Whitepaper: From Leibniz' Quest to Dirac Notation: Toward a Digital Epistemology for Reasoning with Uncertainty in Patient-Centric Learning Healthcare Systems

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Abstract

At the dawn of the scientific age, before modern scientific disciplines had clearly marked boundaries, Leibniz was a polymath on the quest for a language that would enable reasoned discourse to be resolved by calculation (or formal inference), using mathematically precise notation, across different intellectual traditions. A language for scientific reasoning and learning that may uplift humanity, by improving its way of encoding, remembering and use of knowledge.

In our days of clearly marked disciplinary boundaries in science, we may now have more tools at our disposal to revisit his dream. Enabled by scientific progress and increasing capture of human knowledge in digital forms. Facilitated by the binary representation that Leibniz invented, as it now appears in the form of bits and bytes in our computers. Increasingly enabling a new interplay between human and machine intelligence, new ways of encoding (uncertain) knowledge, and new ways of organizing work.

Reflecting on related problems, we propose a contemporary interpretation of Leibniz' vision as a '*digital epistemology'* for the age of AI in medicine. Focused on difficult medical cases where science-enabled decision making by patients and healthcare professionals is non-trivial. Reasoning, within that *digital epistemology*, is based on Dirac notation and derived split-complex vector spaces as a mathematical foundation, a scientific paradigm that was designed for addressing such problems. This *digital epistemology* for learning and reasoning in *learning healthcare systems* allows continuous updating, considering difficult cases for science-enabled medical decision making in its design. Aiming to bring more 'epistemic humility' into the design of learning systems, knowing that difficult cases exist in abundance, and require special attention at system level. To allow such learning systems to discover and validate the most informative patterns in patient data, combining human and machine intelligence, that help us improve the system's ability to guide decisions towards the best possible outcomes even in these difficult cases. To achieve this, Open Science-style transparency is used in that digital epistemology's scientific logic, rather than 'black box AI', including its encoding of uncertainty, contradictions, and conflicting recommendations.

With increasing FAIRification (i.e. the process of making health-related data Findable, Accessible, Interoperable, and Reusable), and new health data spaces (federations across health data silos), we propose that we soon have improved frame conditions for building such learning systems using the proposed digital epistemology. To enable the discovery and validation of the most informative patterns hidden in patient trajectories in complex cross-silo data landscapes, for better health-related decision making by patients and healthcare professionals.

As an example for the emerging paradigm we describe here, we discuss systems designed for the translation of P4 science; i.e. systems that aim to make care more personalized, preventive, participatory and predictive. In other words, health-related systems that aim to enable a paradigm shift from mostly reactive (sick) care and isolated data silos, to a more patient-centric, collaborative and connected, preventive and more proactive healthcare paradigm that is designed to avoid bad outcomes. To personalize care better, in everyday health-related decisions, integrating patient knowledge and medical expert knowledge in its decision making.

In that context, we see an increasingly important role in such patient-centric decision making for AI and digital twins, including the modeling and simulation of patient trajectories. With particular attention to trajectories we can consider difficult cases for science-enabled decision making. In other words, trajectories that do not map well to the medical knowledge and evidence landscape, i.e. *unguided patients* who are clearly different from the populations studied in large clinical studies.

Hence we propose that this *digital epistemology* (for unguided patients in *learning healthcare systems*) will enable the implementation of a new generation of digital systems that can improve our ability to learn informative patterns in the trajectories of some of the most difficult cases, to find better ways to improve their outcomes (and care experience) considering limited resources and uncertain knowledge. Compared to well-established approaches that are currently used widely in healthcare, which were mostly designed for cases for which we have more robust evidence to guide decisions, it emphasizes the importance of representing and integrating uncertainty in relevant knowledge, conflicting recommendations related to difficult cases, different diagnostic hypotheses that point to different decisions, and special needs of implementing more personalized preventive care. Across expert medical knowledge and patient knowledge. How can such a digital system learn to find the most informative and relevant patterns to guide decision making in difficult cases, including endotype modeling, while properly acknowledging the underlying epistemological complexity? To enable the design of learning systems that are more patient-centric, that build actionable patient knowledge using science and cutting-edge AI, and that help us learn what works best in the most difficult cases that require such a comprehensive knowledge fusion approach.

1 Introduction

In the late 17th century, *Gottfried Wilhelm Leibniz* (1646-1716) dreamed of a *characteristica universalis* – a symbolic logic through which all (or most) human disputes could be resolved by calculation (or formal inference). An epistemological [1] dream that has inspired and puzzled many, as it remains mostly elusive, apart from systems deployed in narrowly scoped areas that can be modeled well with mathematical calculations, e.g. many engineered systems (Milkov, 2006).

The various paradigm shifts [2] experienced by the Physics community since the 19th century reinforced the key role of mathematics as a solid, trusted scientific foundation of the field, for its epistemology [2] (Weigert, 2023). Knowing that the human mind often struggles to comprehend theory related to quantum mechanics and relativity, but can learn to 'trust the math' if it is scientifically robust and useful (Gibney, 2025; Dine, 2022; Robson & St. Clair, 2022). More than three centuries after Leibniz' quest, we have made considerable progress in many areas of science, enabled by many paradigm shifts, to now consider revisiting his dream. Leibniz' main passion played a key role in that, namely the power of mathematics as a language and way of thinking that can be more precise than natural language. Mathematics has indeed become a robust foundation for a great variety of sciences (and science-based progress in many fields). As it helped to expand our ability to represent and disseminate what we learned, in areas related to science-enabled decision making, data science, statistics, probabilistic reasoning, causal inference, and also in artificial intelligence (AI). However, today we also face problems of understanding the 'inner workings' of modern 'black box AI', especially in areas such as medicine, where robust explainable decision making and related scientific learning is crucial, requiring a reasoning approach that both humans and machines can relate to (Raposo, 2025). Increasing the tension between what machines (AI) can come up with, to solve problems, and what many humans can easily understand.

Despite all this wonderful progress, with increasing specialization and demarcation of disciplinary boundaries in science comes the challenge of how to cross disciplinary boundaries. Such *transdisciplinary boundary crossing* implies the crossing of what we may call 'epistemological fields', i.e. clusters of similar epistemologies in science that agree on many norms, beliefs and rules related to what counts as valid (high-quality) knowledge, as a contrast to subjective, personal opinion. Each epistemological field using different shared notions of encoding, using and judging knowledge that enable an epistemological community to act in concert, i.e. performing innovation within the boundaries of a particular paradigm (or 'Disciplinary Matrix') [2]. As that community develops its own language for effective coordination among experts that belong to that field. Considering that such epistemological fields, with increasing specialization at work in professional communities [3], may at times not agree on the best way to judge the quality of knowledge (for a particular use case and related decision making where diverse inputs from multiple fields are desired).

[1] We refer to 'epistemology' (and 'epistemological' concepts) throughout this text, using a broadened meaning that is aligned with the Oxford Dictionary's definition of 'epistemology' as "The theory of knowledge, especially with regard to its methods, validity, and scope, and the distinction between justified belief and opinion." Our use goes beyond the philosophical definition, toward applications in the context of an Open Science toolkit we aim to develop. Other definitions of epistemology exist." See also our glossary.

[2] The term 'paradigm shift' is based on Thomas Kuhn's work on the history of scientific revolutions. Note that in his later work he preferred to use the term 'Disciplinary Matrix' (roughly matching his original notion of 'paradigm'), with emphasis on the power of 'exemplars' in paradigm construction.

[3] From a patient perspective this may look quite different, so that notion is under-represented in such a perspective focusing on expert communities. At system level, in healthcare organizations, since the time of Leibniz, there is a trend to increasing specialization that affects how organizations work, and make decisions. In preventive care, for example, knowledge outside healthcare organizations is likely a key factor for success, but often not sufficiently involved in system design compared to professional communities with their epistemologies and biases (note the 'participatory' aspect of P4, see Appendix). Being serious about the patient-centric approach then also means to tap into non-scientific non-expert knowledge where it helps us learn.

Here, it is important to note that the medical domain is rich in such epistemological interactivity across scientific disciplines and medical specialties, as its decision-making logic often relies on their aggregated knowledge (Rillo & Carillo, 2023). Since the days of Leibniz, medicine has become increasingly scientific, increasingly 'precise' in its diagnostic and therapeutic logic (from visible symptoms down to the molecular biology of disease), thus moving forward in terms of increasingly precise science-enabled decision making, science-informed personalization of care, and increasingly sophisticated medical reasoning that should in the end enable better care decisions leading to better care outcomes. However, if we want to fully take advantage of all this impressive scientific and technical progress for improving medicine and patient outcomes further, the problems described in this whitepaper make us wonder about the need to develop new kinds of solutions, i.e. to create more room for new paradigms to emerge and develop. So we can learn how to best navigate all these epistemological fields and sciences (including those that are not integrated well yet into medical epistemology [5]) in a way that enables the best possible decision making, and the effective dissemination of what we learned. Our focus here, in this context, is on the most difficult cases for such care decisions, where current science-based medical knowledge is too weak for reliably guiding decisions. In other words, such difficult cases in terms of care decision making provide interesting material for learning about the limitations of currently established paradigms used in science-based medical decision making, and how we learn from the outcomes of past decisions.

So far, the medical domain has already gathered considerable experience with the application of science (and, in particular, its mathematics-based toolkit) for enabling the discovery and validation of *informative patterns* in patient datasets that capture important information related to what happened in such difficult cases. Pioneering work, for example, was performed in collaborative, transdisciplinary [4] communities consisting of different kinds of physicians and scientists, working closely together with patients on a specific set of well-defined problems, i.e. in a context that requires *epistemic bricolage* [5] to create new kinds of solutions across epistemological fields, for understanding such difficult cases. In collaborative diverse communities that share the goal of learning how to inform better decisions in healthcare in that specific area where such *epistemic bricolage* is approached by intensive collaboration. Selecting, together, what seems most relevant for such bricolage. Developing a shared language that enables effective bricolage.

