timely and efficient delivery of health care system and public health indicators, and standard and special reports	Timely and efficient decision support for clinical, management, and financial decisions
Barriers	Lack of interoperability standards and siloed sectoral stewardship	Siloed vertical stewardship
Opportunities	Digitized workplaces in health care and cross-sectoral health care governance structures (SHC[a])	Digitized workplaces in health care, secure integration platform (XRoad), national EHR[b] (EHIS[c]), data and data exchange standards, and national-level clinical decision support
Principal conclusions	Align the roles of the stakeholders and engage the participants in a standardized data flow	Align the roles of stakeholders and standardize the event-driven sharing of EMRs[d]

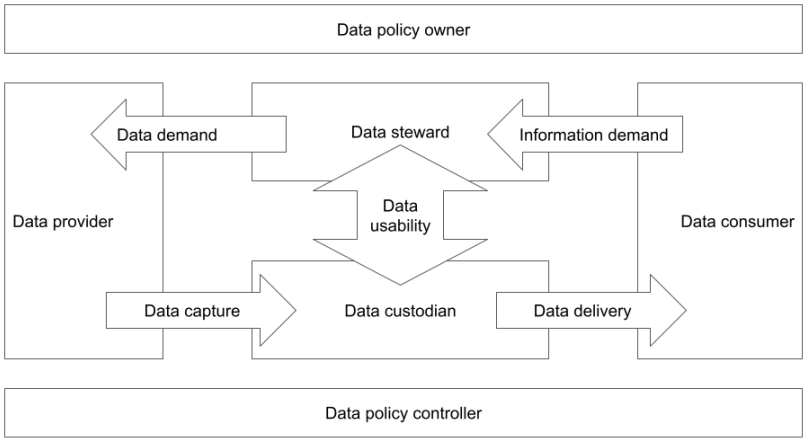
[a]SHC: Saudi Health Council.

[b]EHR: electronic health record.

[c]EHIS: Estonian Health Information System.

[d]EMR: electronic medical record.

Figure 4. A conceptual overview of the data governance roles and relationships used as a base for mapping the actual organizational structure of the countries. A policy for multiple data use supports resolving demand and supply between data providers and consumers. The policy establishes authority and responsibility for pervasive data stewardship and custodianship.



Discussion

Principal Findings

The study maps the common thread of thought from 2 distinct projects in the Kingdom of Saudi Arabia and Estonia, assessing the potential of secondary use of health care data and supporting governmental decisions. The projects apply comparable frameworks and methods, allowing the comparison of the barriers, opportunities, and conclusions. The findings include both the frameworks used and the conclusions made. The framework of assessment defines 2 dimensions of analysis. First, there is the need to identify and improve data sharing flows between data providers and consumers. The analysis investigates multiple purposes of data, data and exchange standards, stakeholders' governance, and shared data management platforms. Second, the framework considers the maturity of the data sharing implementation. The maturity assessment measures the level of institutionalization of health data sharing. The second part of the framework was included and applied only to the project in Estonia.

The assessment revealed opportunities and barriers in the secondary use of health data. Starting with the opportunities, the included institutions demonstrated high levels of digitization in the workplace. In the Estonian case, we also experienced advanced integration platforms and interoperability standards implemented nationally. The latter has supported the development of sophisticated solutions for national electronic health record and clinical decision support. However, the countries have maintained a fragmented organization of data stewardship, which has not been able to coordinate the need for data. In both cases, the assessments concluded with a recommendation to implement pervasive data stewardship to align the need for data.

While many countries have digitalized information necessary for clinical work and described the data relatively well, especially in most European countries and North America, unified routines and applications for the secondary use of digital data in health care are largely still being planned.

In Sweden, more than 100 health care quality registries collect individual-based clinical data for research and improvement of health care delivery [26]. In Estonia, 6 medical registries and databases collect, process, and distribute data about health and medicine [27]. Studies propose that clinical quality registers can be cost-effective and yield significant investment returns [28]. The number and quality of the registries indicate success in the secondary use of health care data. The registries also introduce data capture, integration, and delivery costs for secondary use. These professional specialty or national quality registries are often developed and managed in silos, leading to high maintenance costs and challenges in interoperability.

