THE LEARNING
HEALTHCARE PROJECT

REALISING THE POTENTIAL OF
LEARNING HEALTH SYSTEMS

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Foundation

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Contents

Preface

The Learning Healthcare Project at Newcastle University was founded in 2014, with funding from The Health Foundation; we issued our first report, *The Potential of Learning Healthcare Systems [1]*, the following year. Since then, we have collaborated on national and international policy relating to Learning Health Systems.

We predicted that the five years to 2020 would see increasing efforts to learn from routine data, improvement of user interfaces, and the further development of outcome measures and outcomes-based reimbursement. We also expected to see progress on interoperability, the development of platform components, more interorganisational networks and greater acceptance of data sharing by patients. There has been international movement towards these goals, but not as much as we had expected. This report reflects our richer understanding of the sociotechnical complexity involved in developing a Learning Health System and presents tools that can help to manage it.

Since the publication of our first report, we have been contacted by organisations around the world, seeking advice on how to build a Learning Health System. While there can be no one-size-fits-all blueprint, in this report, we present a framework for considering the key sociotechnical challenges. We also provide links to practical resources that organisations may find helpful as they progress towards their own vision of a Learning Health System.

This report is a child of the Covid-19 pandemic. Our work and our workshops moved online, but more broadly; we witnessed an acceleration in the shift to digital healthcare. Hopefully the Learning Health System concept can channel the "dash for digital" and help to avoid wasteful spending on siloed systems that don't work together.

Most importantly, we hope that you enjoy our report. Please get in touch to feedback, to share your experience or if you would like to collaborate.

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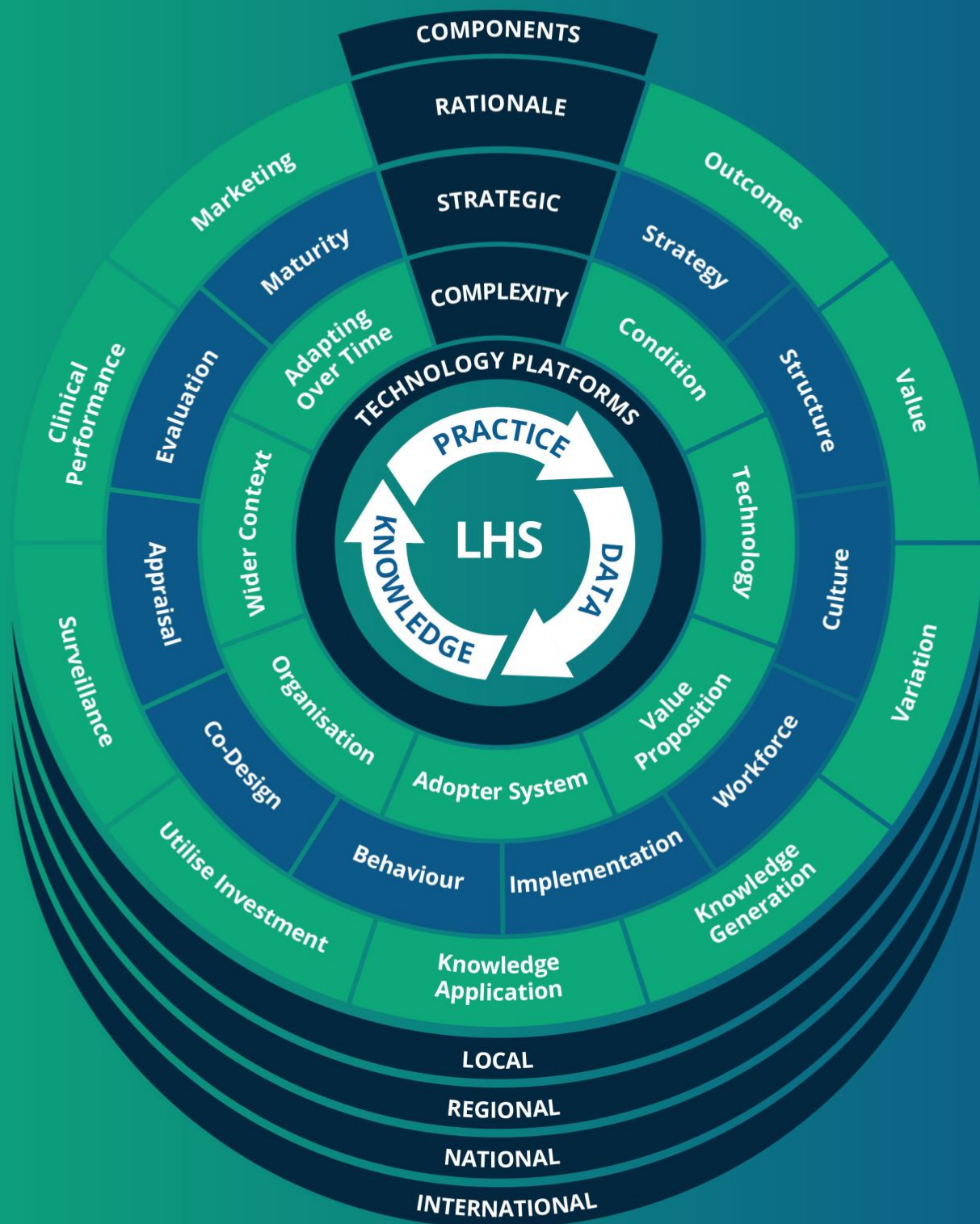
Figure A.
Learning Health System Framework

Executive Summary

A Learning Health System is described as a health system in which outcomes and experience are continually improved by applying science, informatics, incentives and culture to generate and use knowledge in the delivery of care. A Learning Health System can also improve value, reduce unjustified variation, support research and enhance workforce education, training and performance.
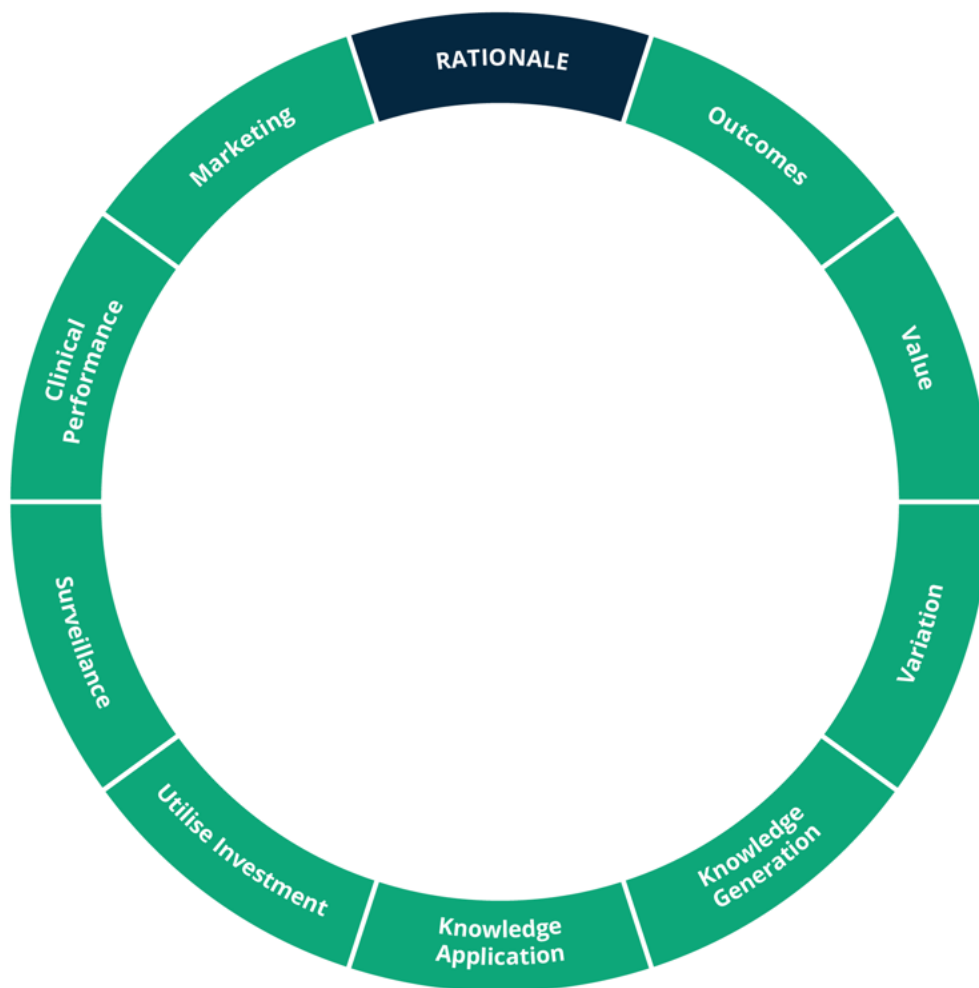
This report presents a framework for considering the key challenges facing anyone building a Learning Health System (Figure A). The fractal nature of a Learning Health System means that conceptually, many of the challenges are the same, whatever the system's scale – from a small medical practice to an international health system.

THE LEARNING
HEALTHCARE PROJECT

At the hub of our framework are the technical building blocks for organisational learning, that enable data generated from practice to create knowledge and for that knowledge to be put back into practice.

Data must be generated from practice (Practice to Data):
It must be captured, stored, accessed and protected. The quality and provenance of data must be ensured, and it must be sharable and understood between settings.

Knowledge must be generated from the data (Data to Knowledge):
There are many ways to generate knowledge. Randomised trials are familiar in clinical medicine, but there is also a range of quasi-experimental analytic methods. Artificial Intelligence is only the latest field to offer methods of generating insight. More traditional engineering approaches also have a role, as do qualitative methods. Knowledge generation cannot be entirely automated and learning communities have a place at the heart of any Learning Health System.

Knowledge must be put into practice (Knowledge to Practice):
It is not enough to publish knowledge in books, journals and reports. It must be put into practice. Clinical guidelines, for instance, can be represented in a standardised, machine-readable and computable form that can guide decision making at the frontline.

Platforms:
While each Learning Health System is a unique and complex system of technologies, people and policies, there are usually common infrastructural elements.
These can often be procured as platforms, freeing the health system to focus on the unique and high-value elements of its Learning Health System.

Understanding and managing complexity in a Learning Health System:

Healthcare is complex, a fact that must be reflected in any Learning Health System. The Nonadoption, Abandonment, Scale-up, Spread and Sustainability (NASSS) Framework suggests seven domains in which the complexity of a Learning Health System can be considered: condition/illness, technology, value proposition, adopters, organisations, the wider system and adaptation over time. Considering a proposed Learning Health System within this framework can aid in design, implementation and evaluation.
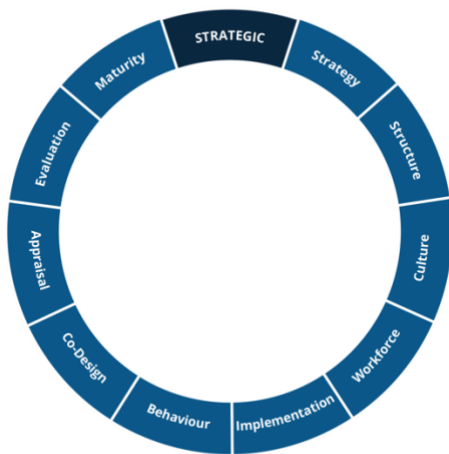
Strategy in a Learning Health System:

A Learning Health System requires strategic direction, a culture of learning and a scientific approach to implementation. Individuals and organisations will have to change their behaviour. It must be co-designed by the stakeholders and continually evaluated.

These elements of our framework are represented in Figure A and described in detail throughout this report, with links to a huge range of useful resources.

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Introduction and Rationale for a Learning Health System
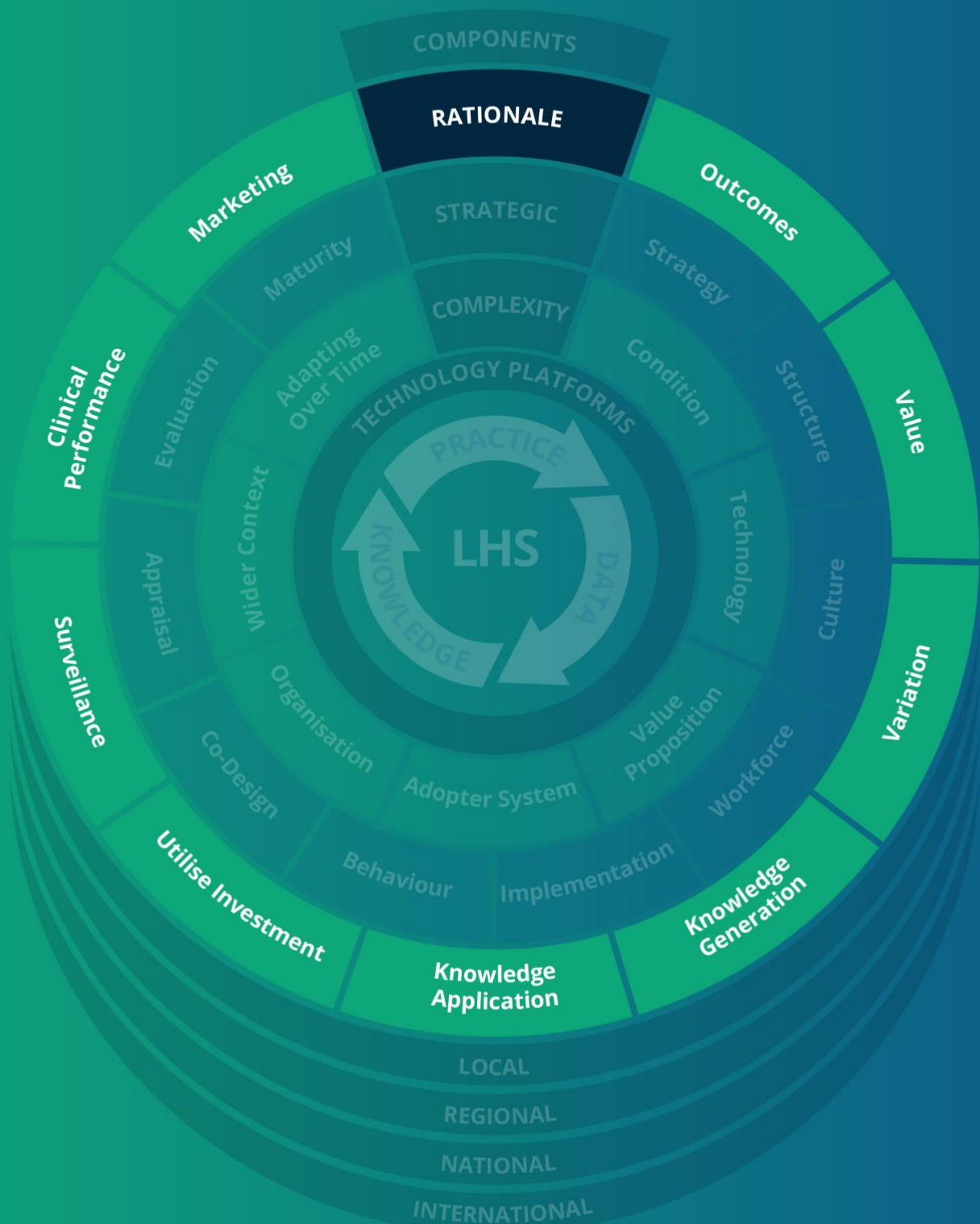
This report offers guidance for building a Learning Health System, focusing on tools, models and frameworks that might be helpful. However, it is not a "how to" guide. Indeed, there is no model for building a Learning Health System that can be "lifted and shifted". Learning Health Systems are complex by nature and must be co-designed with local stakeholders.

We aim to refresh "The Potential of Learning Healthcare Systems" [1], which was published in 2015. Here, we supplement the interviews and workshops conducted for that report with five new expert workshops, a purposeful literature review and six more years of experience building Learning Health Systems.

Figure A provides a framework for thinking about the components of a Learning Health System which is mirrored by the sections of the report. This first section describes how a group of stakeholders might determine their **Rationale for developing a Learning Health System** (the outer ring of Figure A). The next section discusses the **Technical Building Blocks of a Learning Health System** (the hub of Figure A). Next, we explain why **Understanding and Managing Complexity in a Learning Health System** is about more than just technology (the ring marked 'Complexity'). The final main section explains the key **Strategic Considerations in a Learning Health System** (the ring marked Strategic).

A Learning Health System can operate at any scale, from a team to a small provider organisation, or from a regional group of organisations to a national or even international system [2]. The elements considered in this report are relevant at each scale, as illustrated by Figure A.

What is a Learning Health System, and why would you want one?

Many years before the concept was applied to healthcare, a learning organisation was defined as "an organization skilled at creating, acquiring, and transferring knowledge, and at modifying its behaviour to reflect new knowledge and insights" [3].

The idea was introduced to healthcare in 2007 by the United States Institute of Medicine (IoM, now the National Academy of Medicine) [4], which later defined it as a system in which "science, informatics, incentives, and culture are aligned for continuous improvement and innovation, with best practices seamlessly embedded in the delivery process, [with] patients and families active participants in all elements, and new knowledge captured as an integral by-product of the delivery experience" [5].

On the face of it, the definitions above are comprehensive, but not very specific. Almost any health system can claim to be a Learning Health System, in that there are scientific processes, informatics and incentives in play. Knowledge is usually captured in some form or other, and most systems at least claim to seek improvement. However, there are few, if any systems in which these elements are fully

aligned for continuous improvement and innovation.

Importantly, the focus is on collecting data to generate knowledge and applying it to improve practice (the hub of Figure A).

In most cases, data come from Electronic Health Records, clinical registries or other routinely collected sources. Data are analysed by communities of practice or by a range of quantitative methods, often devised by academic health centres, public bodies or commercial organisations [6]. The knowledge generated is then used to change practice by informing deliberative processes or by directly feeding decision support systems.

Learning Health Systems have been called many different things, including data hubs, living labs, innovation or informatics hubs, learning networks, learning laboratories, community-clinician participatory data healthcare research, data driven improvement initiatives, interventional informatics, practice-based data networks, circular data-driven healthcare, Learning Healthcare Systems and Rapid Learning Health Systems [6].

It is important to recognise that a Learning Health System is an ongoing journey rather than a destination; the very concept of a Learning Health System is that there is always something new to learn [7]. They conduct similar activities regardless of scale, giving them a fractal property. This means that many elements will be reusable as Learning Health Systems scale up. Figure A shows that each of the elements considered in this report can

be co-designed at the local, regional, national and international level.

There is necessarily an interdisciplinary science developing around the Learning Health System concept, evidenced by the formation of new university departments [8], conferences [9, 10] and an academic journal [11].

The rationale for developing a Learning Health System often includes some or all of the following, which were explored in more detail in the earlier Learning Healthcare Project report [1]:

To improve patient outcomes and experience:
While most health systems seek to improve the quality and safety of care, many fail even to measure comprehensive and robust outcomes. A Learning Health System with the ability to deliver actionable knowledge to the point of care could enable improvements to patient outcomes and experience.

To provide better value healthcare:
Patient outcome and patient-level costing data can enable Value Based Healthcare Delivery [12]. This may reduce the cost for a given outcome – in other words, doing things right. Perhaps more fundamentally, a Learning Health System can inform priorities for resource allocation – doing the right things.

To reduce unjustified variation:
A Learning Health System can identify variations in outcomes and in the availability of health interventions by geography or by subpopulation. It can highlight health inequalities or positive deviants, and apply behaviour change

methods to address such variations [**13**].

To generate generalisable knowledge:
A Learning Health System can empower research. It can help identify potential participants for traditional randomised controlled trials. It can enable low-cost monitoring or long-term follow-up of participants, by tracking when they interact with the health system. It can host prospective pragmatic trials or retrospective observational studies. It can generate evidence that is relevant to small sub-populations or those with comorbidities or polypharmacy [**14**], and can deliver evidence for policymaking at the population-level.

To optimise the use of knowledge and evidence for decision making:
A Learning Health System can improve the use of research evidence, staff knowhow, learning from experience and organisational memory. It can close the loop by delivering knowledge back to the front-line, in a form that is likely to be acted upon. It can also monitor the impact of that action.

To identify and track epidemiological phenomena in near real-time:
The Covid-19 pandemic has highlighted the importance of real-time health surveillance systems. These can be developed on top of the infrastructure required to support other Learning Health System functions [**15**].

To maximise the benefits of technological innovation and investment:
Many health systems have invested vast resources into Electronic Health Records

(EHR) and other Health IT infrastructure. Without investment in something like a Learning Health System, EHRs often represent little more than a clunky version of paper notes. A Learning Health System can exploit the newly available data and increase the value of existing Health IT infrastructure.

To expand the education, training and performance of clinicians:
A Learning Health System can enable performance feedback and personalised professional development using routinely collected clinical data [**16**].

Marketing (Because it sounds good):
In some cases, the Learning Health System concept has been used as a marketing label, applied to existing systems. This is due to the vagueness of the definitions above. It risks diluting and discrediting the concept, but it can have benefits. If it provides a set of organising principles for existing activities, it can point the way to more strategic future developments.

Stakeholders should review their current systems before establishing a Learning Health System, identifying how it may address any existing issues. This could take the form of a simple SWOT (Strengths, Weaknesses, Opportunities, Threats) [**17**] or PESTLE (Political, Economic, Sociological, Technological, Legal, Environmental) [**18**] analysis, or it could use the more comprehensive NASSS Framework (outlined later). This will provide the basis for a strategy to deliver the right Learning Health System.

Case studies

No two Learning Health Systems are the same, but there is much to be learned by studying examples and considering what succeeded, and in what circumstances.

A recent review of the literature identified 68 Learning Health System case studies across 20 countries [19]. A previous Learning Healthcare Project report and associated website described many other examples [1]. This report is illuminated by several additional examples that have been identified from the literature and our workshops. They are referenced throughout the report and summarised below. Most relate to components of a Learning Health System, though some are full Learning Health Systems in their own right.

Learning Health System	Details
Better Care Programme (HDR UK) [20]	A UK-wide hub and spoke funding and collaboration network designed to support the development of Learning Health Systems that integrate clinical practice, large-scale data and advanced analytics in a cycle of continuous improvement.
Evelina London Children and Young People's Health Partnership [21, 22]	An interagency model to provide coordinated and tailored care for children and young people in South London. Anticipatory care is enabled using a population health model supported by primary and secondary care data systems.
Geisinger Health System [23]	Geisinger is an integrated health system in Pennsylvania, USA, that has embraced the Learning Health System concept to drive continuous care improvement.
HealthTracker [24]	A well-evaluated Australian clinical decision support tool that incorporates ten different clinical practice guidelines into a single on-screen algorithm on the clinician's desktop. It provides estimates of cardiovascular risk and suggests further investigations and lifestyle changes.

Learning Networks [25]	The Learning Network approach has been pioneered by Cincinnati Children's Hospital. In 2007 it started with ImproveCareNow, a Learning Health System for Inflammatory Bowel Disease, and now covers many other conditions. It has scaled up and spread the concept by sharing its common framework, methods and processes with other institutions.
Local Health and Care Records [21]	A group of regional interagency information-sharing initiatives across England, based on the Learning Health System concept.
Mayo Clinic Platform [26]	A ten-year strategic initiative aiming to transform healthcare by delivering data, care, diagnostics and management platforms that could support a Learning Health System.
Mobilizing Computable Biomedical Knowledge [27]	An international community led by the Department of Learning Health Sciences at the University of Michigan. Their goal is to ensure that biomedical knowledge in computable form is Findable, Accessible, Interoperable and Reusable (FAIR).
Nightingale Learning System [28]	In response to the Covid-19 pandemic, the NHS in England converted a London convention centre into the first of the country's Nightingale Hospitals, expanding treatment capacity. A learning system was built into the organisational architecture of the facility.
Open Lab Newcastle [29]	Open Lab is a research group that works on advanced Human-Computer Interaction (HCI), digital citizenship, sustainability, design futures, social innovations and machine learning. The group essentially creates sociotechnical learning systems in health and beyond.
Rapid cycle randomized testing at NYU Langone Health [30]	A Learning Health System was developed by embedding randomised tests of quality-improvement interventions within an existing healthcare system, using routinely collected data.
National Institute for Health and Care Excellence (NICE) [31]	NICE produces national guidelines across health and social care. It aims to support a Learning Health System by broadening its scope from single condition, narrative guidelines, to structured recommendations encompassing multi-morbidity, polypharmacy, and wider health system considerations.
NHS Digital [32]	The English health system's data hub aims to enable a national Learning Health System, using cradle-to-grave longitudinal health data on the entire population.

OpenClinical [33]	A collaboration between University College London, Oxford University and Deontics Ltd., created to maintain an open access and open-source repository of medical knowledge in a machine-readable format.
Optum Labs [1]	A US research partnership with access to the health records of over 100 million patients, Optum Labs has used structured data and Natural Language Processing to enable a research-based Learning Health System.
PatientsLikeMe [29, 34]	A US-based web platform that allows patients around the world to share their health-related experiences and outcomes in a highly structured format. The data can be used by individual patients or researchers to learn from the experience of each patient. This information has also been linked to biological data and used to train AI algorithms.
Scottish National Decision Support Programme [35, 36]	A development programme aligned to the broader national health strategy that focuses on improving outcomes in key areas. Each decision support tool is developed through a participatory co-design process, engaging all stakeholders.
TRANSfoRm [37]	An EU-wide programme to enable a Learning Health System, this could improve patient care by speeding up translational research, enabling more cost-effective Randomised Control Trials and by deploying diagnostic decision support.