Understanding the epistemological impact of the work done by the field called *Evidence-Based Medicine* (EBM) is of particular importance here. EBM has contributed considerably to make medicine more scientific, enabled by a math-based 'evidence paradigm' [6] which is used increasingly to inform science-enabled decision making in many modern health care systems (Sackett, 1996; Robson, 2016). Within the EBM paradigm, RCTs (*randomized controlled trials*, a particular type of clinical trial) play a crucial role, being considered the most robust, generally applicable method for gathering reliable evidence. To separate clear causation from correlation [7], e.g. about a care decision involving a new drug or diagnostic which may provide extra value compared to an already widely used treatment. In the last decades this has become a dominant paradigm for furthering scientific progress in medicine, guiding the generation of

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[4] We use the term 'transdisciplinary' rather than 'interdisciplinary' as it is not only about an interface between two different disciplines but about knowledge from several disciplines and across epistemological fields (not only 2). Such transdisciplinary work may need to be more encouraged to better deal with some of the problems outlined in this paper. See also footnote 5 (bricolage).

[5] While physicians and scientists, in collaborations, often experience considerable overlap in their epistemologies, a strong participation by patients can create particular epistemological challenges. Bricolage, in this context, is a way of developing a shared language and understanding in such complex communities, e.g. when comparing clinical research endpoints and what really matters to patients and their families. See Levi-Strauss (1962) for a seminal text that contrasts the notion of Bricolage with the mindset of an engineer or scientist.

[6] A simplified version is captured in the 'pyramid of evidence' with randomized controlled trials (RCTs) at the top of this pyramid, as the most reliable type of evidence for causation, and real-world evidence (RWE) derived from healthcare data as a less reliable type of evidence within that paradigm, for making medicine more scientific

[7] We only touch briefly on this very important problem here. Note also many new emerging paradigms related to causal modeling in the field, e.g. to extract patterns from 'messy' real-world health data.

trusted evidence even in some rare diseases that were once considered difficult cases including diagnosis (Triposkiadis & Brutsaert, 2025). However, note that there are a range of issues, currently under debate, with the methods that are commonly used for the generation of evidence in scientific publications, e.g. the over-emphasis of the notion of *p-values* and *statistical significance* in many biomedical publications (Ioannidis, 2005). With this we can expect that EBM is not a static system but also prone to undergo paradigm shifts over time.

While traditional, more 'bureaucratic' [8] healthcare models often struggle to integrate the patient's experience and knowledge into shared decision making, cutting-edge digital approaches often aim to find a better balance between the needs of the system and the individual, aiming at a more complete picture around the case (beyond expert epistemologies) that combines information from different sources about the patient history, past decisions, current state and trajectory (CDS Innovation Collaborative, 2025). Note that this may include information in narrative form describing a patient's lived experience. However, it is non-trivial to integrate all this expert and patient knowledge to make it available for a patient to reason and navigate all kinds of accessible options that could impact the patient's health (including but not limited to services offered by healthcare systems).

It is widely acknowledged among health innovation experts that such science-based advances in medicine (in the last 300 years, since the days of Leibniz) have strongly improved health outcomes and life expectancy of populations, especially in the last 100 years or so (GBD 2019 Demographics Collaborators, 2020; Deaton, 2013; Oeppen & Vaupel, 2002), in many countries that have been able to build strong healthcare systems for their populations. However, in their work today, despite all the great science, physicians still face difficult decisions quite often. Such difficult cases are often about an incoming case not fitting well into current medical categories, reasoning and its science-based evidence landscape [9], reminding us of the challenge traditional bureaucratic systems face as they struggle with incoming cases that do not fit their category-to-process organizational cognition (Rebhan, 2025) [8]. In particular, EBM with its RCT-based evidence model may help to guide real-world cases that are highly similar to the patient populations investigated in those high-quality clinical studies (considering their inclusion and exclusion criteria), but it can't reliably guide cases that are too different from the characteristic of those studied populations [10]. When a case is similar enough to apply EBM-based clinical care guidelines can be a difficult decision in itself.

Such '*unguided patients*' (above-described difficult cases) are discussed here as a focus application for our *digital epistemology*. They are cases in which science-enabled decision making in healthcare is difficult, because a) the case does not match well [11] any EBM-based evidence that can guide care decisions (i.e. by not being similar enough to the populations EBM studied), or b) they match multiple guidelines for different populations but then result in conflicting recommendations (Damarell, 2020). Note

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[8] A key property of bureaucratic systems that is relevant here is the tendency to quickly force-fit an incoming case to a set of fixed categories that inform the selection of an appropriate process (Rebhan, 2025). While many incoming cases may fit those categories reasonably well, the atypical cases who do not fit well provide a challenge to the system that it may not be able to resolve well, too often resorting to simple force-fitting of such cases to its categorical system. During system design, it may have been assumed that any incoming case will fit a limited set of categories in this category-to-process bureaucratic logic. Also, incentive systems can hinder other responses.

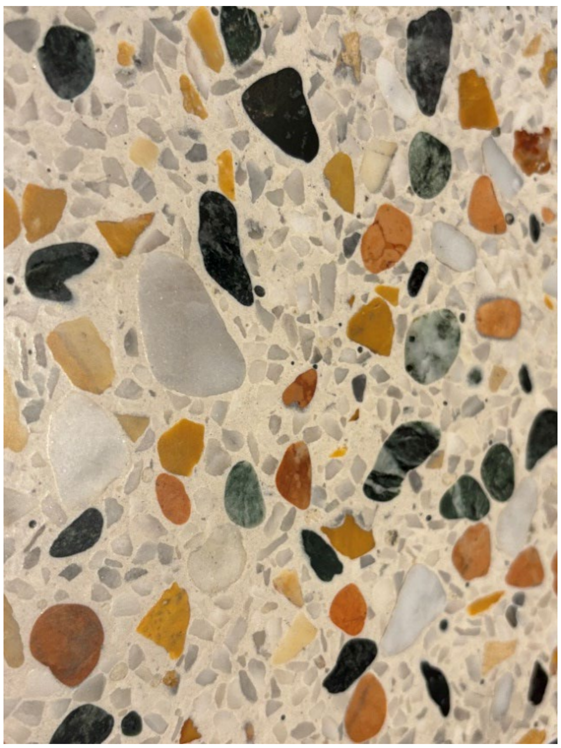
[9] Imagine a landscape of EBM-based evidence as hills and valleys, with the highest hills are peaks of strong (RCT-based) evidence that can guide care decisions well, while further down, in the valleys, this is not the case. See Fig. 1 also.

[10] A cohort of similar patients that is being studied, here, depends a lot on how similarity is defined, and what we consider 'similar enough' to include a case in the cohort. Like in a swarm of fish, some are closer to the center of the swarm, some more on the edge. This may relate to a case being considered guided or unguided. If a patient matches particular RCTs and their inclusion and exclusion criteria may be the easiest starting point.

[11] If a case (patient with a particular profile) matches EBM-based evidence or not may not be a binary decision (it matches, or it does not), but we would expect many grey area cases in which there is some similarity to the populations EBM focused on but also a concern that known differences to those populations could affect confidence in a decision to follow EBM-guided care (without any adjustment considering such differences)

that such cases includes situations in which patients may not match well the genetic/ethnic or gender composition of the populations EBM studied with RCTs as those may show a particular bias e.g. towards certain Caucasian subpopulations that are easier to recruit into RCTs [12].

Examples for such *unguided patients* can include ethnicities and genders that are under-represented in EBM-based evidence, less-studied rare disorders, complex multi-morbidity cases that are often excluded in RCTs (e.g. patients with chronic kidney disease co-morbidity), and well-known diseases for which insufficient EBM-based evidence exists to guide care decisions (e.g. what to do once first-line therapy has failed). Also, EBM-based evidence is often biased towards later stages of disease (with strong symptoms) that are easier to study with current clinical research approaches, resulting in major gaps in the EBM evidence landscape when we want to use EBM-based evidence to inform decisions about the personalization of *primary prevention,* to keep populations healthy (in organizations emphasizing the *preventative* principle of P4, see below). [13]



For such different kinds of *unguided patients* who unfortunately fall into such gaps (or grey areas) in the EBM landscape (Fig. 1, on the left), it may not be obvious how to approach science-based, robust decision making in care due to the lack of robust evidence. We argue that, with increasing digitalization of patient trajectories and healthcare processes, we can record the decisions that were made in such difficult cases (by physicians, patients and others) and, importantly, the outcomes, and then find ways to learn what works best for which trajectory, even if they are unguided patients. As cutting-edge *Learning Health System* approaches are being developed to facilitate such learning based on past decisions, it implies a search for *informative patterns* in these patient trajectories that correlate with better outcomes [14]. Including complex combinations of big and small decisions made by different actors that correlate with good outcomes. Creating a new innovation area including a role for Open Science communities that could help healthcare systems learn how to deal with such difficult cases, how to enable such learning in a way that fits the special situation of these cases.

See *Fig. 1* above for a visual metaphor of the landscape we discussed above. We can see areas with dark colors that are rich in evidence that can confidently guide care, and areas with much lighter colors that are less rich in such trusted evidence. An individual patient trajectory (current state and past decisions, history) would fall somewhere in that landscape, e.g. a) within a dark color area, b) nearby, or

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[12] While EBM does not solely rely on RCTs and there is increasing interest in considering 'real-world evidence' e.g. in situations where it is difficult to study populations with RCTs (Sheldrick, 2023), the EBM community has a clear preference for well-designed RCTs that decrease the influence of confounders, as the most reliable type of evidence. If there is a lack of RCT-based evidence to guide medical decisions then the *unguided patients* challenge present itself.