Regardless of the advanced information systems in hospitals, the health care system in the Kingdom of Saudi Arabia spends considerable time and resources collecting statistical data. There is much manual processing due to the lack of standards for integration and semantics. The same applies to Estonia; despite the common health data interoperability standards and transport system, secondary use of health care data is often in silos and needs additional effort. In the Kingdom of Saudi Arabia and Estonia, the data consumers coordinate their needs directly with the data providers, reinforcing the traditional model of form-based reporting. The form-based approach introduces duplication at the data capture; one may call it secondary capture. To avoid resource wasting and duplication, collecting the data consumers' need shall be part of the standards of primary data capture.

In Estonia, the advanced semantic interoperability of the clinical documents shared via the EHIS enables the automation of clinical decision support [29-32]. Such features include drug-drug interaction alerting, context-driven suggestions of clinical guidelines, and automatic patient summaries based on clinical documents. These features increase the use of data but only inside the vertical of clinical decision-making. The EHIS could also facilitate data flows for public health, health care management, and clinical research decision-making.

The stakeholders of health care data need to cooperate through a strategic digitalization process. Often, the participants are not aware of the discontinuity of the data flow. The study in Estonia indicated that the participants were relatively satisfied with the data management tools and their engagement in the flow. Instead, they reported problems with data quality and governance. The users expressed their frustration regarding duplicate data capture but could not relate it to the low alignment of the processes. We hypothesize that the interview results indicate disruptions in the data flow. The respondents struggled to find source data to fill in the data entry forms for secondary use. Designing and managing a flow that connects data capture with a single consumer is relatively easy, ensuring satisfaction with the tools and participation. Only a helicopter view of the landscape of data needs shows the shortcomings of governance and the chronic waste of capturing the same data repeatedly. Efficiency in the secondary use of data starts from the health care policy establishing clear goals and management.

Single-purpose capture of data and single-purpose databases are indicators of the low secondary use of health care data. The data flow design should follow the principle of "collect once and use multiple times." The studied cases reveal the barriers built between the domains of information purpose. The health care system extends over 6 ministries in the Kingdom of Saudi Arabia. It takes a long time and heavy work to combine data across the borders of the governance verticals. In Estonia, where the organization is more straightforward, data collection for different purposes is still split between different data consumers, resulting in independent data flow designs without proper interoperability. For example, health care providers must simultaneously record the exact data for clinical decisions, management, funding, statistics, and research. The new policy shall require the unification of the demand of data consumers into a single standard of data capture.

The analysis of health data sharing challenges in the Kingdom of Saudi Arabia and Estonia demonstrates that the digitization of the workplaces, integration of information systems, and advanced semantic interoperability are insufficient for secondary use on a large scale. A prerequisite for secondary use is a health care policy that emphasizes the need for the continuity of the data flow. The health policy should address governance of the data and stakeholders without introducing central bottlenecks for innovation. The policy should guide parties to map the impacts of their data processing and increase the value of their data through greater secondary use. A health data sharing system shall reward the measurable secondary use of data assets.

Advances in the digitization of health data and integration of information systems open the way to the digitalization of health care processes. Shared data enables the coordination of activities of a digital process. Stewards and custodians must govern health care data through the diverse organizations, workplaces, and information systems landscape. Data governance conceptualizes and carries out stewardship responsibilities based on data access, custodianship, and use policies [33]. The conceptual framework for data governance by Abraham et al [6] suggests structural, procedural, and relational mechanisms. The structural and relational mechanisms include establishing clear organizational responsibility and communication. The governments in demand for greater secondary use of health care data shall establish data policy with precise coordinating mechanisms.

We saw that digitalizing data providers and consumers is insufficient for efficient secondary use of data. There is a need for a DHP that enables data and information sharing. However, having a DHP only for clinical data is insufficient. For secondary use, the stewardship must include the requirements of all targeted consumers. This recommendation is also very much in line with the observation from a 2021 report that calls for more substantial public-patient participation in the secondary use of health data [2].

There is an ever-growing demand for better data and information for decision-making. Modern health care and research depend on data from various domains, including education, environment, and social care. It is an ongoing effort to analyze and integrate the new demand for data.

