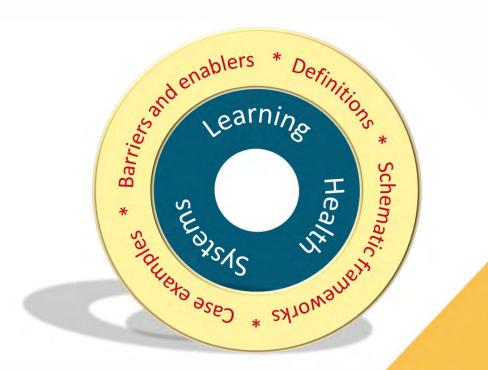# MAPPING THE LEARNING HEALTH SYSTEM: A SCOPING REVIEW OF CURRENT EVIDENCE
A WHITE PAPER

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Table of Contents

List of Abbreviations

Abbreviation	Explanation
D2K	Data to knowledge
DEDUCE	Duke Enterprise Data Unified Content Explorer
eHR	Electronic health record
FDA	Food and Drug Administration
IT	Information technology
IoM	Institute of Medicine (now the National Academy of Medicine)
K2P	Knowledge to performance
KaaS	Knowledge-as-a-Service
LHS	Learning health system
OHTM	Ottawa Health Transformation Model
P2D	Performance to data
PBRN	Practice-based research network
PREM	Patient-reported experience measure
PROM	Patient-reported outcome measure
QUERI	Quality Enhancement Research Initiative
VHA	Veterans Health Administration

List of Abbreviations

"Learning is not attained by chance, it must be sought for with ardor and attended to with diligence." - *Abigail Adams*

Executive Summary

The concept of a learning health system (LHS) has been gaining traction for over a decade as we increasingly realise that current health systems are not fit-for-purpose. The Institute of Medicine (IoM; now the National Academy of Medicine) described an LHS as a health system where "science, informatics, incentives, and culture are aligned for continuous improvement and innovation, with best practices seamlessly embedded in the care process, patients and families active participants in all elements, and new knowledge captured as an integral by-product of the care experience."[1] In the age of "big data" and artificial intelligence, there is enormous potential to harness the data that health systems generate, such as clinical information from electronic health records (eHRs), imaging, and genomics, to create new knowledge to improve care and health outcomes. With increasing challenges on health systems to deliver high-quality care within fiscal constraints, the LHS as a concept is increasingly being embraced by researchers, funders, managers, and clinicians as a means to embed the capture, analysis, and translation of new knowledge into the practice of healthcare delivery. We conceptualise an LHS as an ongoing journey rather than a destination – there is always something new to learn to continuously improve health systems. Of course, to advance knowledge on the development, implementation, and sustainability of LHSs we need to know the scope of current knowledge.

We therefore consolidated current understanding related to LHS definitions, schematic frameworks, barriers and enablers, as well as analysed LHS case examples to inform and stimulate further development and adoption of LHSs. Our knowledge synthesis is based on a scoping review of journal articles, review articles, journal commentaries, editorials, books, and book chapters on the LHS concept published from 2016 to 2020. Two-hundred and seventy-two papers were included in our synthesis. We sought to derive from this information critical lessons for the future adoption, adaptation, and scaling of LHSs.

We used a mixed methods approach for our knowledge synthesis. Our synthesis was guided by the IoM 2013 report *Best Care at Lower Cost: The Path to Continuously Learning Health Care in America*,[1] which described four 'dimensions' of an LHS with either one or two 'characteristics' under each dimension. During our analysis, we identified another dimension of an LHS, 'Structure and Governance', that was not adequately captured by the original IoM dimensions or characteristics. We used the original four dimensions and their corresponding characteristics for the analysis of the definitions and case examples. For the analyses of the LHS schematic frameworks and barriers and enablers, we included the 'Structure and Governance' dimension. The dimensions and characteristics that guided our analysis and synthesis are listed in Table 1.

Table 1. Dimensions and characteristics of LHSs

Dimensions	Characteristics	Source
Science and Informatics	*Real-time access to knowledge*	IoM 2013[1]
	Digital capture of the care experience	IoM 2013[1]
Patient-Clinician Partnerships	*Engaged, empowered patients*	IoM 2013[1]
Incentives	*Incentives aligned for value*	IoM 2013[1]
	Full transparency	IoM 2013[1]
Continuous Learning Culture	*Leadership-instilled culture of learning*	IoM 2013[1]
	Supportive system competencies	IoM 2013[1]
Structure and Governance	*Policies, governance, and regulations aligned to facilitate research, collaboration, and learning*	This review

LHS Definitions and Terminology

Although the body of literature referring to LHSs has been growing very rapidly over the last decade, many publications simply mention the LHS concept or include it among keywords or conclusions without addressing or defining the term. Over two-thirds (n=191) of the publications in our review provided a definition of an LHS. Ninety-seven different reports and papers were cited as the sources of these definitions, with many publications (n=55) citing more than one source. Eighteen different IoM reports were cited as reference sources for definitions a total of 140 times, and 77 non-IoM sources were cited a total of 131 times. Seven publications included an LHS

Most common words in the 191 LHS definitions listed in the reviewed publications

definition without providing any citation in direct relation to their wording. Across publications, core definitions included concepts of achieving healthcare quality improvement by analysing data, embedding data analysis and intelligent decision-making into routine care delivery processes, and changing culture to support the adoption of these changes.

LHS Schematic Frameworks

In 74 publications, we identified 63 unique frameworks depicting the functioning of an LHS. Although many were variations on a theme, the IoM's 2013 schematic framework[1] and the frameworks developed by Friedman and colleagues[2-4] were reproduced most often. We used the five dimensions and seven characteristics (Table 1) to describe the schematic frameworks. In addition to, but separate from the modified IoM dimensions, we added three terms to further categorise the components of the schematic frameworks: 'Ongoing Cycle of Learning', 'Research Translation', and 'IT System Only' (IT; information technology). Within schematic frameworks, the most frequently identified IoM dimension was 'Science and Informatics', with the IoM characteristics 'Real-time access to knowledge' included in 37 different frameworks and 'Digital capture of the care experience' represented 44 times. 'Patient-Clinician Partnerships' was another common dimension, while the components 'Ongoing Cycle of Learning' and 'Research Translation' were also frequently identified. Eight schematic frameworks were concerned only with the functioning of data technology infrastructures within the healthcare organisations ('IT System Only'). All frameworks included elements of routine, embedded, and continuous data collection. Networks and collaborative structures that bring together interdisciplinary teams, patients, and managers also commonly featured in framework schematics. Very few authors drew on existing health system theory literature when developing their frameworks. One notable exception explicitly included implementation science and precision medicine as critical components of an LHS framework.[5]

Barriers and Enablers to LHSs' Development and Implementation

Barriers to the development, implementation, and functioning of an LHS were discussed in 218 publications, and enablers were discussed in 256. Barriers and enablers were categorised using the five dimensions and eight characteristics outlined in Table 1. Common barriers were related to the 'Science and Informatics', 'Incentives', and 'Structure and Governance' dimensions (120, 105, and 125 papers, respectively), while barriers related to 'Continuous Learning Culture' and 'Patient-Clinician Partnerships' were less frequently mentioned (73 and 56 papers, respectively). The most common enablers fell into the 'Science and Informatics', 'Incentives', 'Continuous Learning Culture', and 'Structure and Governance' dimensions, which attests the importance of these more "human" LHS dimensions (184, 133, 151, 118, respectively). Enablers related to 'Patient-Clinician Partnerships' were the least commonly mentioned (95 papers).

Our findings align with previous studies that suggested the implementation of 'Science and Informatics' technical solutions for incorporating research and clinical

Most common words used in the 11 articles in our review that addressed at least four barriers and at least four enablers

data into practice was a critical barrier or enabler of an LHS.[6] Papers addressing the patient's role and 'Patient-Clinician Partnerships' centred around the ethical tensions between patient privacy, data ownership, and secondary use of data originally collected for clinical purposes. The perceptions of some patient groups, ethics committees, and funding bodies that secondary data analysis to support quality improvement activities constitutes research, and therefore requires ethics approval and patient consent, were frequently considered barriers to the full realisation of an LHS. These perceptions limit patient participation, data access, completeness, and usability. Proposals to increase data access include more frequent meaningful involvement of patients in co-design and co-production of research and quality improvement systems, financial incentives for patients to participate in research, opt-out consent systems for data access, and automatic de-identification of data.

In relation to 'Structure and Governance', clinical, institutional, and national governance policies and payment structures were often discussed. Consistency of regulations across health system sectors (e.g., state and local or private and public institutions) was seen as a key enabler to data collection, analysis, and re-use.[7, 8] Appropriate regulatory oversight can also facilitate the uptake of research discoveries in the clinical setting while ensuring that ethical, legal, and social obligations are met.[9, 10]

Case Examples of Systems on the Journey to an LHS

We uncovered 68 emerging or established LHS examples described in 98 papers. Almost two-thirds (n= 42) of these LHSs were based in the United States of America (USA), and seven were multi-national networks. The rest were spread across 19 other countries. The identified LHSs operated at local, regional, national, and international levels, as well as in public and private healthcare delivery settings. The most common descriptions of LHSs (33 in total) centred on the technology implemented in a health system (e.g., data networks or platforms). Practice based research networks (PBRNs) or learning communities underpinned by robust data networks or platforms, or both, were also commonly discussed. To showcase international perspectives of implemented LHSs, we selected four case studies of systems that self-identified as an LHS: Geisinger Health System in the USA, the Santeon Farmadatabase in the Netherlands, the Veterans Health Administration (VHA) in the USA, and the Ottawa Hospital in Canada. These include two large, integrated health systems (one publicly funded (the VHA) and one privately funded – Geisinger), one LHS operating at the level of a local medical centre (Ottawa Hospital), and one national LHS data network (Santeon Farmadatabase). Geisinger and the VHA embodied many of the IoM's four dimensions and their corresponding characteristics of LHSs. In both systems, paying clinicians a salary was seen as an incentive for moving from volume-

Most common words in the six reviewed articles used as the basis of our case example profiles

based care practices to value-based care. Furthermore, empowering patients to contribute to decision making and to take more control of their own healthcare were integral to establishing and maintaining an LHS. All four systems were underpinned by sophisticated and easily accessible data and analytics platforms.

Discussion

Overall, we found convergence around the definitions of what constitutes an LHS. However, there remain inconsistencies in the concept of what LHSs are and do – or perhaps it is more accurate to say that there are many pathways to an LHS. Although technological solutions to collect, analyse, share, and use data in the health system were viewed as central enablers to the development of LHSs, these platforms in themselves do not constitute a functioning LHS. In the current LHS literature, there is a strong focus on knowledge generation, translation, and improvement of patient care as supported by data and analytics platforms. There is less emphasis on the important factors that support the development of LHSs, such as organisational culture, incentives, and human capabilities (staff skills, research literacy, and buy-in). This imbalance may act as a barrier to the widespread adoption of the LHS vision, which requires considerable behavioural and organisational change.[11] Our findings suggest that cultural factors, such as increasing collaboration between health professionals and researchers, health professional research literacy, patient involvement and co-production of care, and incentives to shift to value-based care, need to be more explicitly addressed to advance the development of LHSs.

The more "human" LHS dimensions 'Continuous Learning Culture' and 'Incentives', and our added dimension 'Structure and Governance', were also less apparent in studies and seldom depicted in identified LHS schematic frameworks. Only one schematic framework specifically considered the importance of implementation science in negotiating the real-world complexity involved in creating a functioning LHS.[5] Research focused on the cultural and contextual aspects has the potential to inform implementation and adoption processes when conceptualising, developing, and operationalising LHSs.

The LHS concept places a strong emphasis on patient involvement, however this was not extensively covered in the literature. The characteristic 'Digital capture of patient experience' was rarely conceptualised in terms of patient experiences. The definitions and application of this characteristic were more about analysing care encounters, tests, prescription, and procedures therefore we suggest that this characteristic should be renamed as the "Digital capture of the care journey." We also noted that the capture and use of health provider experiences in an LHS was largely absent. Healthcare provider experiences are essential for the adoption of the LHS vision at the frontlines of care. Therefore, to accurately capture both patient and clinician experiences, we propose an additional characteristic "Digital capture of patient and healthcare professional experience" be added to LHS models.

A focus on LHS theory rather than practice was a prevailing theme in the literature. The LHS schematic frameworks described in recent publications were mostly conceptual in nature, rather than descriptions of frameworks that underpinned adopted systems. Furthermore, few studies discussed emerging or adopted LHSs, although the four chosen case examples attest to the feasibility of operationalising the LHS vision in some health systems. This reflects that we are in the early stages of the LHS journey, with the underlying theories still being advanced. Nevertheless, schematic frameworks are useful to those wanting to implement and evaluate LHSs, providing guidance on which components may be needed to achieve desired outcomes.

We found no long-term rigorously designed evaluations of LHSs that provide measurement of progress with clinical outcomes, patient, and healthcare provider experiences or economic analyses. This is a significant gap and must be addressed to capture lessons to support progress, translation, and scaling up of LHSs. Incorporating outcomes from rigorous evaluations is central to the development of more fully functioning LHSs.[3]

Conclusions

Given the variability of terminologies used to conceptualise LHSs and the absence of outcome evaluations, there is currently uncertainty about the scalability and transferability of LHS models. This variability is also a strength, as diverse approaches and structures provide potential for adaptations to different local contexts. We emphasise the need for rigorous evaluations to strengthen the evidence base in this rapidly evolving area of healthcare innovation. We identified 'Structure and Governance' as a pivotal consideration for LHS implementation that was not adequately addressed in the identified LHS models or definitions. We believe that 'Structure and Governance' – not only of an LHS itself but also of the environment into which LHSs are implemented – needs to be carefully considered to optimise fit with local health delivery structures, workforce, policy, and financing arrangements.