[13] One important factor here is the ability to recruit participants into studies, if they do not yet experience symptoms strong enough to motivate them to participate in a study. Also, such preventive studies can be difficult to finance.

[14] Basically, the main point of EBM is to use good science to properly distinguish causation from correlation in its evidence base. To optimize care processes for unguided patients based on correlations alone may be problematic.

c) far away from it. Highly similar patient trajectories would be close to each other, considering the sequence of events in the trajectory (for an example, see Kapur et al. (2022)). Outside those dark spots we can see various colors, with the different shades of reddish brown indicating that there is some potentially informative science that may be relevant in healthcare decisions, but it's more patchy, less robust and not at the level of high-quality RCT-based evidence from large studies. Darker brown spots may have evidence from smaller studies, for example. The part of this landscape that is relevant for our discussion on unguided patients is therefore heterogeneous as well, with many colors found in small and large spots. With different degrees of uncertainty in potentially relevant scientific knowledge.

How large such *unguided patient* populations are in a typical healthcare population is non-trivial to quantify at present [15], given the lack of attention to this way of framing the problem in previously designed healthcare systems' digitalization efforts, and a lack of consensus on how to count such cases reliably and reproducibly. Is it somewhere between 20-50% of a typical all-comers population entering a hospital for a variety reasons?

Therefore, we try to shine the light of attention on the problem of science-enabled decision making for *unguided patients*, based on their digitalized trajectories, hoping that they will receive more attention by different innovators in the near future, to further develop the science they need. To help us learn about the extent of the challenge, what common situations look like that we may be able to generalize and disseminate, how new roles can help organizations deal with them before they are force-fitted, and how learning loops can help us improve outcomes and patient / provider experiences. We would expect that with the increased use of EHR (electronic healthcare record) systems, improved digital capture of the patient experience, more sophisticated decision support systems, health data spaces using federated learning and analytics (such as PHEMS[16]), better patient participation in decision making, better digital twins and AI-enabled learning from trajectory data, and a combination of those (e.g. using epistemic bricolage), will help us develop new kinds of solutions, together with those who are willing to collaborate on this using Open Science principles (UNESCO, 2021).

We propose that the *digital epistemology* described in this whitepaper (see below for specifics) may help us design improved *learning healthcare systems (LHS)*, that aim at finding new, more patient-centric ways of improving care outcomes and experience for *unguided patients*. Helping us find the most *informative patterns* in the patient trajectory data to enable good care decisions for such difficult cases, even if modeling across health data silos is required to enable such learning. Assuming that patient outcomes and insights are tracked well enough to enable well-designed learning loops in such LHS, as originally outlined in the paradigm of *value-based health care* (Porter, 2010) [17] - knowing that such learning will be difficult or impossible if appropriate definitions of success and meaningful progress are not well tracked.

In addition to the types of *unguided patients* described above, there is a trend towards more proactive and preventive care models that will add further fuel, increasingly emphasizing 'health maintenance' [18] as an ambition, implying a paradigm shift in organizational and digital design related to healthcare. As mentioned above, the problem of *unguided patients* is about the lack of evidence within the EBM

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[15] A baseline approach could map if a patient would have fit the inclusion / exclusion criteria defined for a particular large RCT that provided much of the trusted evidence, for example. However, this does not account for all biases in the composition of the study population in the RCT, e.g. ethnicity, genetics, socio-economic status. Also, often it's a more complex mix of studies that leads to care recommendations e.g. using the Cochrane process https://www.cochrane.org/evidence/why-our-evidence-trusted

[16] A European health data space for pediatric hospitals that see a lot of unguided patients, see https://phems.eu/

[17] VBHC (value-based health care) can only work if outcomes are tracked and used in feedback loops that help improve how care works, and how care decisions are made. Patient-reported outcomes (PRO) are clearly an enabling tool here. However, many healthcare organizations struggle to track outcomes and build solid feedback loops to enable VBHC, for a variety of reasons. Again, this can only work if the organization is serious about it, and has sufficient slack to invest in such innovation (and bringing in relevant expertise to make it work).

[18] Health maintenance is about maintaining physical and mental health in populations, e.g. in many P4 ecosystems (see Appendix). Example: the health of working-age populations has effects relevant for employers.

paradigm, as a basis for science-enabled robust decision making in care. When healthcare systems try to shift to more proactive and preventative care models, they will face a lack of EBM-grade evidence in such relatively healthy populations and early stages of disease with no or only mild symptoms. In principle it is possible to design an EBM-based strategy to fill such evidence gaps, but at present it is unclear how it would be resourced and implemented within a reasonable time frame (to enable organizations that have prioritized health maintenance and prevention, as in section 3.1).

As this *unguided patients* situation unfolds in front of our eyes, we can see new forms of collaborative transdisciplinary community-based learning emerge, facilitated by new health data spaces similar to the EHDS (European Health Data Space; European Commission, 2022) and the SwissHDS (Swiss Health Data Space[19]) that allow to do science on patient trajectories. Across the parts of the patient trajectory that were previously fragmented, hidden in health data silos. Over time, as those data spaces become a reality that is adopted by different users, we may accumulate a variety of (potentially) *informative patterns* found using sophisticated analytics and AI [20] in those complex data landscapes, e.g. combinations of very different 'data points' such as quantified blood-based circulating biomarkers, narrative patient insights and outcomes, SNOMED-coded clinical events and health state models (Rebhan, 2017) in patient trajectories. Such complex *informative patterns* could in turn help to identify and describe particular types of *unguided patient* populations in ways that differ from traditional approaches for describing populations in medical publications [21]. Even if such populations do not map well to current diagnostic procedures and diagnostic coding practices [22]. With AI increasingly adopted in that context to aid in the discovery, study and annotation of such informative patterns (see a few emerging trends described in Allam et al., 2021).

Considering the importance of gaining mechanistic insights into the disease patho-biology that could help to guide care decisions, a promising subset of *informative patterns* would help us model the elusive 'endotype' [23] in clusters of similar *unguided patient* trajectories, and how that endotype model relates to the more easily visible phenotype / symptoms observed in the clinic (or 'at home' or 'at work', in the patient experience). Beyond what healthcare systems record on their side, with their digitalized medical logic about a particular case here, e.g. in EHR [24] systems, the integration of patient knowledge, experience and outcomes is likely to be a key factor in building a more complete picture of a patient trajectory; however considering that this may provide a formidable *epistemological field* crossing challenge which takes us beyond medical epistemology [25]. Here, we propose a patient-centric approach that considers the patient's knowledge as it taps into expert medical knowledge as well as other knowledge that is relevant, depending on the patient's health goals and aspirations.

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[19] https://www.digisante.admin.ch/de/swiss-health-dataspace-de

[20] AI is good at pattern recognition and connecting multiple sources of data, which can be difficult for human brains to recognize and connect, making it possible to see informative patterns in unguided patients that human doctors may not see.

[21] Exemplified by the classic Table 1 in medical publications that describes the characteristics of the population that was studied, including demographics, selected quantified biomarkers, and clinical code frequencies

[22] An example would be the SNOMED approach for diagnostic coding, one of the most comprehensive toolkits. https://www.snomed.org

[23] *Endotype* is the mechanism that is driving the development of the visible part of disease (phenotype) as it shows up as symptoms considered in diagnostic processes. In other words, the biology of disease that is less visible ('hidden from sight') but important for modern medical decision making, e.g. related to disease subtype.

[24] Electronic Health Record digital systems can, in principle, contain patient trajectory data that reflect what happens in healthcare systems, including past decisions and hopefully also outcomes

[25] As patients are usually not heavily trained in medical knowledge and logic, so when capturing their experience and insights we enter different epistemology that is less standardized, more influences by social context and culture etc. Therefore, the use of natural language is often preferred here to capture insights that are complementary to medical epistemologies and clinical coding systems (e.g. SNOMED).

Such efforts to record multiple perspectives about a patient trajectory (in a balanced way, from a system and individual's [26] perspective) is then likely to help us find out what the most *informative patterns* are, as it increases the chance of discovering new *informative patterns* that so far have not been considered by those used to focus their attention to medical epistemology only. Aiming to find a healthy balance between system-level optimization (driven mostly by medical professionals and operational optimization experts in healthcare systems, using medical epistemology) and improved participation and engagement of patients and their knowledge / insights / data [26]. In LHS that emphasize the discovery of such *informative patterns* in *unguided patient* trajectories using a P4 approach aimed at improved health maintenance and prevention, such a balance between system and individual focus will not only inform personalization strategies that learn from what works best, but also how to build trust and solid relationships to enable collaborative progress.

To help us design such a new generation of *LHS* that can help us figure out such *unguided patient* trajectory challenges in a new way, this paper situates Barry Robson's *digital epistemology*, grounded in Dirac notation and derived split-complex vector space (Robson, 2007; Robson, 2014; Robson, 2016; Robson & St. Clair, 2022; Deckelman & Robson, 2014), as a design frame, and a philosophical, scientific and technical successor of Leibniz's dream [27]. In the medical domain, with its traditions of generating and using scientific evidence for robust decision making, focusing on *unguided patients* and related decision making, i.e. cases where EBM-grade evidence is lacking and new paradigms are needed to build outcome-based learning loops in LHS.

Note that, while Barry Robson's *digital epistemology* may also be useful outside the medical domain (in non-medical domains that can benefit from improved 'epistemic humility' in the design of similar kinds of learning digital systems [28]), our discussion here is restricted to applications in the medical domain.