Limitations

The study reports the findings from 2 projects from 2 countries. The findings present certain commonalities but still have a limited generalizability for different contexts. Countries or regions searching for advice may present circumstances that demand noticeably different strategies for their digital health improvement. It is also essential to understand the role of the frameworks when trying to replicate the results. For practical reasons, a solid framework is essential for such projects, as effective planning, execution, and analysis require a rigid structure. However, the choice of a framework indicates the researcher's focus and may lead to a limited space of findings. The studied projects develop policy suggestions for health data governance on the national level. Controlled empirical validation of the suggested policies is nearly impossible. The conclusions mainly depend on the internal validity of the research, where we build on the experience of the involved stakeholders and findings from similar experiments.

Conclusions

In this study, we have analyzed 2 projects that assessed and provided advice for the national-level improvement of the secondary use of health care data. The study provided an overview of the projects' backgrounds, frameworks, methods, and results. Finally, we discussed the main advice from the projects. The study shows that 2 high-income countries with very different health care systems have comparable issues with the secondary use of health care data. National-level secondary use shall build on an overarching data policy that enables horizontal stewardship to coordinate requirements of a diverse landscape of health care data consumers.

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Authors' Contributions

JM and PR were the main contributors to both studied projects, and ZS was a leading contributor in the case of the Kingdom of Saudi Arabia. DD worked on the structure and methodology of the study. TN, one of the leading developers of Health Information Sharing Maturity Model (HISMM), contributed to the required details and reviewed the results concerning HISMM adoption.

Conflicts of Interest

None declared.

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Abbreviations

CMMI: Capability Maturity Model Integration
DHP: Digital Health Platform
EHIF: Estonian Health Insurance Fund
EHIS: Estonian Health Information System
HISMM: Health Information Sharing Maturity Model
MoH: Ministry of Health
MoSA: Ministry of Social Affairs
NHIC: National Health Information Center
NIHD: National Institute for Health Development
PHC: primary health care
SHC: Saudi Health Council
WHO: World Health Organization

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Curriculum Vitae

1. Personal data

Name: Janek Metsallik
Date and place of birth: 13 April 1971, Pärnu, Estonia
Nationality: Estonian

2. Contact information

Tallinn University of Technology (TalTech), School of Information Technologies, Department of Health Technologies
E-mail: janek.metsallik@taltech.ee
ORCID: 0000-0001-9929-2258

3. Education

PhD studies (ongoing) - Tallinn University of Technology (TalTech), School of Engineering, doctoral programme Mechanical Engineering (MAPD02)
Dissertation title: *Interoperability and Governance in National Digital Health: A Framework-Based Argument for Integrative and Knowledge-Driven Approach*
Supervisors: Peeter Ross; Dirk Draheim
1998 - Tallinn University of Technology, Master's Degree
Thesis: *Applying CMM 2nd level practices in Estonia*
Supervisor: Leo Mõtus
1990 - Tallinn Polytechnics, specialisation: *Electronic computers, instruments and devices* - Electronics Technician Diploma thesis: *"Charging device for batteries of portable radio receivers for simultaneous interpretation"*

4. Fields of research

ETIS research field: 4. Natural Sciences and Engineering; 4.9. Medical Engineering
CERCS research field: T115 Medical technology

5. Language competence

Estonian - native
English - professional working proficiency
Russian - limited working proficiency

6. Institutions and positions

2015-present - Tallinn University of Technology (TalTech), School of Information Technologies, Department of Health Technologies - **Expert of E-Health**, **Lecturer of Healthcare Information Systems** (Digital Health MSc program at TalTech, MSc programs at RSU, MSc program at FH Joanneum)

7. Professional focus

Enterprise and solution architecture in digital health; national-scale EHR/HIE and interoperability (incl. standards-based and conceptual modelling).
Academic work at TalTech since 2014; international consulting roles in national digital health programmes since 2013.