Technical Building Blocks of a Learning Health System
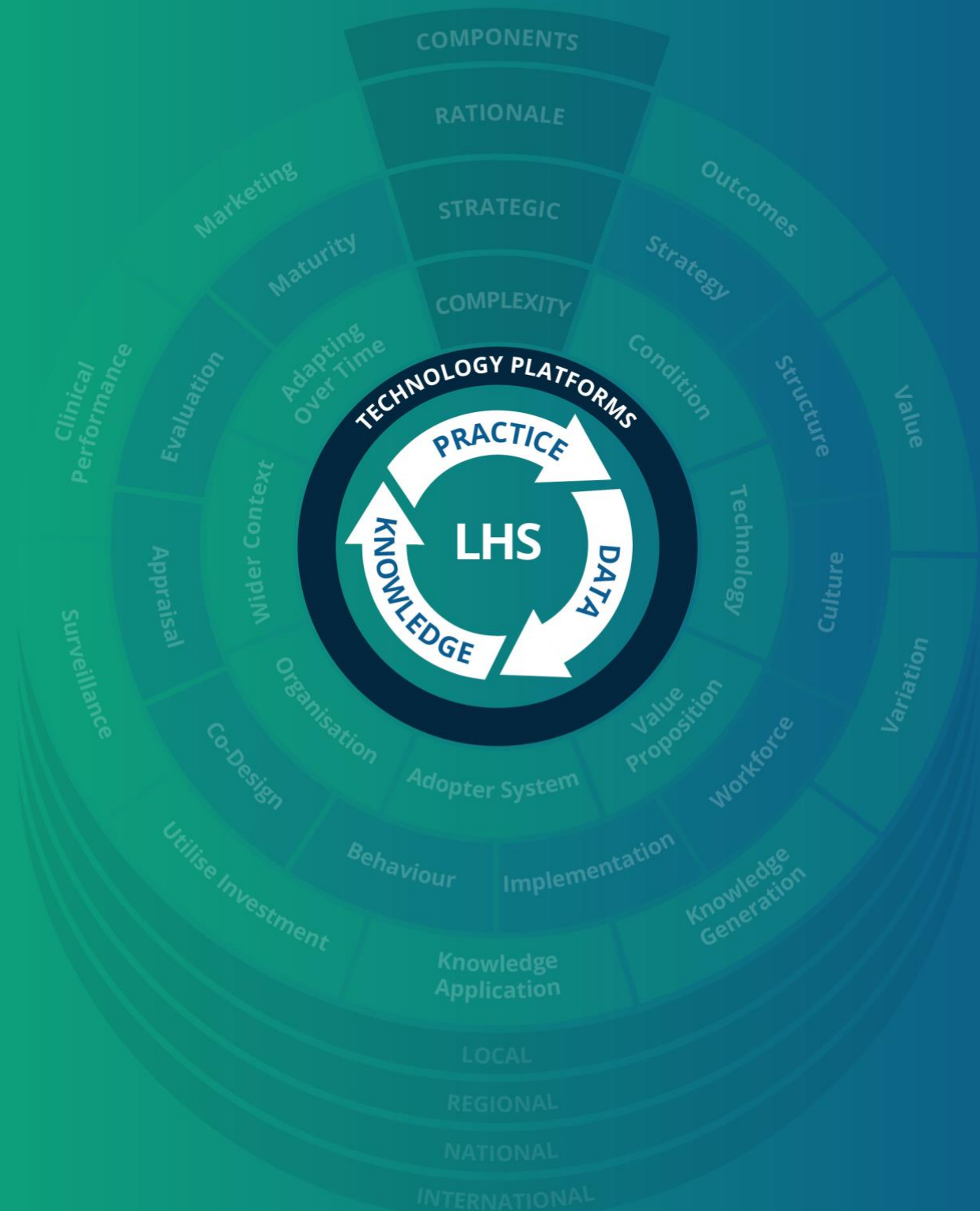
Our earlier Learning Healthcare Project report [1] described the building blocks of a Learning Health System in detail. Here we will summarise that work, expanding on new developments.

Learning Health Systems have been described as learning cycles at scale [38]. Once a decision is made on what to study, organisational Learning relies on data being derived from practice (Practice to Data), knowledge being generated from the data (Data to Knowledge), and knowledge being transferred back into practice (Knowledge to Practice). This is illustrated by Figure A, which in turn forms the hub of the wheel in Figure A. Each of these stages is described below.

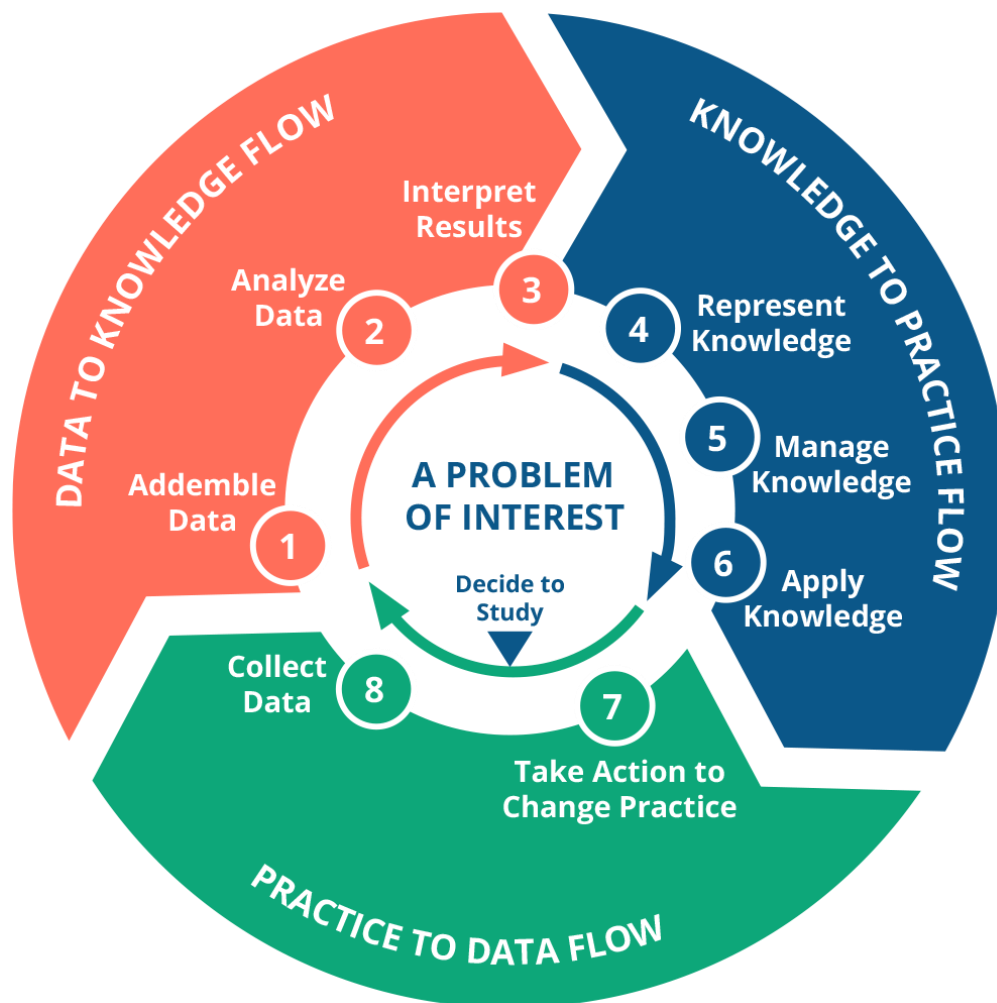*Figure A Adapted from Flynn et al.'s [38] view of the learning health cycle of the Learning Health System*

Other models [39] explicitly consider "information" and "wisdom", as well as "data" and "knowledge". This is often helpful in considering how specific Learning Health System cycles operate.

However, for the purposes of this report, data and information are considered together, as are knowledge and wisdom.

Practice to data

In a Learning Health System of any scale, informatics provides an opportunity to learn from every patient who is treated. The first step is to collect and assemble data that accurately represents what is happening within the system. This can include data on patients that is generated within healthcare organisations or elsewhere, as well as data on staff, facilities, finance and the environment.

Data Capture

There are different approaches to collecting data [40]. On an Electronic Health Record (EHR), highly structured input fields can be used to capture structured data or Natural Language Processing (NLP) can be applied to make sense of free text [1] (see Optum Labs Box). NLP systems vary in their performance in different contexts and do not currently offer an acceptable solution across settings. Some providers that lack electronic records still rely on clinical coders to extract data from handwritten patient notes. Structured data, such as genomic or pathology results, can flow from labs when coding standards are agreed.

Optum Labs

Optum Labs is a UnitedHealth-owned US research partnership that has access to the health records of over 100 million patients. It found that clinicians prefer not to use structured fields and often leave them blank. Accordingly, Optum opted to codify around 70% of its data from EHRs using NLP [40]. This real-world evidence has been used to validate and complement Randomised Controlled Trials.

Data collected outside healthcare settings can be useful: for example, from smartphones, apps, wearable technology, online communities and social media [41]. The Covid-19 health system response has shown how patients can be supported remotely with data on their vitals, eg blood oxygen levels flowing back to clinicians in real time via mobile apps [42].

It was thought that these many sources of data could be routed back into EHRs, which would act as central repositories for each provider. However, issues with performance, the ease of access to interfaces for importing and extracting data to and from EHRs, and the ongoing challenges of interoperability between EHRs have limited this approach. Many providers rely on data warehouses to hold data from multiple sources, and other platforms have emerged to manage data flowing in from outside the clinic and between multiple organisations. Many now advocate completely separating the EHR front end from the data.

The focus is often on quantitative data, but it is not always possible to measure some important factors through quantitative metrics [43]. It is therefore also vital that a Learning Health System can capture qualitative data, such as experience and narrative. This can be achieved through a number of methods, such as interviews and focus groups, as well as mass-participation tools for capturing and visualising narratives from across a population [44]. Health systems can also embed opportunities for comment and feedback into routine practice, such as providing feedback links in electronic decision support screens or free text options in staff or patient surveys.

Data Quality and Provenance

Within a Learning Health System, data are analysed to generate knowledge that can be applied to practice. If the data driving that process is inaccurate, incomplete or out of date, the insights generated will be incorrect, resulting in poor decisions and possibly even harming patients. Data are often derived from multiple sources and may undergo processing by multiple parties. The technique of describing the history of data items, where they came from, how they came to be in their current state and who has acted upon them, is known as data provenance [45].

Routinely collected data are particularly prone to poor data quality because it is often generated as a by-product of care provision. Those generating the data are often unaware of how it will be used and interpreted beyond direct care. Improving data quality requires a multilevel, sociotechnical effort with patients and staff at the front line, clinical coders, system designers and analysts (see DQMI Box).

Data Quality Maturity Index

The Data Quality Team within NHS Digital have created the automated Data Quality Maturity Index (DQMI), which is used to assess the quality of data submitted by providers across four metrics:

- Coverage: has data been received from all expected data suppliers?
- Completeness: do data items contain all expected values?
- Validity: does data satisfy the agreed standards and business rules?
- Use of default values: percentage of times that the default value is selected.

Results of the Data Quality Maturity Index are published and fed back to data providers to drive improvements.

This index cannot, however, detect several important aspects of data quality. For example, it would not necessarily pick up inaccurate data flowing from a provider. This currently requires familiarity with the data set, the providers, historical data and the clinical environment where the data are generated.

Geisinger Health System

Geisinger Health System is a leading US non-profit integrated healthcare system. It has aspired to become a Learning Health System since 2014 and has embraced patient-engaged research. When investigating data quality, the Geisinger team found that the most accurate data items tend to be those that are most frequently viewed, and that are viewed by several stakeholders. Sharing data with patients has therefore proved an effective way of improving data quality.

Data Storage and Access

In Learning Health Systems that span more than one organisation, data can be stored and accessed through centralised or distributed networks. In a centralised network, the data are uploaded, in real-time or periodically, to a central repository, from which it can be accessed for secondary uses. Hospital Episode Statistics (HES) data from the English NHS is an example of this approach. Each hospital in the English NHS submits data to NHS Digital on a monthly basis. This data are combined into a centralised database, elements of which can be disseminated to others [46].

A benefit of this approach is that it simplifies access to data as only one location needs to be queried. However, although patient data can be de-identified, centralised systems can create concerns over security, proprietary, legal and privacy issues, because patients can sometimes be reidentified and the provider, who may be legally responsible for the security of data that they have collected, loses operational control [47].

By contrast, a distributed network configuration leaves the data holder in control of its protected data. The US Food and Drug Administration (FDA)'s Sentinel program [48], an active surveillance system for monitoring the safety of FDA-regulated medical products, is a good example.

Through this approach, queries are sent to each node (organisation) in the network. Each node returns (often aggregated) results to a coordinating centre, using an agreed common data model. A mapping must be agreed between each node and the common data model, if the individual nodes represent data differently. Moreover, multiple queries are needed to obtain complete data.

Distributed implementation is therefore more complex than the centralised approach. However, it overcomes many of the privacy issues, and the participating organisations maintain operational control of their data [49]. They may even choose to review each query before releasing the data.

Data can be disseminated for analysis (bringing the data to the analysis). Alternatively, the analysis can be carried out within a secure environment operated by the data controller (bringing the analysis to the data). The latter option has become increasingly popular as a way to reduce the risk of patient-identifiable data being accessed without authorisation. Traditionally, queries were performed in a secure

room, from which data could not be removed. More recently, the secure room has been replaced by a secure web-based portal, where analysis can be conducted. NHS Digital has developed such a Data Access Environment, which permits authorised organisations to analyse data and extract aggregate results, but not patient-level data [**50**].

Information Governance

Information Governance (IG) is critical to maintaining trust in a Learning Health System, ensuring that individuals can trust organisations to use their data fairly and responsibly [**51**]. Data must be obtained, held, used and shared within a robust, ethically based IG framework.

In the UK, IG is underpinned by the General Data Protection Regulation (GDPR). This European Union regulation is unaffected by Brexit, having been passed into UK law by the Data Protection Act 2018 [**52**]. The legislation applies to anyone who collects information about individuals; it is upheld by the Information Commissioner's Office [**53**], which provides detailed guidance on its application. In the US, data sharing is regulated by the Health Insurance Portability and Accountability Act that regulates patients' data use and disclosure [**54**].

In the United States, access to "protected health information" (identifiable) is governed by the Health Insurance Portability and Accountability Act. Covered entities (clinicians, insurers, medical service providers, business associates) must obtain written permission from patients to share data unless it is needed to facilitate treatment, payment or

operations, or for legal reasons. Most of the activities of a LHS would fall into the facilitation of treatment or operations category.

General Data Protection Regulation
Under GDPR and the UK Data Protection Act, organisations must establish and publish a basis for the lawful processing of data. There are six lawful bases [**53**]:
A. Consent: The individual has given clear consent for you to process their personal data for a specific purpose.
B. Contract: The processing is necessary for a contract you have with the individual, or because they have asked you to take specific steps before entering a contract.
C. Legal obligation: The processing is necessary for you to comply with the law (not including contractual obligations).
D. Vital interests: The processing is necessary to protect someone's life.
E. Public task: The processing is necessary for you to perform a task in the public interest or for your official functions, and the task or function has a clear basis in law.
F. Legitimate interests: The processing is necessary for your legitimate interests or the legitimate interests of a third party, unless there is a good reason to protect the individual's personal data which overrides those legitimate interests. This lawful basis cannot apply if you are a public authority processing data to perform your official tasks.

Data protection regulations have often been viewed as a challenge for Learning

Health Systems [49]. They must be carefully considered and resourced when planning a Learning Health System.

Interoperability

Interoperability is the ability of one system to work with another. Learning Health Systems are often networks of networks, rather than single unified systems [55]. It is therefore usually necessary to share and use data that has been collected and stored in different systems. This requires standards for [56]:

- The terminologies and classifications used to describe things that exist in the real world
- The structure and format of data
- The transport of data
- The security of data

There are many different approaches to achieving interoperability [57], with the appropriate choice depending on the particular use case [1]. To move data from one provider to another so that it can be viewed is relatively straightforward. It does not matter how it is transmitted, providing it is appropriately labelled. However, if it is to be analysed, then it needs to be standardised; this is much more difficult [1].

Even within a single organisation, there are often multiple separate systems that are divided by speciality and function, such as pharmacy, radiology, or laboratory. This presents problems for linking a person's data together and can lead to duplication of data. It gives rise to the need for a lot of "plumbing" technologies [58] . There is therefore a

lot of work involved in generating a longitudinal record, even for an individual. Longitudinal data presents an additional problem because systems and data representations often change over time [59]. The nations of the UK each have an NHS number that facilitates this process, while in the US, there is no universal healthcare identifier.

Data collection is often the first point of failure. While true interoperability requires consistent data collection, there is often no agreement on acceptable values. For example, biochemistry results are recorded differently in different places. These could be standardised on their way into the EHR, rather than requiring complex mapping steps at a later stage [49].

In England, the NHS Digital Data Standards Team (IReS) [60] maintains terminology and classification products for the nation. These include:

- SNOMED CT: A structured clinical vocabulary used in EHRs [61]
- The Dictionary of Medicines and Devices (dm+d): Identifiers and descriptors of licenced medicines [62]
- ICD-10: A classification of diagnoses [63]
- OPCS-4: A classification of interventions and surgical procedures [64]

NHS Digital has legal powers in England to mandate the submission of data by providers, in a pre-set format at given intervals [65]. This overcomes many interoperability issues [65]. However, when extracting richer data from EHRs and other systems, the coding

structures used by providers can create major challenges [66].

At the regional level in England, there have been efforts [199]to create interoperability networks between providers [200] . More recently, many of these have been funded centrally through the Local Health and Care Records programme. However, each region has taken a different approach to sharing data for direct care and secondary uses [21]. There are opportunities for researchers, policymakers, managers and industrial partners to collaborate around the new LHCR infrastructure.

In addition to those administered by NHS Digital, other standards commonly applied within LHSs include:

Terminologies and classifications:
- LOINC: A classification of health measurements (eg, laboratory studies, radiology results, vital signs)
- CPT: Billing codes for procedures

Structure and format:
- Consolidated-CDA: an XML-based standard format for export of clinical data
- OMOP: A clinical data model to organize data in different domains (i.e. diagnoses, laboratory studies, medications)

- i2b2: A clinical data warehousing and analytics research platform primarily used by researchers

Security:
- HTTPS: a secure protocol for data transport

Transport:
- FHIR: A standard for defining data resources and transmitting them via an API
- HL-7: An older standard for defining and transmitting data
- DICOM: the standard format for transmission of imaging data

There is a long-held view that there are insufficient requirements or incentives in place to achieve interoperability [58]. In the US, the Office of the National Coordinator for Health IT (ONC) has implemented regulations set out in the 21st Century Cures Act (2016) [67], which improve interoperability by using an Application Programming Interface (API) approach [59]. While many in the industry have welcomed this move, it has been opposed by some EHR vendors and others, who cite concerns over privacy, feasibility and costs [68]. The success of this measure will be determined through careful monitoring, assessing whether it can provide a model for other countries [69].

Data to knowledge

Once data are consistently obtained in a standardised, comprehensive, exchangeable, analysable form, they must be used to derive knowledge. Within Learning Health Systems and clinical informatics more generally, the emphasis has often been on the collection, storage, analysis and dissemination of data. Too often, health systems collect reams of data but lack the means of converting them into reproducible, generalisable knowledge [**57**]. This section will signpost some important methods for deriving knowledge from data.

Data and knowledge

Knowledge is the insight produced by processing data. The data might be of any form, and the processing could be conducted by humans or machines. Knowledge can include instructions to complete a task, a predictive model, the results of an experiment, a physical law, a practice guideline, or anything else that can be known.

Knowledge can be generated using a wide range of qualitative and quantitative methods. In a Learning Health System, the data collected is often the product of a knowledge-generating process. For example:

- Data that incorporates clinician judgment, assessment, and expertise, such as structured reasons for ordering a test or stopping a medication
- Data that synthesises more basic data elements, such as risk scores or predictions

- Data that indicates trajectory or trend
- Data that patients directly contribute and that reflects lived experience, such as patient-reported outcomes, experience and satisfaction
- Data that reflects staff experience
- Data generated through randomisation or quasi-randomisation to minimise bias

NYU Langone CTPA

At NYU Langone Health, a clinical decision support tool was created to help clinicians optimise the ordering of CT pulmonary angiograms for the detection of pulmonary emboli. The tool incorporated an automatic risk calculation. During the design phase, clinicians noted that they trusted their clinical intuition more than the risk score. The decision support tool therefore incorporated specific reasons for ignoring the risk score, including "high clinical suspicion". In a number of cases, patients with low risk scores were still sent for tests, based on high clinical suspicion; subsequent analysis showed that these patients were just as likely to have a pulmonary embolism as those with high risk scores. This indicated that "high clinical suspicion" was a very valuable prognostic data element.

Randomisation and the Learning Health System

Among the most sophisticated methods of creating value added data is to embed trials within routine care. Randomised trials are now the mainstay of knowledge generation in clinical medicine and have been widely adopted by other industries, rebranded as A/B testing. Randomisation is particularly valuable in situations in which there is likely to be substantial bias in observational data (eg selection bias, regression to the mean, differential loss to follow up). While they remain rare in health system operations and implementation, there are many opportunities for randomised studies in the health system beyond tests of novel therapeutics. Interventions can be studied versus usual care (no additional intervention).

However, sometimes healthcare providers object to randomisation because they don't want to withhold a perceived beneficial intervention. Capacity-constrained interventions (such as intensive case management or post-discharge telephone calls) are excellent opportunities to randomise while still providing the intervention to the same number of people: converting data collected on convenience and often biased sample to data collected on an unbiased, randomized population. Interventions being given to all those eligible are also excellent candidates for randomisation without withholding care by randomising the intervention form, content, frequency or delivery.

Randomisation can take place at any level (patient, clinician, hospital unit, ambulatory practice, health system) depending on the target of the intervention. Randomisation can be simple (intervention vs none) or can involve more complex designs. Factorial designs allow simultaneous testing of multiple [70] different interventions – important given the multicomponent nature of many health system interventions – or of multiple variations of the same intervention (eg changes in both content and timing). New statistical methods allow for "fractional" factorial designs that do not test every single possible iteration, but efficiently test those of most interest. Adaptive trials allow for changes in group allocation or intensity as the trial progresses to optimize sample size and speed of the trial [71].

Pure randomisation is not always practical when embedding randomisation into routine care. In such cases, quasi-randomisation (eg, week on/week off, randomisation by odd vs even medical record number) is often an option. In such cases, it is important to minimize potential bias. For instance, randomisation by odd vs even record number is likely to be more truly "random" than randomisation by first letter of last name, since patients from certain racial or ethnic backgrounds might be more prevalent in certain letters. Randomisation by sequential week on/week off is likely to be less biased than randomisation by day of the week, given that there are known differences in clinical severity and volume by day of week.

In cases where it is desirable for the intervention to be given as is to everyone, a randomised Stepped Wedge Design can be employed, in which clinicians or units/practices begin the intervention at randomly assigned

sequential time periods [72]. This allows for control group comparisons across the intervention period while still enabling everyone to receive the intervention.

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NYU Langone Health Exemplar Box

NYU Langone Health in New York, USA, established a rapid randomised quality improvement project unit and randomised over a dozen interventions in its first year. The health system was able to rapidly determine the effectiveness of a variety of interventions, including community health worker facilitation, post-discharge telephone calls, mailer outreach, and electronic clinical decision support [30]. A similar system has been implemented at Vanderbilt University Medical Centre, with the aim of creating generalisable knowledge [183].

</div>

Quasi-experimental analyses

Randomised interventions can often use very simple analytics, such as Chi square tests for categorical outcomes or t-tests for normally distributed continuous outcomes. However, because unobserved confounders are typically only equally distributed among groups in randomised studies, non-randomised interventions require more complex analyses, as bias between groups is likely. For situations in which randomisation is not possible, quasi-experimental analytic methods can often be used. These methods all have in common some form of comparison to the intervention group, whether by time or by a different cohort. All of these methods can also incorporate statistical adjustment for confounding factors, such as differences in demographics or comorbidities between patients.

Difference-in-differences analysis

Also known as a controlled before and after study, this method compares the difference in average outcomes before and after an intervention in a control population to those in the intervention group. It assumes that trends in the control and intervention group were similar in the pre-intervention period, and that those trends would have remained similar in the absence of the intervention. It further assumes that no changes besides the intervention affected the intervention group, and that the intervention did not affect the control group. It is essential to explore the validity of these assumptions when conducting such an analysis, because they are often not met.