Our scope here is the discussion of applications of this *digital epistemology* in patient-centric *learning healthcare systems (LHS)*, which aim to a) improve care for patients that fall into gaps in the EBM evidence landscape, i.e. *unguided patients* , b) shift to more proactive and preventive care and health maintenance for their populations by learning how to personalize preventive care, using the P4 approach. Such applications of our *digital epistemology* need to consider how systems and people [29] learn in a digitally connected care organization, increasingly supported by federated *health data spaces* that enable the discovery of *informative patterns* across traditionally separated health data silos. Bringing new possibilities for more complex cross-silo patterns to emerge that are relevant for improving the care for *unguided patients* [30]. Note that both a) and b) come with the requirement to deal with different kinds of uncertainty including *epistemic uncertainty* (imperfect knowledge in the context of science-enabled decision making; see Appendix).

As healthcare systems can be very different from each other, e.g. in different countries and regions, we use the example of Switzerland to illustrate this further. Considering that Switzerland has a particular healthcare system, population, decentralized culture, federated tech scene, silo'ed digitalization of patient trajectories to overcome, and pioneering community culture in medicine. Relevant aspects in that Swiss

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[26] Cultures that are less individualistic may need a more comprehensive perspective of the social context around the individual. This may also be a factor to consider even in Europe, e.g. with migrant populations. See also Seebode (2013) for a patient-centric perspective on this.
[27] We approximate the 'essence' of his dream here as a form of reasoning across 'knowledge atoms' understandable to both humans and machines, enabling an epistemology that has a high degree of 'epistemic humility' in the sense that it knows its own imperfection well and then learns how to improve by updating its beliefs (in the sense Bayes' once described it).
[28] e.g. to better treat unguided cases who do not fit organizational cognition well, i.e. cases that do not fit the set of categories used by an organization for classifying incoming cases: see Rebhan, 2025
[29] people, here, include healthcare professionals and non-experts (patients, their families, others)
[30] Healthcare systems are often fragmented, and so are their data landscapes. By enabling cross-silo modeling of a patient trajectory, we have a more complete picture of that trajectory and a better chance of finding patterns that we missed before.

landscape include *LHS* efforts that aim to track patient trajectories with outcomes for unguided patients, including related national and regional digitalization programs, AI-enabled digital decision support in healthcare, and a variety of relevant technical / scientific efforts. *P4 ecosystems* [31] that combine all those aspects to enable a shift towards more proactive and personalized care will be given special attention (see the Appendix for a definition of *P4 ecosystems*, beyond classic notions of P4 medicine in the Systems Biomedicine literature [32]).

2 From Leibniz' vision to hyperbolic reasoning over imperfect health knowledge

Leibniz's goal was twofold: to create a universal symbolic language (*characteristica universalis*) and a formal calculus (*calculus ratiocinator*) that could encode reasoning across domains. He envisioned modular, recursive symbols representing *knowledge atoms* [33], logical operations performed via manipulation of these atoms, and the resolution of complex reasoning problems through symbolic computation. As a mathematically grounded polymath, he tried to generalize and connect across the emerging scientific epistemologies that were accessible to him at the time (Milkov, 2006). Further encouraged in later phases of his effort by letters from Bouvet about 'ancient reasoning over symbols' [34] that may be considered a previous polymathic attempt at such 'computation', being quite distinct in the 'way of thinking' from the epistemologies and mathematics accessible to Leibniz in Europe (Berkowitz & Cook, 2015).

Interpreting Leibniz' epistemological vision in its historic and cultural context, we can note that many intellectuals in his age in Europe had a fascination for sophisticated designs behind seemingly complex machines, the role of precise computation in it, enabled by progress in mathematical calculation and scientific reasoning, as engineering developed as a field that could create increasingly complex machines with such paradigms. In other words, we can imagine his generation of European intellectuals as 'owning' those scientific paradigms, being inspired by all the good things they will create for humanity. In that historic context, we can imagine his vision as a kind of generalization of the available calculus that would work beyond these engineered systems, to help humanity solve many other important problems related to the use of knowledge and reasoning. Such a more general calculus should then allow those who master it to cross many different areas of human knowledge, including intersectional problems where different *epistemological fields* and their languages and symbols overlap (see above). In the context of our paper

[31] P4 ecosystems in this context are basically a subtype of learning healthcare systems, focused on making healthcare more P4 i.e. more preventative, personalized, predictive and participatory. Aiming for improved health maintenance at population level. See the Appendix, section 3.1 and https://www.linkedin.com/pulse/p4-ecosystems-recent-progress-2024-michael-rebhan-x6mqf/

[32] Original definitions of P4 medicine emerged from the Systems Biology and Systems Biomedicine academic community around Leroy Hood, in the early days of genomics, proteomics and related technologies that promised to provide insights into human patho-biology. Here, our perspective on it reflects our view on progress made in 20 years, considering translation of such P4 science into healthcare systems, organizational aspects of P4 ecosystems, startup-led ecosystems and consumer-centric P4-related services

[33] His notion of 'knowledge atoms' and 'logical operations' has to be interpreted in its historic context, considering that in his time, such language was used more 'playfully' from a modern perspective, while meanings have narrowed in our time. In his age, there was a widespread fascination to new possibilities enabled by mathematics and, in particular, 'algebraic thinking' with symbols and logic in many domains of life.

[34] Bouvet, at the time, had just gained access to precious documents held by scholars near the Chinese emperor, as he proposed a cross-cultural intellectual exchange between European science culture (math-based) enabling precise engineering, while the Chinese scholars helped him understand what they cherished in Asian ancient logic e.g. in the form of hexagram-based cosmological logic. Leibniz was excited about the exchange with Bouvet on this, as it seemed to fit well with his new 'binary logic' that later enabled digitalization of knowledge (encoding information as 0 and 1 sequences, or, in Chinese, as 'yin' and 'yang' encoding). From a contemporary perspective his understanding, through Bouvet, of that hexagram logic may have been superficial in some parts, as Leibniz had limited information and was focused on finding something that could make his binary logic more universal. One interpretation of this exchange with Bouvet is that it further encouraged Leibniz to pursue his epistemological vision, even if it is difficult.

here, this is the interpretation of his vision that we propose, knowing that there is considerable debate about the meaning of his vision (Milkov, 2006).

In medicine, knowledge and reasoning often taken an ‘Aristotelian approach to truth’, by forcing a decision about a statement being either ‘true’ or ‘false’, i.e. using Boolean logic (Alencar, 2024). For example, a clinical *lab value* measuring a blood-based circulating biomarker informing about a physiological health state is either below or above a threshold that separates ‘normal’ from ‘abnormal’ values. To simplify decision making in hectic work situations in healthcare systems, and to minimize required training for professionals. Is a particular symptom ‘present’ or ‘absent’? Due to its simplicity such Boolean logic is popular, easy to learn, disseminate and implement, and therefore omnipresent. Also, in digitalized decision support systems that are widely used. An Open Science example for such Boolean logic being implemented in a clinical decision context and related decision support systems is CQL (*Clinical Quality Language*), a project developing a standard that medical professionals and digital systems in medicine can understand [35], including those working in low-resource environments which may not have access to the latest technology for clinical decision support.

When facing health-related decisions that go beyond such Boolean logic, probabilities are often used to express a degree of uncertainty about a situation, e.g. a probability of developing severe complications after a surgery. Those probabilities typically are somewhere between 0 and 1 (or expressed in %, i.e. between 0 and 100%). In terms of probabilistic reasoning over medical knowledge, *Bayes Nets* are able to express conditional probabilities where the probability of an *event A* occurring can change if *event B* occurred first. In other words, there is a conditional probability, regarding those two events, written as $P(A|B)$. For example, if a patient is diagnosed with type 2 diabetes (event B), the probability of a diagnosis of diabetic renal complications (event A) after x years in that patient may have increased. In many situations such *Bayes Nets* composed of such conditional probabilities can express medical reasoning relatively well, so they have found their way into many decision support systems, to complement what can be expressed with simple Boolean logic (e.g. in the form of *decision trees)* (Ni et al., 2010; Lucas, 2001). However, there are fundamental problems, related to the previously mentioned important distinction between causation and correlation (how to properly capture it), and the difficulties when using such probabilistic approaches to encode knowledge about describing bidirectional influences between event A and event B (event A influencing the probability of B and vice versa).

Therefore, attempts were made to develop new knowledge and reasoning frameworks for health that would overcome the well-known limitations of Boolean logic and Bayes Nets for robust decision making in increasingly digitalized healthcare contexts (Lucas et al., 2004; Hunter & Williams, 2012; Friedman et al., 2014). Here, we argue that the problem of improving science-enabled decision making for *unguided patients* in *learning healthcare systems* is especially relevant, in the context of such efforts. To enable faster system-level (organizational) learning around the above-described *informative patterns* in patient trajectories, including those enabling endotype modeling. Such cases require special attention, in terms of our ability to combine many different and distributed weak signals that are hard to interpret using simpler medical logic.

The *digital epistemology* we propose here for such purposes is based on the work of *Barry Robson* [36] and his collaborators, building on earlier work by *Paul Adrien Maurice Dirac* (1902-1984) on what is often referred to as *Dirac notation*. Inspired by the ability of Dirac’s approach to encode more complex but real knowledge situations such as the representation of probabilistic and sometimes seemingly contradictory states in quantum mechanics, which would not fit the above simple logic (restricted to Boolean logic and Bayes Net style probabilistic reasoning), Robson et al. developed a language for encoding complex situations in medical decision making that could not be represented well with a combination of Boolean logic and Bayes Nets. The result of those efforts, the knowledge encoding language Q-UEL *(Quantum*

[35] https://github.com/cqlabio/cqlab-typescript, https://cql.hl7.org/

[36] As the CEO of *The Dirac Foundation*, Barry Robson was inspired by Dirac’s earlier work, and worked on its extension into the *digital epistemology* described here, including Q-UEL and HDN as key pillars of it

Universal Exchange Language), encodes medical 'knowledge atoms' in a particular *hyperbolic vector space,* using split-complex vectors and their scalar products. As a second step, a bespoke automated reasoning approach for Q-UEL, called *Hyperbolic Dirac Networks* (HDN) was developed (Robson, 2014; Robson, 2016; Robson & St. Clair, 2022; Deckelman & Robson, 2014). This used a vector algebra that can operate on knowledge encoded in this hyperbolic vector space. Here, special attention was given to situations in which knowledge is incomplete, weak or conflicting, and hence difficult to use for medical decision making based on probabilistic knowledge networks as bidirectional general graphs. A key design feature of this *digital epistemology* is to avoid the constraint of Bayes Nets being unidirectional in their conditional probabilities, only from event B occurring first to event A shifting its probability due to B having occurred (Polotskaya, 2024) [37]. The ability to encode *bidirectional* influences, from event A influencing B and vice versa, is considered important here, in the design of Robson's *digital epistemology* (Robson, 2014).