8. Professional employment (summary)

2018-present - The World Bank Group - *eHealth Architecture Consultant*
Saudi Arabia (Dec 2018 - May 2020): National Health Information Management System; Ukraine (since Aug 2023): digital health projects.
2013-present - Independent consultancy (Itarc Consult OÜ; Abtram29 OÜ; DocuMental OÜ; partners) - *Digital Health Architect*
Selected assignments (selection): Estonia NHIS-Rescue Service integration (2014-2015); laboratory portal and B2B integrations (2015-2016); ITU/WHO digital health capabilities catalogue input (2015-2016); Estonia CDA→FHIR/event-based exchange transformation consulting (2019); DocuMental clinical decision support (2019-...); Pre-Visit primary care case coordination system (2021-2023); Architecture Panel member for next-generation NHIS (Estonia, 2022-...); strategy reviews (Uzbekistan 2021; Rwanda 2023); National Health Data Analytics Master Plan Development MoH Romania (2023-2024), Digital Health Reform - Elektron "Salomatlik", MoH Uzbekistan (since 2024).
2017-2020 - Ministry of Healthcare, Mongolia - *Enterprise Architecture Consultant*
2016-2018 - SYNLAB Eesti OÜ, Estonia - *Chief Architect*
2006-2011 - Hewlett-Packard OY & Estonian eHealth Foundation, Estonia - *Chief Solution Architect*
2011-2015 - Danske Bank A/S (Estonian branch) - *System Architect*
2000-2005 - Media Menu International AS - *System Architect*
1995-2000 - Abobase Systems AS - *Senior Developer*
1993-1995 - Ektaco AS - *Software Developer*

9. Computer skills (selection)

Programming: Java; Lua; SQL; XML/XSLT; Bash
Architecture and modelling: UML; Sparx EA
Tooling: Git/Gitea; Docker; Maven; Eclipse; LaTeX; Pandoc; Markdown
Domain/standards: HL7 CDA/FHIR; ISO 13940 (ContSys); ISO 23903

10. Defended theses

1998 - Master's thesis: *Applying CMM 2nd level practices in Estonia* (TalTech; Leo Mõtus)
(PhD thesis ongoing.)

11. Publications (ETIS)

- Kankainen, K. J. I.; Erm, R.; Metsallik, J.; Piho, G.; Ross, P. (2025). *Experiences translating and introducing ISO 13940 ContSys in Estonia: challenges and perspectives.* In: *Proceedings of MIE 2025*, IOS Press (SHTI 327), 378-382. DOI: 10.3233/SHTI250348.
- Kankainen, K. J. I.; Erm, R.; Metsallik, J.; Piho, G.; Ross, P. (2025). *Method for ContSys-based semantic annotation of the Estonian law of obligations.* In: *Proceedings of MIE 2025*, IOS Press (SHTI 327), 373-377. DOI: 10.3233/SHTI250347.
- Bossenko, I.; Metsallik, J.; Piho, G. (2025). *Terminology quality Checklist for medical terminology developers and evaluators.* Zenodo. DOI: 10.5281/zenodo.14609493.
- Metsallik, J.; Draheim, D.; Sabic, Z.; Novak, T.; Ross, P. (2024). *Assessing opportunities and barriers to improving the secondary use of healthcare data at the national level: A multi-case study in the Kingdom of Saudi Arabia and Estonia.* *Journal of Medical Internet Research*, 26, e53369. DOI: 10.2196/53369.
- Ross, P.; Metsallik, J.; Kankainen, K. J. I.; Bossenko, I.; Mäe, C.; Maasik, M. (2023). *Health Sense: universaalse andmemudeli ja raviteekondade järjepidevuse standardi väljatöötamine...* 1-87.

- Bertl, M.; Metsallik, J.; Ross, P. (2022). *A Systematic Literature Review of AI-based Digital Decision Support Systems for Post-traumatic Stress Disorder. Frontiers in Psychiatry*, 13, 923613. DOI: 10.3389/fpsyt.2022.923613.
- ITU-WHO team et al. (2021). *Digital Health Platform Handbook: Building a Digital Information Infrastructure (Infostructure) for Health*. WHO; ITU.
- Metsallik, J.; Ross, P. (2021). *Testing the Applicability of Digital Decision Support on a Nationwide EHR*. In: *ICDEc 2021 Proceedings*, Springer (LNBIP 431), 134-146. DOI: 10.1007/978-3-030-92909-1_9.
- Metsallik, J.; Ross, P.; Draheim, D.; Piho, G. (2018). *Ten years of the e-Health system in Estonia*. CEUR-WS 2336, 6-15.
- Metsallik, J.; Ross, P. (2018). *Das eHealth-System in Estland - Estonian Nation-wide Health Information System. Experience since 2008*. In: *Praxisbuch eHealth* (Kohlhammer), 266-284.