Interrupted time series

This method (also known as a repeated measure study) essentially examines whether an intervention a) changed the absolute level of an outcome and b) changed the trend by which that outcome was changing over time [73]. This gives it some advantages over difference-in-differences analysis, in that it accounts for pre-intervention trends and can be conducted without a control group [74]. However, it requires similar assumptions that underlying trends would have continued unchanged and that [75] no other changes affected the population in the intervention period. A comparative interrupted time series can also be constructed, which compares

differences in outcomes over time between control and intervention groups [76].

Regression discontinuity

This method is useful when there is a specific point at which an intervention is applied (ie a target laboratory result, a qualifying income, a population percentage). It examines differences in outcomes for subjects immediately on one side or another of the intervention qualifying point [77]. These subjects are expected to be otherwise similar except for the arbitrary cut point qualifying them for intervention. If a substantial difference is found between those just on one side of the dividing line and those on the other, the intervention can be considered effective [75].

Causal inference

Observational studies are typically limited by an inability to detect causality; we can conclude that outcome B is often associated with intervention A but not necessarily that A caused B. A ream of statistical techniques has been developed to try to disentangle causality from association. Structural equation modelling analyses causal paths prespecified by the investigator on the basis of hypothesized relationships [78, 79]. Directed acyclic graphs (DAGs), commonly used in Bayesian analyses, similarly can be constructed to model and study causal relationships. Instrumental variables can serve as artificial randomizers to help mitigate selection bias [80].

Artificial control groups

There is a ream of methods for constructing artificial control groups to use in standard analyses through matching or similarity analyses. While these should be employed with caution, given the high risk for unmeasured confounding that cannot be accounted for in the matching process, they nonetheless can be useful to reduce bias in comparisons with unselected control groups. Propensity score matching, Mahalanobis distance matching and coarsened exact matching are commonly used methods [81].

Statistical process control

Borrowed from manufacturing, statistical process control methods examine whether outcomes are stable over time – within expected statistical variation – or whether they vary in a random fashion or in a non-random fashion (special cause variation). This is an alternative method of examining time-series data. In the case of an intervention, one would look for special cause variation in the intervention period using control limits established in the baseline period. Special cause variation has been defined as [82]:

- Any point above or below three standard deviations (99.7%)
- A run of at least eight consecutive observations above or below the mean, or 12 of 14 successive points above or below the mean
- Two of three points more than two standard deviations away from the mean (and on the same side of the mean)
- At least four out of five successive points on the same side of the mean and more than one standard deviation from the mean

Machine learning and artificial intelligence

The newest methods of generating knowledge from data have come from the field of artificial intelligence. Broadly speaking, these approaches use all data available, rather than a prespecified subset, to learn patterns. While the promise of AI in healthcare has so far exceeded its application, there have been some promising examples of new knowledge generation from AI analyses of data – for instance, discovering undiagnosed disease [83], identifying new subtypes of disease [84], predicting future events [85, 86], optimising treatment selection [87] and managing complex [88] medications.

Generating knowledge from local experience

In some cases, pure descriptive statistics may suffice to generate useful insight. For example, consider a new service from Stanford University; if there is a question about a patient's optimal treatment or ultimate prognosis, the tool can rapidly query the EHR of all other, similar patients[89] "Green Button" query would return a descriptive summary of what happened in similar case studies, which could help guide clinician decisions in the absence of stronger evidence. Of course, this approach can be limited by small samples and is prone to bias. More complex statistics could also be applied, to more robustly match similar patients or to generate stronger predictions.

Engineering approaches to generating knowledge from data

It is not always necessary to generate reams of complex statistics to gain knowledge from data. Visual or qualitative representation of data can also often generate important insights.

Process mapping enables a visual representation of the various stages of a particular activity and can identify redundancies, waste and gaps. Alternate versions of process maps include swimlane maps, which organise steps by location or discipline; service blueprinting, which divides steps into those that are visible to the end-user and those that are not [90]; patient experience mapping, which depicts typical emotional reactions and lived experience at each stage of a [91] process; and lean value stream mapping, which focuses on time, waste and material use at each step of the process [92].

Qualitative methods

Knowledge generation within a Learning Health System is not the preserve of machines. Many of the most powerful insights come from people, working alone or in groups. People are uniquely well-equipped to make sense of and manage complex sociotechnical environments that may defy quantification. Each person has a unique perspective, which can be captured within a Learning Health System.

Qualitative methods are invaluable to the Learning Health System. Interviews, focus groups, direct observations/ethnography, user feedback and free text comments in surveys are examples of approaches that can generate insights into WHY and HOW systems are functioning. This in turn provides essential insights into WHAT can be measured quantitatively

[93]. Indeed, it is difficult to imagine a successful Learning Health System that does not make use of qualitative methods.

Learning communities

Learning Communities have a place at the heart of any Learning Health System. A Learning Community is a group of stakeholders who come together in a safe space to reflect and share their judgements and uncertainties about their practice and to discuss ideas or experiences to collectively improve [94]. This can extend to governance and improvement of the Learning Health System, along with knowledge generation.

Learning Communities require members, facilitators and sponsors. They must be co-designed. The Learning Community Handbook [94] contains detailed evidence on the rationale for Learning Communities, as well as guidance on establishing and running such groups. It suggests a four-phase cyclical development process [94].

- **Phase 1 – Negotiating the Space:** Working with the sponsor to give permission, resources and time for people to join a safe space. An agreement must be reached on the facilitator, metrics and reporting mechanisms.
- **Phase 2 – Co-Design Process:** The group takes ownership of the Learning Community. Ground rules and processes are agreed.
- **Phase 3 – Facilitating Learning Communities:** Sessions take place, including presentations and discussions. Collective learning is captured, and reporting arrangements agreed. The community reflects on the process.
- **Ongoing – Reflection and Evaluation:** This will form part of each session and can comprise regular, standalone sessions.

Learning Communities should foster a positive error culture, where people feel comfortable talking about their mistakes and organisations see them as an opportunity for improvement. As well as generating knowledge, Learning Communities can build trust, capacity, skills, confidence and agency for change among members. They can challenge members, provide reassurance and help members deal with uncertainty. They can be action-focused and sustainable, with low overhead costs [94].

The Department of Learning Health Sciences at the University of Michigan has produced a practical guide [95] to operationalising a Learning Community for a Learning Health System. This provides detailed guidance on building a Learning Community around a problem of interest, illustrated by the case study of a gastroenterology community.

Knowledge to practice

Generating knowledge is not the ultimate aim of a Learning Health System. Rather, the goal is to continuously improve health and care. For this to happen, the knowledge generated in the previous steps must be translated into action or mobilised. This section outlines how knowledge within a Learning Health System can be represented in a machine-readable format and applied at the front line.

Representing and managing knowledge

A Learning Health System can generate knowledge, but it must also integrate knowledge generated beyond the system: in previous studies, for example. Often knowledge is represented in books, journal articles, clinical guidelines and protocols. It can be passed on through formal and informal education or training. It can be used to redesign care environments and health interventions. These processes are often slow. These will all continue to be valuable ways of representing knowledge within a Learning Health System, but in order to scale-up and speed-up the process of knowledge improving practice, knowledge must be consumable by the computer systems in use at the frontline.

NHS Library and Knowledge Services

In England, the national NHS Library and Knowledge Services team procures a clinical decision support tool for all NHS staff and learners, enabling seamless access to a high-quality digital knowledge resource. It has supported knowledge management within the health service, providing a toolkit that covers traditional and digital forms of knowledge [86]. It offers e-learning on the [184] a suite of techniques through which users can articulate and share their learning from experience. Library and Knowledge Services in general are becoming more, rather than less, important within Learning Health Systems [185]. The English service has been shown to return significant value.

There have been efforts to standardise the representation of knowledge so that it can be applied at scale within a Learning Health System. OpenClinical.net, a collaboration between University College London and Oxford University, maintains an open-access and open-source repository of medical knowledge in a machine-readable format. OpenClinical uses the PROforma process modelling language to create machine-readable clinical guidelines, clinical algorithms, etc [39].

A more recent example is provided by Mobilizing Computable Biomedical Knowledge (MCBK), a new international community led by the Department of Learning Health Sciences at the University of Michigan. The group's goal is to ensure that biomedical knowledge in computable form is Findable, Accessible, Interoperable and Reusable (FAIR). MCBK has formed multidisciplinary workgroups to develop key aspects of the solution:

- Standards
- Technical Infrastructure
- Trust & Policy
- Sustainability & Inclusion

Once knowledge is computable, processes can be automated; it can be fed into decision support systems to help guide decisions, or it can be used to assess the delivery of care against the knowledge base. These uses reduce the time taken for new knowledge to improve care, compared to the traditional system, which relies on the knowledge being published in a journal, read, acted upon and audited.

The Learning Healthcare Project collaborated with the Faculty of Clinical Informatics, NICE, the British Computer Society, HDR UK and HL7 UK to run a workshop on Mobilising Computable Biomedical Knowledge, inspired by the global MCBK community [27]. The knowledge generated by the workshop is available in traditional forms, including video recordings [96] and as a series of seven journal articles, forming a special issue of BMJ Health & Care Informatics [97].

National Institute for Health and Care Excellence

The National Institute for Health and Care Excellence (NICE) [**186**] produces knowledge in the form of evidence-based guidance to the English NHS. This knowledge is based on evidence developed through a range of scientific methods [**187**] and interpreted through a deliberative committee process [**186**]. Figure B shows the range of guidance produced over the last 20 years.
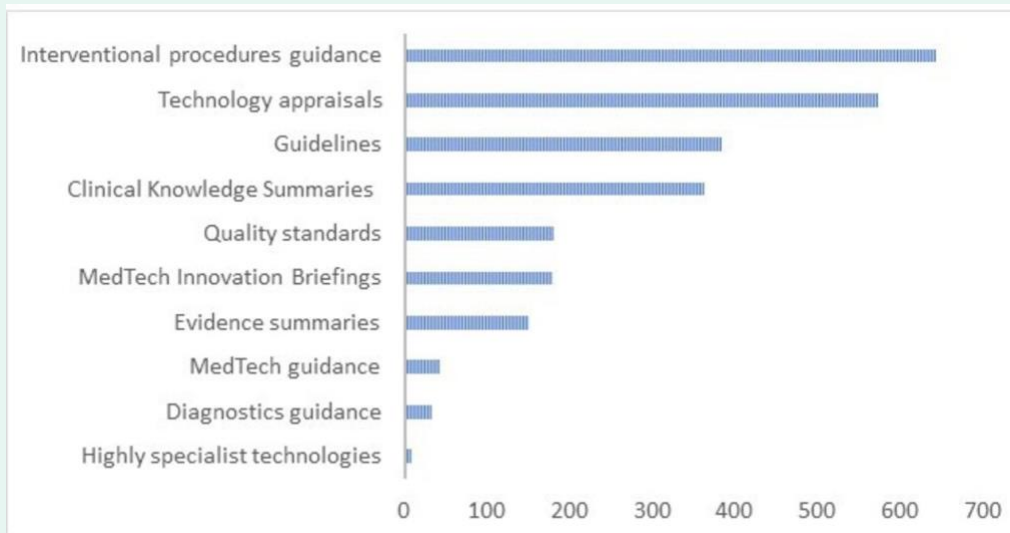

*Figure B NICE Products produced over the last 20 years [**188**]*

The MCBK workshop explored NICE's ambition to broaden its scope from single condition, narrative guidelines to structured recommendations encompassing multi-morbidity, polypharmacy and wider health system considerations [**189**].

The NICE team have considered their current products against the AHRQ 4 levels of knowledge (Figure C). While currently the products are primarily narrative, there is an ambition to make their recommendations – and the evidence that underpins them – more structured, to aid maintenance and surveillance. Although NICE has explored the potential for reverse engineering structured guidance from previously generated narrative guidance, the group has found it to be inefficient and potentially unsafe. Instead, NICE considers a co-production model to be a better way of bringing together the guideline development committee and those who produce the executable guidance.
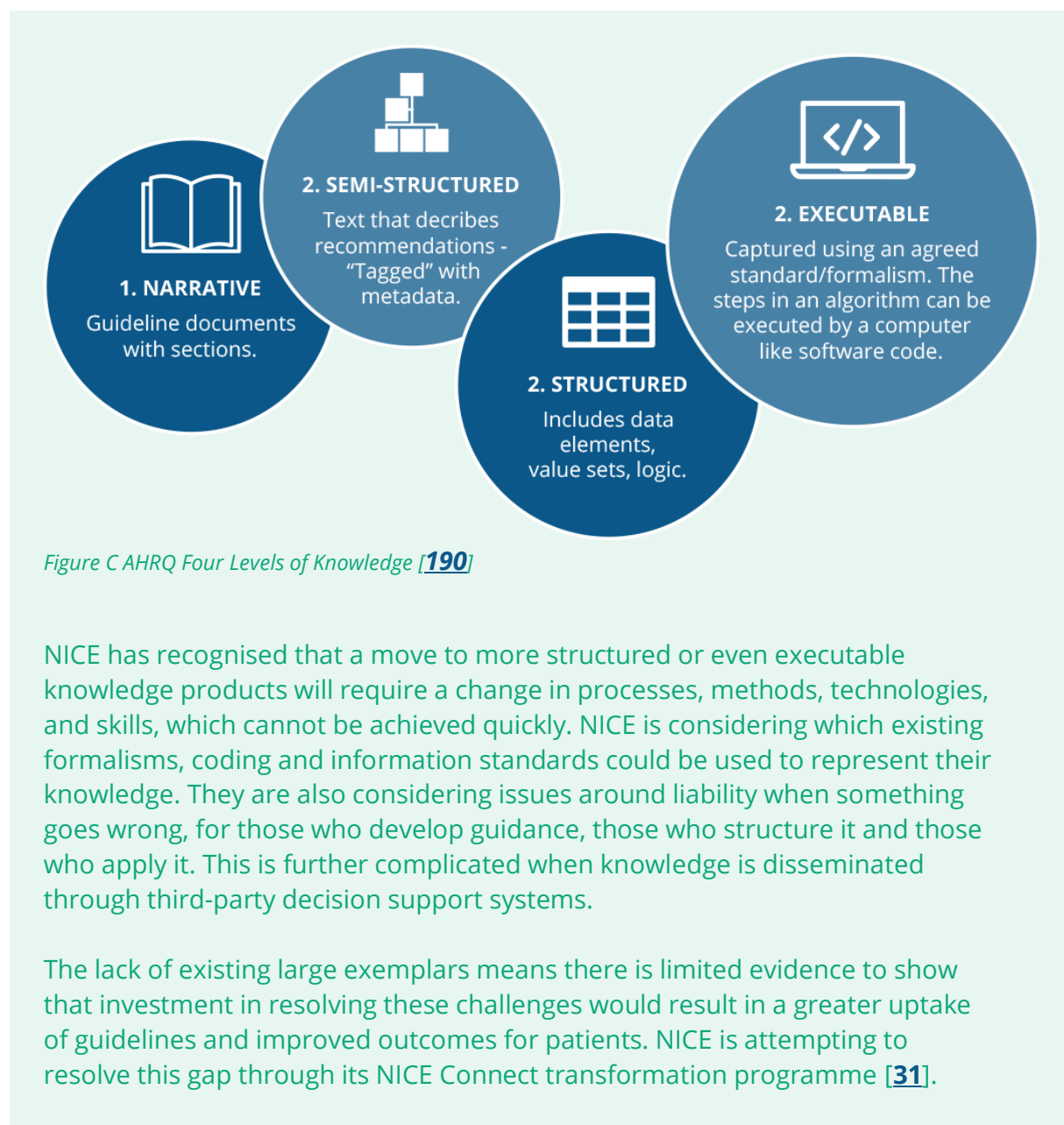
*Figure C AHRQ Four Levels of Knowledge [**190**]*

NICE has recognised that a move to more structured or even executable knowledge products will require a change in processes, methods, technologies, and skills, which cannot be achieved quickly. NICE is considering which existing formalisms, coding and information standards could be used to represent their knowledge. They are also considering issues around liability when something goes wrong, for those who develop guidance, those who structure it and those who apply it. This is further complicated when knowledge is disseminated through third-party decision support systems.

The lack of existing large exemplars means there is limited evidence to show that investment in resolving these challenges would result in a greater uptake of guidelines and improved outcomes for patients. NICE is attempting to resolve this gap through its NICE Connect transformation programme [**31**].

Challenges for Medical Knowledge Providers

In a session led by BMJ Best Practice, the MCBK workshop explored the challenges that Medical Knowledge Providers face in getting knowledge into practice [**41**, **98**]. This was supplemented by a session focusing on the associated technical [**98**] challenges [**99**, **100**]. These sessions highlighted seven challenges that should be considered by any organisation seeking to mobilise computable biomedical knowledge:

- **Size of the task:** BMJ Best Practice covers over 1,000 topics, while NICE [**41**] has published over 2,000 products. Maintaining these catalogues alone is a huge undertaking, yet they represent only a very small fraction of total medical knowledge.

- **Standards:** These are necessary to make knowledge interoperable between systems. SMART on FHIR (for building Apps on health platforms) [**101**], Guideline Interchange Format [**102**], CDS Hooks (for clinical decision support) [**103**], and openEHR (for EHRs) [**104**] are in use, along with a range of other open and proprietary standards.

- **Making knowledge computable:** This is known as knowledge formalisation. All background knowledge is made explicit, along with the common sense required for interpretation. Meanwhile, ambiguity is removed, enabling interpretation by a machine [**99**]. This is a highly skilled process with scope for error and harm to patients.

- **Inference:** To use computable knowledge in areas like clinical decision support, it must be manipulated to produce actionable outputs. This process is called inference. Logical or probabilistic reasoning combines knowledge, such as a guideline, with specific data about individual patients. For example, does the patient require a CT Head? This reasoning can exploit IF-THEN rules (eg IF patient meets any of these criteria THEN perform CT Head). It becomes much more difficult if there are multiple conflicting knowledge sources, multi-morbidities or if the accuracy of the knowledge is uncertain.

- **Outcomes:** As seen in the NICE example (See NICE Box), there is a need to trace the ways that computable knowledge impacts on patient outcomes as well as process measures, in order to justify investment and improve systems.

- **Safety:** Computable knowledge that is intended to be applied at the point of care can cause harm. In England, compliance with clinical safety standards DCB0129 (for manufacturers) [**105**] and DCB0160 (for deploying organisations) [**106**] is mandatory under the Health and Social Care Act 2012 [**107**]. Under the Medical Devices Regulation published by the European Commission in 2017, software such as a clinical decision support system would be classed as a Medical Device [**108**], so would need to be registered with the Medicines and Healthcare Products Regulatory Agency (MHRA) and audited by a notified body [**109**].

- **Professionalism:** Clinicians need problem solving and procedural skills, healthy attitudes and professional behaviours, which cannot be replaced by computable knowledge. It is important to recognise the limits of such systems.

Progress on Mobilising Computable Biomedical Knowledge

Despite much technological progress, the goal of Findable, Accessible, Interoperable and Reusable (FAIR) [110] knowledge has still not been widely achieved. Much knowledge is not computable, as it resides in books, articles, PDFs etc that are proliferating faster than clinicians can consume.

Most computable knowledge is in formats that lack common standards, such as proprietary decision support systems. Systems rarely address the real-world complexity of multimorbidity, polypharmacy, resource constraints etc. This limits the development of Learning Health Systems and causes patient safety issues, particularly when

knowledge is encoded within systems that cannot be readily evaluated [111]. When such systems malfunction, large numbers of patients can be impacted [112].

Those developing computable biomedical knowledge can benefit from the open-source tools, infrastructure and repositories developed by MCBK and others [38, 113]. They can also publish their knowledge objects for peer review and reuse [114].

It is important to note that in practice, the evidence applied to decisions [115] does not necessarily comprise the most "scientific" or objective items. Decision makers often prefer local knowledge and the experience of near neighbours. This judgement can be difficult to codify in a computerised system. It may be sensible for an organisation to start computerising knowledge in areas that are characterised by the most agreement and least complexity; however, the richest opportunities may lie beyond.

Scottish National Decision Support Programme

This workshop explored a new Scottish programme to mobilise knowledge through decision support systems [35, 36]. It is aligned to the broader national health strategy and focuses on improving outcomes in key areas. Each decision support tool is developed through a participatory co-design process, engaging all stakeholders. It has developed a technology architecture to facilitate joined-up development across partners in health, academia and industry (Figure D), which could be applied elsewhere.
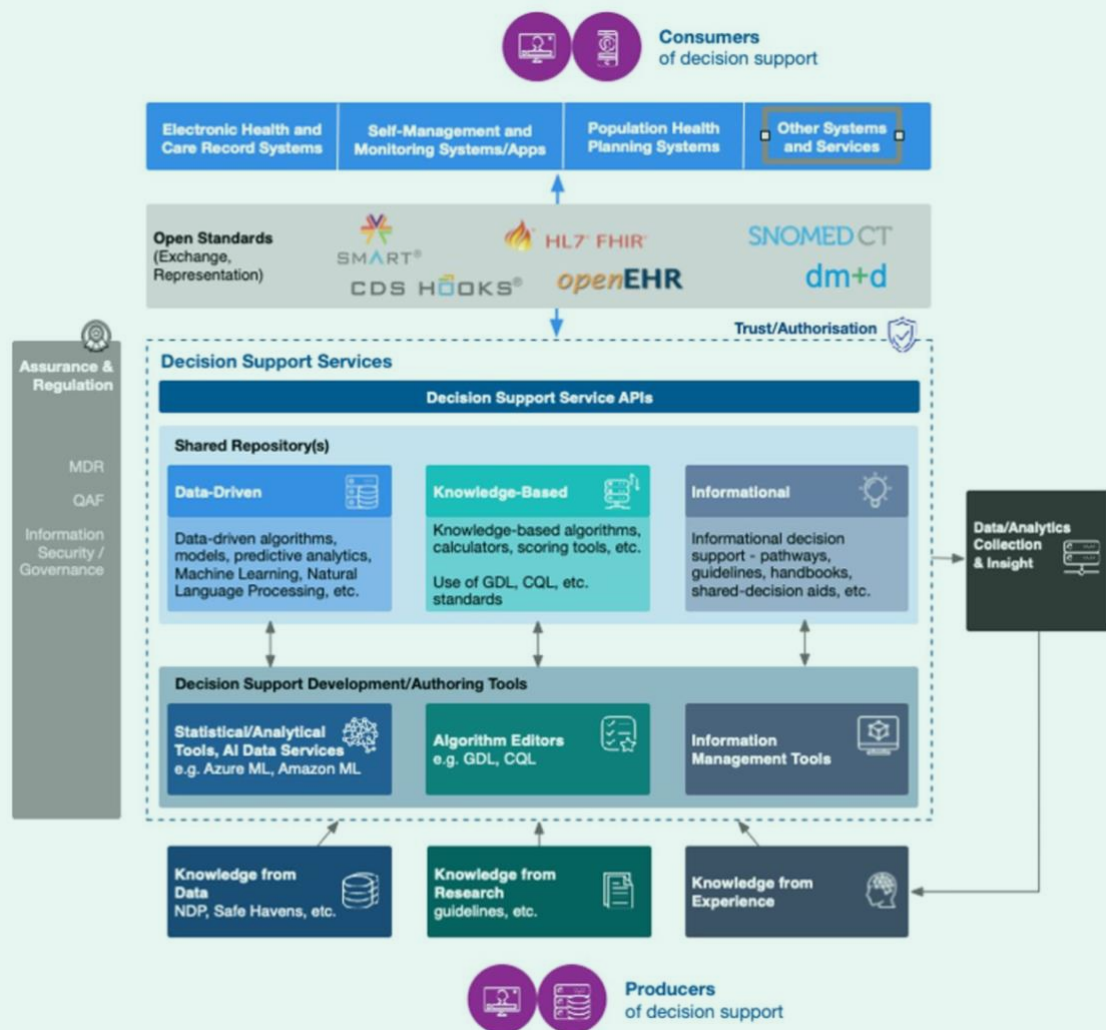

Figure D A reusable technology architecture for decision support

Platforms

A Learning Health System is a complex system that cannot be lifted and shifted from one organisation to another. Still, many aspects of its infrastructure are common across organisations. Early examples – such as TRANSfoRm [116] or FDA Mini-Sentinel – had to develop a distributed network infrastructure and rules for operation before deploying the Learning Health System, making them very expensive. It is analogous to recreating a new version of the Internet every time a new website is launched.

However, the development of platforms has made it affordable for even small organisations to build Learning Health Systems. A platform is a set of systems that work together to deliver specified functions according to agreed standards. These are functions that are likely to be required by many organisations. It forms a base on which organisations can build more specific functions.

Recent years have seen the emergence of platforms offering IT, data, governance, user interfaces, Application Programming Interfaces, workforce solutions and clinical outsourcing. Platform providers include large IT companies (cloud providers), Electronic Record System vendors, academic groups and even healthcare providers.

A Platforms workshop was held to inform this report and to understand the implications of such developments for Learning Health Systems [41]. The workshop brought together a range of platform providers and users. The Mayo Clinic's approach to platforms was presented as an exemplar, and its general applicability was discussed.

NHS Digital has developed [32] a national Data Services Platform on AWS Cloud that is capable of landing data from every English healthcare provider. The platform manages and de-identifies the data, before making it available for analysis to anyone with authorisation, all within a secure, web-based Data Access Environment. Because this is cloud-based, NHS Digital can offer the Platform as a Service to other organisations that do not have an in-house capability.