The concept of an LHS is exciting and holds much promise. However, the LHS field needs to continue developing theory, as well as focusing on implementing and embedding LHSs into practice as the concept increasingly matures. Although some authors claim to have established LHSs, we believe there is little room for proclamations that simply state "we have an LHS" – the very concept of an LHS is that systems are constantly adjusting and that learning is continuous. An LHS is more of a journey than a destination. As we look to the future, a greater emphasis is needed on developing implementable strategies for LHS adoption at different levels (micro, meso, and macro) of health systems, and on the evaluation of adopted LHS models, to support the broader realisation and ongoing development of the LHS vision.

Background and Rationale

Health system performance can be succinctly summarised in just three numbers: 60-30-10. That is, on average, 60% of care delivered in the system is in line with guidelines (either evidence-based or consensus-based), 30% of care is of little or no value to the patient, and as such is waste, and 10% results in patient harm.[12] To increase high-quality care and shift the dial on the 60-30-10 status quo – a state of performance which has dogged health systems for approximately 30 years – Braithwaite et al. (2020) have recommended the adoption of a learning health system (LHS) approach.[12] To understand whether this is possible, we first need to understand the current knowledge, application, and benefits of LHSs.

Over a decade ago, the Institute of Medicine (IoM; now the National Academy of Medicine) proposed an LHS as a new model for health systems that rapidly integrates the best available evidence into the front lines of healthcare delivery. The goal of an LHS was to address challenges to health systems, including the persistence of iatrogenic harms, inefficiency, and healthcare waste, whilst leveraging the ever-increasing amounts of clinical and research data that largely remain unused by the health system.[13] Achieving this goal requires establishing information technology architectures to enable synthesis, analysis, and use of the massive amounts of data already being collected in the health system, including from new technologies in the areas of genomics and artificial intelligence. However, technology infrastructure is only one piece of the puzzle – an LHS additionally requires changes to clinical and organisational practices, a skilled and resourced workforce, the empowerment of patients and communities, and the realignment of incentives and governance structures. A fully functional LHS has enormous potential to make knowledge generation, quality improvement, and a culture of learning embedded within, and automatic to, everyday practice.[14, 15] This is clearly an appealing concept.

In its 2013 report *Best Care at Lower Cost: The Path to Continuously Learning Health Care in America*,[1] the IoM identified four key, inter-related dimensions of an LHS: 'Science and Informatics', 'Patient-Clinician Partnerships', 'Incentives', and 'Continuous Learning Culture' (Table 2).[1] The 'Science and Informatics' dimension is characterised by the ability to access, capture, and synthesise in real-time the increasing amount of data generated during the course of clinical care, through research, new technologies, and from patient experiences. Digital platforms, such as eHRs, disease registries, mobile devices, and apps provide a wealth of data to generate real-time knowledge to feed back into the system to improve the quality of care and patient safety. The IoM also envisions a patient-centred health system wherein the patient, their family and other caregivers are more fully, and genuinely, partners with clinical teams. This concept of patient-centredness extends beyond the direct relationships between patients and clinicians and shared decision making, to include patient involvement in the governance structures of healthcare organisations, for example, patient representatives on hospital boards and committees for better care quality and patient experience.[16]

The importance of aligning the incentives for health systems, health professionals, researchers, patients, funding bodies, and organisational culture to realise an LHS is also acknowledged.[17] The system must have policies and processes that encourage efficiency and continuous improvement, incentivising high-value care while reducing the provision of low-value care. Organisational transparency is required surrounding all aspects of care, such as outcomes, processes and costs, to make available the necessary information for quality improvement.[18] An LHS also relies on leaders that facilitate a culture of collaboration and adaptability, and skilled staff that are trained and
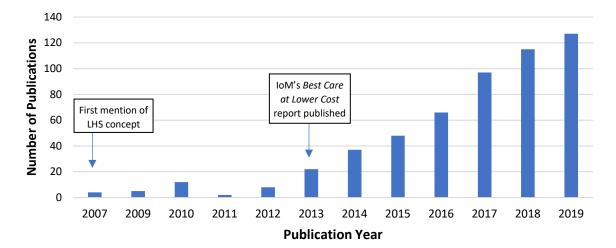
encouraged to have agency to support the continuous refinement of system processes for continuous improvement.[19, 20]

Table 2. Key dimensions and characteristics of an LHS as identified by the IoM (2013)[1]

Dimensions	Characteristics	Description
Science and Informatics	*Real-time access to knowledge*	Best available evidence incorporated into clinical decision-making processes to improve the quality of care and patient safety.
	Digital capture of the care experience	Digital platforms (e.g., eHRs, disease registries, mobile devices) utilised for the real-time capture, production, and application of knowledge based on best available data.
Patient-Clinician Partnerships	*Engaged, empowered patients*	Patients, families, and caregivers are full partners in a patient-centred system.
Incentives	*Incentives aligned for value*	Policies actively encourage ongoing evaluation of care given and improvement of processes and support the provision of high-value care and reduction in wasteful practices. Incentives should be aligned across sectors, including health providers, health delivery systems, and patients, to provide better outcomes, improve efficiency, and increase engagement.
	Full transparency	All aspects of care, including safety, quality, processes, costs, and outcomes are recorded and available to stakeholders (patients, health professionals, managers) to improve patient care and decision making.
Continuous Learning Culture	*Leadership-instilled culture of learning*	Leaders instil a culture of collaboration and adaptability to support the learning process.
	Supportive system competencies	Staff training, skill building, and support to enable continuous refinement of processes and system improvements is implemented.

Since the concept was first proposed over a decade ago, there have been numerous efforts to create LHSs at different scales. These have included large government organisations,[21] private corporations,[22] disease specific consortia that bring together health professionals from across organisations,[23] and clinical microsystems such as intensive care units, emergency departments, or chronic disease clinics.[24]

Parallel to the growing number of efforts to embrace the LHS vision in real-world settings, there has been an expansion in the literature on LHSs. Since the 2013 IoM report,[1] the number of peer-reviewed papers using "learning health system" or related terms (e.g., "learning healthcare system" and "learning health care system") in the abstract, full text, or as keywords has increased steadily. Over the last four years alone, there have been nearly three times as many papers published on LHSs as were published in the previous eight (Figure 1).

Figure 1. Scopus search results for peer-reviewed papers using "learning health system" or similar terms in the abstract, full-text or as keywords

Reflecting the increased interest in this area, previous reviews have examined the literature on underlying theories and implementation of LHSs.[6, 25] A 2016 review by Budrionis and Bellika[25] found global interest in the potential improvements to healthcare systems promised by an LHS. Most of the literature in their review focused on LHS theory while fewer papers reported on LHS implementation and even fewer papers reported on LHS evaluations. Empirical results demonstrating improved patient outcomes or economic benefits were largely absent. This may be unsurprising because health systems can be resistant to orchestrated change, and when change occurs it can be slow and unpredictable.[26] Budrionis and Bellika's[25] findings also reflected the relative novelty of the LHS concept in 2016, which would account for the fact that there were few extant, empirical examples, and limited demonstrated impact. We know from previous studies that implemented health system changes may not be evaluated or evaluation results may not be reported in the peer-reviewed literature,[27] and this may limit the utility of literature reviews that concentrate only on peer-reviewed literature.

In a scoping review that examined peer-reviewed LHS literature between 2007 and 2017, Platt et al. (2020) found many articles on LHS theory and very few articles on the outcomes of implemented LHSs.[6] The included literature consisted primarily of discussions of integrating data from eHRs into clinical practice, the importance of organisational culture, and the ethics of data access and re-use for clinical efficacy and safety.[6] 'Patient-Clinician Partnerships' were rarely discussed.[6] The use of data, regardless of the initial reason for the data collection, to support rapid virtuous cycles for continuous learning and improvement of care delivery, is identified as one of the central enablers of an LHS.[28] However, the ongoing lack of clarity about patient consent and privacy requirements for secondary data re-use has limited adoption of LHSs.[14] Enabling patient participation in an LHS and regulatory clarity around data use and re-use need to be addressed to move LHSs from theory to practice.[6]

Another reflection of the emerging nature of this field is the lack of consensus in the literature on the terms used to refer to an LHS. In the literature, LHSs have variously been called "learning healthcare systems",[13] "learning health care systems",[8, 29] and "learning health systems".[11, 15] While the difference between the first two terms is a matter of convention, the third category reflects a more substantive distinction. "Healthcare systems" refer to a more limited domain centring on the organisations, agencies, and institutions that provide health services, while "health systems" connote larger social ecosystems comprising population and public health concerns.[30] Given that our analysis took a global perspective, we used the more inclusive term "learning health system" throughout this paper, but also digested literature that used the alternative terms.

Objectives

We aimed to describe recent advances in LHS theory and practice to consolidate current knowledge related to definitions, schematic frameworks, and barriers and enablers to the development and adoption of LHSs. We sought to identify adopted LHSs and to describe these as case studies. Guided by the key dimensions and characteristics of LHSs proposed by IoM, we aimed to identify current strengths, limitations, and gaps to inform future directions in the realisation of the LHS vision.

Methods

Design

We conducted a scoping review of recent LHS literature.[31, 32] The search strategy was developed by JB, YZ, MW, and CLS. We used an iterative team approach with regular meetings of all authors to ensure consistent understanding of the purpose of the review, and to reach consensus at each step of the review process, including the search strategy, screening according to inclusion and exclusion criteria, and data extraction. To enhance our understanding of how LHSs work in practice once they are embedded in the health system, we selected several examples of operationalised LHSs from the included articles to profile as case studies.

Search Strategy

We searched PubMed and Scopus using the terms "learning health* system*". The search was limited to include publications written in English and published between January 2016 and May 2020. Full texts of papers were downloaded into Endnote and duplicates were removed.

Selection Criteria Processes

We screened the full text of potentially relevant papers against our inclusion and exclusion criteria (Table 3). Our selection criteria were intentionally broad to enable us to include papers containing information on any of the key areas of interest:

1) LHS definitions and terminology,

2) LHS schematic frameworks,

3) barriers and enablers to LHSs' development and implementation, and

4) case examples of systems on the journey to an LHS.

Publications were excluded if "learning health system" or similar terms were only mentioned in the keywords, abstract or conclusions, without discussing LHS issues elsewhere, or if they were only referenced as a general enabler of healthcare improvement without providing specific information or commentary on at least one of our four key areas of interest (Table 3).

Seven reviewers (AV, CLS, GK, IM, HG, LE, and MW) independently assessed the articles against the inclusion and exclusion criteria (Table 3). Any discrepancies among reviewers' judgements to include

or exclude were reviewed by two authors (AV and CLS) in consultation with YZ and JB, acting as project sponsors, when needed.

Table 3. Inclusion and exclusion criteria

Criteria	Inclusion	Exclusion
Language	English language	Languages other than English
Types of publications	Journal articles, review articles, journal commentaries and editorials, books, and book chapters	Grey literature
Publication date	Published January 2016 – May 2020	Published before January 2016 or after May 2020
Data	Contained at least one of these: an LHS definition, an LHS schematic framework, perceived barriers and enablers to LHS development and implementation, profile of one or more operational LHSs (with descriptions of how key LHS characteristics had been implemented)	"Learning health system" and related terms were only used in the abstract, keywords, or conclusion, and not discussed elsewhere in the paper, or the paper did not include information on one of the four focus areas of our review

Data Extraction and Analysis

Data were extracted from each of the included articles on our four areas of interest into a purpose-designed Excel sheet. The relevant information for each area was extracted by one or more of the reviewers (AV, HG, LE, CLS, GK, and IM).

LHS Definitions and Terminology

For the definitions, we extracted verbatim sentences wherein the author(s) described what an LHS is (e.g., a virtuous learning cycle) or the components of an LHS (e.g., databases, research networks) or its purpose, and recorded any reference(s) cited. We analysed which publications were cited and the frequency with which authors cited these publications to support their LHS definitions. This provided a measure of the influence of previous publications on the current conceptualisation of LHS.

We also performed a text analysis in NVivo software (Version 12 Plus; QRS International) to determine word use frequency, excluding common words (e.g., "the", "for", "a", etc.) and grouping together similar words (e.g., "improvement", "improve", "improving", etc.), to understand the language used to describe LHSs (Table 4a).

LHS Schematic Frameworks

Schematic frameworks of LHSs were identified from the included publications. Frameworks were analysed and information about the overall functioning of an LHS (e.g., the flow or interrelation of various system components and processes) was extracted. Framework features were first deductively mapped according to the four LHS dimensions proposed by the IoM, and the added fifth dimension 'Structure and Governance' identified by us as we reviewed the literature. The dimension 'Structure

and Governance' included policies, governance, and regulations that support a continuous learning system. To enable a richer description of frameworks, the eight characteristics were used to classify information emerging from our full-text review (Table 4).[1] The schematic frameworks were also assessed for using three new terms to categorise their components: 'Ongoing Cycle of Learning', 'Research Translation', and 'IT System Only', which were inductively identified during the review. 'Ongoing Cycle of Learning' was defined as a continual process of capturing knowledge through data analysis from clinical practice and other sources (e.g., research) and systematically reincorporating it back into the system to support learning. 'Research Translation' was defined as prioritisation of using research data and knowledge to directly support improved care. Schematic frameworks that depicted information technology systems (for example, data networks and platforms for the collection, processing, and analysis of eHRs) as constituting the sole or dominant element of an LHS were categorised as 'IT System Only'.

If a framework was reproduced in its entirety in another publication, we counted the number of times a characteristic or component was included in each unique framework and the total number of times including duplications. Frameworks were also classified as either theoretical or implemented and whether they applied to a whole system (i.e. considered the functioning of health systems across disciplines and conditions – for instance, the functioning of entire national healthcare ecosystems) or was condition/discipline –specific (e.g., cancer or wound care). The coding categories are summarised in Table 4a.