12. Research projects (ETIS)

- **TEM-TA105** "Digital health for a whole and healthy society" (01.01.2024-31.12.2028). PI: Peeter Ross. Financier: Estonian Research Council.
- **F21009** "Development of universal data model and continuity of care processes…" (01.02.2021-30.04.2024). PI: Peeter Ross. Financier: Norway Grants Programme "Green ICT".
- **LEP18020 (RITA1/01-42-07)** "Clinical pilot projects of personalised medicine…" (01.01.2018-31.05.2021). PI: Peeter Ross. Financier: Estonian Research Council.
- **F17128** "DocuMental" (01.05.2017-31.10.2017). PI: Janek Metsallik. Financier: Enterprise Estonia.
- **F16002** "Assessment of terms for the development of clinically valid…" (01.09.2015-30.09.2016). PI: Peeter Ross. Financier: Enterprise Estonia.
- **LMIN15035** "Feasibility study for the development of digital decision support systems…" (30.03.2015-30.06.2015). PI: Peeter Ross. Financier: Ministry of Social Affairs.

13. Supervised dissertations (ETIS; selection)

- 2025 - Scharlett Hansson: *Metamodel Development in Data Catalogue Using Immunisation Report Dataset* (co-sup: Aivi Saar)
- 2025 - Nikita Andrianov: *Advancing Adolescent Comprehensive Sexuality Education in Europe…*
- 2025 - Veera Ruže: *AI-Driven Framework for Dynamic Integration of Real-Time Medical Knowledge…*
- 2024 - Aleksander Tali: *Metamodel and Method for E-health Systems Landscape Mappings*
- 2024 - Meeri Vainola: *Time and Motion Study… Type 2 Diabetes Mellitus…*
- 2024 - Oduware Oduware: *Digital Knowledge Management in Healthcare: a Scoping Review*
- 2024 - Hamzah Shaikh: *Analysis of Frameworks in e-Health Program Implementation* (co-sup: Peeter Ross)
- 2024 - Herman Matis Eek: *Improving Secondary Data Use in Public Health Through Structured Data Capture…*
- 2023 - Kristian Talviste: *Using Process Mining to Evaluate the Data Capturing Optimization… DocuMental*
- 2023 - Rene Allkivi: *A Roadmap for the Rapid Maturation of the Text-Dialog System* (co-sup: Kristian Juha Ismo Kankainen)
- 2021 - Kristjan Krass: *Data quality in health information systems - completeness and timeliness* (co-sup: Taavi Päll)

- 2021 - Carmen Mäe: *A comprehensive analysis of the inputting and storage of data received by Estonian optometrists…*
- 2020 - Anni Männil: *Using the Time and Motion Study Method… Family Physicians' Time Utilization…*
- 2020 - Ivelisse Rodriguez Aguirre: *Feasibility Study of Sclerosis Multiple Registry…* (co-sup: Katrin Gross-Paju)
- 2019 - Maiko Sado: *Visualising Trends in Alcohol Use Disorder…*
- 2019 - Heidi Urmet: *Mapping the NICE Evidence Standards Framework…*
- 2018 - Kerli Norak: *Estonian Family Physicians Usage and Satisfaction with Drug-Drug Interaction Alert System* (sup: Tanel Ross; Janek Metsallik)
- 2018 - Hakki Jankat Var: *Effectiveness of Web and Computer-based CVD/T2DM Interventions…*
- 2018 - Turan, Muhammet Bilal: *Effectiveness of Smartphone Application Based Weight Management Interventions…*
- 2018 - Jibuti, Shota: *A Situational Analysis Of Pharmacovigilance System In Georgia*
- 2017 - Raid, Anna-Liisa: *The Quality and Usability of Data in Estonian Health Information System for Analysing Waiting Times*
- 2016 - Rudkovska, Ievgeniia: *Laboratory results visualization techniques for athlete's personal decision support*
- 2016 - Toks, Kadri: *Soccer Players Fitness and Health Status Monitoring System…*
- 2015 - Puppart, Egle: *Creating a New E-Service and Patient Portal… minu.synlab.ee*