Platform thinking requires a new level of collaboration with industry and other partners; public trust is important and has been damaged by previous ill-conceived initiatives [117]. Ideally, partners would develop long-term relationships.

Platform providers represent another useful group, with the potential to bring cross-sectoral experience to bear on the challenges faced by Learning Health Systems. Often healthcare organisations come to platform providers with a clear project that they have worked up. They might also consider collaborations with industry where they are not entirely sure of their next move, so that they can become "thinking partners" [41]. This clearly requires careful procurement governance.

Mayo Clinic Platform

The Mayo Clinic has a 10-year Platform Strategic and Operating Plan that aims to transform healthcare by 2030 [**26**]. It involves three building blocks:

- **A Data Platform** on the Google Cloud. Google does not have access to the data, but provides analytics, metadata characterisation, search etc. Mayo created a de-identification process in collaboration with the Office for Civil Rights. It built FIHR-based interfaces to query the data and created subtenancies on the cloud, where innovators could access but not export de-identified data.
- **A Virtual Care Platform** enables video consultations for ambulatory care, remote monitoring for acute care at home and asynchronous sharing of pictures, results etc.
- **A Remote Diagnostic and Management Platform** that can collect data, perform an action and return a result. This has already been used to ingest DICOM objects from other providers and return radiation oncology treatment regimes. Mayo is planning to ingest data from smartphones and wearables, apply algorithms and return actions.

These building blocks allow departments to build their own use cases. Mayo is working with its EHR vendor to bring new search functionality into the record and to allow patients to better navigate their potential care journeys. They have also developed an "AI Factory", allowing clinicians to develop algorithms by themselves. Platform thinking has involved a cultural transformation, requiring constant engagement with all parts of the organisation.

In future, smaller providers may be able to subscribe to the platform products that larger providers create. They could consume products and contribute data. Some organisations manage the digital implementation but then fail to realise change on the ground. It requires a multimodal change involving workforce, buildings, facilities etc. The Mayo example suggests that business transformation rather than technology is the biggest challenge.

Understanding and Managing Complexity in a Learning Health System
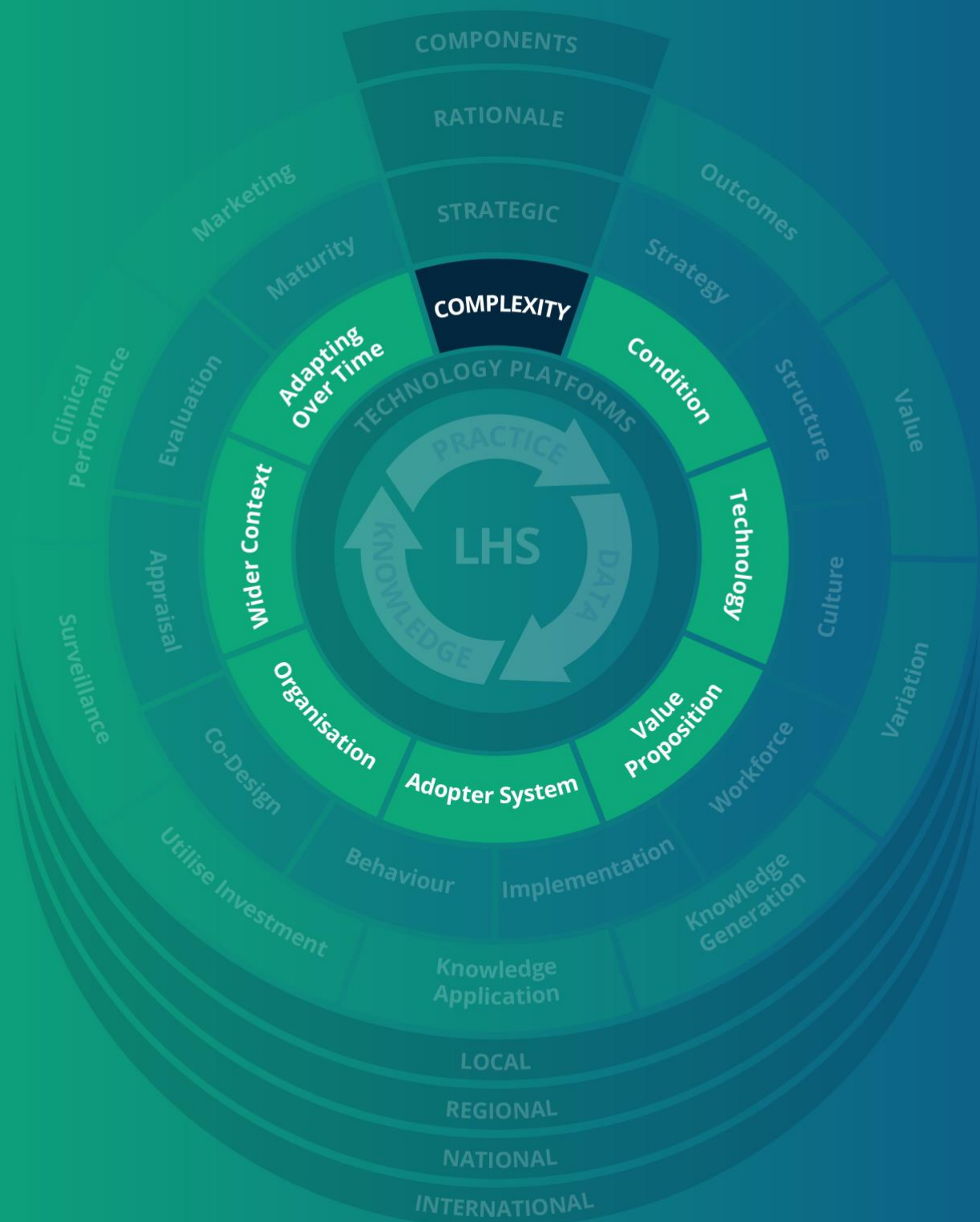
Learning Health Systems could revolutionise healthcare practice. They have the potential to enable personalised, proactive services, capturing and analysing clinical data that can continuously inform and improve health decision making and practice [118, 119] . But six years after the first Learning Healthcare Project report [1] and 13 years since the IoM popularised the concept [120], no nation, region or individual healthcare provider has fully realised this promise. Previous sections have discussed the delivery of knowledge to the point of care. This is necessary, but more is needed to ensure this knowledge actually influences practice.

In the traditional "pipeline" model of healthcare innovation, basic research progresses to the prototype stage, before moving to Randomised Controlled Trial, publication and guideline production, resulting in a change in practice [121].

Early Learning Health System thinking recognised the limitations of this model. Randomised Controlled Trials could not answer all the clinical questions about the wide variety of real-world patients. Even when evidence existed, it was often not widely employed [122]. Learning Health Systems offered an improvement, showing how routinely collected data could provide answers to more questions and how digital systems could deliver that knowledge to the point of care. The pipeline became a cycle, but it maintained a stepwise nature.

Our original report covered a range of complex challenges in developing a Learning Health System, based on our study of international exemplars. These challenges included comorbidities, technology, interoperability, data quality, Information Governance, regulation, ethics, leadership, behaviour change, value, and patient, clinician and organisational acceptability [1].

Until this point, there has been no accepted framework for considering these challenges when planning, implementing and evaluating Learning Health Systems, with most effort so far spent on developing the technical aspects of the systems. Consequently, we have not seen widespread adoption, scale-up and spread of Learning Health Systems.

Complexity in the Learning Health System

Healthcare is increasingly recognised as a complex adaptive system [123]. Snowden [124] outlined the characteristics of a complex system:

- A large number of interacting elements
- Non-linear interaction – minor changes can produce disproportionate consequences
- Emergence – the whole is greater than the sum of its parts
- Elements evolve with one another and with the environment in an irreversible way
- While it may appear predictable in retrospect, this is misleading:

external conditions and the system are constantly changing

- Agents and the system constrain one another over time, unlike an ordered system (where the system constrains the agent) or a chaotic system (no constraints)

The Cynefin Framework [125] can be used to understand whether a given system is Obvious/Simple, Complicated, Complex, Chaotic or Disordered. This understanding
can suggest the most appropriate way to intervene (
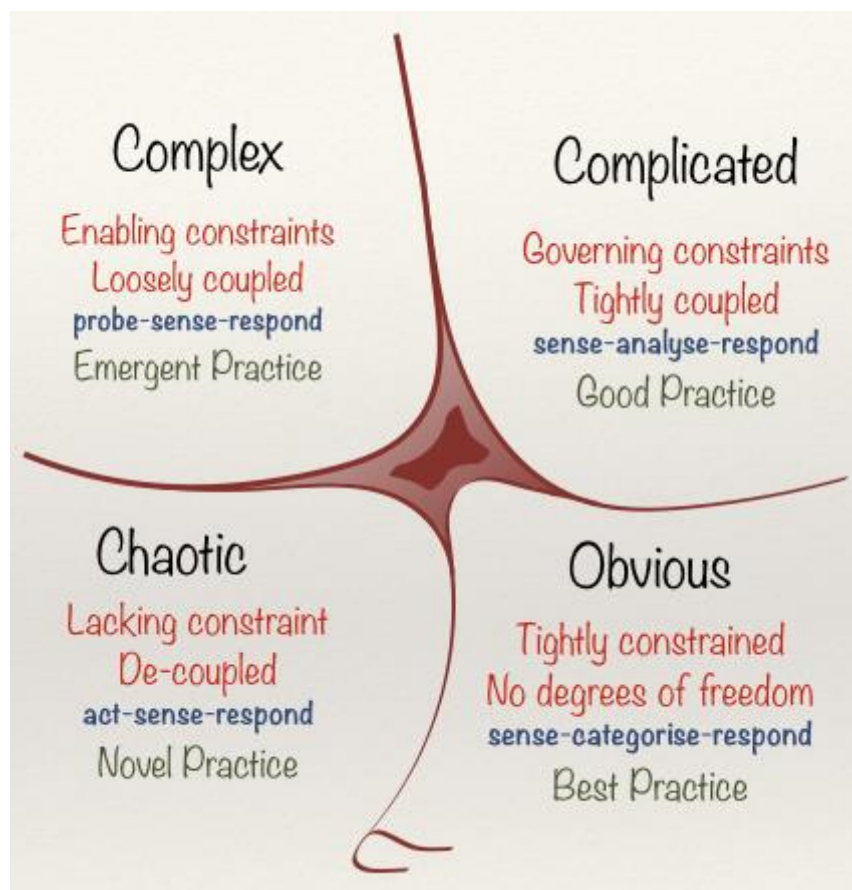Figure E):

Figure E A representation of the connection strengths of the Cynefin framework (D. Snowden, 2010)

Simple Context: These are process-oriented systems in which there is clear cause and effect and best practice can be established. The solution is obvious to everyone. For example, a system for allocating patients to child or adult services: if their age is under 18, allocate to child services, and if their age is 18 or

greater, allocate to adult services. A command-and-control approach can be effective in such systems, and extensive discussion is unnecessary.

Complicated Context: Cause and effect is still present, but it may not be obvious. There could be multiple right

answers, and expertise is required to analyse the situation: for example, building or repairing a piece of medical equipment. Good practice is therefore more appropriate than best practice. With enough time, at least one right answer can usually be found.

Complex Context: Complex systems are in constant flux, so cause and effect break down. The whole is greater than the sum of its parts. Snowden uses the analogy of a Ferrari (complicated but static) and a rainforest (complex). While an expert can take the Ferrari apart and put it back together, a rainforest is more than the sum of its parts. Command and control management, fail-safe plans and defined outcomes do not work in complex contexts, due to their unpredictability. Instructive patterns emerge by setting up many parallel, safe to fail experiments, and a way forward can be determined by amplifying interventions that work and dampening those that do not [126]. Learning Health Systems generally fall into this complex category.

Chaotic Context: This is a crisis situation. The relationship between cause and effect is impossible to determine and constantly changing. Searching for the right answer is futile and immediate action is required to establish stability, allowing the situation to move from chaotic to complex. A directive leadership approach is required, but this is also a time when innovation can be accelerated; hence

the term, "never let a good crisis go to waste".

Disordered Context: It is not clear which context prevails, and there are multiple perspectives. Resolution lies in breaking the situation down into its constituent parts, each of which can be assigned to one of the other contexts.

Understanding which context describes a particular situation can help determine the most likely successful approaches. Situations can also shift between contexts. For example, a complex situation can become complicated when it is better understood, or a simple situation can become chaotic as a result of complacency.

For some experts, uncontrolled complexity explains the failure of many health IT interventions, including those associated with Learning Health Systems [127]. Complex systems may require alternative, more human approaches to governance and improving outcomes [128].
In 2017, Greenhalgh et al. [127] reviewed 28 technology implementation frameworks and integrated the findings with 400 hours of ethnographic observation and 165 semi-structured interviews. They used this to develop the Nonadoption, Abandonment, Scale-up, Spread, and Sustainability (NASSS) Framework for Health and Care Technologies.

The NASSS Framework identifies a range of challenges across seven domains, each of which can be classified as simple, complicated or complex, in line with the Cynefin Framework [124]
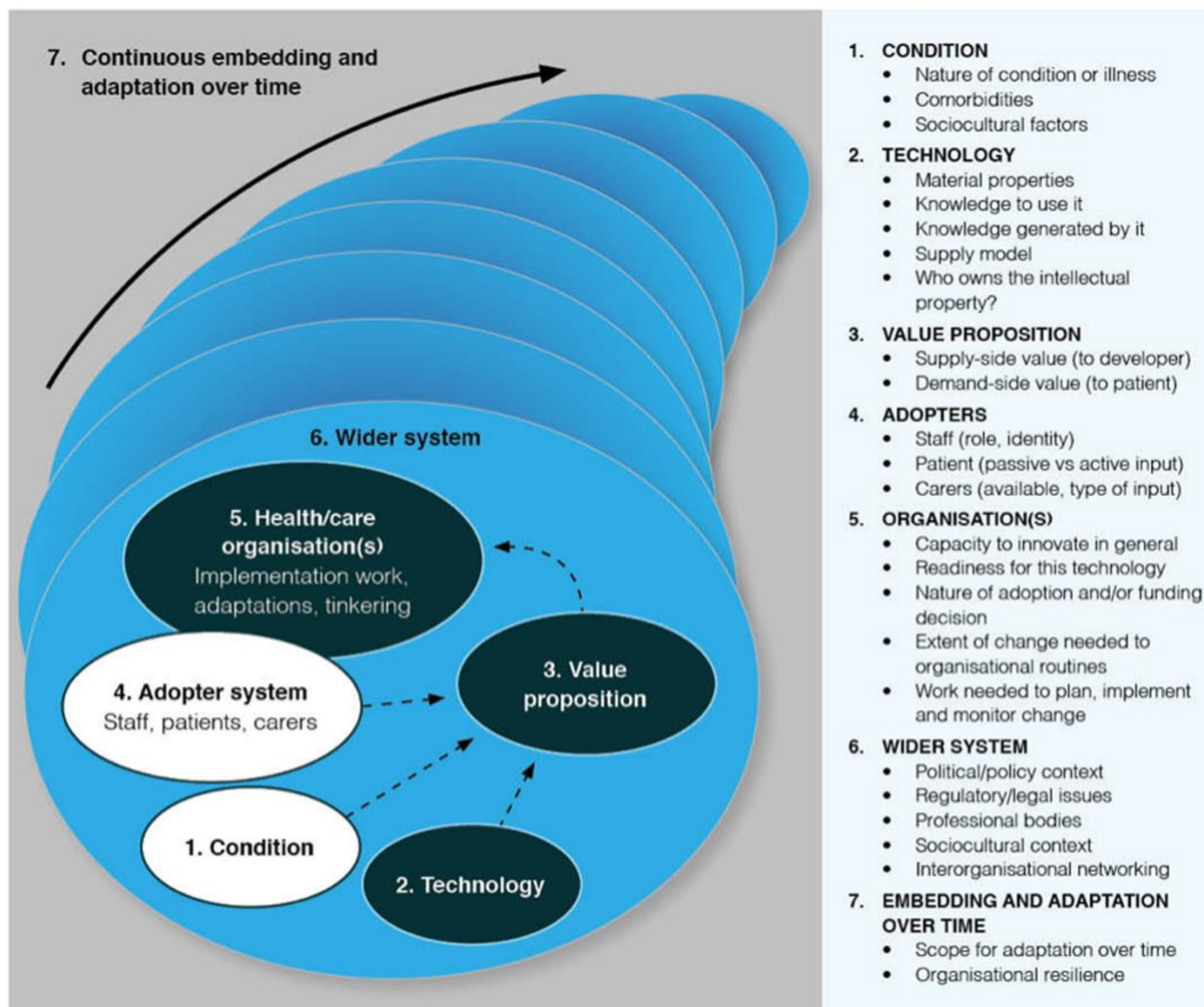

Figure F The NASSS Framework [24]

An expert workshop was held to inform this report, chaired by Prof Greenhalgh and attended by a group of experts in Learning Health Systems and implementation science [129].

The workshop considered how the NASSS Framework could be applied to Learning Health Systems, using four exemplars (See boxes below).

HealthTracker

A Clinical Decision Support Tool which incorporates ten different clinical practice guidelines into a single on-screen algorithm on the clinician's desktop. It provides estimates of cardiovascular risk and suggests further investigations and lifestyle changes. The tool was deployed in 60 general practices in Australia. A series of evaluations showed some positive impacts from deployment, but also wide variations in the tool's use between clinicians and practices[24].

PatientsLikeMe

PatientsLikeMe [34] is a US-based web platform that allows patients around the world to share their health-related experiences and outcomes in a highly structured format. It was established by brothers Jamie and Ben Heywood after another brother, Stephen, was diagnosed with Amyotrophic Lateral Sclerosis (ALS). Since 2011, patients have been able to record their experiences of living with a large range of other conditions. The platform now has 750,000 members. The data can be used by individual patients or researchers to learn from the experience of each patient. This data has also been linked to biological data and used to train AI algorithms. Recent studies have shown the platform's peer-peer connections improve self-management and self-efficacy for users.
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Children and Young People's Health
Partnership (CYPHP)**

The Evelina London CYPHP model [**22**] provides coordinated and tailored care for children and young people that is responsive to their needs. It integrates primary and secondary physical health, mental health, social care and education through Multidisciplinary Team meetings. Anticipatory care is enabled by using a population health model that allows for early identification and intervention through primary and secondary care data systems. The model combines routine health administration data with patient-generated data via a portal, giving children's health teams the information to plan care that is appropriate to a child's physical, mental, and social needs. Templates embedded in electronic health records, guidelines, and decision support tools promote evidence-based care and systematic collection of data on quality of care and outcomes. The data generated is combined with other evidence to enable continuous improvement in a Learning Health System.
The Evelina London CYPHP model covers two inner-city boroughs of South London (Lambeth and Southwark) with poor child health outcomes and high Emergency Department attendance rates for children and young people, emergency hospital admission and hospital appointment use. The Evelina London CYPHP model is being implemented across general practices, schools and hospitals.

TRANSFoRm

The TRANSFoRm project [**37**] developed technology to enable a rapid Learning Healthcare System that improves patient care by speeding up translational research, enabling more cost-effective Randomised Control Trials and by deploying diagnostic decision support. The project brought together a multidisciplinary consortium of 21 partner organisations from ten EU member states and was deployed on multiple EHR systems across several countries.

The following sections outline how each domain (
Figure E) can be applied to understand the level of complexity within a Learning Health System, illustrated by the examples above.

The Condition

The success of a Learning Health System depends on the clinical scenario in question. Previous studies have found that only a fraction of potential patients was deemed suitable for new technology because of the complexity of their condition, comorbidities or sociocultural situation. In reality, most patients are an exception to the general model.

The **HealthTracker** tool produced lifestyle recommendations suitable for patients with a structured lifestyle. However, those at risk of cardiovascular disease often had mental and physical comorbidities, as well as sociodemographic factors that made it difficult to comply with preventative lifestyle changes.

PatientsLikeMe began by covering one serious, fatal, and untreatable condition – ALS. Over time, it expanded to include a wide range of other conditions, starting with other neurological conditions like MS and Parkinson's. It then broadened out into other chronic conditions, such as mood disorders, autoimmune and rheumatological diseases, as well as oncology and rare diseases. Patients with more serious conditions with fewer treatment options were more likely to engage in the platform continuously. For example, non-terminal chronic conditions like psoriasis had less uptake [191]. Patients waiting for an organ transplant were highly engaged while on the waiting list, but much less so once they had successfully undergone surgery[34].

CYPHP is a model of healthcare for children and young people, as well as a health system strengthening initiative. It therefore benefits patients and populations across multiple conditions. Guiding principles include anticipatory care, biopsychosocial care, and equity. Services are tailored to need using child-specific data gathered through a patient and parent portal, together with system-level administrative data and registries. CYPHP integrates care for children and young people across primary and secondary care, joining up mental and physical health and placing prevention and health promotion at the heart of the service.

TRANSFoRm initially focused on diagnosis in abdominal pain [**116**]. This is a well-defined field, but one that involves biopsychosocial complexities. The project later focused on colorectal cancer, which is more tightly defined [**37**].

The Technology

Usability and dependability have often been cited as reasons for the failure of technology interventions. There has often been a failure to adequately prototype and test systems. There is also a risk that technology-produced data could be misinterpreted by patients or clinicians, particularly if it does not directly measure the underlying illness. Skills and training requirements can also be a barrier to scaling and spreading the initiative. Systems that are plug and play/off the shelf, which can be replaced by other, equivalent systems, avoid the risk of lock in or provider failure.

HealthTracker was co-designed with clinicians and was visually appealing, but technical glitches disrupted workflows and slowed down the EHR, so many clinicians stopped using it.

PatientsLikeMe established a reliable cloud-based database with an appealing user interface. Complexity was minimised by avoiding an interface with Electronic Record Systems. Over time, more advanced analytical capabilities were developed, but the system remained easy to use, in some ways resembling a dating website.

CYPHP's core technologies are population health registers from primary and secondary care, used to identify risk or diagnoses; shared interoperable clinical notes between primary and secondary care; and a patient or parent portal that supports self-referral, collecting biopsychosocial data to help tailor care to need, and providing health promotion and supported self-management information. The patient portal connects to a research database, enabling participation in formal research evaluation, with patient or parent consent [**22**].

TRANSFoRm built a decision support system and a user interface from reusable components. It also used an ontology to overcome the challenge of interoperability between EHRs [**116**]. Building and sustaining interfaces with each of the EHRs was the most burdensome task [**37**].

The Value Proposition

Who benefits from a Learning Health System? Is it worth developing? If there is no clear business case, a private company will be unable to scale and spread. If there is no value to the organisation (eg hospital, GP practice), then it is equally likely to fail. This value can include benefit to patients or improved efficiency.

Value in healthcare is the outcome created per unit of resource spent. Maximising value means achieving the best outcomes at the lowest cost. It must also address issues of value to stakeholders, such as equity, sustainability and transparency [130]. The Learning Health System can enable the measurement of outcomes and generate improved costing data, allowing for routine measurement and comparison of value within healthcare [1].

HealthTracker had a complex and varied value proposition for government, GPs and patients, making it difficult to assess value as a whole.

PatientsLikeMe had great value to the patients who used it, giving them a feeling of community and sometimes a sense of being believed. It also helped them make decisions about their own care, with many changing clinicians as a result. However, charging patients might have deterred use, while hosting advertisements could damage its independence. The data was valuable to researchers, pharmaceutical companies and to the medicines' regulator. This was the primary source of funding (alongside grants) and enabled a peak turnover of millions of dollars in revenue per year. For example, it helped analyse the impact from the launch of a new drug. It had limited value to the health system, in which many clinicians ignored the data, although some found it useful to help compare their practice with the community.

CYPHP delivers value to patients and families through more joined-up and safer care, reduced delays and better quality. For example, specialist nurses and doctors work and share data between hospital, primary care, and community organisations to support children. The system also provides access to additional expertise for clinicians, linking clinicians in teams across organisational and professional boundaries. There was concern that additional need might be uncovered that could not be met by existing commissioner budgets. Indeed, CYPHP's population health approach to early identification and universal coverage has uncovered unmet need: for example, 45% of children in the community with asthma have poorly controlled symptoms requiring clinical support. However, early intervention and joined up care has delivered cost savings, and the service is cost-effective and commissioned. Moreover, the population health management approach has reduced inequalities in access to care, delivering higher levels of early intervention to the children who need it most [**22**].
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TRANSFoRm was shown to improve diagnostic accuracy in some situations and was acceptable to patients and GPs. However, there were concerns that it might result in increased demand on other parts of the system if deployed more widely [**37**].

The Adopter System

The staff, patients and carers who adopt and use a Learning Health System are critical to its success. Previous studies [127] have shown that staff sometimes abandon technology because of usability issues, but more often do so because of threats to their scope of practice, fear of job loss or concerns over the safety/welfare of patients. Patients often abandon technology because of usability and the amount of work required of them. Technology may not be used due to weak social networks or a lack of skills among carers, so these assumptions must be made explicit.