Table 4a. Coding categories for LHS definitions and terminology and LHS schematic frameworks

LHS Definitions and Terminology Coding
• Reference(s) cited to support the wording of the LHS definition(s) used in the included papers • Frequency of citation for each publication referenced • Word frequency count from verbatim definitions
LHS Schematic Frameworks Coding
Characteristics and Components Depicted within Framework[*]
Characteristics (n=8)[+] • Real-time access to knowledge   • Leadership-instilled culture of learning • Digital capture of the care experience   • Supportive system competencies • Engaged, empowered patients   • Policies, governance, and regulations aligned to • Incentives aligned for value   facilitate research, collaboration, and learning • Full transparency **Components** • Ongoing Cycle of Learning   • Research Translation   • IT System Only

Status	**Applicability**
• Theoretical • Implemented	• Whole system • Condition/discipline-specific

[*] Characteristics and components (except 'IT System Only') can be coded to more than one framework.
[+] "n=" indicates the number of dimensions or characteristics where used in the coding for each key area.

Barriers and Enablers to LHSs' Development and Implementation

Data on perceived barriers and enablers were categorised into the five dimensions and eight characteristics outlined below (Table 4b) by grouping discussions of factors that facilitate or inhibit the development or implementation of LHSs. Identified barriers could include obstacles to developing, implementing, or improving the sustainability of an LHS. Enablers included specific recommendations or conditions that facilitated any of these areas, such as policies or guidelines, culture of the existing health system, data sharing systems, and data analytics infrastructure.

Table 4b. Coding categories for LHS barriers and enablers

Coding of Barriers and Enablers to LHSs	
Dimensions (n=5)	**Characteristics (n=8)**
Science and Informatics	• *Real-time access to knowledge* • *Digital capture of the care experience*
Patient-Clinician Partnerships	• *Engaged, empowered patients*
Incentives	• *Incentives aligned for value* • *Full transparency*
Continuous Learning Culture	• *Leadership-instilled culture of learning* • *Supportive system competencies*
Structure and Governance	• *Policies, governance, and regulations aligned to facilitate research, collaboration, and learning*

✝"n=" indicates the number of dimensions or characteristics where used in the coding for each key area.

Case Examples of Systems on the Journey to an LHS

We classified each paper as focused mainly on LHS theory or on an LHS currently functioning or implemented to some extent in a health system. Theoretical papers focused on the underlying rationale, components, or requirements for establishing an LHS, but did not discuss an operational LHS. Papers categorised as implemented provided information about a specific LHS (either emergent or established). From the papers on implemented LHSs, we recorded the country or countries participating in the LHS to determine, as a proxy, the prevalence of LHSs worldwide. Through an iterative process based on our full-text review, we also classified these LHSs into one of six types: 1) data networks or IT platforms, 2) practice-based research networks (PBRNs) and other types of learning communities, 3) PBRNs/learning communities with robust data networks/platforms, 4) local providers or clinical microsystems (e.g., a local hospital or single intensive care unit), 5) regional-level private providers, and 6) large-scale public providers. We used these categories to determine the scale and breadth of LHSs identified in the literature (Table 4c).

For the case studies, a descriptive overview of the scope of the self-identified LHS (e.g., system level, approximate number of patients or services provided) was developed. We then mapped examples from the information publicly available about health organisations and systems identifying as operational or emergent LHSs onto the four IoM dimensions and their corresponding characteristics

from the IoM 2013[1] report (Table 4c). This enabled us to determine the extent to which the case examples addressed the dimensions that the IoM listed as important to creating an LHS.

Table 4c. Coding categories for case examples

Coding of Case Examples of Systems on the Journey to an LHS
Coding for All LHSs Identified

• Country where LHS operationalised
• Type of LHS
    1. data networks or IT platforms
    2. practice-based research networks (PBRNs) and other types of learning communities
    3. PBRNs/learning communities with robust data networks/platforms
    4. local providers or clinical microsystems
    5. regional-level private providers
    6. large-scale public providers

Coding for Case Examples		
Dimensions (n=4)	**Characteristics (n=7)**	
Science and Informatics	• *Real-time access to knowledge*	• *Digital capture of the care experience*
Patient-Clinician Partnerships	• *Engaged, empowered patients*	
Incentives	• *Incentives aligned for value*	• *Full transparency*
Continuous Learning Culture	• *Leadership-instilled culture of learning*	• *Supportive system competencies*

✦ "n=" indicates the number of dimensions or characteristics where used in the coding for each key area.

Results

Our search identified a total of 430 publications. Eight duplicates were removed. Of the remaining 422 publications, 148 were excluded because the LHS term and similar terms were only referenced in the keywords and/or the abstract, or the concept of an LHS was discussed as a general enabler of healthcare improvement without specific information or commentary on the LHS characteristics. Two-hundred and seventy-four articles were included in the analysis (Appendix 1).

1. LHS Definitions and Terminology

Over two-thirds (n=191) of the 272 included publications provided some form of definition of an LHS, and these publications cited 97 different reports and papers as the sources of their definitions; 55 cited more than one source. The IoM was the most frequently referenced source for LHS definitions with 141 citations to 18 different IoM reports; its 2013 report *Best Care at Lower Cost: The Path to Continuously Learning Health Care in America*[1] was the most cited. Seventy-seven non-IoM sources were cited a total of 133 times, with Friedman et al. (2015), Friedman et. al. (2010) and Etheredge (2007) the most frequently cited.[2, 28, 33] All other non-IoM definition sources were cited fewer than

four times each, with the majority (n=53) cited only once. Seven publications provided their own LHS definition without providing any citation in direct relation to their wording (Figure 3). For additional detail on the sources of LHS definitions across the literature, see Supplementary Tables 1a, 1b, and 1c in Appendix 2.

Figure 3. Citation sources for LHS definitions

*Citation Sources:
- **IoM (2013):** Institute of Medicine. Best Care at Lower Cost: The Path to Continuously Learning Health Care in America. Washington (DC): The National Academies Press; 2013.
- **IoM (2007):** Institute of Medicine. The Learning Healthcare System: Workshop Summary. Olsen L, Aisner D, McGinnis JM, editors. Washington (DC): National Academies Press; 2007.
- **IoM (2011):** Institute of Medicine. Digital Infrastructure for the Learning Health System: The Foundation for Continuous Improvement in Health and Health Care: Workshop Series Summary. Washington (DC): The National Academies Press; 2011.
- **Other IoM reports:** Report published by IoM; not one of the three listed above.
- **Friedman et al. (2015):** Friedman C, Rubin J, Brown J, Buntin M, Corn M, Etheredge L, et al. Toward a science of learning systems: a research agenda for the high-functioning Learning Health System. Journal of the American Medical Informatics Association. 2015;22(1):43-50
- **Friedman et al. (2010):** Friedman C, Wong AK, Blumenthal D. Achieving a Nationwide Learning Health System. Science Translational Medicine. 2010;2(57).
- **Etheredge (2007):** Etheredge, L.M. A rapid-learning health system. Health Affairs (Millwood). 2007;26(2).
- **Oher non-IoM sources:** Report published by a source other than the IoM and not previously listed.
- **Definitions without citations:** No citation given with definition wording.

Language Used to Define LHSs

Across the 191 publications that provided definitions, common terms and statements related to "quality improvement", "data", "evidence", and "integrated" or "embedded" processes. The 20 most frequently used words are closely related to the main concepts covered by the definitions which are centred on achieving improvements in patient care through the use of data to continuously advance knowledge (Table 5).

The prominence of such terminology reflects both the central objectives and the ideal functioning of an LHS. At the core of the LHS vision is the idea that knowledge generation and translation should move away from the current reliance on ad hoc interventions and become automatic to day-to-day operations. In an LHS, information technology systems, clinicians, and administrators ideally work together and make continual adjustments to their activities based on the best available evidence from all available sources (e.g., clinical outcomes, patients' experiences, research findings). Such responsiveness to new evidence on the part of people and machines would be built into the system. Given that the principal aim of an LHS is to improve quality of care for patients, it is unsurprising that, aside from words that form part of the LHS term itself, "improvement" and "patient" (and their derivations) were the most frequently used terms across LHS definitions (162 and 136 occurrences, respectively).

However, the dominant terminology also reflects specific gaps in the way the literature presents LHSs. There was more attention devoted to the technical processes through which new knowledge can be generated and absorbed into the system, but relatively less discussion of organisational culture, and the human capabilities (behavioural change, skills, training and staff buy-in) needed to make such processes possible. For example, despite their presence in the 2013 IoM definition, terms such "culture", "incentives", and "participation" do not figure among the most common words in LHS definitions across the literature (Table 5).

Table 5. Twenty most frequent words and terms (including derivatives) in 191 LHS definitions identified from the reviewed papers (NVivo analysis)*

Word	Count	Word	Count	Word	Count	Word	Count
health	330	patient	136	practice	101	evidence	80
system	301	data	134	healthcare	90	process	77
care	282	continuously	122	delivery	87	generate	76
learn	247	knowledge	119	research	85	clinical	74
improvement	162	LHS	101	medicine	83	new	69

Word frequency counts based on verbatim language from definitions in 191 papers. Counts include words sharing the same stem – for example, the count for the word "system" includes the number of mentions of "systems" and "systemic". All listed words have been presented in their singular form, regardless of whether plural forms were more prevalent.
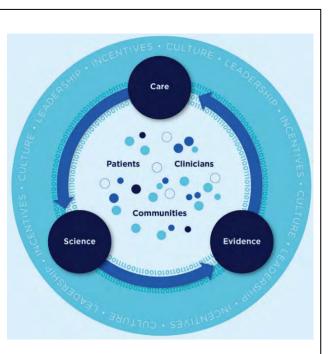
2. LHS Schematic Frameworks

Seventy-four papers (27.0%) included at least one schematic LHS framework. Two-thirds presented a framework developed by the authors themselves (n=50, 67.6%), while 24 papers either reproduced

or adapted the frameworks of others. A total of 63 different frameworks were reviewed by the research team. The most commonly reproduced frameworks were those created by the IoM (2013) (Box 1)[1] and Friedman et al. (2017) (Box 2).[3]

Box 1. IoM LHS schematic framework*

In the *Best Care at Lower Cost* report, the IoM (2013) presented a vision of a USA healthcare system where science, information technology, incentives, and care culture are brought together seamlessly to produce high-quality healthcare. At the centre of their vision lies the building of an LHS, characterised by a continuous cycle of knowledge, development, improvement, and application. The critical nodes in this framework include: the development of new scientific knowledge (science); the translation of science into clinical evidence of efficacy (evidence); and the application of efficacious interventions through effective care delivery (care). The IoM's framework also shows that a critical factor in a productive LHS is the engagement of patients, family members, and community.

Source: Institute of Medicine. Best Care at Lower Cost: The Path to Continuously Learning Health Care in America. Washington (DC): The National Academies Press; 2013.

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Most of the frameworks depicted a learning cycle using arrows to illustrate flow and continuity, such as the knowledge to data to performance cycle outlined in the framework by Friedman et al. (2017) (Box 2). Other authors provided alternative views of the LHS learning cycle, either in terms of the number of cycle stages,[34] or in terms of supporting infrastructures.[35] For example, Greene et al. (2012)[34] expanded on Friedman's cycle to include six distinct phases that are inherently iterative and include: scanning and surveillance; design (blending of research evidence with frontline workers' experience); implementation (multifaceted strategy); evaluation (predefined, with timely feedback); adjustment (allows for refinements to be made using evidence); and dissemination (including both internal and external stakeholders).[34]
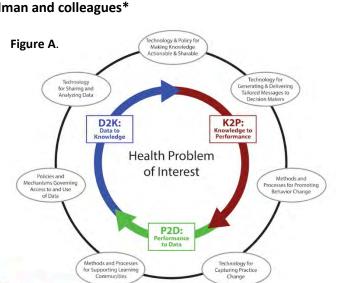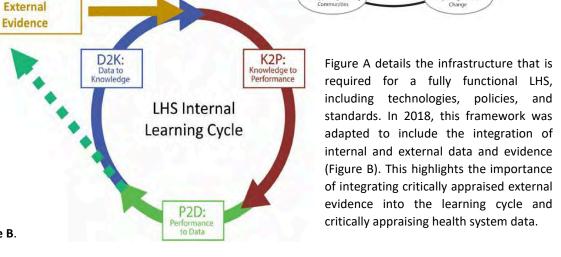
Box 2. LHS schematic frameworks by Friedman and colleagues*

The frameworks by Friedman et al. (2017) depict the basic learning cycle at the heart of the LHS. Each cycle begins with conversion of data to knowledge (D2K), followed by application of this acquired new knowledge to transform practice (K2P). The capture of practice changes and the consequences of these changes generate new data (P2D), which completes the cycle and initiates the next iteration. Successive iterations of the cycle aim to continue to identify best practices and improve outcomes.

Figure A.

Figure A details the infrastructure that is required for a fully functional LHS, including technologies, policies, and standards. In 2018, this framework was adapted to include the integration of internal and external data and evidence (Figure B). This highlights the importance of integrating critically appraised external evidence into the learning cycle and critically appraising health system data.

Figure B.

Figure A. Source: Friedman C, Rubin JC, Sullivan K. Toward an Information Infrastructure for Global Health Improvement. *Yearb Med Inform*. 2017;26(1):16-23.
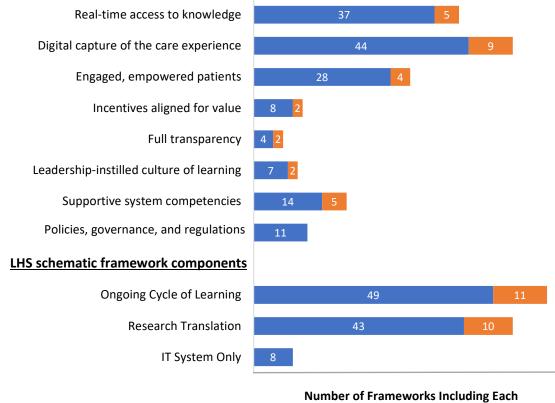
Figure B. Source: Guise JM, Savitz LA, Friedman C. Mind the Gap: Putting Evidence into Practice in the Era of Learning Health Systems. *J Gen Intern Med*. 2018;33(12):2237-9.