Elulookirjeldus

1. Isikuandmed

Nimi: Janek Metsallik
Sünniaeg ja -koht: 13. aprill 1971, Pärnu, Eesti
Kodakondsus: Eesti

2. Kontaktandmed

Tallinna Tehnikaülikool (TalTech), Infotehnoloogia teaduskond, Tervisetehnoloogiate instituut
E-post: janek.metsallik@taltech.ee
ORCID: 0000-0001-9929-2258

3. Haridus

Doktoriõpe (pooleli) - Tallinna Tehnikaülikool (TalTech), Inseneriteaduskond, doktoriõppekava *Mehhanotehnika* (MAPD02)
Väitekirja pealkiri: *Koosvõime ja valitsemine riiklikus digitaaltervises: raamistikupõhine käsitlus integreerituse ja teadmuspõhisuse toetuseks*
Juhendajad: Peeter Ross; Dirk Draheim

1998 - Tallinna Tehnikaülikool, magistrikraad
Lõputöö: *Tarkvara Võimete Küpsuse Mudeli teise taseme võtmepraktikate rakendamine Eestis*
Juhendaja: Leo Mõtus

1990 - Tallinna Polütehnikum, eriala: Elektronarvutid, -riistad ja seadmed - elektroonikatehnik
Diplomitöö teema: *"Sünkroontõlke portatiivsete raadiovastuvõtjate akude laadimisseade"*

4. Teadusvaldkond

ETIS teadusvaldkond: 4. Loodus- ja täppisteadused ning tehnika; 4.9. Meditsiinitehnika
CERCS teadusvaldkond: T115 Meditsiinitehnika

5. Keeleoskus

Eesti - emakeel
Inglise - professionaalne töökeel
Vene - piiratud töökeel

6. Asutused ja ametikohad

2015-tänaseni - Tallinna Tehnikaülikool (TalTech), Infotehnoloogia teaduskond, Tervisetehnoloogiate instituut - **E-tervise ekspert**

7. Teadustöö põhisuunad

Digitervise arhitektuurid ja platvormid; riiklikud terviseandmete infosüsteemid ja andmevahetus; koosvõime ja standardid (ISO 13940, ISO 23903, HL7 CDA/FHIR); kliiniline otsustustugi; tervise-andmete teisene kasutus ja andmehaldus; andmekvaliteet ja raviteekonna järjepidevus; digitervise kogukondade küpsusmudelid.

8. Töökogemus (kokkuvõte)

2018-tänaseni - The World Bank Group - *e-tervise arhitektuuri konsultant*
Saudi Araabia (dets 2018 - mai 2020): National Health Information Management System; Ukraina (alates aug 2023): digitervise projektid.
2013-tänaseni - sõltumatu konsultatsioon (Itarc Consult OÜ; Abtram29 OÜ; DocuMental OÜ; partnerid) - *digitervise arhitekt*
Valik töid (selection): Eesti NHIS-Rescue Service integratsioon (2014-2015); laboriportaal ja B2B integratsioonid (2015-2016); ITU/WHO digitervise võimekuste kataloogi sisend (2015-2016); Eesti CDA→FHIR / sündmuspõhise vahetuse transformatsiooni konsultatsioon (2019); DocuMental kliiniline otsustustugi (2019-...); Pre-Visit esmatasandi juhtumikoordineerimise süsteem (2021-2023); järgmise põlvkonna riikliku tervise infosüsteemi arhitektuuripaneeli liige (Eesti, 2022-...); strateegiadokumendi ülevaatused (Usbekistan 2021; Rwanda 2023); National Health Data Analytics Master Plan Development Rumeenia Tervishoiuministeeriumile (2023-2024), Digital Health Reform - Elektron "Salomatlik", Usbekistani Tervishoiuministeeriumile (alates 2024).
2017-2020 - Ministry of Healthcare, Mongoolia - *ettevõttearhitektuuri konsultant*
2016-2018 - SYNLAB Eesti OÜ, Eesti - *peaarhitekt*
2006-2011 - Hewlett-Packard OY & Estonian eHealth Foundation, Eesti - *juhtiv lahendusarhitekt*
2011-2015 - Danske Bank A/S (Eesti filiaal) - *süsteemiarhitekt*
2000-2005 - Media Menu International AS - *süsteemiarhitekt*
1995-2000 - Abobase Systems AS - *vanemarendaja*
1993-1995 - Ektaco AS - *tarkvaraarendaja*