This supported previous analysis that "those on the front line of care (clinicians, staff, patients) navigate change through their small part of the system, adjusting to their local circumstances, and responding to their own interests rather than to top-down instructions" [123].

Digital exclusion is a major concern for patient-facing systems. In the UK, 7% of the population lack internet access, while almost 12 million people do not possess the digital skills considered essential for going online [131]. There are broad government initiatives to improve digital inclusion, but providers who offer digital services must also ensure that patients without the necessary skills or resources are not disadvantaged.
Some individuals have ethical concerns about how their data might be used [19]. Clarity around Information Governance (see above) and the use of

participatory co-design (see below) are key to resolving such concerns.

Fewer than one third of GPs used **HealthTracker** for more than half of eligible patients. This was ascribed to a combination of technical and sociocultural reasons, as well as unwritten clinical assumptions. For example, alerts that appear after the clinician has decided to do something can cause cognitive dissonance.

PatientsLikeMe was eagerly adopted by patients, reaching 750,000 members. As discussed, adoption varied by condition and by age and gender. The stage of illness was also important, with people more likely to sign up at diagnosis or when their condition changed. Patient activation [192] was another important factor. Little effort was made to drive adoption by clinicians; PatientsLikeMe did not employ any senior clinicians.

CYPHP's Learning Health System adopters include patients, parents, and professionals. The portal was developed from another effective portal and linked to existing EHRs. There have been a number of issues from a professional perspective. For example, it was a challenge to achieve interoperability between

primary and secondary care clinical notes, but practical work-around solutions were found, and care effectively crossed boundaries. Concerns about professional liability and accountability within a multi-agency, multidisciplinary system were overcome through developing a partnership with shared governance for the programme, with clinical governance agreed by clinical teams. CYPHP was successfully adopted because it moved from disruption to embedding new ways of working within business-as-usual systems, using a combination of "hearts and minds", parent power, clinical common sense and effective management.

TRANSFoRm was only adopted by a trial group. It was clinician-facing and was shown to be acceptable to GPs [**37**].

The Organisation

The organisation's capacity and readiness for change will influence the uptake and scale-up of Learning Health System interventions internally. The decision on whether to fund and support a Learning Health System will be influenced by the business planning, yet it is often impossible to predict costs and benefits in advance. Many healthcare organisations are already working at capacity and are focused on relatively short-term financial, process and regulatory targets. There may be limited uptake for Learning Health System elements that are unaligned with these targets or demand upfront investment for long-term payback.

A Learning Health System is not just an IT project. Ideally, within a healthcare provider or even a national system, Informatics, Quality Improvement, Research, Library, Performance, HR, Training departments and others would be working together to deliver the Learning Health System strategy.

Elements of a Learning Health System that are viewed as a public good – such as the contribution of data to publicly funded research with open access to results – may be seen as a luxury, only affordable for organisations that trade on their national reputation or dominate their market [1]. Other organisations may require additional incentives to participate.

Organisational slack can make this process possible. The work involved in implementation is often extensive and underestimated at the planning stage, while there must be a shared vision about what the Learning Health System can realistically achieve. In some cases, innovation can be achieved by working with another, more innovative organisation.

Poor technical and support infrastructure meant that some organisations could not support **HealthTracker**. There was also a varying capacity for innovation and quality improvement, while the size and governance structure had an impact. Some small practices struggled to support the change, while others benefited from streamlined decision making. In other practices, inflexible job roles hindered use.

PatientsLikeMe sought but did not achieve adoption by existing healthcare organisations.

CYPHP is a clinical-academic programme functioning as an Active Learning Partnership. It brings together three Foundation Trust hospitals (including a mental health provider), primary care providers, local authorities, public health organisations, commissioners and a university institute. It is a formal partnership with shared decision-making and governance. Building trust took time but has resulted in profound change being embedded across the system. CYPHP is supported by a mixed funding model, including a hospital charitable foundation and local Clinical Commissioning Groups (CCGs). A twin-track evaluation programme includes both pragmatic NHS service evaluation and a rigorous research-standard evaluation, providing new knowledge about effective models of care for children and young people.

TRANSFoRm required cooperation from several EHR vendors for whom participation was not always a priority. This resulted in delays [**37**].

Wider Context

The wider institutional, policy and sociotechnical context is often identified as a key factor in the failure to move from a demonstration project to a transferable and sustainable mainstreamed service. This context can include policy, political, IG, interoperability, legal, market, IP and regulatory considerations.

HealthTracker implemented existing guidelines but had limited success in securing endorsement from well-established professional societies. Attempts to embed it within the reimbursement model failed because of the novelty of the idea.

PatientsLikeMe expanded beyond patient-reported experiences and outcomes to become a biobank. It raised a $100 million investment and secured a critical technology partnership with a Chinese genetic research firm, growing to 250 staff. Shortly afterwards, a review by the Committee on Foreign Investment in the US (CIFUS) ordered a divestment by the Chinese firm as part of the wider deterioration in US-China relations. This prompted the rapid sale of PatientsLikeMe in 2019 and the loss of a significant part of the workforce.

For **CYPHP**, Information Governance and public trust have been central. There have been a number of challenges, such as competition rules and pressures to maintain organisational financial balance. However, policy has supported cooperation, crucially through building relationships at all levels of organisations: executive, managerial, clinical and administrative. A strong patient focus has also been key to success. Ensuring the flow of data between organisations requires a complicated set of data-sharing agreements; this enables data flow between multiple providers, for direct clinical care, service evaluation and research. Intra-organisational liability has also presented challenges, but a Partnership approach, as described above, has enabled effective, shared governance at organisational and clinical levels.

TRANSFoRm started as an EU-funded project. The UK's participation in such schemes following Brexit is uncertain [**37**].

Adapting over Time

By its nature, a Learning Health System will change during its implementation and beyond. To succeed, it must be able to adapt. Likewise, the organisation must have the resilience to respond to critical events and maintain a flexible approach.

HealthTracker required knowledgeable staff and was hard to sustain when staff turnover was high. There were challenges in updating the software in response to bugs and competing systems emerged over time. Eventually, the regulatory system caught up, and created opportunities to align with reimbursements and broader digital strategy.

PatientsLikeMe grew and adapted over time, moving from start-up to mature business, expanding its user base and generating revenue and investment. It was subject to an unforeseen international event (outlined above) that came close to destroying the business. It continues to operate at a different scale, and it remains to be seen how it will develop in future.

CYPHP technology and organisational structures have evolved as the network of organisations has grown and funding has become available. The involvement of university partners has ensured flexible learning capability. Being part of this organisational landscape has helped CYPHP to adapt to changes like new EHRs and new patient administration systems.

TRANSFoRm has found that maintaining interfaces with a range of EHRs as they change has been a huge challenge and threatens sustainability [**37**].

Applying the NASSS Framework to Learning Health Systems

The expert workshop found that the NASSS Framework could be applied to a broad range of Learning Health Systems. Moreover, the understanding gained could help select projects to fund, as well as aiding in their design, implementation and evaluation. Some NASSS domains will be more important than others for a given Learning Health System, while some may not merit consideration. The framework could be applied to the entire Learning Health System or separately to the components within an umbrella Learning Health System. It is likely to be most effective if used to guide a comprehensive discussion, rather being applied mechanistically.

The NASSS Framework has been deployed within a series of tools called NASSS-CAT (Complexity Assessment Tool) [132]. The NASSS-CAT Tools Box describes each tool and when it should be used. These tools should be applied to Learning Health System components as they are being designed, implemented and evaluated.
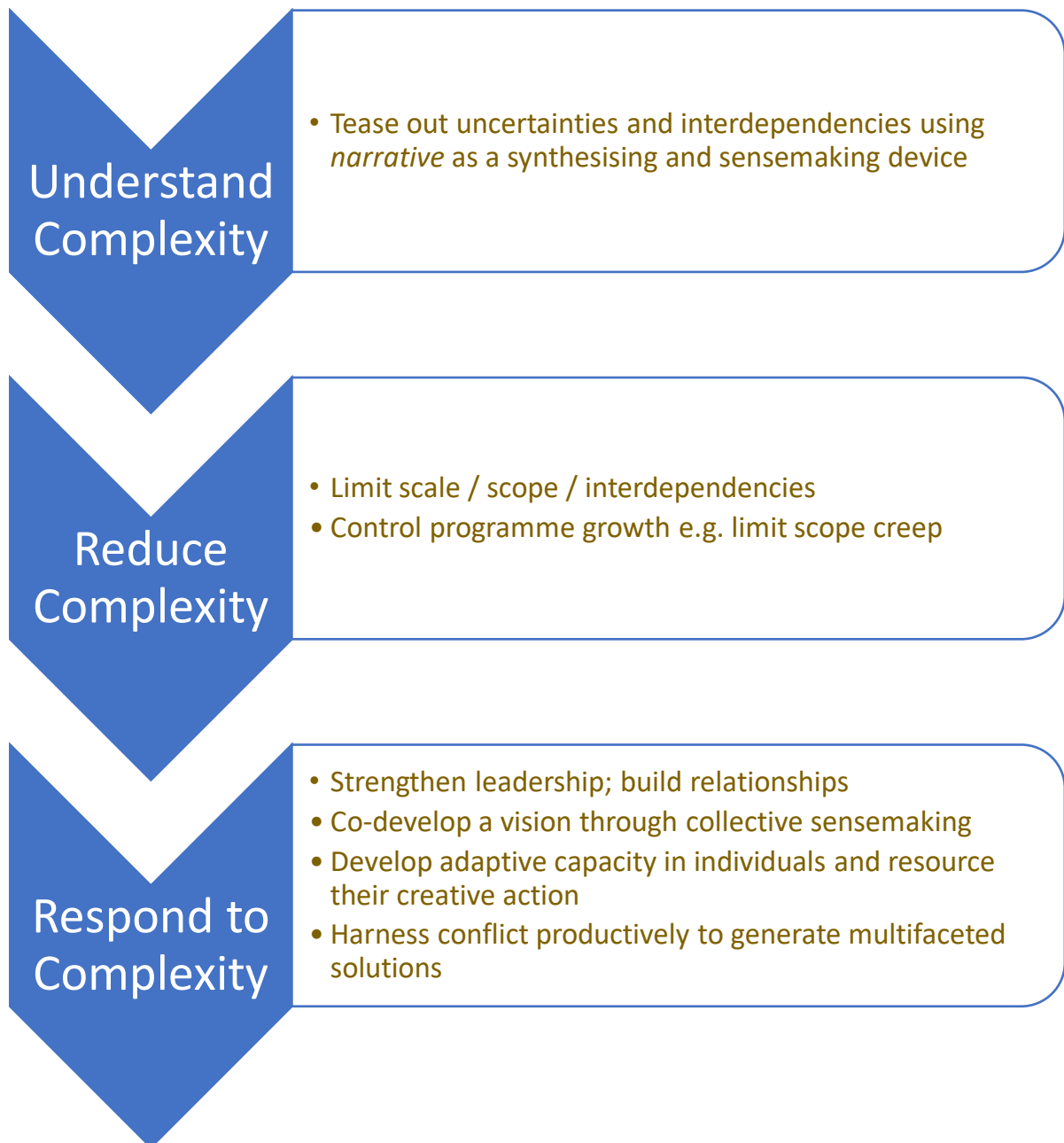
The aims of these tools are summarised in Figure G

Understand Complexity

- Tease out uncertainties and interdependencies using *narrative* as a synthesising and sensemaking device

Reduce Complexity

- Limit scale / scope / interdependencies
- Control programme growth e.g. limit scope creep

Respond to Complexity

- Strengthen leadership; build relationships
- Co-develop a vision through collective sensemaking
- Develop adaptive capacity in individuals and resource their creative action
- Harness conflict productively to generate multifaceted solutions

Figure G The NASSS-CAT (Complexity Assessment Tool) [1]

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[1] Adapted from a presentation by Prof Greenhalgh to the workshop on applying NASSS to Learning Health Systems.

Reducing and Responding to Complexity

Greenhalgh and colleagues have adapted existing [133] principles for managing complexity, so that they are relevant to the development of a Learning Health [134] System. They suggest that teams:

Acknowledge unpredictability: Designers of interventions should contemplate multiple plausible futures. Implementation teams should tailor designs to the local context and view surprises as opportunities.

Recognise self-organisation: Designers should expect their designs to be modified, perhaps extensively, as they are taken up in different settings; implementation teams should actively capture data and feed it into the adaptation process.

Facilitate interdependencies: Designers should develop methods to assess the nature and strength of interdependencies; implementation teams should attend to these relationships, reinforcing existing ones where appropriate and facilitating new ones.

Encourage sensemaking: Designers should build focused experimentation into their designs; implementation teams should encourage participants to ask questions, admit ignorance, explore paradoxes, exchange different viewpoints, and reflect collectively.

Develop adaptive capability in staff: Individuals should be trained not merely to complete tasks as directed but to tinker with technologies and processes and make judgments when faced with incomplete or ambiguous data.

Attend to human relationships: People must work together to embed innovation, solving emergent problems using give-and-take and "muddling through".

Harness conflict productively: There is rarely a single, correct way to tackle a complex problem, so look upon conflicting perspectives as the raw ingredients for multifaceted solutions.

Strategy in a
Learning Health System
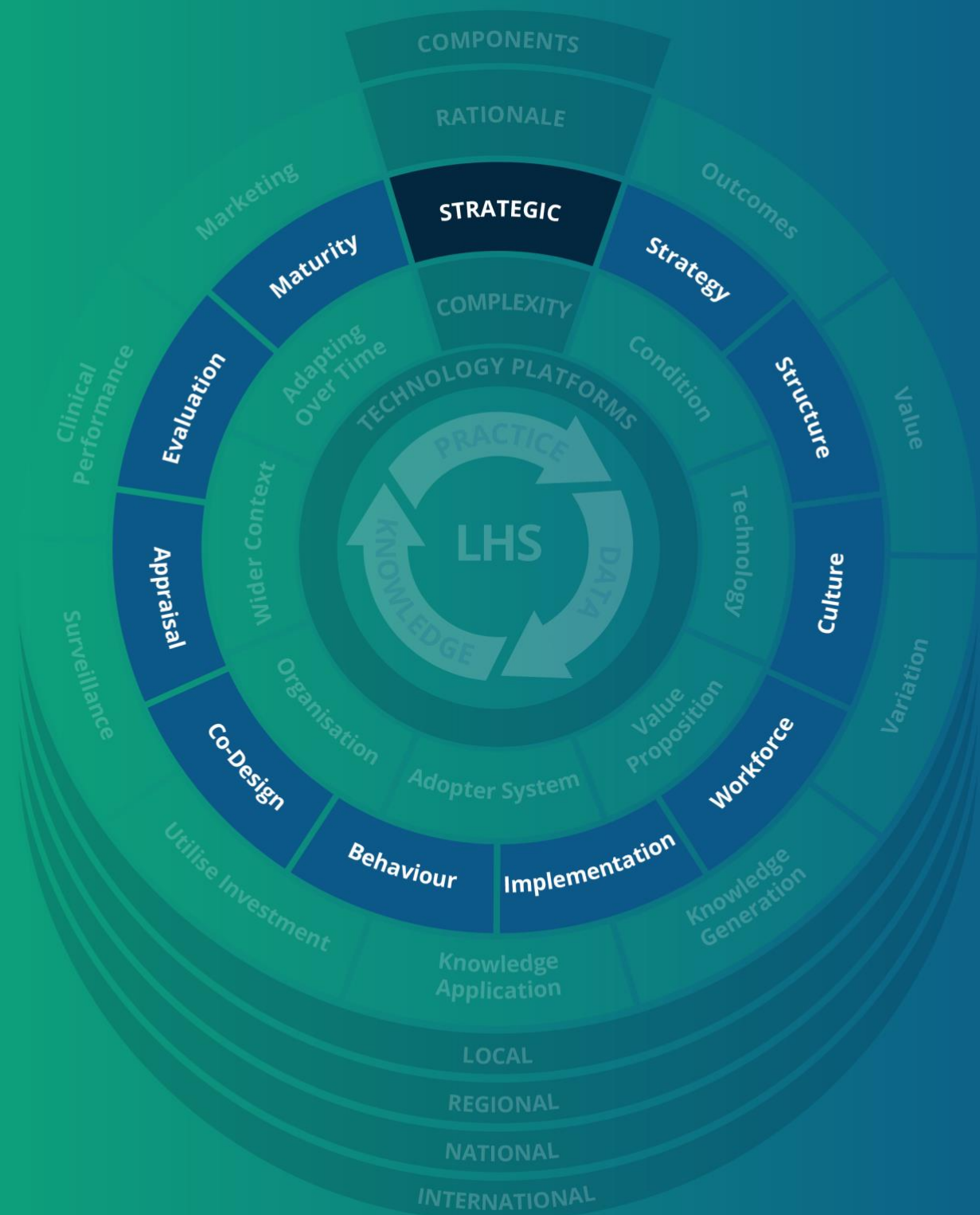
Strategic direction is required to build a Learning Health System. A culture of learning and innovation will ensure that individuals are motivated to participate, while a scientific approach to implementation will increase the likelihood of success. Individuals and organisations will have to change their behaviour in ways that may not come naturally. All stakeholders must have a hand in designing a system that will change the way they work or are treated. The system must be continually evaluated, and its maturity understood.

This section offers advice on how these objectives can be achieved.

Strategy and Organisation

Strategy generally involves setting goals and priorities, determining actions to achieve these goals, and mobilising resources to execute the actions [135]. It is often thought of as a deliberate, explicitly stated plan, but can also be viewed as a "pattern in a stream of decisions" [136]. While much strategy literature addresses competition in business or war, it is not always obvious how this applies to healthcare, particularly in public systems [137] or to a Learning Health System. Ultimately, strategy is a set of inter-related choices on how a team or organisation will deliver value [138].

The Learning Health System can be a vague concept and there are almost limitless ways in which it could be organised. A given organisation must choose what sort of Learning Health System will best meet the needs of its stakeholders. A strategy can help to make this explicit. Like every other element of a Learning Health System, strategy must be co-designed by the stakeholders. There are many guides and tools that can assist with this process [139-142]. For larger programmes, strategy consultancies can take an organisation through the process, though it is also essential to develop strategic thinking capabilities within the Learning Health System.

Once a strategy has been developed, people and resources must be organised to deliver it effectively. This is sometimes known as the Target Operating Model (TOM) or an Organisational Architecture. An organisation wishing to become a Learning Health System can create a TOM that describes how its people, processes and technology should be deployed [143]. Such an approach can be helpful in a complicated environment. It can orientate stakeholders to their role in delivering the strategy and can aid in planning long-term investments like infrastructure and training. It has been employed by NHS Digital, the recent NHS London Nightingale hospital, and other healthcare organisations [28]. It necessarily makes assumptions about the future. Because this is often not possible within a complex system, the operating model must itself be subject to learning and change.

If misapplied, this mechanistic systems approach can have drawbacks. Longwinded multi-year strategies can be out of date by the time they are published and cannot respond to emerging threats and opportunities.

This was highlighted by the Covid-19 pandemic.

McCrone and Snape consider strategy within the different domains of Snowden's Cynefin Framework [144] (see
Figure E). In a complex Learning Health System, strategy might be better thought of as a verb than a noun: a continual process, rather than a masterplan. It is a series of safe-to-fail experiments (see
Figure E – Probe, Sense, Respond). Learning comes from those that fail, as well as those that succeed. Successes can be amplified by attracting more resources. As evidence from experiments accumulates, an environment can move from complex to merely complicated, because cause and effect becomes better understood and more stable.

A Learning Health System can have a shared purpose or mission, while individuals and groups can have autonomy to develop complementary microstrategies and safe-to-fail experiments [144]. The infrastructure of a Learning Health System can enable such an approach (see NYU Langone Health exemplar box). Over time, a Learning Health System that is complex at the enterprise level can have lower-level functions that are simple or complicated, lending themselves to more traditional strategic planning and TOM approaches.

A Learning Health System may well exist within a wider organisation, such as the NHS or another funding network. These organisations might have requirements for traditional long-term plans, which

can limit strategic innovation. This can, however, be helpful in planning long-term investments, like infrastructure or training.

An alternative approach is the actor-oriented learning network organisational form, proposed by Britto et al., which aims to facilitate co-production and cooperation at scale to improve healthcare (See Learning Network Box). This has three components [145]:

- **Aligning participants around a common goal:** Mission, vision and values are visible and shared. There is transparency and learning between teams. Stakeholders understand how they can get involved, while leadership and co-design are distributed.

- **Standards, processes, policies and infrastructure to enable multi-actor collaboration:** These can be shared across centres to reduce costs and customised as required. Leaders have dedicated time to ensure that these elements are continuously improved using standardised Quality Improvement methods.

- **A commons where information, knowledge, resources and knowhow to achieve the goal are created and shared:** As well as data registries, other platforms can be used to share different resources within and between networks. This leads to the development of a shared knowledge base.

Culture

The most widely cited definition of an Learning Health System – from the Institute of Medicine (IoM) [120] – discusses an alignment of science, informatics, incentives and culture for continuous improvement and innovation.

The need for a culture change is often noted to include learning, innovation, information use, sharing and implementation and research [146]. More broadly, there are frequent calls to change the culture of health and society [147]. Organisational culture has been categorised in three layers [147]:

- **Visible manifestations:** The distribution of services and roles, the physical layout of facilities, established pathways of care, staffing practices, reporting arrangements, dress codes, reward systems, established ways of tackling quality improvement and clinical governance.
- **Shared ways of thinking:** Values and beliefs used to justify the visible manifestations and the rationales for doing things differently, such as prevailing views on autonomy, dignity, evidence and service improvement.
- **Deeper shared assumptions:** The unconscious underpinnings of day-to-day practice, such as assumptions about the role of patients, carers and different professionals.

These layers are learned, shaped and reinforced through training and experience. There may be subgroups with different cultures within any given system (eg clinicians and managers). Such cultures can help deliver organisational goals; on the other hand, they can undermine drives for change. This is a fundamental source of complexity within healthcare. The multidisciplinary, often multi-agency

nature of a Learning Health System increases the risk of culture clashes [19].

There are many quantitative tools for assessing organisational culture, but they often lack evidence. There is no one tool that is appropriate in all circumstances [148]. Another approach, which recognises the constraints of measuring complex systems, is to explore culture through narrative [149].

While culture is clearly important, it is not always possible to determine a causal relationship with performance within a complex system. Equally, it is not easy to influence culture in a predictable way. Even so, the King's Fund has produced a tool to help organisations assess their culture and identify targets for improvement in six areas [150]:

- **Inspiring vision and values:** Leaders should communicate an inspiring, ambitious vision.
- **Goals and performance:** Goals should be set at every level, from board to frontline staff, then measured on patient outcomes and patient feedback.
- **Support and compassion:** Everyone should treat colleagues with respect, care and compassion.
- **Learning and innovation:** Teams should take time to review, debate and improve performance. Quality and safety improvement should be a priority for all. Everyone should welcome feedback.
- **Effective teamwork:** Leaders should ensure effective teamwork and inter-teamwork, within and across organisational boundaries.

- **Collective leadership:** Everyone (including patients) should take responsibility for the success of the organisation, not just a few leaders at the top.

Workforce

At the heart of a Learning Health System is a multidisciplinary team bringing together the right people, skills, specialisms and subject matter expertise. The nature of the work will determine the make-up of this team, but a multidisciplinary Learning Health System could include patients, clinicians, researchers, designers, strategy and operational delivery staff, information analysts and other support professions. The team may not all be directly employed; some might be seconded, some could be contractors or consultants, while others may be employed by platform providers. Leadership within each of these groups and organisational leadership understanding and buy-in will also be essential, given the scope of a Learning Health System [151].

Learning Health Systems are unlikely to reduce the number of clinical professionals required. Indeed, many of the same skill categories will continue to be required, but the content of those skills and the context in which they are applied may differ in the following ways [152]:

- **Communication skills:** These will need to extend to online modes
- **Personal and people development:** Professionalism, teaching, personalised lifelong

learning, management and leadership will take on new dimensions

- **Health, safety and security:** Online issues, cybersecurity, information governance and digital ethics will become more important
- **Service improvement:** As services become more digitised, staff will need the skills to optimise these systems
- **Clinical effectiveness:** Staff will need to understand the theoretical frameworks underpinning clinical assessments, investigations and interventions that utilise technology
- **Equality and diversity:** Digital inclusion will be central to accessing care

Clinicians may also need some new skills. They may need to:

- Become more aware of how the data they record might be used by the system [**153**]
- Be able to interpret results of routine data analytics [**7**, **40**, **49**].
- Become more confident with an element of research in their role [**40**]
- Be capable of leveraging data from non-healthcare system sources [**153**]
- Be able to interpret and act upon feedback on their practice [**23**]
- Be able to live with continual change [**153**]

These needs have been captured by the Faculty of Clinical Informatics Competency Framework [**154**].

Many of the skills and disciplines required to develop a Learning Health System are in short supply and take many years to develop, so the Learning Health System should be part of a long-term workforce or people strategy.

Implementation Science

Implementation Science is the scientific study of methods to promote the systematic uptake of research findings and other evidence-based practices into routine practice, to improve the quality and effectiveness of health services [**155**].