Applications of this *digital epistemology* will thus enable us to go beyond unidirectional probabilistic reasoning in medicine as enabled by Bayes Nets. For example, in chronic disease management, e.g. in cardio-renal-metabolic diseases (see 3.2), feedback cycles in the form of patho-physiological loops involved in what makes co-morbidities difficult to manage in healthcare cannot be properly represented with Bayes Nets.

As a consequence, we propose this *digital epistemology* as the logical next step in improving medical reasoning and epistemology, after the shift from Boolean logic to Bayes Nets style probabilistic reasoning. For building learning loops in LHS that learn, using trajectories of unguided patients. To find ways of improving outcomes and experience for such patients, even if EBM-grade evidence to guide their care is relatively weak.

Our *digital epistemology* consists of the following core elements:

- **Mathematical foundation**: Barry Robson's extension of Dirac notation into split-complex vector space enables us to go beyond combinations of Boolean logic and Bayes Nets (Robson & St Clair, 2022), as a foundation of Q-UEL and HDN
- **Q-UEL**: The language for encoding medical knowledge, e.g. a patient's state and potential hypotheses, decisions or actions related to that patient's state (Robson, 2007, Robson, 2014)
- **Hyperbolic Dirac Nets (HDN)** enable reasoning over knowledge encoded in Q-UEL (Robson, 2014)
- **Automation**: Processes for automatically converting existing medical data into Q-UEL and HDN, including automated quality control (Robson & Boray, 2018)
- **Digital systems** providing user-friendly interfaces to such integrated, complex knowledge and reasoning, to facilitate the discovery and validation of *informative patterns* related to unguided patient care, using the Q-UEL + HDN digital core (including patient-centric agentic AI)
- **System designs** that link all the above to human knowledge, behavior, decisions, education and other human activities that can affect a person's health state

Reminding ourselves of Leibniz' vision about 'knowledge atoms', logical operations and reasoning using symbolic computation over these knowledge atoms, Q-UEL basically provides the language for encoding medical knowledge atoms, while HDNs perform the 'calculation' (reasoning) over the knowledge atoms using relevant vector algebra. Leibniz' vision was not focused on medicine as a domain, as our *digital epistemology* is, but it is quite possible that with some adaptation, similar approaches may also develop outside the medical domain (however, we do not explore this further in this paper).

While our *digital epistemology* (described in this whitepaper) is a science-based paradigm for building patient-centric LHS, we noted that in the humanities the notion of a digital epistemology can have a different flavor, that may be complementary (e.g. as input in Design Thinking). For example, Ingvarsson's

[37] Cp. Joshua Pearl's do-calculus, as it sets probabilities to 1 (assuming certainty), 'what-if studies' in medicine

digital epistemology notion that views knowledge as a complex living web with many different kinds of relations, including causal effects that are a focal point for EBM, but also many other kinds of relations that help human cultures adapt to environmental changes, shift organizational cognition and respond to technological disruptions (Ingvarsson, 2021). Such '*epistemic bricolage'* across epistemologies in science and the humanities may help to find ways to balance the medical system's perspective and the individual's (patient) perspective in healthcare, as outlined above.

The way knowledge is digitally encoded, to better capture the real complexity of difficult cases and their trajectories, is important here. To avoid forcing reality into an over-simplified logical frame that does not work well for robust scientific decision making, for unguided patients. Q-UEL (Robson, 2014; Robson, 2016; Robson & St. Clair, 2022; Deckelman & Robson, 2014) is a language that was designed to enable such progress. Q-UEL manages uncertainty, by associating each statement of knowledge with a pair of bidirectional probabilities encoded in a single *split-complex scalar value* [38], thus overcoming the unidirectional and acyclic constraints of Bayes Nets[39].

With this, our *digital epistemology* allows the integration of health-related knowledge, symbolic logic and probabilistic reasoning, in a vector space representation of belief systems [40] that can evolve through further observation. Being designed to learn, very much in the spirit of Bayes' original thoughts about the ability to 'update beliefs' (our knowledge) with new data, giving ample space for different kinds of uncertainty and contradictions, in the way knowledge is captured and used for reasoning to enable increasingly robust decisions in LHS. Without forcing over-simplification and arbitrary decisions in modeling complex realities in healthcare.

In terms of the different sources of knowledge it can handle, it can also use knowledge that was automatically extracted from natural language, which can provide a much larger amount of (potentially lower-quality or mixed-quality) knowledge than is typically available in highly structured form, e.g. as knowledge triples encoded in RDF [41]. Learning, here, in this *digital epistemology*, is modeled as a transformation on vectorized knowledge atoms, e.g. of a patient's current state and a potentially fitting diagnosis, risk or other care decision. Note that in its design it does not carry a bias towards certain types of knowledge but allows for considerable flexibility in the incorporation of the patient's experience and outcome expectations, in addition to the medical epistemologies used by healthcare organizations in their operations. Being able to handle all these different sources of knowledge is important, as it can increase our chance of finding *informative patterns* to inform the care of unguided patients, e.g. by considering distributed weak signals that may otherwise be overlooked in classic frameworks.

Coming back to the EBM paradigm and its RCT-based evidence generation approach, as it helps to improve current decision logic in healthcare by updating Boolean logic (e.g. thresholds or new options) or Bayes Nets in decision support systems. Such EBM evidence is often summarized by medical expert communities that develop clinical guidelines for particular populations to facilitate the use of EBM evidence in clinical practice (Higgins et al., 2024). Developers of decision support systems then often try to encode such logic in their systems to make EBM evidence and derived guidelines (including algorithms) easily available in healthcare contexts when it is most appropriate and fits a particular case

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[38] like the complex number based on i that squares to -1 but now based on the split-complex number h (rediscovered by Dirac) that squares to +1. It was rediscovered by Dirac and is fundamental to Quantum Field Theory, and when used in the absence of i it allows Dirac notation to be applied to the everyday world of human experience. Avoiding i leads to the notorious predictions of quantum mechanics as wave mechanics.

[39] As with Dirac's approach, probabilistic elements of knowledge expressed with bidirectional probabilities can also be built up from vectors and matrices in which the elements have, in this case, h-complex values.

[40] The system 'holds itself up' because the *representation* of states (basis vectors) is defined by the very scalar overlaps they compute, and the operators acting on them are defined by their action on that same basis

[41] https://www.w3.org/TR/rdf11-concepts/ - It also allows the distinction of assertions extracted from natural language from other types of encoded medical knowledge, treating it in a consistent probability-theoretic way according to Popper's principle (Robson, 2015)

and decision. But as *unguided patients* do not benefit much from EBM evidence to inform care, the question of the design of LHS and their digital infrastructure and medical logic poses itself here.

In this context, in the last 10 years or so, the scientific paradigm of n-of-1 trials [42] is emerging as a potential future extension of well-validated EBM methodology, with potential relevance for at least some unguided patients (Kim-McManus et al., 2024). This methodology toolkit for personalizing care for atypical cases was designed with patients in mind who do not fit EBM-guided care logic well (Lillie, 2011). Here, several treatment switches can be combined with biomarkers (or other observations) that indicate positive or negative treatment response. To find the best treatment approach for that particular patient, considering their complex trajectory, history, and special needs. For example, if the patient is quite different from the populations studied by EBM, the n-of-1 trial approach may be considered appropriate to achieve better personalization of care. From a statistical perspective, it includes an ambition to find ways to move from the discovery of *informative patterns* as pure correlations (and related endotype modeling) towards insights into causation, e.g. using Bayesian modeling (Samuel et al., 2023). This could be an area of emerging synergies with the *digital epistemology* described here, as such n-of-1 trials accumulate precious longitudinal data (i.e. trajectories) about a patient's response to different treatments, if biomarkers are available to quickly assess treatment response before the next treatment switch happens. This may facilitate the discovery of *informative patterns* with a potential re-use in other patient populations, e.g. those with similar endotypes that influence treatment response and biomarker profile.

For a discussion of underlying mathematics in our *digital epistemology*, the role of the split-complex (hyperbolic) vector space, and major additions since Dirac's original work, see Deckelman & Robson (2014) and Robson & St. Clair (2022). For a gently narrative introduction without any mathematical notation, see our Appendix (those who are very comfortable with mathematics may want to skip that part in the Appendix).

Note that related mathematical approaches such as *Clifford Algebras* (Breuils et al., 2022) and other hyperbolic vector spaces may provide alternative paths to solutions. In recent AI research it was found that such hyperbolic (complex) spaces have clear advantages over classic Euclidean spaces, e.g. regarding the learning of hierarchical representations in AI [43] (Nickel & Kiela, 2017; Karsala et al., 2025).

Research into approaches for the automatic conversion of existing medical data in common formats into Q-UEL and HDN have shown that a method based on *information theory* promises to be able to transform complex data landscapes into the bidirectional relations encoded by Q-UEL in a robust way, e.g. using the k-method (Robson, 2014). This approach could also help enable the discovery of new *informative patterns* that combine weak signals, while imposing less assumptions and beliefs than classic methods. Which could facilitate the discovery of *informative patterns* for improving the care of unguided patients, and the interpretation of data generated in n-of-1 trials.