9. Arvutioskused (valik)

Programmeerimine: Java; Lua; SQL; XML/XSLT; Bash
Arhitektuur ja modelleerimine: UML; Sparx EA
Tööriistad: Git/Gitea; Docker; Maven; Eclipse; LaTeX; Pandoc; Markdown
Valdkond/standardid: HL7 CDA/FHIR; ISO 13940 (ConTSys); ISO 23903

10. Kaitstud lõputööd

1998 - magistritöö: *Applying CMM 2nd level practices in Estonia* (TalTech; Leo Mõtus)
(Doktoritöö pooleli.)

11. Publikatsioonid (ETIS)

- Kankainen, K. J. I.; Erm, R.; Metsallik, J.; Piho, G.; Ross, P. (2025). *Experiences translating and introducing ISO 13940 ConTSys in Estonia: challenges and perspectives.* In: *Proceedings of MIE 2025*, IOS Press (SHTI 327), 378-382. DOI: 10.3233/SHTI250348.
- Kankainen, K. J. I.; Erm, R.; Metsallik, J.; Piho, G.; Ross, P. (2025). *Method for ConTSys-based semantic annotation of the Estonian law of obligations.* In: *Proceedings of MIE 2025*, IOS Press (SHTI 327), 373-377. DOI: 10.3233/SHTI250347.
- Bossenko, I.; Metsallik, J.; Piho, G. (2025). *Terminology quality Checklist for medical terminology developers and evaluators.* Zenodo. DOI: 10.5281/zenodo.14609493.
- Metsallik, J.; Draheim, D.; Sabic, Z.; Novak, T.; Ross, P. (2024). *Assessing opportunities and barriers to improving the secondary use of healthcare data at the national level: A multi-case study in the Kingdom of Saudi Arabia and Estonia.* *Journal of Medical Internet Research*, 26, e53369. DOI: 10.2196/53369.
- Ross, P.; Metsallik, J.; Kankainen, K. J. I.; Bossenko, I.; Mäe, C.; Maasik, M. (2023). *Health Sense: universaalse andmemudeli ja raviteekondade järjepidevuse standardi väljatöö-*

tamine… 1-87.

- Bertl, M.; Metsallik, J.; Ross, P. (2022). *A Systematic Literature Review of AI-based Digital Decision Support Systems for Post-traumatic Stress Disorder. Frontiers in Psychiatry*, 13, 923613. DOI: 10.3389/fpsyt.2022.923613.
- ITU-WHO team et al. (2021). *Digital Health Platform Handbook: Building a Digital Information Infrastructure (Infostructure) for Health*. WHO; ITU.
- Metsallik, J.; Ross, P. (2021). *Testing the Applicability of Digital Decision Support on a Nationwide EHR*. In: *ICDEc 2021 Proceedings*, Springer (LNBIP 431), 134-146. DOI: 10.1007/978-3-030-92909-1_9.
- Metsallik, J.; Ross, P.; Draheim, D.; Piho, G. (2018). *Ten years of the e-Health system in Estonia*. CEUR-WS 2336, 6-15.
- Metsallik, J.; Ross, P. (2018). *Das eHealth-System in Estland - Estonian Nation-wide Health Information System. Experience since 2008*. In: *Praxisbuch eHealth* (Kohlhammer), 266-284.