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Key features identified within the different frameworks are presented in Figure 4. The most frequently identified framework feature was the IoM dimension 'Science and Informatics', which covers the characteristics 'Real-time access to knowledge' and 'Digital capture of the care experience'. 'Real-time access to knowledge' was included in 37 different frameworks and 'Digital capture of the care experience' was represented 44 times. The additional components 'Ongoing Cycle of Learning' (49 inclusions in unique frameworks) and 'Research Translation' (43 inclusions in unique frameworks) as well as the IoM characteristic 'Engaged, empowered patients' (28 inclusions) were also frequently included. Eight schematic frameworks were concerned only with the functioning of data technology infrastructures within the healthcare organisations ('IT System Only').

Figure 4. Characteristics, dimensions, and components of LHS schematic frameworks

Characteristics

Number of Frameworks Including Each Characteristic and Component

■ **Unique frameworks** - Characteristic of frameworks that were reproduced in more than one publication were only counted once

■ **Duplicate frameworks** - Count includes all reproductions

In many of the frameworks, the IoM's 'Digital capture of the care experience' was represented as a cornerstone of an LHS. For example, the framework by Finlayson et al. (2016) shows that data-driven decision making is informed by clinical encounters from the past, the results of which will be captured in the eHR system and thus, be used to guide care in the future.[36] The resultant pool of continuously expanding and improving health data is central to their conceptualisation of an LHS. The term "care experience" implies patient-reported measures; however, in most frameworks this term has been used to mean the capture of the clinical journey using eHRs, including clinical encounters, investigations, procedures, and medications, rather than any direct measures of care experience. Melder et al. (2020) specifically included in their framework the capture of patient reported experience and outcome measures (PREMs and PROMs, respectively), in which information is collected and used to facilitate care in real time as well as for service improvement and research.[37] However, PROMs and PREMs were rarely mentioned when authors described 'Digital capture of care experience', relying instead on encounter data extracted from eHRs.
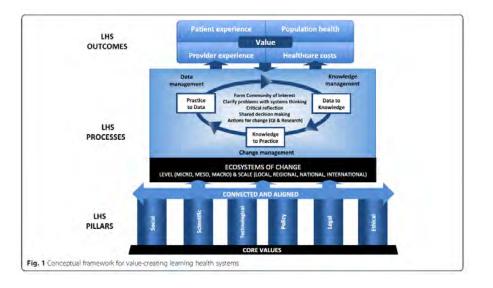
Most of the frameworks also focus on the prioritisation of 'Research Translation' into improved care. For example, Moore et al. (2017)[38] developed a vision for evidence-based practice and practice-based research, which includes a circular model in which data collected within clinical practice informs

research, which generates new knowledge and is used to improve care quality.[38] Furthermore, a distinctive feature of their model was the integration of the preferences and priorities of stakeholders, including patients, clinicians, and scientists.

The most comprehensive framework, with all dimensions, characteristics, and components visually present, was developed by Menear et al. (2019) (Box 3).[30] This framework is one of relatively few that drew explicitly on implementation science theory and included genomic and phenomic characteristics to support advances in precision medicine. This framework is important in its illustration of how the distinctive structures, processes, and outcomes of LHSs tie together with the aim of optimising health system performance and delivering greater value.

Box 3. LHS schematic framework by Menear and colleagues*

Menear et al. defined LHSs as dynamic health ecosystems where scientific, social, technological, policy, legal, and ethical dimensions are synergistically aligned to enable cycles of continuous learning and improvement to be routinised and embedded across the system. Such a dynamic health ecosystem seeks to increase value through an optimised balance of impacts on patient and provider experience, population health, and health system costs. Their framework consists of four key elements: 1) core values, 2) pillars and accelerators, 3) processes, and 4) outcomes. LHS pillars refer to the infrastructure, systems, and resources that provide the foundational supports for LHSs: including scientific, social, technological, policy, legal, and ethical pillars. As part of the policy pillar, Meaner et al. advocated that incentive systems and performance frameworks that foster greater alignment with LHS structures and processes (e.g., incentives for implementing eHR systems, value-based funding models) should accelerate progress toward more rapid LHSs. Further, consistent with the work of Friedman et al. (2017), Menear et al. depict the execution and routinisation of learning cycles as the fundamental processes of LHSs and include three phases: P2D, D2K, and K2P.

Fig. 1 Conceptual framework for value-creating learning health systems

Source: Menear M, Blanchette MA, Demers-Payette O, Roy D. A Framework for Value-Creating Learning Health Systems. *Health Res Policy Syst*. 2019;17(1):79.

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Among the identified frameworks most articulated were *whole system* frameworks, which considered the functioning of health systems across disciplines and conditions – for instance, the functioning of entire national healthcare ecosystems. The *whole system* frameworks depicted a theoretical LHS (e.g., the frameworks developed by Chambers et al. (2016)[5] and Fung-Kee-Fung (2018)[39]) (n=34, 76%). Other

schematic frameworks were condition/discipline-specific (n=14, 22%). Examples of condition/discipline-specific frameworks included those dealing with stem cell research,[40] wound care,[41] renal care,[42] phenotype definitions,[43] irritable bowel diseases,[44] and paediatric pain.[45] One-third of the condition/discipline specific frameworks were identified as extant LHS frameworks (n=5, 36%). One example of a condition-specific and adopted LHS framework was the one developed for a for-profit consortium of wound care clinics (Box 4).

Box 4. LHS schematic framework for wound care by Serena and colleagues*

This framework is a practical example of an implemented condition-focused LHS, illustrating how a network-based LHS was achieved through a consortium of wound care clinics. For this project, a purpose-built eHR was selected for wound care documentation that continuously generates real-world evidence for use in wound care research, by collecting all patient data at points of care using structured programming and provides wound-specific clinical practice suggestions that standardise usual care. Research-related patient and wound data elements have been embedded in the data collection framework of the EHR. The Research Consortium, which consists of 12 clinics in the USA, with 51 providers using the same wound care-specific eHR, transmits structured clinical data to the USA Wound Registry. The USA Wound Registry calculates quality measures for the provider and facilitates clinical practice improvement initiatives. Provider performance reports compare the provider to the aggregate Consortium provider performance. Performance reports and information gleaned from comparative effectiveness research are learning opportunities, which help the provider improve quality of care. Comparative effectiveness findings are used to improve clinical decision support within the wound care-specific eHR enabling patients to benefit from knowledge gained. The USA wound registry transmits to The Centers for Medicare & Medicaid the information necessary for the provider to access payments through the Merit-based Incentive Payment System. The USA Wound Registry deidentifies registry data and prepares analytical datasets for clinical research. Real-world patient data are used for market research and comparative effectiveness research.
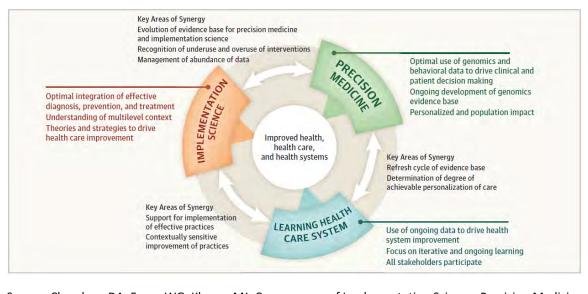

Source: Serena TE, Fife CE, Eckert KA, Yaakov RA, Carter MJ. A New Approach to Clinical Research: Integrating Clinical Care, Quality Reporting, and Research Using a Wound Care Network-Based Learning Healthcare System. *Wound Repair Regen*. 2017;25(3):354-65.

*Reproduced with permission from Wiley and Sons

The schematic framework developed by Chambers et al. (2016) was unique in its depiction of the potential synergies between implementation science, precision medicine, and the LHS (Box 5).[5] Unlike most other frameworks, Chambers et al. highlighted the importance of implementation science in complementing clinical research. Implementation science considers the importance of context to achieve improvement, particularly take-up of evidence, in real-world settings. A plethora of theoretical models from implementation science identify fundamental elements that influence successful implementation.[37] Implementation science is integral to an LHS because healthcare is dynamic and context-dependent and needs to be informed by real-world complexities for its constant improvement.

Box 5. Schematic framework by Chambers and colleagues featuring an LHS*

Chambers et al. suggested "repositioning the formal health care delivery sector as a set of nimble organisations that focus on ongoing system improvement by capturing data at the clinical encounter and using those data to inform ongoing clinical and community practice" (p.2). LHSs were defined as being "designed to improve care over time, using continuous quality improvement strategies, and seek to integrate a range of scientific methodologies at the point of patient care" (p.2). If successful, these health systems offer an opportune setting for the findings of the USA Precision Medicine Initiative to be incorporated into day-to-day clinical care, provided that precision medicine advances can adapt to and integrate within incredibly diverse clinical and community practice settings. Chambers et al. suggested that implementation science is intended to support this integration by providing evidence-based strategies (e.g., system change interventions, training, supervision, quality monitoring tools) to improve the integration of genomics and other precision medicine interventions within real-world practice. As shown in their framework, implementation science can substantially add value to LHSs, and in turn, the precision medicine can reshape current thinking about and approaches to research-practice translation.

Source: Chambers DA, Feero WG, Khoury MJ. Convergence of Implementation Science, Precision Medicine, and the Learning Health Care System: A New Model for Biomedical Research. *JAMA*. 2016;315(18):1941-2.

*Reproduced with permission from the American Medical Association

3. Barriers and Enablers to LHSs' Development and Implementation

Two-hundred and twenty of the included papers discussed at least one barrier to LHS development or adoption, and 256 papers discussed at least one enabler (Table 6). Most of the papers discussed more than one of the five LHS dimensions outlined below. The discussed concepts often cut across the LHS dimensions. For example, 'Real-time access to knowledge' (in the 'Science and Informatics' dimension) could be inhibited or facilitated by patients' willingness to share their data ('Patient-Clinician Partnership') and by the policies that regulate collection and use of patient data ('Structure and Governance'). Nearly half of the papers referred to factors under our 'Structure and Governance' dimension, including policies, governance, and payment structure when describing barriers and enablers (Table 6).

Table 6. Barriers and enablers of LHSs classified according to the five LHS dimensions, and the number of dimensions discussed

LHS Dimensions	Barriers N (%)	Enablers N (%)
Science and Informatics	120 (44%)	184 (68%)
Patient-Clinician Partnerships	56 (21%)	95 (35%)
Incentives	105 (39%)	133 (49%)
Continuous Learning Culture	73 (27%)	151 (56%)
Structure and Governance	125 (46%)	118 (43%)
Number of Dimensions Discussed		
None	54 (20%)	16 (6%)
1-2	137 (50%)	124 (46%)
3-4	74 (27%)	106 (39%)
5	7 (3%)	26 (10%)

Science and Informatics

'Science and Informatics' was the most frequently addressed aspect of an LHS (Barriers: 120 papers, Enablers: 184 papers) (Table 6). Although technological advances, such as eHRs, data warehouses, and web-based interfaces to access databases were viewed as essential enablers to support progress toward functional LHSs, many concerns about accessing and using these were raised.

Science and Informatics Barriers to LHSs

Authors cited barriers, such as lack of infrastructure, including data warehouses, data marts, national repositories of clinical data,[46] and systems to capture PROMs[3, 47] as significant challenges to creating and expanding LHSs (Table 7). There were concerns about the types of data available, fragmentation in data collections,[48-50] and potential bias in data collection (e.g., over-representation of sicker patients).[51, 52] The validity of data was questioned due to potential data entry errors,[51, 53] limited

reproducibility of clinical data,[10, 54] and data coded for reimbursement and administrative purposes not being suitable for clinical decision making.[55] Scarcity of data on specific conditions, especially rare diseases, can cause problems for developing programs to improve clinical decision making, such as predictive modelling or machine learning because of, for example, overfitting of data.[34]

Problems with interoperability of data systems and platforms were commonly cited as a barrier to real-time access. Interoperability has been defined as: "the ability of a system to exchange electronic health information with and use electronic health information from other systems without special effort on the part of the user."[56] Interoperability is limited by a lack of standardisation for data definitions and coding between systems.[57-61] Data for individual patients are often held on multiple, separate systems, which have unique access and security protocols and function on different software platforms.[56, 62] In many cases, automated tools for data extraction[63] and data mining are not available, and data extraction and analysis has to be done manually.[64]

Challenges with data entry and data extraction continue to impede the digital capture of care.[10, 65] Poorly designed systems, including eHRs, that are not aligned with clinical workflows,[66] heterogeneous tools used to collect PROMs and PREMs,[67] and the use of paper forms[68] limit data accessibility and usability. Mining data that is in human-readable form (e.g., free-text in eHRs[57, 66, 69] and published in peer-reviewed journals[4]) is also limited by the speed and accuracy of current tools, including natural language processing technology.[41]

Other barriers to accessing data included information ownership and custodianship (e.g., researchers' or companies' proprietary data)[7, 10, 48] and research data published in peer-reviewed journals.[4] Lengthy delays in publishing research also inhibit the timely integration of new evidence into the healthcare system.[70]

Science and Informatics Enablers for LHSs

For many commentaries, eHRs are the cornerstone of an LHS. These contain increasingly massive amounts of patient data that can be accessed, analysed, and used to improve care.[3, 71, 72] Natural language processing for clinical free-text data mining and the use of these data by machine learning platforms to process information, develop predictive models that can be applied to individual patients, and provide actionable knowledge, are viewed as important enablers of LHSs.[41-47, 73] However, as previously mentioned, the technology for natural language processing is still under development.

Several examples of web-based systems that are designed to facilitate access to large scale data collections to support LHSs were identified in our review. The Duke Enterprise Data Unified Content Explorer (DEDUCE) and Health Sciences South Carolina are examples of large-scale data warehouses that have front-end web-interfaces to allow clinicians and researchers to access longitudinal, de-identified patient data.[71, 74] These types of warehouses draw data from multiple data sources, including registration and billing systems, and eHRs, and contain data on millions of patients.[65, 74]

Knowledge-as-a-Service (KaaS) platforms are another example of web-based systems created to facilitate access to large-scale data and automatically overcome interoperability issues posed by human-readable information.[72] These cloud-based computing platforms are designed to integrate biomedical knowledge (such as research outcomes contained in publications or quality improvement documents) to provide on-demand advice to clinicians and researchers. KaaS systems are intended to overcome current limitations, including data security, reliability, and format consistency, and to improve automation to reduce the current reliance on human intervention to synthesise knowledge (Table 7).