Regarding the digital systems providing user-friendly interfaces to such complex knowledge and reasoning with Q-UEL and HDN, to help a patient navigate a great variety of options, knowledge and potential decisions, we are currently in an early stage. However, as new LHS are entering the phase of system design (e.g. see section 3.1), this may provide an opportunity to upgrade their digital foundations as well, once it is clear what level of emphasis the new system will have on *unguided patient* trajectory

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[42] n-of-1 trials are less about average effects in populations as in many EBM studies, but more about the personalization aspect of P4, i.e. that particular patient with that particular profile even if it does not fit well into classic EBM methodology, guidelines or clinical research traditions. When using multiple treatment switches and biomarkers that help to understand efficacy and safety trade-offs quickly, Bayesian-style probabilistic modeling can be used to increasingly tease apart causation and correlation. How to best extract informative patterns from a collection of n-of-1 studies is an active area of clinical research. In the context of the proposed digital epistemology discussed here, the importance of epistemic humility being properly captured in the learning healthcare system, as well as the belief updating aspect may be focal points for synergy verification as data from n-of-1 studies accumulate

[43] their exponential volume expansion naturally matches the exponential branching of hierarchical structures — which is why hyperbolic embeddings are effective for hierarchies

problems outlined here. For example, such a system may find a balance between a) areas where classic approaches work well and can be deployed also in the new organization, e.g. where EBM-grade evidence is strong, b) areas where new approaches such as the one outlined here are needed to improve the care of unguided patients, allowing safe prototyping while monitoring the decisions made by physicians and patients, and their outcomes. For safety reasons it would therefore be advised to first build further confidence in the approach before influencing any medical decisions using the approach described in this whitepaper. On the other hand, patients are already using a variety of tools available to them to navigate health-related decisions, so the question poses itself if what we propose here could provide added value, e.g. by helping them make better decisions, build more solid health-related knowledge and improve health outcomes using an approach similar to n-of-1 trials.

3 Swiss landscape

Switzerland has been selected as an example context here for several reasons: a) the emergence of the new *Visana VIVA* preventive healthcare model and the synergistic 8P innovation framework (Bernier, 2024) fits the above-described problem of *unguided patient trajectories* in a preventive care context (see 3.1 below), as it provides an example of a new system design for P4-based healthcare [44], b) the SPHN (*Swiss Personalized Health Network*) collaborative communities of physicians, scientists and patients, and their approach to the collaborative, inclusive design of prototype *LHS* for unguided patients through patient-centric research initiatives, c) nationally-coordinated efforts in the next 10 years coordinated by *digiSanté*, including the planned Swiss Health Data Space (SwissHSD), as they may increase chances of finding new kinds of *informative patterns* across health care data silos to inform the care of *unguided patients* [45], d) progress made in Oncology centers in Switzerland in improving care for unguided patients, using a multi-omics rapid endotyping approach [46], e) the emergence of a highly collaborative and transdisciplinary pediatric community in Switzerland, as it develops a more holistic, science-based approach to the personalization of care including diagnostic challenges related to rare disorders and n-of-1 trials [47]. Also note that many of the authors on this whitepaper are Swiss residents, and through their work are familiar with different aspects of the Swiss situation that is relevant here.

3.1 P4 medicine and unguided patients, a new frontier – in Switzerland and beyond

The VIVA care and insurance model, designed by Swiss Medical Network (SMN) and Visana (a health insurance), implemented in three different rural regions in Switzerland, organizes integrated care delivery using a health system design that emphasizes preventive care, early detection of disease and health risks, and early intervention strategies, to keep people healthy, and avoid bad health outcomes where possible. In other words, this model emphasizes health maintenance at population level for the population that signed up to the VIVA model. It uses a bespoke health economic model (using capitation) to improve the alignment of provider incentives to this organizational goal. In this context, Bernier et al. (2024) have developed the 8P frame, to extend the classic P4 principles (to make medicine more *Predictive,*

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[44] It is a LHS in the sense described here, matching the 4 principles of P4 (make medicine more preventive, personalized, predictive and participatory) to maintain the health of the population. This entails a high level of attention on unguided patient trajectories, as most EBM-grade evidence is focused on classic healthcare models when patients are more sick with more severe symptoms.

[45] https://www.digisante.admin.ch/de/swiss-health-dataspace-de

[46] https://eth-nexus.github.io/tu-pro_website/ Rapid endotyping, here, is performed through the fast analysis of a tumor biosample from that patient, using a combination of different lab-based and computational methods, including genomics, transcriptomics, proteomics and other omics technologies that help us understand the endotype that is driving disease progression. See also the personalized combination therapy design approach tested in the Rapid-01 clinical trial in Switzerland, using *pharmacoscopy*.

[47] https://swisspedhealth.com/

Preventive, Personalized, Participatory) by adding 4 additional system design principles (*Purpose, Platform, Performance Sharing and Pooling*). Providing an example for a paradigm shift in organizational design in health. Which entails the challenge of finding smarter ways to personalize and deploy preventive care at population level, a new competence for Swiss healthcare systems, at that scale [48].

Note that organizations outside Switzerland have a longer history of implementing such models, e.g. Kaiser Permanente in the US [49].

As outlined above, such efforts require a bespoke digital foundation to enable robust decision making and system-level learning, even in cases that are not well-informed by EBM-grade evidence (and EBM-derived guidelines that encode logic and algorithms derived from that evidence). In this context, a patient-centric *LHS* has to figure out how to implement evidence-based algorithms that guide care decisions in a way that work in that particular population and setting, in addition to all those cases that would be considered atypical or not fitting into classic diagnostic categories at all. When shifting towards more proactive care, health maintenance and prevention, this organizational shift beyond the 'safe zone' of EBM-guided care captured well in high-confidence clinical guidelines becomes even more acute as EBM-level evidence tends to be weak in early stages of disease when symptoms are absent or quite weak.

In other words, such complex, atypical patient trajectories (Allam et al., 2021) from unguided patients (as defined above) and P4-style preventive care organizational transformations (such as the above examples) push us beyond established EBM paradigms for robust science-enabled decision making in health. Pushing us to explore new paradigms that are based on science, transparent mathematical foundations, e.g. using Open Science collaborative principles that facilitate cross-organizational and transdisciplinary learning on what works well in which setting.

In that context, it is reassuring that the proposed *digital epistemology* has been shown to fit the scientific foundational principles of EBM very well (Robson, 2016), while it also enables opportunities to explore new scientific paradigms that give special attention to complex knowledge and reasoning situations, including epistemic uncertainties and conflicting evidence, that are likely to be especially impactful for unguided patients.

Considering the difficulty of finding such new paradigms when similarities between patient trajectories (and informative patterns they may contain) are less obvious, we may find inspiration in cutting-edge approaches to the use of multi-omics tumor biosample profiling for endotype modeling in the *Tumor Profiler* project in Switzerland [50] as well as efforts related to earlier and improved diagnosis of rare disorders in pediatric care in Switzerland [51]. In those transdisciplinary innovation programs we can observe a trend towards the increased use of multi-omics profiling for unguided patients to find patterns related to endotype (disease-driving biology / physiology) that may help to find the most appropriate treatment. [52] We would expect that as such efforts mature, they will learn where the most informative patterns are likely to show up, to make such efforts economically sustainable.

However, the Swiss healthcare and health data digitalization landscape also provides a number of challenges in this context: a) digitalized health data being available for research at the appropriate level of quality, with the definition of quality depending on intended data use, b) fragmentation in the landscape of

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[48] 'a smarter way' in this context is essentially to build an 'organizational cognition' (and ability to learn at system level) beyond classic category-to-process bureaucracy systems (Rebhan, 2025), which tend to force-fit incoming cases (patients) into a set of categories that match the more frequent cases. In medicine, finding this 'smarter way' is important not only for patients and their outcomes, but also for the sustainability of the healthcare system itself with its limited resources.

[49] https://healthy.kaiserpermanente.org/washington/health-wellness/preventive-care

[50] https://tumorprofilercenter.ch/

[51] https://swisspedhealth.com/

[52] This is conceptually similar to the challenge outlined in Rebhan (2025) about an organization noticing that an incoming case does not fit the categories it uses to assign a process to that case.

healthcare organizations reflected in digital connectivity gaps in a particular patient trajectory [53] (data being stuck in health data silos), c) healthcare providers can be overwhelmed with administrative burden in their workday, and may be reluctant to engage in such innovation as proposed here, d) data being 'AI-ready' [54] in the context of FAIRification, apart from some data subsets that have already reached that level (overlaps with a), e) a bias towards hospital episodes [55] in the Swiss digitalized health data landscape, with many gaps in other areas of healthcare important for more preventive healthcare (covering earlier stages of disease and health risk monitoring).

3.2 Cardio-renal-metabolic patient populations and population health

Cardiovascular diseases (CVD), chronic kidney diseases (CKD) and chronic metabolic diseases (CMD) are highly prevalent in many geographies, causing considerable burden for patients and their families, healthcare systems, payors and other stakeholders. These diseases share risk factors, epidemiological patterns and pathophysiological connections. Therefore, it is not surprising that they show a tendency to overlap, in patient trajectories, resulting in considerable co-morbidity. It has been suggested to increasingly coordinate care decisions in this space, across different healthcare providers and medical specialties - and to shift care towards a more proactive model focused on those shared risk factors, by personalizing preventive care and focusing more on early risk detection. For example, if a patient gets a CKD diagnosis to also assess (and then monitor, over time) CVD and CMD risks (Ndumele et al., 2023).