The fact that it takes on average 17 years for Evidence-Based Practices (EBP) to become routine [**156**] is a widely cited driver for the development of Learning Health Systems. Discourse on Learning Health Systems often assumes that knowledge delivered to the point of care – such as through a decision support system – will actually change practice. Despite positive efforts to integrate knowledge delivery with clinical workflow [**62**], previous sections of this report have shown that this is slow and variable, something that is supported by the literature [**157**]. Indeed, the Learning Health System concept itself is approaching the 17-year milestone without becoming routine practice.

Traditionally, the efficacy of individual interventions has been studied in isolation in a controlled environment. As discussed in previous sections, Learning Health Systems are complex, rather than controlled environments. It can be more important to optimise their real-world effectiveness by ensuring that they are used correctly, rather than seeking to understand their efficacy in a lab.

Learning Health Systems are likely to require an implementation strategy: an integrated package of discrete approaches ideally selected to address identified barriers to implementation success [156]. For example, these might include behaviour change, training, feedback, incentives, learning collaboratives and community engagement. The focus is on the successful integration and use of the Learning Health System elements, rather than their individual efficacy.

Implementation Science is a common source of failure for Learning Health Systems. However, there are many guides available [156] and an extensive academic literature [158]. Large Learning Health Systems will benefit from a team of Implementation Scientists, but even smaller Learning Health Systems would profit from tapping at least some external expertise.

Behaviour

To realise an improvement in practice, a Learning Health System often requires patients, clinicians and others to change their behaviour. There are many theories and models that can be deployed to understand and aid this process. The Behaviour Change Wheel (BCW) (Figure H) [159] is a systematic approach to designing, implementing and evaluating behaviour change interventions in any setting. It is based on a collection of existing theoretical frameworks.

The BCW represents a theory of what drives behaviour and how it can be influenced in different situations. This leads to an accessible and rigorous process that can be integrated into a Learning Health System, increasing the likelihood that the knowledge generated will result in behaviour associated with better outcomes.
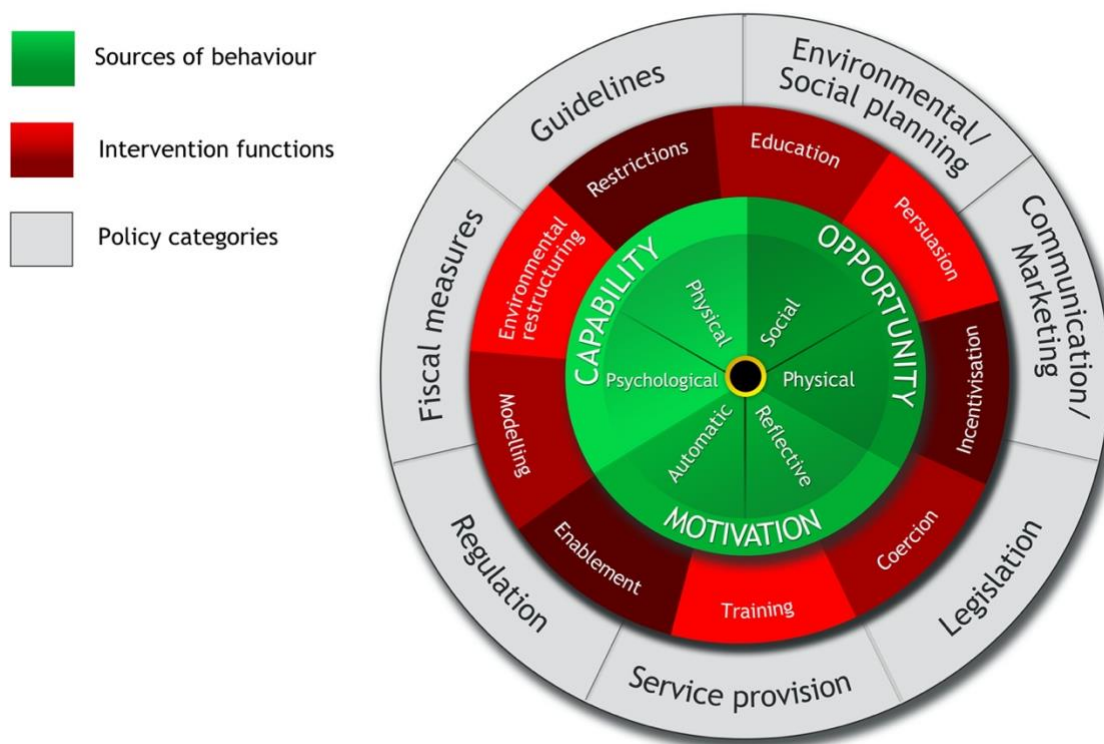

Figure H The behaviour change wheel [159]

The hub of the BCW is concerned with understanding the behaviour that has to be changed. This is achieved using the COM-B model (
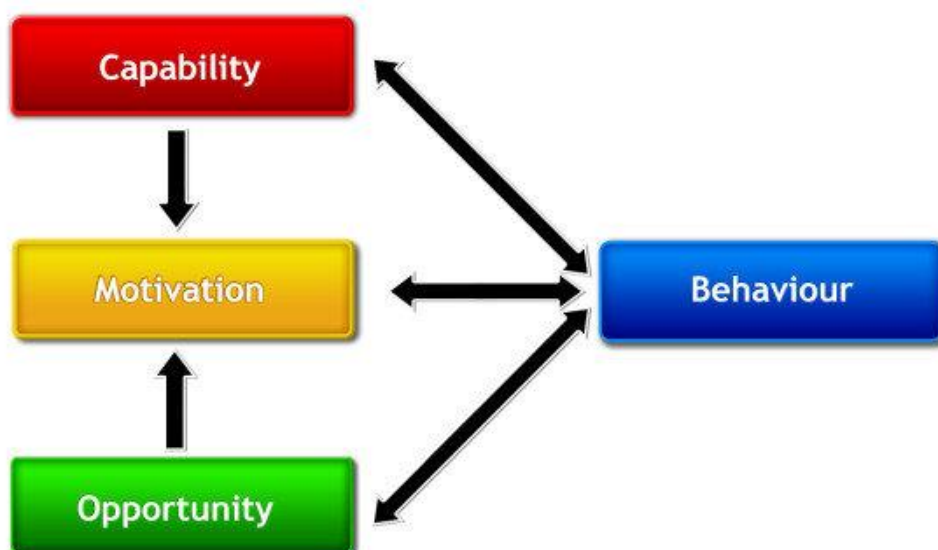
Figure I).

Figure I The COM-B Framework for understanding behaviour; reproduced from the behaviour change wheel [159]

Changing the behaviour of an individual, group or population requires a change in capability, opportunity and motivation, or some combination of the three. Standardised questionnaires have already been developed [159] to capture the drivers of a particular behaviour.

The next circle in the wheel outlines the possible intervention functions. These are broad categories of means by which an intervention can change behaviour: Education, Persuasion, Incentivisation, Coercion, Training, Enablement, Modelling, Environmental Restructuring and Restrictions [159].

The BCW guide provides a matrix that links the COM-B model to the intervention functions [159]. For example, if the barrier to behaviour change is identified as Physical Capability, then Training and Enablement are potential functions that the intervention could serve. If the barrier to change has been identified as relating to Reflective Motivation, then the intervention could serve the functions of Education, Persuasion, Incentivisation and Coercion (or a combination of these).

The final element on the BCW is the set of possible policy categories: seven ways that policy could deliver the intervention. These include Communication/Marketing, Guidelines, Fiscal Measures, Regulation, Legislation, Environmental/Social Planning and Service Provision [159]. Again, a matrix has been created in the BCW guide that links intervention functions to policy categories.

In order to operationalise the BCW, the intervention functions are linked to Behaviour Change Techniques (BCTs), which are the smallest active components of an intervention and designed to change behaviour (eg self-monitoring, goal setting, action planning etc). A taxonomy of 93 techniques has been developed that can be used to describe BCTs used in interventions. The most frequently used BCTs have been

mapped onto the intervention functions of the BCW.

The BCW enables a theoretical and systematic approach to intervention design. The COM-B model can be used to analyse user data and help "diagnose" what needs to shift in order for change to occur. Guided by matrices in the BCW guide, the most appropriate intervention functions, policy categories and BCTs for the context, behaviour and population of the intervention can be selected [159].

Elements of this process could be automated within a Learning Health System. Crucially, evidence could be collected on the effectiveness and cost-effectiveness of each of the BCTs in various situations, resulting in further learning. There are examples of the BCW being integrated in the design of mHealth apps [160]. Behaviour change will be necessary for patients, clinicians and organisations to adopt elements of the Learning Health System, and to ensure that they act on the evidence generated.

The BCW has been constructed from an analysis of existing frameworks and has been assessed in terms of its reliability in practice [159]. If it is to improve healthcare outcomes, any Learning Health System must have a method for delivering behaviour change [7]. It is also important to note that these approaches operate best in a well-understood system and may fail to produce reproducible results in a complex system.

Participatory co-design

This report has emphasised the importance of stakeholder involvement when designing the elements of a Learning Health System. It has described how the stakeholders are critical to understanding the true complexity of what may superficially look like a technical undertaking. This process has been called many things – co-design, co-production, co-creation, patient-centred design, patient engagement and more. All of these differ in subtle but important ways. This report is not concerned with these distinctions, but simply that those developing Learning Health Systems find an approach that meets their needs.

Design is a creative process to solve complex problems [161]; user-centred design brings stakeholders into the process. ISO 9241-210 is the international standard in Human-centred Design for Interactive Systems [162]. NHS Digital has created a set of NHS Design Principles based on this standard [163]. They can be usefully applied when developing each element of a Learning Health System.

The co-design approach emerged as a way of engaging representatives of stakeholders in the system development lifecycle. This emphasises the realisation of ideas that work in reality [164, 165], as well as the application of knowledge and the production of prototypes [38, 94]. The history of these developments has been traced from Hippocrates to the Learning Health System [166]. Involving potential users in participatory co-design aims to

sustain their contribution to ongoing improvements [164]. A set of core principles has been suggested [167]:

- **Democracy:** Include representatives of all stakeholders who will be affected by the new system. The aim is to increase diversity of experience, values and knowledge, while fostering trust among those involved. Careful attention should be paid to ensure that the participants are representative of the full range of stakeholders.

- **Mutual Learning:** Participants will learn from each other and from themselves as they reflect on the work. Efforts must be made to ensure that all participants are able to engage.

- **Capture Tacit or Latent Knowledge:** Assess the needs of stakeholders, including those that are not easily observable. Tacit needs are conscious but not expressed, while latent needs are subconscious and cannot be expressed in words.

- **Collective Creativity:** Stakeholders can work together creatively in a way that encourages the development of values and embeds them in the product. Certain tools and facilitation techniques may stimulate creativity more than others.

Participatory co-design offers a reliable, responsible and ethical approach to the development of Learning Health Systems. However, because it can seem resource-intensive, it is sometimes neglected by developers who fail to grasp the true complexity of a project.

A workshop was held in collaboration with Open Lab – Newcastle University [29] to explore how co-design and participatory design approaches could be applied within a Learning Health System. It brought together a group of 20 Learning Health System experts, clinicians, patients, technology providers and software design researchers.

The workshop featured extensive group collaboration on a range of design-based research methods, tools, and techniques, and followed a design thinking process [168]. It was held online due to the Covid-19 outbreak. This entailed using Zoom, with breakout rooms and a brainstorming and design software (Miro board) that provided a vast virtual collaboration space for collaboration. Key to this workshop was condensing the design thinking process in manageable blocks and rapidly move from idea to presentation within a few hours as a 'taster' approach [169]. It was more of an abridged sprint [170, 171] to rapidly transform an idea to a prototype.

Open Lab

Based at Newcastle University, Open Lab is a research group that works on advanced Human-Computer Interaction (HCI), social innovation, digital citizenship, sustainability, design futures, social innovations and machine learning. With its multidisciplinary and cross-disciplinary groups, Open Lab researchers address imminent challenges in healthcare, education and social justice. Much of the work undertaken by Open Lab designers and collaborators engages the perspectives of "normal citizens" in participatory design, co-design and collaborative design. This aims to bridge the gaps between technology, scientists and society; effectively, Open Lab creates sociotechnical learning systems in health and beyond.

The workshop aimed at eliciting the participants' objectives, perspectives, requirements and concerns by testing a menu of participatory co-design tools on a Miro board (Figure J). The groups were asked to apply the various participatory co-design tools in an invented Learning Health System scenario. These tools were sourced from online, open-source databases of design tools: Service Design Tools [172], Design Kit [173] and Right Question [174].
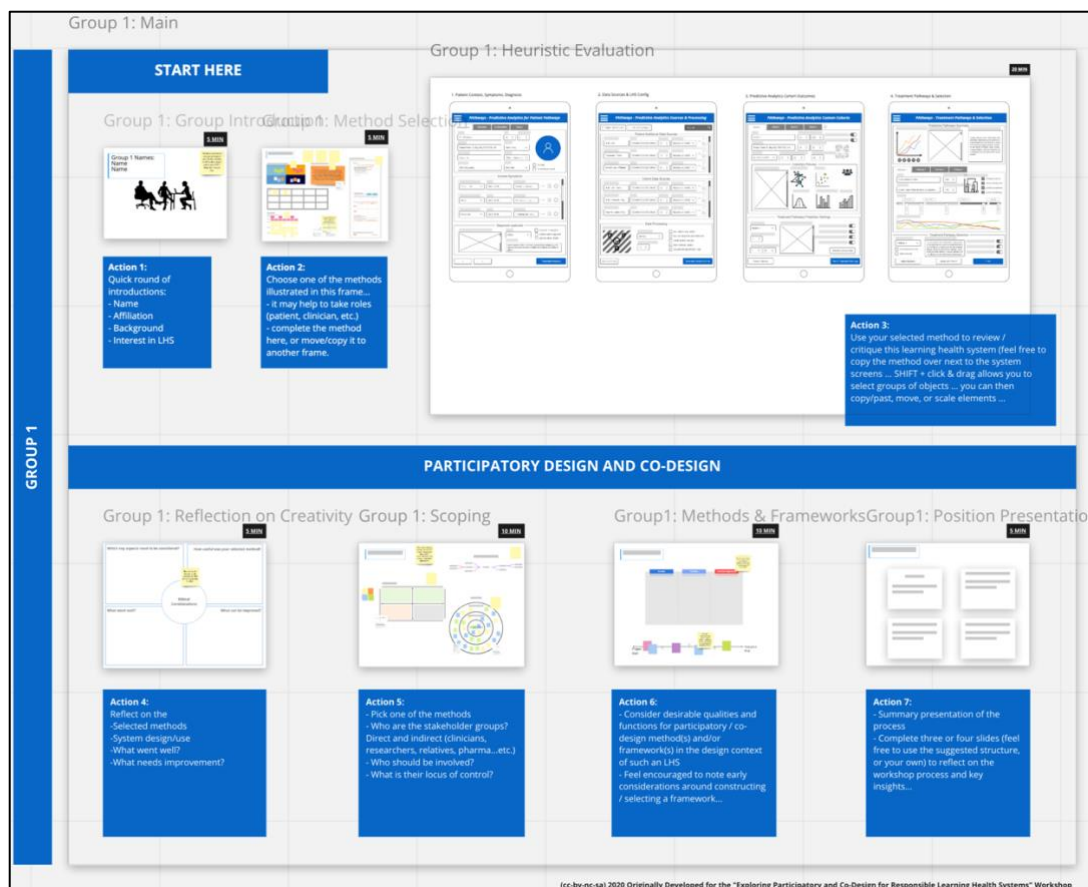

Figure J. Overview of a sample collaborative board for the co-design workshop.

There is limited evidence for how to select the most appropriate tools [167]. In the workshop, participants selected a range of tools to address the same challenges, illustrating that the choice of tool can be influenced by the task, the stakeholders, and by the type of knowledge sought. Participants noted that each tool provided a different perspective on the complexity within the task.

There are also many overarching frameworks to guide participatory co-design. Each framework can be assessed against the core principles listed above, the ISO 9241-210 standard and the preferences of the Learning Health System stakeholders and developers. The Point of Care Foundation [175] offers a guide and toolkit for running Experience-based co-design projects. The Good Things Foundation: Digital Health Lab [176] offers a step-by-step guide to co-design in health that could be applied to a Learning Health System. Teams can review these and other approaches to find the best fit for their stakeholders.

Participatory co-design should not be viewed as a one-off process within a Learning Health System, but as an integral, continuous process. By definition, a Learning Health System must continually learn. This learning and its application must be mediated by participatory co-design at every stage.

Appraisal

An expert workshop was commissioned to inform this report on the issues around evaluating Learning Health Systems [177]. It became clear during the evaluation workshop that the scope should be expanded to include appraisal: ie deciding if a project should proceed. There is no single route for an organisation to decide to implement a Learning Health System. The initial idea may come from staff within the organisation, who have read about or experienced such systems elsewhere. It may come as part of a partnership or collaboration, such as forming an Integrated Care System [178]. It may be part of a national strategy that advises or mandates the development of such systems.

Implementing a Learning Health System is usually not an "all or nothing" decision. It will often be built on legacy systems and existing Quality Improvement capability and may not require an organisation-wide decision. Smaller initiatives could be rolled out within departments, with delegated authority. Often, the influence of the person or group proposing the idea – or who will eventually implement the idea – is just as important as hard evidence. A Learning Health System is also more likely to be implemented if it aligns with the organisation's goals. Organisations sometimes seek evidence yet fail to challenge the methodology used to generate it.

The HM Treasury Green Book [18] presents widely used guidance on conducting an appraisal, covering the following topics:

- **Rationale for intervention:** Why something needs to be done, including objectives and outcomes

- **Options generation:** A longlist of the options for delivering the stated outcomes
- **Shortlist options appraisal:** Comparing the different options
- **Valuation of costs and benefits:** A comparison with "business as usual"
- **Distributional analysis:** The impact on different groups in society
- **Uncertainty:** Applying sensitivity analysis to variables that might change
- **Optimism bias:** Adjusting for the appraiser's tendency to overestimate benefits and underestimate costs
- **Risk:** Accounting for the impact and likelihood of risks that might occur and how they can be mitigated

Following an initial appraisal, the organisation might be persuaded to launch a large project, or they could prefer a pilot study with limited scope. Pilot studies can be a powerful way to test hypothesised impacts and feasibility. They can start to identify knock-on impacts on other services, though they sometimes miss important interactions because of their limited scope.

Evaluation

Learning Health Systems are expensive and impact the health of large populations, so it is important to understand how effective and cost-effective they are. Although failure is an important source of learning and can help others to decide whether and how to join a Learning Health System, organisations are generally less enthusiastic about publicising failures

than successes [179]. In writing this report, it was difficult to find published examples of Learning Health Systems that had failed, while a recent review found no published rigorous evaluation of a Learning Health System [19]. Another systematic review found 43 articles relating to 23 Learning Health Systems (local, regional and national) that reported outcomes. Only six articles were judged to provide high or medium quality evidence[6].

However, the authors have personal experience of several relevant projects that did not meet their anticipated objectives. Health IT research also cites a high failure rate [179], so it is likely that important learning is being missed.

The sociotechnical nature of Learning Health Systems makes them difficult to evaluate. Although the Medical Research Council (MRC) guidance on Developing and Evaluating Complex Interventions [180] remains a gold standard guide, the field has developed significantly since it was published in 2008, and Learning Health Systems present novel challenges. MRC and National Institute for Health Research (NIHR) have commissioned an update to the guidance [180].

Evaluation generally seeks to compare one intervention with another, or to no intervention at all. Because of their heterogeneity, it is not possible to be prescriptive about the methodology that should be used to evaluate a Learning Health System. An evaluation can examine structural or functional aspects of a Learning Health System against a maturity model (see below), but ultimately, success depends on the

extent to which each learning cycle improves patient outcomes.

The MRC guidance states that randomised trials are the most robust evaluation method. They can prevent selection bias: systematic differences between those who do and do not receive the intervention. Such methods might randomise individuals or groups of participants, such as an entire hospital. Stepped Wedge Designs can be appropriate when a new intervention is being rolled out to a population in phases, but such methods are often impractical within a Learning Health System.

Traditional randomised controlled trials are often not feasible in Learning Health Systems, where the intervention changes rapidly and may not be easily isolated. The MRC guidance cautions that non-randomised designs are most useful where the effects of the intervention are large or rapidly follow exposure, and where the effects of selection, allocation and other biases are relatively small.

The MRC guide offers a range of approaches for dealing with such biases, including conventional covariate adjustment using a regression model, and extensions such as instrumental variable and propensity score methods. It concludes, however, that the interpretation of small effects from non-randomised studies requires particular care and should draw on supporting evidence where possible.

Traditional controlled evaluation methods might not be appropriate in many complex environments. Constant change may make it impossible to generalise the finding from one evaluation to another environment. Plan, Do, Study, Act (PDSA) cycles or Lean approaches – which evolve a solution suited to the environment – might be more appropriate. These were traditionally used at the local level with rapid cycles but can work at larger scales. They are based on manufacturing industries and measurement is built into the process.

Qualitative evaluation methods can add an additional dimension. They generally explore how people make sense of the world and experience events. Qualitative data could be collected through direct or participant observation, interviews, focus groups and from documentary analysis. For example, a qualitative study might explore how it feels to be a patient with a long-term condition and aim to gain insight into how people make sense of and manage these situations.

In the context of Learning Health Systems, a qualitative evaluation could try to explore user acceptability issues and the barriers and facilitators to implementation. A qualitative evaluation of usability and engagement could also inform the potential design and development of Learning Health Systems, as well as helping to understand if people/patients are managing their condition better and the impact on their quality of life.

A decision maker may be interested in a wide range of measures to determine whether an intervention was effective. For example, whether it caused harm, introduced inequality, had effects beyond health (social care, education, justice, employment, etc). They may

want to differentiate between individual and population measures. It may be important to understand how the intervention works.

True outcomes may be long term and it could be necessary to measure proxies that are impacted more rapidly: for example, high blood pressure as a proxy for later heart disease. This requires evidence of the downstream impact of the proxy on the real outcome of interest. To model this, it may be necessary for the investigator to narrow their question down to a very specific active ingredient. This is ultimately reductionist and could lead to a focus on very specific measures, missing the broader interactions. It is important to be aware of these limitations.

It is necessary to identify the active ingredients and actors in a complex intervention and to include them in the evaluation. It is also important to think about whether these active ingredients have interactions that the evaluation might fail to capture. This requires talking to the people delivering the interventions, who are likely to know where the interactions occur.

Quantitative economic methods can be used to compare two or more interventions in relation to their cost and consequences. Commonly used methods include cost effectiveness, cost-utility and cost-benefit analysis. There are methods to compare and quantify the value of different outcomes, but they involve trade-offs.

When evaluating Learning Health Systems that change over time, it should be noted that the most appropriate outcome measures may also evolve, as may the available data. It could therefore be appropriate to alter or update the evaluation methodology. An evaluation can also help explain how and why an intervention succeeded or failed. A logic model can be a useful tool for planning the evaluation strategy, representing a hypothesis or "theory of change" on how an intervention works. This can help prioritise and structure data collection and analysis to explore the main aspects of an intervention, as well as the relationships between these aspects. It is important to include a wide range of factors. The NASSS Framework outlined above can help develop a comprehensive analysis of factors across all seven of its domains.

Given the challenges we have outlined, an organisation may well need external support from a university, consultancy, government or other organisation to complete an evaluation. Common reasons to bring in an external organisation include:

- To provide extra capacity
- To provide expertise that the organisation does not possess in-house
- To provide an independent perspective and reduce conflicts of interest

Maturity

In addition to evaluating an outcome, it can also be helpful to assess the maturity of the processes within a Learning Health System. Maturity refers to the degree to which a process is able to achieve a specific objective in a predictable way [181].

The maturity of the underlaying technical infrastructure within a healthcare provider can be assessed using a maturity model, such as those developed by Healthcare Information and Management Systems Society (HIMSS) [182]:

- **EMRAM:** The Electronic Medical Record Adoption Model
- **AMAM:** The Analytics Maturity Adoption Model
- **CCMM:** The Continuity of Care Model
- **INFRAM:** The Infrastructure Adoption Model

These can provide a baseline assessment of an organisation's infrastructure, a roadmap for prioritising improvements, a measure of improvement and a community of peers. While these are all necessary, they are not enough to determine the maturity of a Learning Health System. It is not just a piece of technology, whose speed or capacity can be easily quantified. It is a complex, constantly changing, sociotechnical system, intended to meet a unique and evolving set of needs. It is therefore important to consider how well a Learning Health System is aligned with the needs and resources of the stakeholders implementing it.

Lannon et al. [181] propose a process maturity assessment tool aimed specifically at Learning Health Systems. The tool takes the form of a capability maturity grid covering six domains:

- **Systems of Leadership:** Purpose, understanding the system, measuring the system, planning for improvement etc
- **Governance and Management:** Policies, processes, controls, oversight, norms etc
- **Quality Improvement:** Systematic and continuous actions towards measurable improvements in outcomes
- **Community Building and Engagement:** Structures and processes to enable all stakeholders to become involved
- **Data and Analytics:** Collecting, validating, organising and standardising data relevant to the system's purpose
- **Research:** Generating knowledge through a range of research methods.