12. Uurimisprojektid (ETIS)

- **TEM-TA105** "Terve Ühiskonna Digitervishoid" (01.01.2024-31.12.2028). Vastutav täitja: Peeter Ross. Finantseerija: Sihtasutus Eesti Teadusagentuur.
- **F21009** "Universaalse andmemudeli ja raviteekondade järjepidevuse standardi väljatöötamine lähtudes rahvusvahelistest uue põlvkonna terviseinfosüsteemide standarditest" (01.02.2021-30.04.2024). Vastutav täitja: Peeter Ross. Finantseerija: Norway Grants Programme "Green ICT".
- **LEP18020 (RITA1/01-42-07)** "Personaalmeditsiini kliinilised juhtprojektid rinnavähi ja südame-veresoonkonna haiguste täppisennetuses" (01.01.2018-31.05.2021). Vastutav täitja: Peeter Ross. Finantseerija: Sihtasutus Eesti Teadusagentuur.
- **F17128** "DocuMental" (01.05.2017-31.10.2017). Vastutav täitja: Janek Metsallik. Finantseerija: Ettevõtluse Arendamise Sihtasutus.
- **F16002** "Kliiniliselt ning kaubanduslikult kasutatavate personaalmeditsiini toodete ja teenuste arendamisvõimaluste hindamine" (01.09.2015-30.09.2016). Vastutav täitja: Peeter Ross. Finantseerija: Ettevõtluse Arendamise Sihtasutus.
- **LMIN15035** "Personaalmeditsiini rakendamiseks digitaalsete otsustustoe lahenduste arendusuuring" (30.03.2015-30.06.2015). Vastutav täitja: Peeter Ross. Finantseerija: Sotsiaalministeerium.

13. Juhendatud lõputööd (ETIS; valik)

- 2025 - Scharlett Hansson: *Metamodel Development in Data Catalogue Using Immunisation Report Dataset* (kaasjuh: Aivi Saar)
- 2025 - Nikita Andrianov: *Advancing Adolescent Comprehensive Sexuality Education in Europe…*
- 2025 - Veera Ruže: *AI-Driven Framework for Dynamic Integration of Real-Time Medical Knowledge…*
- 2024 - Aleksander Tali: *Metamodel and Method for E-health Systems Landscape Mappings*
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- 2024 - Herman Matis Eek: *Improving Secondary Data Use in Public Health Through Structured Data Capture…*
- 2023 - Kristian Talviste: *Using Process Mining to Evaluate the Data Capturing Optimization…*

DocuMental

- 2023 - Rene Allkivi: *A Roadmap for the Rapid Maturation of the Text-Dialog System* (kaasjuh: Kristian Juha Ismo Kankainen)
- 2021 - Kristjan Krass: *Data quality in health information systems - completeness and timeliness* (kaasjuh: Taavi Päll)
- 2021 - Carmen Mäe: *A comprehensive analysis of the inputting and storage of data received by Estonian optometrists…*
- 2020 - Anni Männil: *Using the Time and Motion Study Method… Family Physicians' Time Utilization…*
- 2020 - Ivelisse Rodriguez Aguirre: *Feasibility Study of Sclerosis Multiple Registry…* (kaasjuh: Katrin Gross-Paju)
- 2019 - Maiko Sado: *Visualising Trends in Alcohol Use Disorder…*
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- 2018 - Kerli Norak: *Estonian Family Physicians Usage and Satisfaction with Drug-Drug Interaction Alert System* (juh: Tanel Ross; Janek Metsallik)
- 2018 - Hakki Jankat Var: *Effectiveness of Web and Computer-based CVD/T2DM Interventions…*
- 2018 - Turan, Muhammet Bilal: *Effectiveness of Smartphone Application Based Weight Management Interventions…*
- 2018 - Jibuti, Shota: *A Situational Analysis Of Pharmacovigilance System In Georgia*
- 2017 - Raid, Anna-Liisa: *The Quality and Usability of Data in Estonian Health Information System for Analysing Waiting Times*
- 2016 - Rudkovska, Ievgeniia: *Laboratory results visualization techniques for athlete's personal decision support*
- 2016 - Toks, Kadri: *Soccer Players Fitness and Health Status Monitoring System…*
- 2015 - Puppart, Egle: *Creating a New E-Service and Patient Portal… minu.synlab.ee*

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