New drugs like GLP-1 and SGLT2 modulators have shown considerable value in such populations, contributing to an increasing interest in smart prevention models. However, healthcare systems often struggle to operationalize such shifts towards more proactive and connected care, i.e. if their original system design was all about a focus on acute care, including related incentives and organizational structures.

In that cardio-renal-metabolic population, we can find subpopulations with elevated genetic risk that tend to experience a faster progression to bad outcomes. An example is the Lp(a)-defined CVD subpopulation with its increased risk of fast-progressing atherosclerosis (Reyes-Soffer, 2022). Will lifestyle interventions be sufficient here, also in later stages of the subclinical phase of ASCVD? When is it too early, for a non-lifestyle intervention, in those with high genetic risk? It all starts for an affected individual when the results from Lp(a) diagnostic testing are available to patients and medical professionals who may then face such questions, e.g. about timing. In Switzerland, under the umbrella of SPHN, CVD patient trajectories have been simulated using a digital twin that models an individual's personal anatomy in the cardiovascular system (Kozerke, 2025, Laumer et al., 2025), in collaboration with the UK Biobank [56] and their imaging effort [57].

When simulating trajectories and outcomes in such cardio-renal-metabolic populations, with their fast-progressing subpopulations, it can be helpful to use tools to simulate various secondary effects of improved health outcomes, i.e. the impact of changes in how we make care decisions. For example, at the level of social impact, as a shift in the health status of this population can affect many stakeholders in society. An example is PALY (Productivity-Adjusted Life Years) as a tool for such estimation. It quantifies health effects related to workforce productivity. With the basic assumption that a healthier population is more productive in many ways, including both paid and unpaid work in PALY estimates. Unpaid work can

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[53] Once the Swiss health data space (SwissHDS) is operational this situation is likely to improve

[54] FAIRification of data as outlined above also relates to the data being ready for use in AI, to make it interpretable for humans and machines. Note that Q-UEL is one of the approaches to enable human-AI collaboration.

[55] Hospital data are heavily biased towards urgent, acute care and later stages of disease progression, when symptoms are severe, while progress towards better preventive care requires more data about earlier stages of disease progression, when symptoms tend to be much weaker.

[56] The UK Biobank generated a large health dataset for an adult population that includes much information on such genetic risks, in addition to medical data that …

[57] An effort to generate imaging data at population level in the UK Biobank enabling the development of digital twins

include informal care for children, the elderly and the disabled, and even volunteering work as well. Related reference work has been performed in Finland, by Janne Martikainen et al. using Finnish population data (Lavikainen et al., 2025; Ademi et al., 2025). With tools similar to PALY we can then learn which measures have maximal effect at population level, where effects show up and how they can be stabilized. See also *elevateHealth* examples below for such modeling and simulation using the IOOI (input, output, outcomes, impacts) approach (section 3.3).

3.3 Agentic AI, digital twins, elevateHealth and related digital trends

In the last years we have seen much technical progress that may help to address the challenge of unguided patient trajectories and more patient-centric LHS designs in new ways. For example:

- Improved reasoning abilities of AI systems including medical and mathematical knowledge
- Improved understandability of expert knowledge and language for patients, also in medicine
- AI systems performing well on medical exams and similar question-answer tasks
- Progress related to agentic AI, multi-agent collaboration, and AI helping to code software

Considering such AI-related trends and their speed, in the next years, we may increasingly see more sophisticated patient-centric LHS emerge that empower patients to navigate a large, complex knowledge landscape related to their health and wellbeing in a better way. For example, agentic AI systems may be developed that achieve a high degree of personalization, considering the knowledge about health and disease that a patient currently has, the language they prefer, the style that works well to keep them engaged etc. to tap into an integrated knowledge landscape, using a reasoning approach that builds on EBM-style scientific reasoning about evidence and confidence, to then explore what works well outside of that space, where it matters to that patient, using informative patterns derived from unguided patient trajectories as inputs. Depending on the level of interest in learning that patient has, such an AI could help that patient to build up health-related knowledge based on increasingly robust reasoning. Across areas of knowledge, epistemological fields (see above), medical specialities and areas of knowledge that are not well understood by healthcare systems yet e.g. regarding the early detection of weak signals that can be used as inputs for such learning.

Agentic AI systems require a language that coordinates what different AI and non-AI agents do collaboratively, and to enable agent outputs to be evaluated and combined in that context. For example, natural language as produced and ‘understood’ by LLMs (large language models) and humans can be used for such coordination, typically with humans in the loop on key decisions and the language used for keeping that human in the loop adjusted to that particular person (Zhou et al., 2025). In that context, humans can be professionals working in healthcare systems, patients and their families, or other actors that collaborate in patient-centric LHS on improving decisions, outcomes, based on digitalized collections of patient trajectories [58].

Such agentic AI may then contain a number of different agents specialized on certain tasks, areas of knowledge and decisions. For example, an agent may focus on modeling the patient trajectory, and how it compares to a reference dataset of patient trajectories. Another agent may use that patient trajectory model to check if it’s an unguided patient trajectory, and then interact with relevant agents to deal with the case accordingly. Yet another agent may try to model endotype-related patterns that could help to improve the prediction of therapy response. And so on.

The *elevateHealth* Open Science community performs modeling and simulation of patient trajectories using a variety of modeling approaches, including Markov state modeling (a particular kind of digital twin

[58] In Europe such efforts would typically operate on a federated technology stack that keeps health data in their data silos while enabling learning and analytics. Synthetic data that represent particular populations may also play a key role esp. in prototyping.

that simplifies access to complex longitudinal health datasets; Laubenbacher et al., 2024). In the context of the patient-centric agentic AI described above, digital twins derived from the available knowledge that is relevant for that particular patient can be used to visualize the likely effects of potential health-related decisions considering what we learned from a larger set of patient trajectories. Up to personally relevant aspects of social impact as captured by the PALY approach (see above). To enable patients to simulate what will happen, in which time frame, if they do X or Y.

Learning at system level, here, also means to learn when updates based on new data from that patient actually help to decrease particular uncertainties captured in the digital epistemology, e.g. as Q-UEL. There may be situations where the opposite can happen, e.g. new data actually increase uncertainties. Note that different actors as mentioned above, e.g. different healthcare professionals, patients and scientists, may have different, complementary perspectives and understanding of uncertainties, which can be captured in Q-UEL. Additional interactivity between *elevateHealth*-style simplistic Markov models and the proposed *digital epistemology* may include a data-driven discovery of health states (Markov states) [59], and for checking consistency between simplistic elevateHealth-style models and the full complexity captured in the digital epistemology.

Specialized LLM-style AIs to model and generate patient trajectories using UK Biobank and Danish data have recently been published, as LLMs are increasingly used in related research (Shmatko et al., 2025). Note that such health LLMs could be used to generate *synthetic datasets* composed of a large number of patient trajectories for prototyping agentic AI work. However, note that any AI work as outlined here in 3.3 needs to consider what we know currently about different biases that affect AI e.g. due to the biases we can describe in the data that were used to train the AI (Nonori et al., 2021).

3.4 Human-centric design, patient empowerment and knowledge

In Switzerland, many of the above-mentioned *SPHN* or *digiSanté* programs emphasize the use of patient-centric, participatory approaches, including increased patient empowerment (Varela et al., 2025), human-centric design of AI-based digital systems, and digitally enabled personalization to better fit digital systems into people's lives (Seebode, 2013). For example, the increased use of patient-reported outcome (PRO) tools to better estimate changes in delivered tangible value for patients, in addition to expert clinical definitions of value, complement the understanding of a patient trajectory, and helps to achieve a better balance between system and individual in system design (see above). Empowerment, here, is also about enabling the personalization of preventive care, tapping into a rich knowledge landscape to help a patient make better decisions related to their health.

With increasing use of digital systems, including agentic AI, as outlined above we will see an improved consideration of the patient experience in a form that can help us with the discovery and validation of *informative patterns* in patient trajectories, even if they are combinations of weaker signals that are distributed across data silos currently.

[59] Typically, health states in Markov models are decided by a team of modelers who make decisions about the simplification of complex realities in the model design. A data-driven approach is possible as well, where the health states are learned from data, and then checked by the modeling team.

4 Outlook

In terms of an outlook, it may help us to understand key differences between the proposed *digital epistemology* (and its relevance for learning based on unguided patient trajectories) and the current medical epistemology used in healthcare decisions. Our *digital epistemology* is not meant to replace the existing one, but to extend it, focused on providing additional value related to the problem of unguided patients, and the design of patient-centric systems, where existing epistemology does not provide sufficient guidance yet. If such an unguided patient is lucky to meet a highly knowledgeable healthcare professional who has all the relevant knowledge [60] to make a good decision on a difficult case, enough time and attention (including the patient's knowledge, experience and insights), not being incentivized to force-fit the case into a diagnostic code that does not really fit - if all these factors are optimal in the moment when a key decision is made, then our case as presented here may be deemed weaker. However, how likely is it, in healthcare system realities with limited resources, limited time, imperfect attention etc. that all factors are optimal at that time? How much time would the patient have to communicate what's missing in the expert's perspective on the problem?

As healthcare shifts increasingly towards smarter personalization of preventive care, we will need digital systems that help us learn how we can improve, build knowledge and make decisions. But hopefully not using an 'over-dose' of black-box AI [61], but something more scientific and robust that can enhance our shared knowledge and reasoning. Even if that patient is not highly educated in relevant scientific paradigms. With Health Data Spaces then improving our ability to see informative patterns across health data silos, agentic AI improving the patient's ability to navigate all this, we may soon be able to witness a new phase of health innovation.