Conclusion

Many organisations are setting a strategic goal of becoming or supporting a Learning Health System. However, Learning Health Systems are complex and constantly changing entities. No two are the same; they can't be lifted and shifted from one environment to another.

That being said, a great deal can be learnt from successful and unsuccessful case studies. While much has been published on Learning Health Systems, the sector to this point has lacked a "go to" repository, containing tools, frameworks and models that might be helpful to those developing a Learning Health System.

This report provides an early step towards such a resource. As well as signposting useful resources, it presents a framework for considering important topics in developing a Learning Health System and an introduction to each of these topics.

No single report can cover this constantly changing field. The Learning Healthcare Project will therefore collaborate with colleagues in the global Learning Health Community, to develop this work into a live online toolkit that can be supplemented by anyone with relevant experience. This will embody the learning philosophy.

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Glossary

Analytics (Data): The process of examining raw datasets to derive new meaning/information about the dataset

API: Application Program Interface, how different software components interact

BCTs: Behaviour Change Techniques

BCW: Behaviour Change Wheel

Behavioural Economics: The use of psychological insights to interpret economic decision making

Big Data: Large datasets that require complex processing, often analysed computationally to reveal patterns or trends

CDRN: Clinical Data Research Network (US)

CDSS: Clinical Decision Support System

CER: Comparative Effectiveness Research

Claims Data: Recorded for health insurance payment systems

Cognitive dissonance: The feeling of unease created by holding two or more contradictory beliefs

Commissioner (Health): Individuals or bodies responsible for planning and funding healthcare delivery

Co-morbidities: Medical conditions occurring together in the same individual

Data Mining: The process of examining datasets to derive new meaning/information

EHR: Electronic Health Record

Evidence Based Practice: The application of best available research findings to clinical practice

False Negative: A result that wrongly indicates a condition or attribute to be absent

False Positive: A result that wrongly indicates a condition or attribute to be present

FDA: Food and Drug Administration (US)

Fractal: An object or concept that appears the same at different scales

GP: General Practice/General Practitioner. Family Doctor.

HIPAA: Health Information Portability and Accountability Act (US)

HES: Hospital Episode Statistics Published data from NHS Digital containing details of all admissions to NHS hospitals in England, derived from Secondary Uses Services data

IG: Information Governance

Implementation Science: The examination of how research and evidence is integrated into healthcare

Informatics: Computer information science, processing data and engineering of information systems

Informed Consent: Permission given with a full understanding of issue

Interoperability: The ability of different systems to communicate

IoM: Institute of Medicine (US)

LHS: Learning Healthcare System

Longitudinal Data: Data collected over a period of time

MDT: Multi-Disciplinary Team

Meta-Analysis: Statistical methods for combining results of multiple studies

Metadata: Data describing other data or the container of other data

N of 1 Trial/Experiment: A trial in which only one individual is involved

Natural Language Processing: The ability of a computer program to interpret human language, eg within free text

NHS: National Health Service (UK)

NICE: National Institute for Health and Care Excellence (England)

Observational Research: A research technique in which participants are not randomised or pre-assigned to an exposure

Open Source Software: Where the original source code is freely available for use and modification

Organisational Theory: The study of organisations and their structures, relationships and interactions

Patient Administrative System: Information systems used to record data about care provided to patients

Payor: A company or agency that pays for health services

PCORI: Patient Centered Outcomes Research Institute (US)

PDF: A file format for capturing and sending digital documents

Polypharmacy: The use of more than one drug in an individual

Primary Care: Healthcare provided in the community as a first point of contact with the healthcare

system, eg a GP

PROM: Patient Reported Outcome Measure

Provider (Health): An organisation in the business of preventing or treating illness, eg a hospital group

RCT: Randomised Controlled Trial

Read Codes: A clinical terminology used in General Practice in the UK and elsewhere

Routine Data: Any data that is collected as part of the normal provision of care

Safe-to-fail: An experiment that can be allowed to fail without catastrophic consequences

Secondary Care: Healthcare provided by a specialist in a hospital or community setting, eg cardiology

Secondary Use: The use of data for purposes other than those for which it was originally collected, such as care delivery data being used for research

Secondary Uses Services: A repository of healthcare data in England

Semantics (Data): The meaning of data

Standards (Data): The rules used for describing, recording and transmitting data

Telemedicine: Remote diagnosis and treatment enabled by telecommunication systems

Translational research: The process of applying knowledge generated by research to real-world problem

XML: Extensible Markup Language

References

[1]   T. Foley and F. Fairmichael, "The Potential of Learning Health Care Systems," The Learning Healthcare Project, 2015. [Online]. Available: **https://learninghealthcareproject.org/wp-content/uploads/2015/11/LHS_Report_2015.pdf**

[2]   C. P. Friedman *et al.*, "The science of learning health systems: foundations for a new journal," *Learning Health Systems,* vol. 1, no. 1, 2017. [Online]. Available: **https://onlinelibrary.wiley.com/doi/full/10.1002/lrh2.10020**.

[3]   D. A. Garwin. (1993) Building a Learning Organization. *Harvard Business Review*. 73-91. Available: **https://hbr.org/1993/07/building-a-learning-organization**

[4]   J. M. McGinnis, D. Aisner, and L. O. Olsen, "The Learning Healthcare System," National Academies Press, Washington (DC), USA, 2007. [Online]. Available: **https://www.nap.edu/catalog/11903/the-learning-healthcare-system-workshop-summary**

[5]   J. M. McGinnis, L. Stuckhardt, R. Saunders, and M. Smith, *Best care at lower cost: the path to continuously learning health care in America*. National Academies Press, 2013.

[6]   J. Enticott, A. Johnson, and H. Teede, "Learning health systems using data to drive healthcare improvement and impact: a systematic review," *BMC health services research,* vol. 21, no. 1, pp. 1-16, 2021. [Online]. Available: **https://bmchealthservres.biomedcentral.com/articles/10.1186/s12913-021-06215-8#Tab3**.

[7]   T. Foley and F. Fairmichael. "Professor Charles Friedman Interview." The Learning Healthcare Project. **http://www.learninghealthcareproject.org/section/evidence/25/50/professor-charles-friedman-%20interview** (accessed.

[8]   University of Michigan. "Revolutionizing Learning, Transforming Health." University of Michigan. **https://medicine.umich.edu/dept/learning-health-sciences** (accessed.

[9]   MCBK. "Annual MCBK Public Meeting." MCBK. **https://mobilizecbk.med.umich.edu/news-events/annual-meetings** (accessed.

[10]   MCBK. "Featured Events." Mobilizing Computable Biomedical Knowledge (MCBK). **https://mobilizecbk.med.umich.edu/news-events** (accessed.

[11]   C. Friedman. "Learning Health Systems." **https://onlinelibrary.wiley.com/journal/23796146** (accessed.

[12]   T. Foley. "LHS Value." The Learning Healthcare Project. **http://www.learninghealthcareproject.org/section/implications/value** (accessed.

[13]   T. Foley. "Positive Deviance." The Learning Healthcare Project. **http://www.learninghealthcareproject.org/section/use-cases/positive-deviance** (accessed.

[14] T. Foley. "Comparative Effectiveness Research." The Learning Healthcare Project. http://www.learninghealthcareproject.org/section/use-cases/comparative-effectiveness-research (accessed.

[15] T. Foley. "Surveillance." The Learning Healthcare Project. http://www.learninghealthcareproject.org/section/use-cases/surveillance (accessed.

[16] T. Shaw *et al.*, "Attitudes of health professionals to using routinely collected clinical data for performance feedback and personalised professional development," *Medical Journal of Australia,* vol. 210, no. S6, pp. S17-S21, 2019, doi: https://doi.org/10.5694/mja2.50022.

[17] M. M. Helms and J. Nixon, "Exploring SWOT analysis–where are we now? A review of academic research from the last decade," *Journal of Strategy and Management,* vol. 3, no. 3, pp. 215–251, 2010. [Online]. Available: https://www.emerald.com/insight/content/doi/10.1108/17554251011064837/full/html.

[18] (2020). *The green book: Central government guidance on appraisal and evaluation*. [Online] Available: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/938046/The_Green_Book_2020.pdf

[19] Y. Zurynski *et al.*, "Mapping the learning health system: A scoping review of current evidence," Australian Institute of Health Innovation, Sydney, Australia, 2020. [Online]. Available: https://research-management.mq.edu.au/ws/portalfiles/portal/134364432/Publisher_version_open_access_.pdf

[20] HDR UK. "Better Care." Health Data Research UK (HDRUK). https://www.hdruk.ac.uk/how-we-use-health-data/better-care/ (accessed.

[21] J. Farenden and I. Singh, "Local Health and Care Record Exemplars: A summary," NHS England, 2018. [Online]. Available: https://www.england.nhs.uk/wp-content/uploads/2018/05/local-health-and-care-record-exemplars-summary.pdf

[22] Learning Health System for CYP. "Learning Health System for CYP." Children and Young People's Health Partnership. https://www.cyphp.org/cyp-professionals/model-of-care/learning-health-system-for-cyp (accessed.

[23] T. Foley and F. Fairmichael. "Geisinger Health System Site Visit." The Learning Healthcare Project. http://www.learninghealthcareproject.org/section/evidence/34/63/site-visit-to-geisinger-health-system (accessed.

[24] S. Abimbola *et al.*, "The NASSS framework for ex post theorisation of technology-supported change in healthcare: worked example of the TORPEDO programme," *BMC medicine,* vol. 17, no. 1, pp. 1-17, 2019. [Online]. Available: https://bmcmedicine.biomedcentral.com/articles/10.1186/s12916-019-1463-x.

[25] ImproveCareNow. "ImproveCareNow " **https://www.improvecarenow.org/** (accessed.

[26] Mayo Clinic. "Platform revolution: Curing more people, reaching more lives, anytime, anywhere." Mayo Clinic. **https://newsnetwork.mayoclinic.org/discussion/platform-revolution-curing-more-people-reaching-more-lives-anytime-anywhere/** (accessed.

[27] MCBK. "Mobilizing Computable Biomedical Knowledge community " **https://mobilizecbk.med.umich.edu/** (accessed.

[28] R. Bohmer, J. Shand, D. Allwood, A. Wragg, and J. Mountford. "Learning Systems: Managing Uncertainty in the New Normal of Covid-19." NEJM Catalyst Innovations in Care delivery. **https://catalyst.nejm.org/doi/pdf/10.1056/CAT.20.0318** (accessed.

[29] Open Lab. "About Open Lab " **https://openlab.ncl.ac.uk/** (accessed.

[30] L. I. Horwitz, M. Kuznetsova, and S. A. Jones, "Creating a Learning Health System through Rapid-Cycle, Randomized Testing," *The new england journal of medicine,* vol. 381, no. 12, pp. 1175-1179, 2019. [Online]. Available: **http://sumry.s3.amazonaws.com/uc/a5d6aec2707df51d9ba9c671a1610f05_SoundingboardNEJM.pdf**.

[31] NICE. "NICE Connect." The National Institute for Health and Care Excellence (NICE) **https://www.nice.org.uk/about/who-we-are/nice-connect** (accessed.

[32] NHS Digital. "Improving our Data Processing." NHS Digital. **https://digital.nhs.uk/data-and-information/data-insights-and-statistics/improving-our-data-processing-services** (accessed 2021).

[33] OpenClinical. "OpenClinical." OpenClinical. **http://www.openclinical.net** (accessed.

[34] PatientsLikeMe. "About PatientsLikeME." **https://www.patientslikeme.com/** (accessed.

[35] A. Wales, "Decision support for Scotland's health and social care: learning from an outcomes-focused approach," BMJ Health & Care Informatics, 2020. [Online]. Available: **https://informatics.bmj.com/content/27/2/e100124**

[36] Medics Academy. "Ann Wales Presentation - UK Workshop on Mobilising Computable Biomedical Knowledge (MCBK)." Medics Academy. **https://www.youtube.com/watch?v=vWEKM2UYBzg** (accessed.

[37] N. Mastellos *et al.*, "Feasibility and acceptability of TRANSFoRm to improve clinical trial recruitment in primary care," *Family Practice,* vol. 33, no. 2, pp. 186–191, 2016. [Online]. Available: **https://academic.oup.com/fampra/article/33/2/186/2404251?login=true**.

[38] A. J. Flynn, C. P. Friedman, P. Boisvert, Z. Landis-Lewis, and C. Lagoze, "The Knowledge Object Reference Ontology (KORO): A

formalism to support management and sharing of computable biomedical knowledge for learning health systems," Wiley Online Library, 2018. [Online]. Available: **https://pubmed.ncbi.nlm.nih.gov/31245583/**

[39] G. Bellinger, D. Castro, and A. Mills. "Systems Thinking." **https://www.systems-thinking.org/dikw/dikw.htm** (accessed.

[40] T. Foley and F. Fairmichael. "Dr Paul Wallace Interview." The Learning Healthcare Project. **http://www.learninghealthcareproject.org/section/evidence/24/66/dr-paul-wallace-interview** (accessed.

[41] T. Foley. "Platforms in LHS Workshop." The Learning Healthcare Project. **www.learninghealthcareproject.org** (accessed.

[42] M. Inada-Kim and T. Donnelly. "Tech supported remote monitoring for COVID-19." NHS England. **https://www.nhsx.nhs.uk/blogs/tech-supported-remote-monitoring-covid-19/** (accessed.

[43] J. Z. Muller, *The tyranny of metrics*. New Jersey, USA: Princeton University Press, 2018.

[44] V. d. Merwe *et al.*, "Making sense of complexity: Using sensemaker as a research tool," *MDPI,* vol. 7, no. 2, p. 25, 2019. [Online]. Available: **https://www.mdpi.com/2079-8954/7/2/25**.

[45] S. Xu, T. Rogers, E. Fairweather, A. Glenn, J. Curran, and V. Curcin, "Application of Data Provenance in Healthcare Analytics Software:

Information Visualisation of User Activities," *AMIA Summits on Translational Science Proceedings,* pp. 263–272, 2018. [Online]. Available: **https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5961786/**.

[46] NHS Digital. "Data, insights, and statistics." NHS Digital. **https://digital.nhs.uk/data-and-information/data-insights-and-statistics** (accessed.

[47] J. S. Brown, J. H. Holmes, K. Shah, K. Hall, R. Lazarus, and R. Platt, "Distributed health data networks: a practical and preferred approach to multi-institutional evaluations of comparative effectiveness, safety, and quality of care," *Medical Care,* pp. 45-51, 2010. [Online]. Available: **https://pubmed.ncbi.nlm.nih.gov/20473204/**.

[48] Sentinel System. "Sentinel System." **https://www.sentinelinitiative.org/about/how-sentinel-gets-its-data** (accessed 2021).

[49] T. Foley and F. Fairmichael. "Dr Jeff Brown Interview." The Learning Healthcare Project. **http://www.learninghealthcareproject.org/publication/5/60/dr-jeff-brown-interview** (accessed.

[50] NHS Digital. "Data Access Environment (DAE)." NHS Digital. **https://digital.nhs.uk/services/data-access-environment-dae** (accessed.

[51] NHSX. "Information governance (IG)." NHSX. **https://www.nhsx.nhs.uk/information-governance/** (accessed.

[52] UK Gov. "Data Protection Act " UK Public General Acts.

https://www.legislation.gov.uk/ukpga/1998/29 (accessed.

[53] ICO. "Data protection and coronavirus information hub." Information Commissioners Office. https://ico.org.uk/ (accessed.

[54] CDC. "Health Information Privacy." Center for Disease Control. https://www.cdc.gov/phlp/publications/topic/healthinformationprivacy.html (accessed.

[55] D. B. Rubin, "On the limitations of comparative effectiveness research," *Statistics in Medicine,* vol. 29, no. 19, pp. 1991-1995, 2010. [Online]. Available: https://onlinelibrary.wiley.com/doi/abs/10.1002/sim.3960.

[56] ONC, "Connecting Health and Care for the Nation: A 10-Year Vision to Achieve an Interoperable Health IT Infrastructure," The Office of the National Coordinator for Health Information Technolody, 2014. [Online]. Available: https://www.healthit.gov/sites/default/files/ONC10yearInteroperabilityConceptPaper.pdf

[57] N. Sebire, C. Cake, and A. Morris, "HDR UK supporting mobilising computable biomedical knowledge in the UK," *BMJ Health & Care Informatics,* vol. 27, no. 2, 2020. [Online]. Available: https://informatics.bmj.com/content/27/2/e100122.

[58] T. Foley and F. Fairmichael. "IBM Site Visit." The Learning Healthcare Project. http://www.learninghealthcareproject.org/publication/6/84/ibm-watson-site-visit (accessed.

[59] T. Foley and F. Fairmichael. "Improving the Underlying Data Focus Group." The Learning Healthcare Project. http://www.learninghealthcareproject.org/section/evidence/12/69/improving-the-underlying-data-focus- (accessed.

[60] NHS Digital. "Data Standards Team." NHS Digital. https://digital.nhs.uk/data-and-information/data-insights-and-statistics/data-standards-team (accessed.

[61] NHS Digital. "SNOMED CT." NHS Digital. https://digital.nhs.uk/services/terminology-and-classifications/snomed-ct (accessed.

[62] NHS Business Services Authority. "Dictionary of medicines and devices (dm+d)." NHS Business Services Authority. https://www.nhsbsa.nhs.uk/pharmacies-gp-practices-and-appliance-contractors/dictionary-medicines-and-devices-dmd (accessed.

[63] NHS. "NHS Classifications ICD-10." NHS Digital. https://isd.digital.nhs.uk/trud3/user/guest/group/0/pack/28 (accessed.

[64] NHS. "NHS Classifications ICD-10 and OPCS-4 eVersion." NHS Digital. https://isd.digital.nhs.uk/trud3/user/guest/group/0/pack/37 (accessed.

[65] NHS Digital. "Data Provision Notices (DPNs)." NHS Digital. https://digital.nhs.uk/about-nhs-digital/corporate-information-and-documents/directions-and-data-provision-notices/data-provision-notices-dpns (accessed.

[66] T. Foley. "Mr Kingsley Manning Interview." The Learning Healthcare Project. http://www.learninghealthcareproject.org/publication/5/103/mr-kingsley-manning-interview (accessed.

[67] Health IT. "ONC's Cures Act Final Rule." Health IT. https://www.healthit.gov/curesrule/ (accessed.

[68] C. Jason. (2020) Epic Leads Almost 60 Health Systems Against Interoperability Rule. *EHR Intelligence*. Available: https://ehrintelligence.com/news/epic-leads-almost-60-health-systems-against-interoperability-rule

[69] M. Savage, A. Neinstein, and J. Adler-Milstein. (2020) Measure The Impact Of The ONC's New Interoperability Rules Now. *Health Affairs*. Available: https://www.healthaffairs.org/do/10.1377/hblog20200701.58142/full/

[70] R. F. Gunst and R. L. Mason, "Fractional factorial design," *Wiley Interdisciplinary Reviews: Computational Statistics,* vol. 1, no. 2, pp. 234-244, 2009. [Online]. Available: https://onlinelibrary.wiley.com/doi/abs/10.1002/wics.27.

[71] P. Pallmann *et al.*, "Adaptive designs in clinical trials: why use them, and how to run and report them," *BMC medicine,* vol. 16, no. 1, pp. 1-15, 2018. [Online]. Available: https://pubmed.ncbi.nlm.nih.gov/29490655/.

[72] S. Ellenberg, "The Stepped-Wedge Clinical Trial: Evaluation by Rolling Deployment," *Jama,* vol. 319, no. 6, pp. 607-608, 2018. [Online]. Available: https://jamanetwork.com/journals/jama/article-abstract/2672617.

[73] R. B. Penfold and F. Zhang, "Use of interrupted time series analysis in evaluating health care quality improvements," *Academic pediatrics,* vol. 13, no. 6, pp. S38-S44, 2013. [Online]. Available: https://www.sciencedirect.com/science/article/abs/pii/S1876285913002106.

[74] S. Devkaran and P. N. O'Farrell, "The impact of hospital accreditation on quality measures: an interrupted time series analysis.," *BMC health services research,* vol. 15, no. 1, 2015. [Online]. Available: https://bmchealthservres.biomedcentral.com/articles/10.1186/s12913-015-0784-5.

[75] S. Desai and J. M. McWilliams, "Consequences of the 340B drug pricing program," *New England Journal of Medicine,* vol. 378, no. 6, pp. 539-548, 2018. [Online]. Available: https://www.nejm.org/doi/full/10.1056/nejmsa1706475.

[76] L. Bernal, J. S. Cummins, and A. Gasparrini, "The use of controls in interrupted time series studies of public health interventions." International journal of epidemiology," *International journal of epidemiology,* vol. 47, no. 6, pp. 2082-2093, 2018. [Online]. Available: https://academic.oup.com/ije/article/47/6/2082/5049576?login=true.

[77] M. ML and B. A., "Regression Discontinuity Design," *JAMA,* no. 4, pp. 381-382., 2020. [Online]. Available: **https://jamanetwork.com/journals/jama/article-abstract/2768094**.

[78] T. N. Beran and C. Violato, "Structural equation modeling in medical research: a primer," *BMC research notes,* vol. 3, no. 1, pp. 1-10, 2010. [Online]. Available: **https://bmcresnotes.biomedcentral.com/articles/10.1186/1756-0500-3-267**.

[79] P. O. Owili, M. A. Muga, B. R. Mendez, and B. Chen, "Quality of maternity care and its determinants along the continuum in Kenya: A structural equation modeling analysis," *PloS one,* vol. 12, no. 5, p. e0177756, 2017. [Online]. Available: **https://pubmed.ncbi.nlm.nih.gov/28520771/**.

[80] J. D. Angrist, G. W. Imbens, and D. B. Rubin, "Identification of causal effects using instrumental variables," *Journal of the American statistical Association,* vol. 91, no. 434, pp. 444-455, 1996. [Online]. Available: **https://www.tandfonline.com/doi/abs/10.1080/01621459.1996.10476902?src=recsys**.

[81] S. M. Iacus, G. King, and G. Porro, "Causal inference without balance checking: Coarsened exact matching," *Political analysis,* pp. 1-24, 2012. [Online]. Available: **https://www.jstor.org/stable/41403736**.

[82] A. Pfadt and D. J. Wheeler, "Using statistical process control to make data-based clinical decisions. ," *Journal of applied behavior analysis,* vol. 28, no. 3, pp. 349-370, 1995. [Online]. Available: **https://onlinelibrary.wiley.com/doi/10.1901/jaba.1995.28-349**.

[83] B. E. Bejnordi *et al.*, "Diagnostic Assessment of Deep Learning Algorithms for Detection of Lymph Node Metastases in Women With Breast Cancer," *Jama,* vol. 318, no. 22, pp. 2199-2210, 2017. [Online]. Available: **https://jamanetwork.com/journals/jama/fullarticle/2665774**.

[84] C. W. Seymour *et al.*, "Derivation, Validation, and Potential Treatment Implications of Novel Clinical Phenotypes for Sepsis. ," *Jama,* vol. 321, no. 20, pp. 2003-2017, 2019. [Online]. Available: **https://jamanetwork.com/journals/jama/article-abstract/2733996**.

[85] M. Pavlou, Ambler, S. G., S.R., O. Guttmann, P. Elliott, M. King, and R. Z. Omar, "How to develop a more accurate risk prediction model when there are few events," *Bmj,* no. 351, p. p.h3868., 2015. [Online]. Available: **https://www.bmj.com/content/351/bmj.h3868.full**.

[86] R. Miotto, B. A. K. Li Li, and J. T. Dudley, "Deep patient: an unsupervised representation to predict the future of patients from the electronic health records," *Scientific reports,* vol. 6, no. 1, pp. 1-10, 2016. [Online]. Available: **https://www.nature.com/articles/srep26094**.

[87] G. Liang, W. Fan, H. Luo, and X. Zhu, "The emerging roles of artificial intelligence in cancer drug development and precision

therapy " *Biomedicine & Pharmacotherapy,* no. 128, p. 110255, 2020. [Online]. Available: **https://www.sciencedirect.com/science/article/pii/S0753332220304479**.

[88] A. Z. Woldaregay *et al.*, "Data-driven modeling and prediction of blood glucose dynamics: Machine learning applications in type 1 diabetes. ," *Artificial intelligence in medicine,* no. 98, pp. 109-134, 2019. [Online]. Available: **https://www.sciencedirect.com/science/article/pii/S0933365717306218**.

[89] C. A. Longhurst, R. A. Harrington, and N. H. Shah, "A 'green button'for using aggregate patient data at the point of care," *Health affairs,* vol. 33, no. 7, pp. 1229-1235, 2014. [Online]. Available: **https://pubmed.ncbi.nlm.nih.gov/25006150/**.

[90] GL Shostack, "Designing Services that Deliver," *Harvard Business Review,* 1984. [Online]. Available: **https://hbr.org/1984/01/designing-services-that-deliver**.

[91] L. K. Hall, B. F. Kunz, E. V. Davis, R. I. Dawson, and R. S. Power, "The cancer experience map: an approach to including the patient voice in supportive care solutions," *Journal of medical Internet research,* vol. 17, no. 5, 2015. [Online]. Available: **https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4468569/**.