Table 7. Examples of barriers and enablers related to 'Science and Informatics' discussed in the publications

LHS Dimension: Science and Informatics		
LHS Characteristics	**Barriers**	**Enablers**

Real-time access to knowledge	• Data quality – bias toward sicker people
	Free text difficult to extract/use
	  • Fragmentation or duplication of data focus on single condition, which can prevent scaling up of learnings
	  • Different timelines of availability of evidence between clinicians and researchers
		• Access to massive volumes of data
		  • Electronic health records (eHRs)
		  • Genomics data
		  • Systems for routine data collection
		  • Data warehouses/repositories/ "marts"

Digital capture of care experience	• Interoperability of systems
	• "Black boxes" in machine learning programs
	• Limitations of natural-language processing tools
	• Suboptimal data quality of eHRs, incompleteness of eHR data
	  • Incomplete data capture (missing information)
	Lack of non-biological data (mental health, socioeconomic, patient preferences)[75]
	• Lack of validation for data
		• Data standardisation across multiple systems/institutions
		• Machine learning/AI
		• Natural language processing capabilities
		  • Cloud infrastructures
		  • Clinical dashboards
		  • Clinical decision support systems
		• Systems that capture PROMs and PREMs

Patient-Clinician Partnerships

'Patient-Clinician Partnerships' were the least frequently addressed LHS dimension. Fifty-six papers mentioned this as a barrier and 95 mentioned patient engagement as an enabler of LHS functionality (Table 6).

Barriers to Patient-Clinician Partnerships in LHSs

Barriers to including patients' and carers' perspectives and information in an LHS included their concerns about privacy, trust in the system, understanding of the utility of data re-use, and computer literacy,[76] as well as ethical issues and regulations around informed consent and use of patient data for research.[8]

Patients' concerns about privacy and the possibility that data can be reidentified may arise from a lack of trust in the data governance and security processes of the systems.[77] In Australia in 2019, the health sector had the most data breaches of any industry.[78] These risks may make patients more cautious about data collection and re-use, including for research purposes, which is essential for building an LHS.[10]

A general lack of understanding by patients of the value of sharing data, how data can be used, and the importance of participating in research were often cited.[79, 80] Patients may be less likely to share

their data when they fail to perceive a direct benefit to themselves.[81] Inadequate explanation of data usage in consent forms, particularly for re-use in research and quality improvement activities, can also create distrust in the system and reduce participation.[82, 83] Currently, only a small proportion of eligible patients participate in research, which can bias analyses and limit the generalisability of results.[54]

Patients may also experience difficulties in using online services to input their data. This was cited as a major reason for a lack of inclusion of PREMs and PROMs in clinical decision making.[76]

From a regulatory perspective, there is a tension between supporting a public good and respecting patient autonomy and privacy.[84] In some instances, privacy and information security governance set by laws and ethics committees limits communication between patients and clinicians (Table 8).[21]

Enablers of Patient-Clinician Partnerships in LHSs

Co-production of research and shared decision making for clinical care has been cited as an enabler that strengthens 'Patient-Clinician Partnerships'.[85] The goals of co-production and shared decision making, broadly speaking, are to create open and ongoing communication and trust between patients and clinicians or researchers and fosters a culture of data sharing and transparency around data use and secondary re-use. This in turn facilitates inclusion of patients' data (e.g., eHRs, PROMs, and PREMs) for use in an LHS.[85]

Communication can be enabled by systems that allow patients to engage with their health providers, access their own eHRs and patient peer-support programs (such as the MyHealtheVet Patient portal and Blue Button program in the USA VHA).[8, 21] Including patients and carers on advisory committees can encourage dialogue around patient data and facilitates patient input into what data is available and how it is used.[16, 86] Raising public awareness of the value of participating in research has also been suggested to benefit LHSs.[84, 85]

Transparency around clinical decision making and research may create trust in the system and allow patients to perceive the benefits of data sharing.[82, 84] This may in turn increase patient involvement, particularly if patients understand that data sharing and re-use has direct benefits to themselves or their community (Table 8).[81]

Table 8. Examples of barriers and enablers related to 'Patient-Clinician Partnerships' discussed in the publications

LHS Dimension: Patient-Clinician Partnerships		
LHS Characteristic	**Barriers**	**Enablers**

Engaged-empowered patients	• Legal/ethical issues–
	  • Consent to use/share data
	  • Privacy, trust issues
	  • Data ownership
	  • "Re-identification" threats
	• Patient lack of understanding how to input data (e.g. telemonitoring)
		• Co-production of care
		  • PROMs and PREMs
		  • Dashboards (accessible by patients and general practitioners) that integrate mobile health apps, wearable monitoring devices
		  • Public/patient awareness campaigns

Incentives

One hundred and five papers referred to disincentives to value-based care or transparency in an LHS. One hundred and thirty-three papers included information about incentives to LHS adoption (Table

6). Many of the enablers mentioned were aspirational in nature, rather than providing a platform of concrete suggestions for improvements.

Barriers to Incentives Aligned for Value and Full Transparency

Perverse incentives or disincentives, misalignment between funding allocations for research and the needs of health systems, and competition over data as well as lack of resources were cited as barriers to creating an LHS.[8, 87] For example, for health professionals, there are disincentives to changing the current fee-based systems (e.g., potential loss of income from a value-based system) and to participating in research (e.g., insufficient compensation for participation).[8, 87] The current health system also tends to be focused on compliance of reporting single adverse events rather than continuous systems improvement.[85]

To secure funding, researchers all too often must align their projects with the priorities and application guidelines of funding organisations. These may not meet the needs of the stakeholders who will use the end results.[88] Long grant cycles also slow the research process and limit timeliness and relevance of research outcomes to those working in the health system. Grant reviewers may not be open to dynamic learning-experiment style proposals and so may be less likely to fund non-hypothesis driven work, which is relevant to those working close to the frontlines of healthcare delivery.[18] Currently, the value of research is still mostly measured in terms of academic outputs, which incentivises publication and dissemination in journals and research databases. This focus on publication of results in journals creates another barrier to access from the lengthy peer-review and publication process.[76] However, current practices do not provide enough support for translation activities nor do they require data collected to be shared with others in the health sector.[89]

There are numerous barriers or potential barriers to using data to develop and integrate best evidence into practice, including competition over data sharing, costs associated with data collection and sharing. For example, the people and organisations who generate knowledge (e.g., health systems, researchers, and healthcare providers) bear the direct cost of data acquisition.[7] However, it is the patients who should benefit from new knowledge gained from data collected about them either through care provision or through research. Data custodians should be incentivised to share data collections freely and transparently while protecting privacy to ensure that patients benefit.[7]

Other concerns addressed in the literature were a lack of transparency and limited access to data on fees charged for different health and medical services. These limit the ability to identify waste and to determine the true costs of care, including out-of-pocket expenses (Table 9).[90]

Enablers to Incentives Aligned for Value and Full Transparency

One strategy for aligning incentives for value is through the employment of salaried clinicians, as this has been observed to encourage practice based on value rather than the number of patients seen or tests and procedures performed. For example, financial incentives in the USA VHA are tied to a limited number of clinical quality goals, which encourages efficient use of resources.[21] Another suggestion is increased transparency around clinicians' outcomes to support patient choice, efficiency, and evidence-based care.[82]

Financial incentives have been suggested to reward health systems and researchers that facilitate data sharing, increase access to data sharing programs, and improve adherence to interoperability standards, as well as to entice patients to share data or participate in research, although there are many ethical concerns about the latter.[7, 10] Increasingly, publicly funded research or data collections

are required to share data and findings through repositories.[90] The automatic de-identification of data in databases or repositories can reduce research waste and increase accessibility (Table 9).[84]

Table 9. Examples of barriers and enablers related to the 'Incentives' dimension discussed in the publications

LHS Dimension: Incentives		
LHS Characteristics	**Barriers**	**Enablers**
Incentives aligned for value	• Focus on volume-based care and not value • Focus on compliance of reporting single adverse events – not on system learning	• Value-based incentives • Salaried clinicians • Improve transparency around outcomes • Alignment of incentives and priorities • Incentivise data sharing between research and health system
Full transparency	• Competition over data ownership among providers • Lack of transparency of costs • Delay in access to research outcomes	• Public funding of research/data collection • (Automatic) de-identification of data

Continuous Learning Culture

Barriers to a 'Continuous Learning Culture' were discussed in 73 papers. One hundred and fifty-one publications discussed enablers of a learning culture (Table 6).

Barriers in Culture to Creating LHSs

Human factors, such as culture, attitudes, and professional norms, were commonly cited as greater barriers to an LHS than technical issues.[67] Lack of trained staff, low staffing levels, and staff time constraints may limit the ability for staff to participate in data collection or translation.[91] At an individual level, staff may view data collection and entry for an LHS as just more administrative tasks and an additional burden to their workload,[92] especially if it disrupts clinical workflows and patient care. If not adequately engaged, staff may not agree with project objectives and decline to provide data, despite ethics approvals.[91] Staff may also be reluctant to participate in reporting errors, which is an essential part of continuous learning cycles, if they fear reprisals from or against other staff.[93, 94]

Differences within and between organisational cultures can create significant challenges. For instance, differences in cultures and norms between clinicians and researchers may result in misaligned priorities and delays in research translation. Clinicians require implementable knowledge that can be rapidly applied in clinical practice, whereas researchers tend to be focused on scientific rigour and the peer-reviewed process, with long lead times (Table 10).[68]

Enablers in Culture to Creating LHSs

Ensuring strong buy-in from stakeholders from the upper echelons of the administration to middle management, to those who work directly with patients or in other ways collect data, reduces the likelihood that people will obstruct the learning process.[76] Cross-institutional collaboration with shared goals supported by structured interactions creates a strong framework for learning. Ensuring that staff are trained on new systems and understand how new systems contribute to quality

improvement, and promoting a science-literate workforce, including genomics literacy, were cited as enablers of LHSs.[29]

Creating a culture of openness that extends within and across organisations and includes researchers and patients can promote transparency, quality improvement and a learning culture. For clinicians, a culture of continuous improvement and shared responsibility for reporting of outcomes is said to be essential to creating and sustaining an LHS. Embedding researchers within clinical practices can improve workforce training and research transparency. For patients, promoting a culture of opt-out for participation in research can normalise participation and enhance the learning cycle (Table 10).[50]

Table 10. Examples of barriers and enablers related to a 'Continuous Culture of Learning' discussed in the publications

LHS Dimension: Continuous Culture of Learning		
LHS Characteristics	**Barriers**	**Enablers**
Leadership-instilled culture of learning	- Collaboration issues - Institutional silos - Time constraints for clinicians to be actively engaged in research activities - Adaptability - Disruption of clinical workflows	- Education and collaboration - Multi-stakeholder participation - Collaboration (cross-institutional, cross-disciplinary, clinician-researcher, etc.) - Improving genomics literacy - Culture of research (within, clinical practices, etc.), of shared responsibility, and of continuous, improvement
Supportive system competencies	- Lack of people within the system trained to do translation - Increased workload for data collection - Fear that feedback will result in action against an individual	- Learning laboratory to test models - Culture of transparency - Science-aware workforce - Embedded researchers to train

Structure and Governance

'Structure and Governance', the new dimension that we identified from the LHS literature in this review, was referred to as a barrier in 125 papers and as an enabler in 118 papers (Table 6).

Structural and Governance Barriers to LHSs

There are a range of legal and ethical issues from researchers' perspective that are barriers to creating an LHS. These include government regulations (at the country and jurisdiction level) that are perceived as burdensome, lengthy ethics, research governance and clinical governance approval processes, lack of financial incentives to create shareable clinical trial data, intellectual property rights, and copyright laws. For example, ethics committee approval processes (including lengthy forms and decision processes, and in many cases the need for approval from multiple individual site committees every time data is used for a different purpose) reduce the amount and types of patient data accessible for research.[8]

Inconsistent or changing regulations can also cause problems within an LHS.[95] Changes in regulations or reporting requirements in routine data collections, registries, or data repositories can result in

providers no longer contributing information. This can adversely affect data comparability over time (Table 11).

Structural and Governance Enablers of LHSs

Governance structures that enable routine sharing of patient clinical data, including consistent regulations across health system sectors (e.g., between local jurisdictions, states, and territories, or between private and public institutions) would help with information dissemination.[83] This could facilitate transparency among key stakeholders, including patients, carers, clinicians, and researchers.[96] Regulations that enable the use of a unique personal identifier (e.g., in national health cards or identity cards) that can be used across all levels of the health system to facilitate data tracking and ease of data mining to provide more holistic information to be used for public interest and healthcare improvement in LHSs.[59]

Regulatory oversight and targeted funding can also facilitate the uptake of research discoveries in the clinical setting while ensuring that ethical, legal, and social obligations are met.[97] For example, funding bodies in Canada have begun specifically requiring researchers to integrate different stakeholders (e.g. patients, decision makers and end-users) in health research[98] and have provided targeted funding for knowledge translation activities to increase the uptake of research outcomes (Table 11).[99]

Table 11. Examples of barriers and enablers in the 'Structure and Governance dimension discussed in the publications

LHS Dimension: System and Governance		
LHS Characteristic	**Barriers**	**Enablers**
Policies, governance, and regulations aligned to facilitate research, collaboration, and learning	• Legal/ethical issues: • Burdensome regulations • Ethics/research approval, • lack of financial incentives to create shareable clinical trial data • Intellectual property rights • Changes in regulation (relaxing reporting requirements so providers stop collecting data)	• Structure • Large, integrated health systems • Central system of identification of people to track data • Governance • Regulatory clarity, institutional guidance on use of data • Reform of institutional review boards • Reform of guidelines and policies on data use, reuse, collection, etc. • Facilitate use of observational data • Private health insurance share cost of research • Participation in learning activities as an ethical obligation for patients

Changes at the governance level surrounding informed consent for research using de-identified data can facilitate data sharing. New regulations in the USA created new exemptions that theoretically "will make some LHS activities easier to accomplish because practitioners can secure limited review and broad consent when a patient enters the system".[100] Under the Dutch regulatory framework de-identified data can be stored without the informed consent of patients.[50] These regulations address key issues in the access to patient data for research and clinical re-use, which, over time, is essential for implementing an LHS (Table 11).