Once we have been able to build an Open Science catalog of such informative patterns in unguided patient trajectories, and a better understanding of the types of unguided patient trajectories that can be found, such information, if well-organized, could help to better connect the efforts of a) those working to improve decision making as outlined above, with b) those who need information about underlying endotypes that drive disease progression in unguided patients, to develop new interventions for these difficult cases. Considering that our knowledge about disease biology is quite patchy in many areas, there may be different ways to describe 'tentative' endotypes, from different angles, as we capture different hypotheses and the evidence that supports them. Without over-simplifying what we know so far about the less studied endotypes, including those active in earlier stages of disease (where we tend to have less EBM-grade evidence but may have animal models to study). To accelerate efforts to improve care decisions and the options available to such unguided patients, through endotype modeling.

While currently widespread, simpler logic such as Boolean reasoning in decision trees and Bayes Nets for probabilistic reasoning can solve many common cases quite well, based on currently available evidence, we argue that unguided patients provide a clear opportunity to apply more sophisticated digital epistemologies such as the one outlined here, to overcome the known limitations of such simpler reasoning and knowledge representation, to bring patient-centric LHS to the next level. Making expert knowledge more accessible to more people as they make health-related decisions.

In that context we plan to build an Open Science initiative with a Python code and synthetic data repository on GitHub, and appreciate any constructive inputs and contributions to that community effort. Therefore, this whitepaper is meant to provide a reference and scope for this Open Science initiative.

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[60] In other words, while a highly knowledgeable individual can make a big difference, it does not mean that this knowledge is accessible to others e.g. within that learning healthcare system.

[61] There may be helpful applications of black-box AI in medicine even if we don't really understand the decision the AI made, but in general, in medicine, we want to use a more scientific approach to decision making, where we can, which can extend our knowledge and improve our reasoning for the benefit of patients and other stakeholders who are interested in good healthcare and healthy, productive populations.

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APPENDIX

4.1 Epistemological Concerns

Epistemologies are frameworks for knowing, with a set of rules and norms about what counts as a valid question, a legitimate method, a credible source, an acceptable proof, a justified belief and a contradiction (and how to handle it). They are socially created and maintained (Lemos, 2020). In the context of Thomas Kuhn's original view on paradigm shifts in the history of science (Kuhn, 1962), such shifts are enabled by a change in epistemology. Different historical periods and cultures have built different epistemologies that facilitate human coordination. As scientific disciplines establish themselves and their boundaries, they create their own epistemology. The proposed *digital epistemology* above involves choosing how we want to know and learn, including complex, uncertain, and evolving domains in medicine, and other areas of knowledge related to human health. In such efforts we may therefore be informed by past epistemologies, evaluating their strengths and blind spots. Epistemology-related questions for building patient-centric LHS may then include a) do we want to preserve epistemic uncertainty rather than de-emphasize it?, b) does it need a transparent handling of assumptions and versioning of knowledge?, c) how to handle edge cases and contradictions?, d) how much can meaning and validity vary by context and perspective?, e) how do algorithmic approaches that work well with machines connect with human sensemaking (patient, experts)? f) can we hold hypotheses in tension, waiting for resolution? How does resolution happen? Some of those questions relate to the overarching notion of *epistemic humility* and transparency of epistemic uncertainties that may not be considered well in past epistemologies. The current wave of innovation related to AI-supported patient-centric decision making may provide an opportunity for re-thinking along such lines to avoid over-reliance on intransparent black-box AI in decision making. Therefore, unguided patients who don't fit well into clinical care guidelines and the EBM evidence landscape help us see the limits of our current medical epistemologies and what we need to improve.

4.2 Different Types of Uncertainty

Hüllermeier & Waegeman (2021) propose that a trustworthy representation of uncertainty is desirable, especially in safety-critical application domains such as medicine and socio-technical systems. Not only as an on-average uncertainty for a particular type of prediction, but for a particular prediction on a particular instance for a particular patient (considering the patient's trajectory in the context of a larger collection of other trajectories). In the AI literature, there is increasing recognition of the need to distinguish different types of uncertainty, with effects in how we model and do machine learning. Basically, in addition to uncertainty caused by randomness (aleatoric uncertainty), a different type of uncertainty is 'epistemic uncertainty', i.e. uncertainty due to weak knowledge. The latter has the advantage that it can be reduced with additional information. In other words, we can reduce 'ignorance' by learning, i.e. by reducing epistemic uncertainty. Therefore, it is also considered the 'reducible' part of uncertainty, in contrast to irreducible parts considered in previous theories about uncertainty. In patient-centric LHS, their system-level learning goals can often be described in terms of reducing such ignorance, through a learning process the aims to reduce epistemic uncertainty, where such reduction is likely to result in improved patient outcomes and other process-level improvements. Considering the principles of value-based health care (Porter, 2010).

4.3 P4 Ecosystems and unguided patient trajectories

Using the meanings behind the fundamental improvement principles of P4 medicine (i.e. to make medicine more *personalized*, *participatory*, *preventive* and *predictive*) we can derive criteria for answering the question of whether a LHS composed of complementary organizations is indeed a P4 ecosystem, or not. If ecosystem-level goals that guide the collaborative effort (i.e. they are used for defining the meaning of success and related KPIs [62]) include making the practice of medicine more personalized, participatory, preventive and predictive - often in addition to other goals, and areas of focus, that are specific to that ecosystem. In addition to criteria derived from those 4 principles, we can define other ecosystem properties as criteria: a) ecosystem orchestration processes that help to manage conflicts (potential negative outcomes) and maximizes synergies (potential positive outcomes) between the participating organizations, b) a way of plugging in for a new organization that wants to join, and c) a shared learning process at ecosystem level that matches at least some Open Science principles (UNESCO, 2021) in the sense that sufficient transparency is designed in to keep the ecosystem engaged.

Therefore, different archetypes of P4 ecosystems would fulfill all those criteria, but in different ways. Traditionally, ecosystem orchestration (Valkokari, 2015; Valkokari, 2023) is centralized, driven by the organization that invited others into ecosystem co-design and risk sharing negotiation. Exemplified by the Integrated Care archetype of P4 ecosystems (section 3.1), the Nightingale archetype for metabolomics-enabled health risk detection and health maintenance for working populations in Finland (Buergel, 2022) and the HiNouNou connected health ecosystem (a patient-centric LHS with digital twins evolving towards agentic AI as described above) [63]. However, new orchestration models that increasingly deviate from classic, top-down ways of organizing may emerge over time, e.g. through decomposing what orchestration is about in ecosystem design. Our whitepaper here relates to P4 ecosystems in terms of a) ecosystems figuring out how to make progress with P4 translation into health care, b) enabling aspects of that shared learning process that require a paradigm shift in its scientific foundations, beyond classic probabilistic modeling and reasoning, and over-reliance on black-box AI or even Boolean logic, c) enable a data-driven refinement of decentralized orchestration models to adjust the level of decentralization where it helps to improve at ecosystem level. In that sense it will be exciting to watch how this space will develop in the next years, and which P4 ecosystems will learn faster and become smarter, using which approach.

4.6 Programming Aspects

A few comments on how to ‘code this in Python’ or other programming languages. For example, in Python, split-complex vectors and relevant vector algebra are not part of the standard distribution of Python or any commonly used libraries. Therefore, some open source code development effort may be needed to facilitate experimentation using code. Note that Q-UEL itself can be considered a programming language. See also the POPPER language, a simplified form of Q-UEL to teach medical students how medical decision support tools are built, based on Q-UEL principles (Robson, 2015).

[62] KPI = key performance indications, used to track an organization’s performance at system level
[63] https://www.hinounou.com/

Glossary of terms

In the spirit of the 'Epistemic Bricolage' as described in this whitepaper, our glossary of terms will focus on vocabulary we used here that may be confusing to some readers, a) as its use here implies a certain semantic distance from commonly used standard meanings, b) as the term is used in a context they are not familiar with, c) as any kind of Bricolage across the sciences and humanities may be uncomfortable to those who prefer to be either scientists or humanities scholars. See also Levi-Strauss (1962) and our comments on that paper's notion of 'Bricolage'. We prefer concise definitions even if they lack precision in some minor semantic aspects.

Bureaucracy: an organization that at its core is a category-to-process system, mapping incoming cases to a fixed set of categories, with processes attached to those categories. During the organizational ossification process (also called organizational aging) the fixed set of categories is increasingly out-of-touch with a changing world surrounding the organization. As a consequence, the ossified organization struggles to learn and adapt by using cases that do not fit those categories well as inputs to the learning process. See Rebhan (2025).

Digital epistemology: an epistemology that enables the transformation of classic *bureaucracies* into more patient-centric, learning systems that can learn from cases that do not fit well their inherited system of fixed categories in organizational cognition, exemplified here by *unguided patients* and their trajectories. Note the more detailed definition in section 2.

Epistemology: The theory of knowledge, especially with regard to its methods, validity, and scope, and the distinction between justified belief and opinion. See footnote 2 for details, regarding the broader semantic field relevant here.

Learning healthcare system (LHS): a digital system that tracks patient trajectories and learns using outcomes, including what happens in healthcare systems but also outside of them. Learning is about improving care decisions.

LLM: a large language model, an AI trained on natural language patterns, and knowledge encoded in natural language.

Patient-centric LHS: a LHS that integrates medical expert knowledge and patient knowledge as it tracks patient trajectories comprehensively to optimize a patient's ability to make good health-related decisions, balancing the healthcare system and patient perspective in the way how it encodes knowledge and reasoning.

Patient trajectory: a dataset of time-stamped health(care)-related events for a single patient, including events related to diagnosis, treatment, outcomes and decisions made. Including events that are recorded by healthcare systems, and those recorded by patients. A set of patient trajectories may consist of patients with the same diagnosis but different treatment approaches and outcomes. See Allam et al. (2021) and Kapur et al. (2022) for a perspective and an AI example.

Unguided patients: a special case of an incoming case that does not fit the organization's fixed set of categories well. Here, a patient who does not fit the evidence landscape. In other words, the patient is not similar enough to those for which a lot of science exists to guide care decisions. See section 1 and 2.