[92] M. Rother and J. Shook, "Learning to See: value-stream mapping to create value and eliminate muda," *Brookline, Massachusetts: Lean Enterprise Institute,* 2009. [Online]. Available:

https://www.lean.org/Bookstore/ProductDetails.cfm?SelectedProductId=9.

[93] E. H. Bradley, L. A. Curry, and K. J. Devers, "Qualitative data analysis for health services research: developing taxonomy, themes, and theory," *Health services research,* vol. 42, no. 4, pp. 1758-1772, 2007. [Online]. Available: **https://pubmed.ncbi.nlm.nih.gov/17286625/**.

[94] L. Wilson and T. Lowe, *The Learning Communities: Collective Improvement in Complex Environments*. Newcastle Upon Tyne, UK: Newcastle University, 2019.

[95] L. Ferguson, M. Dibble, M. Williams, and J. Ferraro, "Operationalizing a learning community for a learning health system: a practical guide," 2020. [Online]. Available: **https://deepblue.lib.umich.edu/bitstream/handle/2027.42/163515/LearningCommunityPracticalGuide_FINAL.pdf?sequence=1&isAllowed=y**

[96] F. o. C. Informatics. "Nick Booth Introduction- UK Workshop on Mobilising Computable Biomedical Knowledge (MCBK)." Faculty of Clinical Informatics. **https://www.youtube.com/playlist?list=PLn7CfTWFFBSzTZtK4bTpo7Q2kBLjr0RUM** (accessed.

[97] J. Wyatt and P. Scott, "Computable knowledge is the enemy of disease " *BMJ Health Care Informatics,* vol. 27, no. 2, 2020. [Online]. Available: **https://informatics.bmj.com/content/27/2/e100200**.

[98] K. Walsh and C. Wroe, "Mobilising computable biomedical

knowledge: challenges for clinical decision support from a medical knowledge provider," *BMJ Health Care Informatics,* vol. 27, no. 2, 2020. [Online]. Available: **https://informatics.bmj.com/content/27/2/e100121**.

[99]   D. Wong and N. Peek, "Does not compute: challenges and solutions in managing computable biomedical knowledge," *BMJ Health Care Informatics,* vol. 27, no. 2, 2020. [Online]. Available: **https://informatics.bmj.com/content/27/2/e100123**.

[100] Faculty of Clinical Informatics. "David Wong Talk - UK Workshop on Mobilising Computable Biomedical Knowledge (MCBK)." Mobilising Computable Biomedical Knowledge (MCBK). **https://www.youtube.com/watch?v=AZCl7xzXkKU&list=PLn7CfTWFFBSzTZtK4bTpo7Q2kBLjr0RUM&index=9** (accessed.

[101] K. D. Mandl and I. S. Kohane, "No Small Change for the Health Information Economy," *The New England Journal of Medicine,* vol. 360, pp. 1278-1281, 2009. [Online]. Available: **https://europepmc.org/article/med/19321867**.

[102] L. Ohno-Machado *et al.*, "The guideline interchange format: a model for representing guidelines," *Journal of the American Medical Informatics Association,* vol. 5, no. 4, pp. 357-372., 1998. [Online]. Available: **https://pubmed.ncbi.nlm.nih.gov/9670133/**.

[103] HL7 & Boston Children's Hospital. "Home Page - CDS Hooks." HL7 & Boston Children's Hospital. **https://cds-hooks.org/** (accessed.

[104] OpenEHR Foundation. "OpenEHR." openEHR Foundation. **https://www.openehr.org/** (accessed.

[105] NHS Digital. "DCB0129." **https://digital.nhs.uk/data-and-information/information-standards/information-standards-and-data-collections-including-extractions/publications-and-notifications/standards-and-collections/dcb0129-clinical-risk-management-its-application-in-the-manufacture-of-health-it-systems** (accessed.

[106] NHS Digital. "DCP0160." NHS Digital. **https://digital.nhs.uk/data-and-information/information-standards/information-standards-and-data-collections-including-extractions/publications-and-notifications/standards-and-collections/dcb0160-clinical-risk-management-its-application-in-the-deployment-and-use-of-health-it-systems** (accessed.

[107] UK Gov. "Health and Social Care Act." Legislation UK. **https://www.legislation.gov.uk/ukpga/2012/7/contents/enacted** (accessed.

[108] UK Gov. "Guidance Notified bodies for medical devices." Gov UK. **https://www.gov.uk/government/publications/notified-bodies-for-medical-devices/notified-bodies-for-medical-devices** (accessed.

[109] UK Gov. "Approved bodies for medical devices."

https://www.gov.uk/government/publications/approved-bodies-for-medical-devices (accessed.

[110] M. D. Wilkinson *et al.*, "The FAIR Guiding Principles for scientific data management and stewardship," *Scientific data,* vol. 3, no. 1, pp. 1-9, 2016. [Online]. Available: https://www.nature.com/articles/sdata201618.

[111] G. Iacobucci, "Computer error may have led to incorrect prescribing of statins to thousands of patients," *The BMJ,* 2016. [Online]. Available: https://www.bmj.com/content/353/bmj.i2742.

[112] Digital Health. "QRisk2 in TPP "fixed" but up to 270,000 patients affected." Digital Health. https://www.digitalhealth.net/2016/06/qrisk2-in-tpp-fixed-but-up-to-270000-patients-affected/ (accessed.

[113] L. McIntosh and C. Shaffer. "Technical Infrastructure." Mobilising Computable Biomedical Knowledge (MCBK). https://mobilizecbk.med.umich.edu/workgroups/technical-infrastructure (accessed.

[114] C. P. Friedman and A. J. Flynn, "Computable knowledge: An imperative for Learning Health Systems," *Learning Health Systems,* vol. 3, no. 4, 2019. [Online]. Available: https://onlinelibrary.wiley.com/doi/full/10.1002/lrh2.10203.

[115] J. Swan *et al.*, "Evidence in Management Decisions (EMD): advancing knowledge utilization in healthcare management," 2012. [Online]. Available: https://www.bl.uk/collection-items/evidence-in-management-decisions-emd-advancing-knowledge-utilization-in-healthcare-management-executive-summary#.

[116] T. Foley. "Professor Brendan Delaney Interview." The Learning Healthcare Project. http://www.learninghealthcareproject.org/publication/5/104/the-transform-project (accessed.

[117] A. Hern. "Royal Free breached UK data law in 1.6m patient deal with Google's DeepMind This article is more than 3 yea." The Guardian. https://www.theguardian.com/technology/2017/jul/03/google-deepmind-16m-patient-royal-free-deal-data-protection-act (accessed.

[118] J. A. Bernstein, C. Friedman, P. Jacobson, and J. C. Rubin, "Ensuring public health's future in a national-scale learning health system," *American Journal of Preventive Medicine,* vol. 48, no. 4, pp. 480-487, 2015. [Online]. Available: https://www.sciencedirect.com/science/article/abs/pii/S0749379714006710.

[119] C. P. Friedman, A. K. Wong, and D. Blumenthal, "Achieving a nationwide learning health system," *Science translational medicine,* vol. 2, no. 57, pp. 29-57, 2010. [Online]. Available: https://pubmed.ncbi.nlm.nih.gov/21068440/.

[120] National Academy of Medicine. "The Learning Health System Series." National Academy of Medicine. https://nam.edu/programs/value-science-driven-health-

care/learning-health-system-series/ (accessed.

[121] J. Braithwaite, K. C. J. C. Long, L. A. Ellis, and J. Herkes, "When complexity science meets implementation science: a theoretical and empirical analysis of systems change " *BMC medicine,* vol. 16, no. 1, p. 63, 2018. [Online]. Available: **https://bmcmedicine.biomedcentral.com/articles/10.1186/s12916-018-1057-z**.

[122] J. Braithwaite, P. Glasziou, and J. Westbrook, "The three numbers you need to know about healthcare: the 60-30-10 Challenge," *BMC medicine,* vol. 18, pp. 1-8, 2020. [Online]. Available: **https://bmcmedicine.biomedcentral.com/articles/10.1186/s12916-020-01563-4**.

[123] J. Braithwaite, "Changing how we think about healthcare improvement," *BMJ,* vol. 361, 2018. [Online]. Available: **https://www.bmj.com/content/361/bmj.k2014**.

[124] D. J. Snowden and M. E. Boone. "A Leader's Framework for Decision Making." Harvard Business Review. **https://hbr.org/2007/11/a-leaders-framework-for-decision-making** (accessed.

[125] D. Snowden, "The Cynefin framework," *YouTube video,* vol. 8, p. 38, 2010. [Online]. Available: **https://www.youtube.com/watch?v=N7oz366X0-8**.

[126] D. Snowden. "7 principles of intervention in complex systems." Cognitive Edge. **https://www.cognitive-edge.com/7-principles-of-intervention-in-complex-systems/** (accessed.

[127] T. Greenhalgh *et al.*, "Beyond adoption: a new framework for theorizing and evaluating nonadoption, abandonment, and challenges to the scale-up, spread, and sustainability of health and care technologies," *Journal of medical Internet research,* vol. 19, no. 11, p. e367, 2017. [Online]. Available: **https://www.jmir.org/2017/11/e367/**.

[128] A. D. Knight, T. Lowe, M. Brossard, and J. Wilson. "A Whole New World: Funding and Commissioning in Complexity." Human Learning Systems. **https://collaboratecic.com/a-whole-new-world-funding-and-commissioning-in-complexity-12b6bdc2abd8** (accessed.

[129] T. Foley. "Nonadoption, Abandonment, Scale-up, Spread and Sustainability in LHS Workshop." The Learning Healthcare Project. **www.learninghealthcareproject.org** (accessed.

[130] L. Hurst *et al.*, "Defining Value-based Healthcare in the NHS," 2019. [Online]. Available: **http://www.cebm.net/wp-content/uploads/2019/04/Defining-Value-based-healthcare-in-the-NHS-Final4-1.pdf**.

[131] Parliament UK. "The role of the Department for Digital, Culture, Media and Sport." Parliament UK. **https://publications.parliament.uk/pa/cm5801/cmselect/cmcumeds/291/29108.htm** (accessed.

[132] T. Greenhalgh *et al.*, "The NASSS-CAT Tools for Understanding,

Guiding, Monitoring, and Researching Technology Implementation Projects in Health and Social Care: Protocol for an Evaluation Study in Real-World Settings," *JMIR research protocols,* vol. 9, no. 5, p. e16861, 2020. [Online]. Available: **https://www.researchprotocols.org/2020/5/e16861/**.

[133] H. J. Lanham, L. K. Leykum, B. S. Taylor, C. J. McCannon, C. Lindberg, and R. T. Lester, "How complexity science can inform scale-up and spread in health care: understanding the role of self-organization in variation across local contexts," *Social Science & Medicine,* vol. 93, pp. 194-202, 2013. [Online]. Available: **https://pubmed.ncbi.nlm.nih.gov/22819737/**.

[134] T. Greenhalgh and C. Papoutsi, "Spreading and scaling up innovation and improvement," *Bmj 365,* p. 365, 2019. [Online]. Available: **https://www.bmj.com/content/bmj/365/bmj.l2068.full.pdf**.

[135] L. Freedman, *Strategy: A history*. Oxford University Press, 2015.

[136] H. Mintzberg, "Patterns in Strategy Formation," *International Studies of Management & Organization,* vol. 9, no. 3, pp. 67-86, 1979. [Online]. Available: **https://www.tandfonline.com/doi/abs/10.1080/00208825.1979.11656272**.

[137] J. Stewart, "The meaning of strategy in the public sector," *Australian Journal of Public Administration,* vol. 63, no. 4, pp. 16-21, 2004. [Online]. Available: **https://onlinelibrary.wiley.com/doi/10.1111/j.1467-8500.2004.00409.x**.

[138] A. G. Lafley and R. L. Martin, *Playing to Win: How Strategy Really Works*. Harvard Business Press, 2013.

[139] HNHS Providers. "Building A Digital Strategy." **https://nhsproviders.org/building-a-digital-strategy** (accessed.

[140] M. E. Porter, "What Is Strategy?," *Harvard Business Review,* vol. 74, no. 6, pp. 61-78, 1996. [Online]. Available: **https://hbr.org/1996/11/what-is-strategy**.

[141] R. P. Rumelt, "Good strategy/bad strategy: The difference and why it matters," *Emerald insight,* vol. 28, no. 8, 2012. [Online]. Available: **https://www.emerald.com/insight/content/doi/10.1108/sd.2012.05628haa.002/full/html**.

[142] R. K. Sondhi, *Total Strategy*. BMC Global Services Publications, 2008.

[143] StrategicCoffee. "How to design a Target Operating Model (TOM)." StrategicCoffee. **https://strategiccoffee.chriscfox.com/2012/12/how-to-design-target-operating-model-tom.html** (accessed.

[144] D. Snowden and R. Greenberg, *Cynefin - Weaving Sense-Making into the Fabric of Our World*. Cognitive Edge, 2020.

[145] M. T. Britto *et al.*, "Using a network organisational architecture to support the development of Learning Healthcare Systems," *BMJ quality & safety,* vol. 27, no. 11, pp. 937-946, 2018. [Online]. Available: **https://qualitysafety.bmj.com/content/27/11/937.abstract**.

[146] S. Scobie and S. Castle-Clarke. "What can the NHS learn from learning health systems?" Nuffieldtrust. https://www.nuffieldtrust.org.uk/files/2019-05/learning-health-systems-v3.pdf (accessed.

[147] R. Mannion and H. Davies, "Understanding organisational culture for healthcare quality improvement," *The BMJ,* vol. 363, p. k4907, 2018. [Online]. Available: https://www.bmj.com/content/363/bmj.k4907.

[148] T. Jung *et al.*, "Instruments for Exploring Organizational Culture: A Review of the Literature," *Public Administration Review,* vol. 69, no. 6, pp. 1087-1096, 2009. [Online]. Available: https://onlinelibrary.wiley.com/doi/abs/10.1111/j.1540-6210.2009.02066.x.

[149] B. Shirai. "Dave Snowden — How leaders change culture though small actions." Medium. https://medium.com/@brixen/dave-snowden-how-leaders-change-culture-though-small-actions-766cd2bf5128 (accessed.

[150] The King's Fund. "Improving NHS culture." The King's Fund. https://www.kingsfund.org.uk/projects/culture (accessed.

[151] R. M. Wachter. "Making IT Work: Harnessing the Power of Health Information Technology to Improve Care in England." GOV.UK. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/550866/Wachter_Review_Accessible.pdf (accessed 2021).

[152] T. Foley and J. Woollard, "The digital future of mental healthcare and its workforce," NHS UK, 2019. [Online]. Available: https://topol.hee.nhs.uk/downloads/digital-future-of-mental-healthcare-report/

[153] T. Foley and F. Fairmichael. "Workforce and Training Focus Group." The Learning Healthcare Project. http://www.learninghealthcareproject.org/section/evidence/12/71/training-and-workforce-focus-group (accessed.

[154] Faculty of Clinical Informatics. "Core Competency Framework for Clinical Informaticians." The Faculty of Clinical Informatics. https://facultyofclinicalinformatics.org.uk/core-competency-framework (accessed.

[155] J. L. Magnabosco, "Innovations in mental health services implementation: A report on state-level data from the US evidence-based practices project," *Implementation Science,* vol. 1, no. 1, p. 13, 2006. [Online]. Available: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1562440/.

[156] M. S. Bauer, L. Damschroder, H. Hagedorn, J. Smith, and A. M. Kilbourne, "An introduction to implementation science for the non-specialist," *BMC psychology,* vol. 3, no. 1, p. 32, 2015. [Online]. Available: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4573926/.

[157] N. Page, M. T. Baysari, and J. I. Westbrook, "A systematic review of the effectiveness of interruptive medication prescribing alerts in hospital CPOE systems to change prescriber behavior and improve patient safety," *International*

journal of medical informatics, vol. 105, pp. 22-30, 2017. [Online]. Available: **https://pubmed.ncbi.nlm.nih.gov/28750908/**.

[158] M. P. Eccles and B. S. Mittman, "Welcome to implementation science," *implementation science,* 2006. [Online]. Available: **https://implementationscience.biomedcentral.com/articles/10.1186/1748-5908-1-1**.

[159] S. Michie, M. M. V. Stralen, and R. West, "The behaviour change wheel: A new method for characterising and designing behaviour change interventions," *Implementation Science,* vol. 6, no. 1, p. 42, 2011. [Online]. Available: **https://implementationscience.biomedcentral.com/articles/10.1186/1748-5908-6-42**.

[160] K. E. Curtis, S. Lahir, and K. E. Brown, "Targeting Parents for Childhood Weight Management: Development of a Theory-Driven and User-Centered Healthy Eating App," *JMIR Mhealth Uhealth,* 2015. [Online]. Available: **https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4526951/**.

[161] T. Väänänen. "Design is the strategy." NHS Digital. **https://digital.nhs.uk/blog/design-matters/2020/design-is-the-strategy** (accessed.

[162] ISO. "Human-centred design for interactive systems." ISO/TC 159/SC 4 Ergonomics of human-system interaction. **https://www.iso.org/standard/77520.html** (accessed.

[163] NHS Digital. "Design principles." NHS Digital. **https://service-manual.nhs.uk/assets/nhs-design-principles.pdf** (accessed.

[164] S. Reponen. "Co-design Framework." **http://results.learning-layers.eu/** (accessed.

[165]   E. B.-N. Sanders and T. B. Eva Brandt, "A Framework for Organizing the Tools and Techniques of Participatory Design," in *Proceedings of the 11th biennial participatory design conference*, 2010, pp. 195-198. [Online]. Available: **https://dl.acm.org/doi/10.1145/1900441.1900476**. [Online]. Available: **https://dl.acm.org/doi/10.1145/1900441.1900476**

[166] M. Batalden *et al.*, "Coproduction of healthcare service," *BMJ Quality and Safety,* vol. 25, no. 7, 2015. [Online]. Available: **https://qualitysafety.bmj.com/content/qhc/25/7/509.full.pdf**.

[167] P. Vandekerckhove, "Generative Participatory Design Methodology to Develop Electronic Health Interventions: Systematic Literature Review," *JMIR Publications,* vol. 22, no. 4, 2020. [Online]. Available: **https://www.jmir.org/2020/4/e13780/**.

[168] R. F. Dam and T. Y. Siang. "5 Stages in the Design Thinking Process." Interaction Design Foundation. **https://www.interaction-design.org/literature/article/5-stages-in-the-design-thinking-process** (accessed.

[169] C. Illuk. "The 2 hour Design Sprint." **https://blog.prototypr.io/the-2-hour-design-sprint-9e2bbc14ee1** (accessed.

[170] Google. "Design Sprints." Google. **https://designsprintkit.withgoogle.com/** (accessed.

[171] J. Knapp, J. Zeratsky, and B. Kowitz, *Sprint: How to Solve Big Problems and Test New Ideas in Just Five Days*. Simon and Schuster, 2016.

[172] Service Design Tools. "Service Design Tools." **https://servicedesigntools.org/** (accessed.

[173] Design Kit. "Design Kit." **https://www.designkit.org/** (accessed.

[174] The Right Question. "The Right Question." **https://rightquestion.org/** (accessed.

[175] P. o. C. Foundation. "EBCD: Experience-based co-design toolkit." The Point of Care Foundation. **https://www.pointofcarefoundation.org.uk/resource/experience-based-co-design-ebcd-toolkit/** (accessed.

[176] Digital Health. "Co-design in Health." Good Things Foundation: Digital Health Lab. **https://digital-health-lab.org/codesign-in-health** (accessed.

[177] T. Foley. "Evaluation in LHS Workshop." **www.learninghealthcareproject.org** (accessed.

[178] NHS. "Future NHS." NHS. **https://future.nhs.uk/system/login?nextURL=%2Fconnect%2Eti%2Fhome%2Fgrouphome** (accessed 2021).

[179] J. Leviss, *HIT Or Miss, 3rd Edition Lessons Learned from Health Information Technology Projects*. Taylor & Francis, 2019.

[180] P. Craig, P. Dieppe, S. Macintyre, S. Michie, I. Nazareth, and M. Petticrew, "Developing and evaluating complex interventions: the new Medical Research Council guidance," BMJ, 2008. [Online]. Available: **https://mrc.ukri.org/documents/pdf/complex-interventions-guidance/**

[181] C. Lannon *et al.*, "A maturity grid assessment tool for learning networks," *Learning Health Systems,* 2020. [Online]. Available: **https://onlinelibrary.wiley.com/doi/full/10.1002/lrh2.10232**.

[182] HIMSS Analysis. "Adoption Model for Analytics Maturity." HIMSS Analysis. **https://www.himssanalytics.org/healthcare-provider-models/all** (accessed.

[183] C. J. Lindsell *et al.*, "Learning From What We Do, and Doing What We Learn: A Learning Health Care System in Action," *Academic Medicine: Journal of the Association of American Medical Colleges,* 2021. [Online]. Available: **https://journals.lww.com/academicmedicine/Abstract/9000/Learning_From_What_We_Do,_and_Doing_What_We_Learn_.96789.aspx**.

[184] NHS. "NHS Knowledge Mobilisation Framework " **https://www.e-lfh.org.uk/programmes/knowledge-mobilisation-framework/** (accessed 2021).

[185] NHS Health EdEng. "Library and Knowledge Services in England." NHS Health Education England. **https://www.hee.nhs.uk/sites/default/files/HEE%20-**

%20Library%20and%20Knowledge%20Services%20Value%20Proposition%20The%20Gift%20of%20Time%20FINAL%20Nov2020_0.pdf (accessed 2021).

[186]   NICE. "Developing NICE guidelines: the manual Process and methods." The National Institute for Health and Care Excellence (NICE). https://www.nice.org.uk/process/pmg20/chapter/decision-making-committees (accessed.

[187]   M. H. Murad, N. Asi, M. Alsawas, and F. Alahdab, "New evidence pyramid," *BMJ Evidence-based Medicine,* vol. 21, no. 4, pp. 125-127, 2016. [Online]. Available: https://ebm.bmj.com/content/21/4/125.

[188]   A. Mitchell, "A NICE perspective on computable biomedical knowledge," *BMJ Health & Care Informatics,* vol. 27, no. 2, 2020. [Online]. Available: https://informatics.bmj.com/content/27/2/e100126.

[189]   Faculty of Clinical Informatics. "Andrew Mitchell - UK Workshop on Mobilising Computable Biomedical Knowledge (MCBK)." Mobilizing Computable Biomedical Knowledge (MCBK). https://www.youtube.com/watch?v=lIHJLRjUjRo&list=PLn7CfTWFFBSzTZtK4bTpo7Q2kBLjr0RUM&index=8&t=135s (accessed.

[190]   AHRQ. "Improving quality of care through clinical decision support (CDS) takes a community." Agency for Healthcare Research and Quality. https://cds.ahrq.gov/cdsconnect/about (accessed.

[191]   S. Jain. "How to Make Healthcare Innovation Work in the Real World—Merck's Partnership with PatientsLikeMe." Medical Marketing and Media. https://www.mmm-online.com/home/channel/suppliers/how-to-make-healthcare-innovation-work-in-the-real-world-mercks-partnership-with-patientslikeme/ (accessed.

[192]   J. Hibbard and H. Gilburt, "Supporting people to manage their health." An introduction to patient activation," The King's Fund, London, UK, 2014. [Online]. Available: https://www.kingsfund.org.uk/sites/default/files/field/field_publication_file/supporting-people-manage-health-patient-activation-may14.pdf

[193]   T. Greenhalgh. "Assessing and handling complexity in technology projects." https://www.researchprotocols.org/api/download?filename=e47188522869f9601723b92bbe0f7b18.docx&alt_name=16861-319949-1-SP.docx (accessed.

[194]   T. Greenhalgh. "NASSS-CAT (Project Version)." https://www.researchprotocols.org/api/download?filename=15d56b11e2f52e9308f7e0a15afb5222.docx&alt_name=16861-319950-1-SP.docx (accessed.

[195]   T. Greenhalgh. "Identifying complexities in your technology project." https://www.researchprotocols.org/api/download?filename=21c2d1bfd3c40e2666e592da19e5bc8d.docx&alt_name=16861-319948-1-SP.docx (accessed.

[196]   D. Neuman, "Qualitative Research in Educational Communications

and Technology: A brief introduction to Principles and Procedures," *Journal of Computing in Higher Education* pp. 69-86, 2014.

[197] IHI. "Introduction to Learning Health Networks." IHI. **https://ihi.webex.com/recording service/sites/ihi/recording/c1f65 d0feafe4361a373e3feab417155/p layback** (accessed.

[198] Institute of Healthcare Improvement. "About IHI." Institute of Healthcare Improvement. **http://www.ihi.org** (accessed.

[199] N. H. S. Alliance. "Connected Cities." Nothern Health Science Alliance. **https://www.connectedhealthcit ies.org/** (accessed.

[200] NHS, "Joining up health and care data," 2021. [Online]. Available: **https://www.england.nhs.uk/dig italtechnology/connecteddigital systems/health-and-care- data/joining-up-health-and-care- data/**.

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