4. Case Examples of Systems on the Journey to an LHS

More than a third (98; 36%) of the 272 articles in our review included profiles of healthcare organisations that were identified by the authors as emergent or more established LHSs. In total, 68 LHSs were described in the 98 papers: 42 in the USA and 19 in other countries, including five in Canada, two in the Netherlands, two in Sweden, two in Taiwan, two in the United Kingdom, and one in each of the following countries: Belgium, Denmark, France, Germany, Kenya, and Spain. The remaining seven LHSs were multi-country networks – including three exclusively European networks,[101-103] three networks spanning multiple continents,[87, 104, 105] and one USA and Canada network.[106]

Of the 68 emerging or established LHSs, the most common type was data networks or platforms (33 LHSs). PBRNs and other types of learning communities were the second most common. PBRNs/learning communities with robust data networks/platforms', local providers or clinical microsystems, regional-level private providers, and large-scale public providers were all less common and almost equally represented (Table 12).

Table 12. Types of LHS described in the literature

LHS Type	Description	Number of LHSs Discussed in the Literature Reference #
Data networks or platforms	Local, regional, national, or international information technology architectures for the collection, storing, sharing, and/or systematic analysis of health data	33 20, 41, 42, 44-46, 49, 50, 57, 62, 68, 70, 74, 87, 91, 101-103, 107-117
PBRNs and learning communities	Local, regional, national, or international PBRNs or other learning communities centred around a particular condition or medical discipline	13 81, 87, 92, 96, 104-106, 118-122
Learning communities with data platforms	Local, regional, national, or international PBRNs/learning communities with robust data networks/platforms	5 87, 123-126
Local providers	Large or small medical centres or clinical units operating at a local level	7 24, 39, 107, 127-130
Regional private providers	Large-scale private healthcare providers operating at a large regional level and serving over half a million patients	5 131-135
Large public providers	Public systems covering either an entire national community or a specific population within a national community	5 9, 47, 53, 136, 137

The four self-identified operationalised LHSs selected as case examples were Geisinger Health System in the USA (Geisinger), the Santeon Farmadatabase in the Netherlands, the VHA in the USA, and the Ottawa Hospital in Canada. These include two large, integrated healthcare providers (one publicly funded and one private), one LHS operating at the level of a local medical centre, and one LHS data network. The LHSs are from three countries to provide an international profile.

Geisinger Health System

Founded in 1985, Geisinger provides healthcare to over three million patients primarily in rural areas of Pennsylvania in the USA. Operating as an integrated system that includes administration, payer, and providers, Geisinger coordinates patient care at multiple levels across a network of hospitals and clinics with around 1.5 million unique visits each year.[86] Geisinger is recognised for delivering quality care at relatively low cost, mainly attributed to a strong focus on managing population health, continual care quality improvement (including promotion of best practice checklists for physicians), and a comprehensive eHR system.[138] Employing doctors on set salaries instead of on a fee-for-service basis aligns with the key characteristic of an LHS, 'Incentives aligned for value' (Table 13).

Geisinger has included the LHS model in their strategic plans since 2014.[139] A multidisciplinary team was established to undertake system-wide efforts to "enhance organizational learning and develop a plan for operationalizing" the LHS model.[22] The group consists of representatives from key departments, including research, clinical innovation, and bioethics, who regularly meet to identify obstacles and solutions to keep moving toward achieving an LHS.[86] In 2015, Geisinger published a framework to guide the implementation of the LHS vision, which included the following key components: Data and Analytics, People and Partnerships, Patient and Family Engagement, Ethics and Oversight, Evaluation and Methodology, Funding, Organisation, Prioritisation, and Deliverables.[22]

Geisinger describes its operation as an integrated system "in which all employees and units – including researchers, providers, and a payer – are part of the overall success of the enterprise".[86] This and the explicit support from the organisation's leadership are viewed by Geisinger as significant strengths and have resulted in the development of conceptual and business models to create a learning culture. The organisation has inclusive advisory boards that draw on multidisciplinary expertise to foster trust and participation across stakeholder groups. This is designed to promote open communication and create functional partnerships with patients, research participants, and the community at large.[86]

The Geisinger LHS framework embeds 'Science and Informatics' through the eHR system, which generates large quantities of patient data owing to the stable routine enrolment of patients into the system. This allows for tracking patient treatment trajectories and outcomes over the long-term. Geisinger maintains a set of security requirements and stores patient data behind a system firewall to protect patient information.[86] These practices support the LHS characteristics of 'Real-time access to knowledge' and the 'Digital capture of the care experience' (Table 13).

Geisinger's informatics infrastructure includes capabilities related to precision medicine and genomics-informed care. In 2007, Geisinger created its MyCode biorepository, which allows participants to contribute genomic data and biospecimens linked to their eHR data. MyCode relies on opt-in consent, and of those approached, 85-90% agree to participate, with over 180,000 patients having contributed their genomic data as of 2018.[86] The MyCode repository and the patient participation it has elicited are examples of 'Engaged, empowered patients' and the 'Digital capture of the care experience' (Table 13). These genomic data can be used in concert with clinical data to enhance understanding of the risk of disease and to enhance the practice of precision medicine. Genomic variants are reported back to patient-participants, while also being deposited into publicly available databases to increase knowledge sharing about genetic variation beyond Geisinger. Geisinger also supports international efforts to develop and implement standards for genomic and clinical data that will increasingly improve the generalisability of data across healthcare information systems.[86] These practices speak to the LHS characteristics 'Incentives aligned for value' and 'Full transparency' (Table 13).

Geisinger's ongoing plans to further develop its LHS capabilities include developing a system to track other local learning health initiatives and identify factors that brought them success, establishing a Geisinger group that will be supported to lead new efforts in experimentation and innovation, and creating working and business models to build on earlier lessons learned. These strategies will be used to help "spread a system-wide culture of organizational learning".[139]

The Santeon Farmadatabase

A network of seven teaching hospitals in the Netherlands, Santeon was founded in 2010 with the aim of promoting collaboration around patient care and boosting quality improvement activities.[140] The hospitals are geographically spread across the Netherlands and serve approximately 13% of the Dutch population. In 2012, Santeon began building a shared medical database for continuous data collection on prescriptions, diagnoses, and patient outcomes from all participating hospitals. The system was spurred in part by a growing awareness of the cost, difficulty, and limited external validity of traditional clinical trials as the primary source of research and quality improvement activities.[50] The building of this shared environment of routinely collected patient data was considered as a key step to establishing a multi-institutional LHS.

Santeon's "Farmadatabase" is now a fully operational data warehouse linking the seven hospitals. As of 2017, it had records on nearly 800,000 unique patients – including 18,741,766 medication orders, 3,366,162 hospital admissions, and 15,930,414 diagnoses.[50] These practices and infrastructure are an example of the 'Digital capture of the care experience' characteristic (Table 13). The Farmadatabase relies on weekly extraction, transformation, and loading of relevant data generated during routine clinical care from the individual hospitals' eHRs. As the hospitals have different eHR systems, the data are normalised for entry into the shared data warehouse based on agreed-upon categories. These regular updates and uniform data formats facilitate observation of comparable trends, for example, in types of admissions, emergency presentations, and patient outcomes. It prevents double data entry and allows the shared data warehouse to evolve alongside the hospitals' individual IT infrastructures.[50] One drawback of the upload procedures from individual hospitals is that a patient who has attended more than one hospital may be counted as separate patients in the database.[50]

Santeon protects patient anonymity by de-identifying the data. The Dutch regulatory framework allows for such anonymous data to be stored without the specific informed consent of individual patients enabling data sharing by default; however, patients can opt-out of the system. Santeon's data storage and protection framework aligns closely with the national provisions and regulations to protect patient privacy while providing choice to patients. This aligns with the LHS characteristics 'Engaged, empowered patients' and 'Full transparency' (Table 13).[50]

As the Santeon Farmadatabase is predominantly a data platform rather than an integrated healthcare provider, several key LHS aspects may be variously applied across the seven hospitals. Characteristics such as 'Incentives aligned for value', 'Leadership-instilled culture of learning', and 'Supportive system competencies' may vary from hospital to hospital (Table 13).

The Farmadatabase provides opportunities for cross-hospital care quality comparisons and benchmarking in line with the LHS characteristics 'Real-time access to knowledge' and 'Full transparency' (Table 13). For example, a benchmarking report on the treatment of patients with community-acquired pneumonia showed a one-day difference in the median time to switch from intravenous to oral antibiotics between some hospitals.[50] The value of the Farmadatabase is

recognised by participating hospitals and future plans include enhancements to enable value-based use of medicines.[50]

Veterans Health Administration

The VHA provides healthcare to nine million military veterans, making it the largest publicly funded integrated healthcare delivery system in the USA. The VHA operates 1,255 healthcare facilities, including 170 hospitals and 1,074 outpatient clinics across the country.[141] The VHA's movement toward the LHS vision has unfolded over several decades.[21] In 1998, the VHA's Quality Enhancement Research Initiative (QUERI) created a national network of academically affiliated, VHA-embedded investigators to work with national, regional, and facility-level VHA leaders on implementing and evaluating changes to routine clinical care. Guided by the LHS vision and drawing on the field of implementation science, QUERI has sought to reduce variation in care quality, improve population health, and operationalise rigorous evaluation of implementation strategies.[142]

The VHA has well-developed internal research capabilities. With a budget of more than US$1 billion per year for research, its studies address subjects from primary healthcare to translational research and have informed VHA policy development and improvements in care quality.[21] The VHA's investment in research and its size provide unique conditions for large-scale evaluations of its care delivery practices. The VHA has sponsored evaluations in high-priority areas such as home- and community-based care, telehealth, suicide prevention, and opioid prescribing risk mitigation.[89] The VHA aims to combine top-down and bottom-up strategies for spreading best practices. For example, conducting centrally-mandated pilot studies can help in the development of evidence-based guidelines, while initiatives like its Diffusion of Excellence program seek to discover how VHA facilities are rewarded for sharing their best practices and to what degree such innovations are adopted elsewhere in the system.[21] Moreover, there are strong academic affiliations in the larger VHA hospitals, with many clinicians holding dual appointments.[21] These practices align with key characteristics of an LHS, namely, a 'Leadership-instilled culture of learning' and 'Supportive system competencies' (Table 13).

The national implementation of eHRs have facilitated much of VHA's research by making available large quantities of population-based data on clinical care and outcomes. Its early adopted eHR system, established in 1992, currently processes approximately 2.4 million lab results, more than 550,000 pharmacy orders, and some 420,000 patient encounters on a daily basis.[21] In addition, routine administrative and clinical data capture is complemented by annual PREMs surveys and by expanded monitoring capabilities through telehealth for patients with diabetes, heart failure, and other chronic illnesses. For VHA clinicians and patients, the eHR system also functions as an information system, providing real-time access to clinical guidelines and electronic reminders and alerts.[21] In addition, the VHA's national Corporate Data Warehouse enables administrators to track specific areas of performance through dashboards at the facility, clinic, or provider level. The Veterans Administration Informatics and Computing Infrastructure, which uses advanced analytic tools and the data warehouse, have accelerated research through machine-learning techniques and natural language processing to extract clinical data captured in text notes.[21] These align with LHS characteristics 'Real-time access to knowledge' and the 'Digital capture of the care experience' (Table 13). The VHA aims to advance the holistic understanding of leadership, culture, process, and incentives that contribute to variations in care quality by augmenting their Big Data platforms with qualitative or Deep Data.[21] The VHA views the growing amounts of electronic health information as key to expanding opportunities for "rapid, low-cost, randomized trials of system interventions".[21, 89]

The VHA values 'Engaged, empowered patients' as an integral to LHS. The My HealtheVet web portal allows patients to access and update their health records, make appointments, and refill prescriptions. Paying VHA clinicians a salary helps to align financial incentives to value-based care rather than volume-based care. Access to multiple dashboards allows clinicians to track care quality relative to their peers, further incentivising high-quality care. As a public agency, the VHA has an obligation to transparency and publicly reports large amounts of data on care quality for both self-auditing purposes and for the benefit internal and external researchers.[21] These practices align with to the LHS characteristics 'Incentives aligned for value' and 'Full transparency' (Table 13).

The Ottawa Hospital

The Ottawa Hospital is a three-campus acute care facility in Canada and one of the main providers of cancer treatment in the Ottawa metropolitan area. In the 2014-2015 fiscal year, it carried out 24,000 oncology consults and received over 110,000 patient visits. Identifying delays to timely diagnosis and treatment for patients with lung cancer, the hospital consciously adopted an LHS vision to redesign its diagnostic processes. This resulted in the Ottawa Health Transformation Model (OHTM) which operationalised LHS thinking at the hospital.[39]

The OHTM was conceived as a consensus approach to address resistance to change, process barriers, and conflicting priorities. It aimed to align a number of key domains: "people (attitudes and cultural norms), processes (redesigned care protocols and revised performance standards), and technology (process-aware measurement and automation) to form a cycle that drives a learning health system that increases adaptability and performance".[39] The OHTM also created a dedicated "transformation team" to support implementation and process improvement. Drawing on systems thinking, lean thinking, and the Theory of Constraints,[39] 12 processes including referrals, triage, diagnostics, assessment, and consultations were redesigned and implemented.

Patients were consulted and engaged in the re-design process over time through semi-structured interviews (Table 13). The OHTM also won buy-in from hospital leadership as well as clinicians, who realised the utility of the aggregated operational and clinical data, and therefore worked to increasingly contribute to it. This positive feedback loop helped bring the care community together in a regional Community of Practice with a goal to learn, optimise patient care, and develop a platform for continued adaption to changing clinical and operational factors.[39] These initiatives align with the LHS characteristics of a 'Leadership-instilled culture of learning' and 'Supportive system competencies' (Table 13).

Process monitoring and business intelligence tools that integrate process-related data were employed to establish a learning cycle and create insights on system performance, available to multiple stakeholders. This enabled generation of local dashboards to track performance metrics at a provincial level, visualisations of the entire patient care trajectory, and alerts and queries to monitor individual and clinical team performance.[39] These initiatives can be mapped to the LHS characteristics 'Real-time access to knowledge', 'Digital capture of the care experience', and 'Full transparency' (Table 13).

As a result of its steps toward an LHS vision, the Ottawa Hospital experienced a 48% decrease in the median patient journey from referral to initial treatment – from 92 to 47 days. A diagnosis is now provided to 80% of referred patients within the provincial target of 28 days. These significant improvements are attributed to the OHTM process which has potential to facilitate improvements in other areas as it is "scalable, replicable, and simple enough to facilitate common understanding among stakeholders, including patients".[39]

Table 13. Examples of ways in which the case example LHSs embody the LHS characteristics

Case Example	Science and Informatics		Patient-Clinician Partnerships	Incentives		Culture	
	Real-time access to knowledge	*Digital capture of care experience*	*Engaged, empowered patients*	*Incentives aligned for value*	*Full transparency*	*Leadership-instilled culture of learning*	*Supportive system competencies*
Geisinger Health System	Robust eHR system[138] that feeds genomic data back into the sequence and allows for data analysis to improve genetic variant annotation, creating a virtuous cycle.[86]	Stable enrolment of patients into eHR system within a robust informatics infrastructure allowing for the tracking patient experiences and outcomes over the long-term.[86] Over 180,000 patients had consented to contribute their genomic data.[86]	MyCode Community Health Initiative (biorepository) relies on opt-in consent, and of those approached, 85-90% agree to participate.[86] Informatics infrastructure with security requirements and stores patient data behind a system firewall to protect patient information.[86]	Paying clinicians a salary so that their remuneration is not based on care volume.[86]	eHR and genomic data variants are reported back to patient-participants, while also being deposited into publicly available databases.[86]	The goal of establishing an LHS has been embraced by the organisation's leadership, who have aimed to develop conceptual and business models for moving toward a learning culture.[86]	Emphasis on continual quality improvement and the promotion of best practices checklists for physicians.[138]

Continued next page

Case Example	Science and Informatics		Patient-Clinician Partnerships	Incentives		Culture	
	Real-time access to knowledge	*Digital capture of care experience*	*Engaged, empowered patients*	*Incentives aligned for value*	*Full transparency*	*Leadership-instilled culture of learning*	*Supportive system competencies*
The Santeon Farmadatabase	Database allows for regular benchmarking between hospitals.[50]	Fully operational data warehouse linking the seven hospitals. Powered by a robust network of hospital pharmacists and containing medicine prescriptions and major clinical outcomes of all the hospitals' patients.[50] Specific records on nearly 800,000 unique patients – including over 18 million medication orders, 3 million hospital admissions, and 15 million diagnoses.[50] Weekly, uniform uploading of patient data to the shared warehouse.[50]	Patient anonymity through de-identification measures [50] Dutch regulatory framework allows de-identified data to be stored without the informed consent of patients.[50] However, the fact that individual patients have little say about what the capture and use of their data limits the degree to which this characteristic is fully realised.	N/A May vary by each hospital within the network.	Database allows for regular benchmarking between hospitals. Dutch regulatory framework allows de-identified data to be stored without the informed consent of patients.[50]	N/A May vary by each hospital within the network.	N/A May vary by each hospital within the network.

Case Example	Science and Informatics		Patient-Clinician Partnerships	Incentives		Culture	
	Real-time access to knowledge	*Digital capture of care experience*	*Engaged, empowered patients*	*Incentives aligned for value*	*Full transparency*	*Leadership-instilled culture of learning*	*Supportive system competencies*
Veterans Health Administration	Driven by the eHR system, the VHA's national Corporate Data Warehouse enables administrators to track specific areas of performance through dashboards at the facility, clinic, or provider level.[21] Providing clinicians with access to multiple dashboards to track quality relative to their peers.[21]	Systemwide eHRs, making available large quantities population-based data on clinical care and outcomes. Daily processing of more than two million lab results, 500,000 pharmacy fills, and 400,000 patient encounters.[21]	Initiatives such as the My HealtheVet web portal allow patients to access and update their health records, schedule appointments, and refill prescriptions.[21]	Paying clinicians a salary so that their remuneration is not based on care volume.[21]	Public reporting of large amounts of data on quality for both self-auditing purposes and for the benefit of unaffiliated researchers. Providing clinicians with access to multiple dashboards to track quality relative to their peers.[21]	strong academic affiliations in the larger VHA hospitals, with many clinicians holding dual appointments, has helped foster a leadership-instilled culture of learning.[21]	Strategy of combining top-down and bottom-up approaches for spreading best practices. Conducting centrally-mandated pilot studies to help develop evidence-based guidelines. Diffusion of Excellence program, launched in 2015, seeks to discover how VHA facilities are rewarded for sharing their best practices and to what degree such innovations are adopted elsewhere in the system.[21]

Case Example	Science and Informatics		Patient-Clinician Partnerships	Incentives		Culture	
	Real-time access to knowledge	*Digital capture of care experience*	*Engaged, empowered patients*	*Incentives aligned for value*	*Full transparency*	*Leadership-instilled culture of learning*	*Supportive system competencies*
The Ottawa Hospital	Process monitoring and business intelligence tools allowed for the local generation of dashboards to visualise and track performance metrics at a provincial level, create alerts and queries to monitor individual and clinical team performance.[39]	Process monitoring and business intelligence tools that integrate process-related data were also employed to establish a learning cycle and create insights on system performance.[39]	Patients were among the stakeholder groups engaged – through interviews – in the system redesign.[39]	N/A Information not readily available in reviewed materials.	Consensus approach to the initiative's creation led to general buy-in among most relevant stakeholders and their ability to access and benefit from the process monitoring and business intelligence tools implemented in the restructuring.[39]	Reported buy-in from leaders of the academic and community hospitals.[39]	Operating with a conceptual focus of a "health region" as a geographic unit of implementation, the OHTM brought about the establishment of a "regional Community of Practice" to engage stakeholders.[39]

Discussion

The rapidly increasing number of publications that discuss the LHS attests to the growing interest and potential benefits of this concept. However, few sources report on mature or advanced LHSs or their evaluations. Although the language used to define an LHS appears to be converging, there remain inconsistencies in how the term is applied. Indeed, we excluded many papers that mentioned the LHS in passing or simply listed it among the keywords but did not discuss the LHS concept at all, suggesting that the term is sometimes loosely applied in the literature. However, the IoM definition published in 2013[1] remains the touchstone definition of an LHS:

> "A learning health care system is one in which science, informatics, incentives, and culture are aligned for continuous improvement and innovation, with best practices seamlessly embedded in the care process, patients and families active participants in all elements, and new knowledge captured as an integral by-product of the care experience."[1]

This definition continues to be the most widely cited in the literature. Even publications that do not reference it directly touch on many of the concepts it contains, particularly in relation to health systems' informatics capabilities, continual efforts toward quality improvement, and capture of new knowledge as an integrated part of care provision and care experience.[80, 143] Many papers reported on the LHS only in terms of the 'Science and Informatics' dimension, suggesting that those working in the field view the availability of information technology and data infrastructures as an essential element of an LHS. In contrast, more "human" elements related to organisational cultures of learning and the empowerment and engagement of patients and their families are less frequently mentioned in the definitions (see Table 5 and Appendix 2). This variability in the definitions may reflect real-world differences in the importance placed on the different characteristics and the pragmatic elements needed to support LHS implementation.

The open-ended nature of the LHS term and its definitions and the variability in their usage can be a double-edged sword. On the one hand, the flexibility allows for the application of the LHS characteristics to a wide variety of initiatives in a range of contexts as demonstrated in our analysis of LHS case examples. However, a lack of shared terminology may affect the understanding of what an LHS is and does and how it can be realised. For example, many organisations across the world may be building LHSs or carrying out LHS activities without explicitly identifying their efforts as LHSs. McLachlan et al. (2018) stated: "the LHS 'community' is fragmented, with groups working on similar systems being unaware of each other's work".[11] Advancing not only a shared definition and terminology, but also an increasingly shared understanding of the LHS concept is fundamental to bringing greater coherence and opening avenues for constructive exchange and collaboration to advance the LHS vision.

Schematic frameworks which depict core operating features are another useful tool to help us to understand the complexities embodied in an LHS.[144] These conceptualisations are also important to guide adaptations and implementation of LHSs for specific local conditions or for specific purposes. Importantly, schematic frameworks can make a great deal of complex information more easily available to policymakers, clinicians, administrators, patient groups, and other stakeholders who can better grasp what is required to achieve an LHS. Even more importantly, frameworks provide a common vision for stakeholders to work from to realise the potential of the LHS vision.

Across the frameworks that we reviewed, we found consistent themes of continuity of data collection, analysis and feedback that support learning cycles for teams, collaboratives, networks, or institutions

that deliver healthcare. Unsurprisingly, the involvement of patients was central to many LHS frameworks. Some included elements of shared decision making in care delivery, including what care is delivered, how it is delivered, and how it aligns with patient needs and expectations. These core characteristics were applicable to various healthcare contexts, as well as to specific diseases, processes, or care delivery settings. An important consideration for achieving an LHS vision is the rigorous evaluation of LHSs embedded in the real-world. Schematic frameworks are useful to those wanting to implement and evaluate LHSs, providing guidance on which components may be needed to achieve desired outcomes. This is important for the future adoption of LHS models at scale.

Despite the potential usefulness of frameworks as described above, most of the frameworks we found were theoretical rather than applied in the real-world of health systems. Few papers that proposed an LHS framework discussed how one might go about implementing an LHS. Such guidance is very much needed to move the LHS model away from theoretical conceptualisations, and closer to practice.

The reviewed literature contained extensive information on examples of barriers and enablers to the development, implementation, and adoption of LHSs, which can support prioritisation of future efforts to implement LHSs. For example, the full potential of collecting large amounts of data has yet to be realised as the ability to mine information from free text in eHRs is still limited.[6] Focusing on developing natural language processing software and KaaS platforms may facilitate the use of such data in the future as the accuracy and specificity of these systems advances.

Conceptualising the secondary use of data collected during the clinical process as a research activity raised concerns related to lengthy ethical approval processes and data custodian permissions.[145] This can enhance rigour, but holds up access to data and delays data analysis, thereby slowing translation of new knowledge into practice.[8] Because of these delays, traditional ethics processes are often bypassed by labelling secondary data analyses as clinician led "quality improvement projects" rather than research.[130] This side-step perpetuates the view that quality improvement occurs through projects rather than being embedded as part of routine clinical practice, as intended in an LHS. Improving relationships between patients and clinicians and trust in health facilities through patient engagement, transparency, and accountability improves patients' willingness to work with current ethical processes and to give permission for the re-use of their data.[146, 147] Faden et al. (2013)[148] was repeatedly cited in relation to rethinking this traditional dichotomy between research and clinical practice while reframing ethics in terms of patients' "obligations to contribute to the common purpose of improving the quality and value of clinical care and health care systems",[149] a position which was supported by other studies.[14, 73, 145, 150] Operationalising these obligations as described by researchers and clinicians requires significant changes to the current legal and policy frameworks governing secondary use of data originally collected for clinical purposes. These factors are included under our 'Structure and Governance' dimension which we believe is an important addition to the four dimensions described by IoM. This dimension which includes, among other things, privacy and data protection laws and health policies that may be beyond the control of people and organisations developing LHSs, is an important consideration, which can enable or constrain LHS development and adoption process.

Translation of evidence into practice can often be slowed by traditional, expensive, and time-consuming research designs, such as cohort studies or randomised controlled trials.[151] Innovative, pragmatic, locally implemented research designs can hasten translation to support LHS adoption.[130, 152] Pragmatic trials, implementation evaluations, and embedded designs based on routine analysis and feedback loops are needed to capitalise on the enormous amounts of data being collected in every health system every day.[10, 90] The literature suggests that in many studies the LHS model is still considered as an idea to be trialled through research projects, however, the essence of an LHS concept

is more about adopting an LHS as the "business as usual" of healthcare provision, rather than projects that have a beginning and an end. Several of the included case studies, for example, Geisinger, VHA, and Santeon, demonstrate the potential for system transformation by adopting an LHS into their "business as usual" plans and practices.

Although patient involvement in the design and delivery of an LHS has been described as a key characteristic of a functioning LHS,[1] it was the least frequently addressed enabler in the literature. The incorporation of PROMs and PREMs has been slow in part due to barriers with integration of these measures into eHRs and their use in the care delivery process. Several papers talked about the care experience; however, the data they provided simply tracked encounters, tests, imaging, procedures, and operations through eHRs.[72, 74] The IoM's characteristic 'Digital capture of the care experience' included under the 'Science and Informatics' dimension is ambiguous. Experiences cannot be tracked through eHRs unless there are direct measurements of experience using either qualitative or quantitative methods (e.g., via PREMs, PROMs, or qualitative measures). The 'Digital capture of care experience' as defined by the IoM, predominantly describes the patient journey through health services, tests, imaging, and medical procedures rather than experience *per se*. Therefore, the terminology "Digital capture of the care journey" may be a more fitting description for this concept and should be considered. Actual measures (qualitative or quantitative) of experience should however still be collected. Furthermore, the care journey is not only important for patients; it is also important to teams of healthcare providers who care for patients, and yet the journeys and experiences of healthcare providers are rarely captured and largely absent from the LHS literature. An additional characteristic "Digital capture of patient and healthcare professional experience", that uses PROMs, PREMs, workforce surveys, debriefing sessions and other qualitative methods should be considered. This is important for the establishment and continuous improvement of LHSs, with healthcare providers being key stakeholders who need to apply new knowledge generated at the frontlines of care.

Although most of the articles in our review focused on theoretical aspects of an LHS, we found 68 examples of emerging or established LHSs. Many originated in the USA. This may be because the IoM, which developed and promulgated the definition of an LHS, is a US institution. Further research is needed to determine if this skew towards the USA reflects a difference in actual implementation across the world, a publication bias in the literature, or simply the use of other terminologies to describe LHS-like activities in other parts of the world.

Our four case studies of LHSs established and functioning in health systems provide insights of how emergent and established LHSs function and how their operations align with LHS dimensions and characteristics identified by the IoM. For example, the practices of Geisinger and the VHA touch on all IoM dimensions of an LHS. These LHSs are large, integrated healthcare providers with well-developed research capabilities, supported by established data platforms. Simon et al. (2020) summed up the critical components of established LHS organisations as those that have "large and well-defined patient or member populations, a comprehensive and well-curated data infrastructure, leaders who champion rigorous public-domain research, and the patience to invest institutional resources for long-term benefit".[90] Despite evidence that large institutions or networks of institutions have an advantage when implementing the LHS vision, we found a number of examples of smaller disease- or setting-specific LHSs, including the "Learn From Every Patient" program of a cerebral palsy clinical team at Nationwide Children's Hospital in the US[24] and a gynaecological cancer testing system at Virgen del Rocío University Hospital in Spain.[127] This validates for us that the LHS concept can be adapted at different scales and in different contexts.

The only LHS dimension clearly exhibited by all four LHS case studies was that of 'Science and Informatics', where 'Real-time access to knowledge' and 'Digital capture of the care experience' featured prominently and were supported by a robust eHR infrastructure in each case.[21, 39, 50, 86] There was less information about 'Engaged, empowered patients', although the reviewed literature on Geisinger and the VHA touched on practices allowing patients to control certain aspects of their health data. [21, 86] All case studies described the involvement of patients in committees and boards governing LHSs, though the influence and agency held by patients in these structures was not clear.

Three of the case studies provided specific details on the 'Incentives' LHS dimension. Geisinger and the VHA both remunerated clinicians with fixed salaries instead of on a fee-for-service basis, a clear example of 'Incentives aligned for value' for healthcare workers.[21, 138] In addition, the literature on those two systems and on the Ottawa Hospital program noted practices such as public reporting of system performance, reporting data back to patients, and opening access to key informatics tools, each of which speak to the question of 'Full transparency' as an important LHS characteristic.[21, 39, 86]

The last – and most human – of the IoM-identified LHS dimensions is 'Continuous Learning Culture' and three of the four case studies spoke to this LHS dimension. The ways in which the 'Leadership-instilled culture of learning' characteristic was manifest in the various LHSs differed, but the literature generally emphasised the importance of leadership having a clear understanding of and desire to implement the LHS vision, often described as "buy-in".[71, 153, 154] It also emphasised the importance of alignment between health professionals and healthcare researchers – who, in the case of large, integrated healthcare providers, were sometimes embedded within the system itself.[21] The concept of the culture of 'Supportive system competencies' was often embodied in the LHSs in the form of system-created opportunities for continued learning and collaboration among health professionals.[87]

One of the essential elements to operationalising an LHS is the ability to learn from previous endeavours. With the exception of the Ottawa Hospital case study, whose steering team has attempted to chronicle their journey to becoming a functional LHS, the profiled LHSs evolved over time through a series of initiatives (such as streamlining eHR integration), rather than through a predetermined LHS blueprint. Clear documentation of the steps taken when pursuing the implementation of an LHS are very much needed for the broader, future realisation of the LHS vision by others who follow these examples. The case studies tended to describe the benefits of an LHS in terms of successfully implemented system components but rarely addressed barriers and how these were overcome.[21, 50, 86] Empirical evidence demonstrating improved health outcomes or other benefits to patients and healthcare providers was limited, although a few examples of process improvement were given.[39, 130] There is a need, therefore, for more systematic documentation and pragmatic trials of LHS models which rigorously assess outcomes and experiences whilst analysing factors that help or hinder implementation in different contexts. This is essential to identify LHS components and implementation strategies that are transferrable or adaptable across contexts. Although none of the case studies provided a fully developed strategy for realising an LHS at scale they do provide important lessons and insights for healthcare organisations seeking to restructure their practices based on the LHS paradigm.

Conclusions

There is no doubt that data systems and technology to analyse and translate large amounts of data to produce information that can be used by clinicians, policymakers, and managers is the crux of an LHS. However, we believe on the basis of our extensive review of LHS literature that data systems and technology alone do not make an LHS – an LHS is much more than a 'Science and Informatics'

infrastructure. The other more human dimensions and characteristics of an LHS – including the interface between stakeholders and technology, learning networks and communities, alignment of care with patient needs through direct input from patients themselves, incentives for healthcare providers and managers to use information to increase value in the system, transparency and disclosure to support learning – are at least equally as important as informatics, although much harder to cultivate. To achieve a functioning LHS, amongst the most important aspects are culture and leadership to support, enable and adopt the other LHS characteristics.

Furthermore, entrenched governance structures, regulations, and laws operating at various levels often inhibit the progress of LHSs. Ethical considerations, privacy legislation, organisational structures, and funding flows that fragment rather than integrate systems, as well as outdated payment systems that incentivise volume rather than value, are important considerations for the progress of LHSs. For this reason, we believe that another category of LHS dimensions – 'Governance and Structure' – is important for the implementation of LHSs in healthcare contexts and should be considered in addition to the original four IoM dimensions.

The characteristic of 'Digital capture of care experience' as defined by the IoM does not currently capture "experience" and we believe it should be renamed to "Digital capture of the care journey" which is more aligned with the definition and application of this characteristic, where most authors talk about encounters, tests, treatments, and procedures derived from eHR. Furthermore, the experiences of healthcare providers are largely absent from the LHS literature. Measuring and using healthcare provider experience is important when developing and operationalising LHSs as after all, the health providers at the front lines are the ultimate users of information and systems embodied in an LHS. An additional characteristic, "Digital capture of patient and healthcare professional experience", should be added to accurately describe and encapsulate both patient and clinician experience through PROMs, PREMs, workforce surveys, debriefing sessions and other qualitative measures.

The potential of the LHS vision to improve patient care, reduce waste and bring about a more sustainable health system is apparent. Indeed, there is little doubt that the LHS vision is being embraced, developed, and implemented at different scales and levels around the world, although there is variation in models and applications. Despite this enthusiasm, rigorous evaluations are lacking. Such evaluations are critical for providing feedback to guide the realisation and ongoing development of this promising model. Considering additional dimensions and characteristics, including structure and governance, capture of patient journeys, and the experiences of patients and of healthcare providers, would further enhance the already exciting concept of an LHS.

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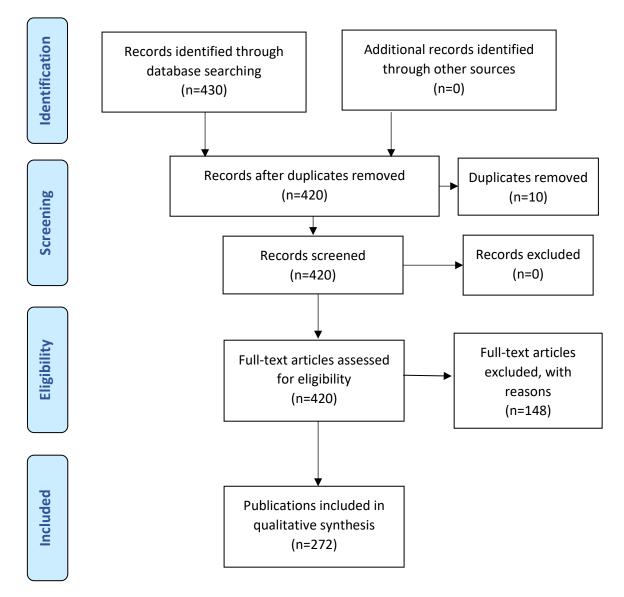
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Appendices

Appendix 1. PRISMA Flow Diagram

Appendix 2. LHS Definitions

Supplementary Table 1a. LHS definition sources: IoM reports

Source and Reference	Definition or Sample Definitions from Cited Source*	Number of Publications Citing
Institute of Medicine (2013)[1]	"A learning health care system is one in which science, informatics, incentives, and culture are aligned for continuous improvement and innovation, with best practices seamlessly embedded in the care process, patients and families active participants in all elements, and new knowledge captured as an integral by-product of the care experience."	53
Institute of Medicine (2007)[13]	"…a learning healthcare system that is designed to generate and apply the best evidence for the collaborative healthcare choices of each patient and provider; to drive the process of discovery as a natural outgrowth of patient care; and to ensure innovation, quality, safety, and value in health care)." "…a healthcare system that 'learns'—one in which knowledge generation is so embedded into the core of the practice of medicine that it is a natural outgrowth and product of the healthcare delivery process and leads to continual improvement in care." "…the *long-term vision* of a learning healthcare system, in which evidence is both applied and developed as a natural product of the care process."	46
Institute of Medicine (2011)[155]	"In the **learning health system**, progress in science, informatics, and care culture align to generate new knowledge as an ongoing, natural by-product of the care experience, and seamlessly refine and deliver best practices for continuous improvement in health and health care." (Emphasis in the original)	14
17 other IoM reports	Examples include: "…a **learning health system** that is designed to generate and apply the best evidence for the collaborative healthcare choices of each patient and provider; to drive the process of discovery as a natural outgrowth of patient care; and to ensure innovation, quality, safety, and value in health care." (Emphasis in the original) - Institute of Medicine (2011)[156] (7 citations) "…a continuously learning health system in which science, informatics, incentives, and culture are aligned for continuous improvement and innovation. In this continuously learning health system, best practices will be seamlessly embedded in the care process, patients and families will be active participants in all elements of the health system, and new knowledge will be captured as an integral byproduct of the care experience." - Institute of Medicine (2015)[157] (4 citations)	28

*Definitions provided are from the cited sources

Supplementary Table 1b. LHS definition sources: non-IoM publications

Source and Reference	Definition or Sample Definitions from Cited Source	Number of Publications Citing
Friedman et al. (2015)[2]	"Though articulated in various forms, the underlying concept is straightforward: harness the power of data and analytics to learn from every patient, and feed the knowledge of 'what works best' back to clinicians, public health professionals, patients, and other stakeholders to create cycles of continuous improvement."	12
Friedman et al. (2010)[33]	"The accumulation through EHR adoption of these computable, liquid, standardized data creates an enormous potential for the U.S. health system to conduct clinical and translational research, assess and improve the quality of health care, and survey the health of the public at speeds approaching real time. These goals can be achieved by moving data, on an as-needed basis, from the panoply of locations where they are collected to one or more investigative centers where they are aggregated and analyzed for a specific purpose. Rapid data aggregation enables the creation of large, scientifically valid samples that can then be used to draw powerful inferences about populations. When this process can happen routinely, with mechanisms in place to establish and maintain public trust that the process is secure and private, the nation will have substantially progressed toward establishing a so-called rapid learning health system".	10
Etheredge (2007)[28]	"A national rapid-learning system could include many databases, sponsors, and research networks. Its databases could be organized by enrolled populations (private health plans, VA, Medicare, Medicaid), providers (multispecialty clinics, academic health centers, specialist registries), conditions (disease registries), technologies (drug safety and efficacy studies, outcomes research), geographic areas (the Framingham Heart Study), age cohorts (the National Children's Study), minority populations (human genome studies), and other ways. With national EHR data, registry, connectivity, reporting, and privacy protection standards, all EHR systems could be compatible and capable of multiple uses; information in one data bank could be supplemented with that from another."	7
74 other non-IoM sources	Examples include: "The 'rapid-learning health system'… leverages recent developments in health information technology and a growing health data infrastructure to access and apply evidence in real time, while simultaneously drawing knowledge from real-world care-delivery processes to promote innovation and health system change on the basis of rigorous research." - Greene SM, Reid RJ, Larson EB (2012)[34] (3 citations) "…the Learning Health System (LHS) model, which seeks to integrate organizational learning across clinical, operational, and research functions of health systems to support improved quality and high value care." - Psek et al. (2016)[134] (3 citations)	104

Supplementary Table 1c. LHS definition sources: unsourced (authors' own definitions)

Source and Reference	Definition*	Number of Publications
Menear et al. (2019)[30]	"We thus define LHSs as dynamic health ecosystems where scientific, social, technological, policy, legal and ethical dimensions are synergistically aligned to enable cycles of continuous learning and improvement to be routinised and embedded across the system, thus enhancing value through an optimised balance of impacts on patient and provider experience, population health and health system costs."	
Harris et al. (2016)[81]	"…a learning health system, in which data gathered from point of care is applied for purposes of quality improvement as well as health services and comparative effectiveness research (CER)."	
Kim et al. (2017)[158]	"…a learning health care system (LHCS), in which patient information, captured at the point of care, is analyzed to assess treatment efficacy, safety, and quality of care, and fed back to improve patient care."	
Daza et al. (2016)[64]	"…a learning healthcare system, a system that is able to generate enough data that can be then analyzed to generate new insights into what works and what doesn't."	7
Alsheik et al. (2019)[113]	"Learning health systems are systems that leverage the experience of every patient to determine the most effective and efficient care that can be offered within their organization. The core requirement of such a system is big data processing of digital health information from within and outside a healthcare organization to provide a new approach to determine diagnostic or treatment pathways and their resultant outcomes and costs."	
Dranseika and Piasecki (2020)[159]	"A Learning Health Care System is one in which data collected from and about patients are analyzed and used to find better ways to care for future patients."	
Squires et al. (2019)[106]	"Learning Health Networks (LHN) improve the well-being of populations by aligning clinical care specialists, technology experts, patients and patient advocates, and other thought leaders for continuous improvement and seamless care delivery."	

* The papers in this table did not give a citation for the wording used in the definition.

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