Artificial Intelligence: Leveraging Disruptive Technology to Improve Reimbursement Decision-Making

Complexities in the Canadian access and reimbursement environment demand that industry, payers and health technology assessment bodies find new ways to collaborate in order to solve significant challenges. Artificial intelligence offers new opportunities to transform research into optimized treatment and disease management for patients. Technology can enable downstream efficiencies while simultaneously bringing important insights to reimbursement decision-making. To remain ahead of ongoing challenges, industry stakeholders must embark on these new paths to facilitate reimbursement. This shift in thinking has the potential to improve cost management while positively affecting patient outcomes, resulting in more personalized health care.

Shelley Epstein

KEY POINTS

- Canada's aging population exposes the gaps in the country's access and reimbursement practices.
- Age-related diseases are rising and the health care system struggles to keep up.
- Health technology assessment bodies and payers need to upgrade their assessment frameworks to account for artificial intelligence (AI) and other disruptive technologies to meet current and future challenges.
- AI is perfectly positioned to apply to all stages of the care continuum.
- Payers are shifting to value-based health care, which can be augmented by AI.

The Canadian access and reimbursement landscape is changing at a rapid pace, due in large part to an aging population and a surge in age-related diseases. Disruptive technologies like artificial intelligence (AI) are creating new avenues for industry, payers and health technology assessment bodies to stay ahead of the curve by shifting to value-based health care augmented by AI.

Challenges in the Canadian Health Care System

THE NEED FOR CHANGE IS ACUTE

Canadians are getting older. According to the Canadian Institute for Health Information (CIHI), by 2037 Canada's senior population will grow by 68% – to 10.4 million individuals over the age of 65.[1] That is in concert with 2019 statistics showing that the average Canadian's life expectancy increased to 80 years for males and 84 years for females.[2]

Advancing age is the most important – and perhaps the strongest – risk factor for complex diseases like cancer and Alzheimer's, which are caused by a combination of genetic, environmental and lifestyle factors.[3] For example, a staggering one in 20 Canadians over age 65 has Alzheimer's disease. The risk of developing Alzheimer's disease doubles approximately every five years after age 65, with one in four Canadians over 85 having it.[4] The risk of cancer also increases substantially with age. A startling 90% of new cancer cases will be diagnosed in Canadians aged 50 and older, with the highest number of new cancers diagnosed in those between the ages of 65 and 69.[5]

Accordingly, there will be increasing demands on our health care system as a result of greater health care

[1] CIHI. Infographic: Canada's seniors population outlook: Uncharted territory. 2017: https://www.cihi.ca/en/infographic-canadas-seniors-population-outlook-uncharted-territory.

[2] Statistics Canada. Table 13-10-0114-01, 2020-01-28: https://www150.statcan.gc.ca/t1/tbl1/en/tv.action?pid=1310011401.

[3] Craig J. Complex diseases: research and applications. *Nature Education*. 2008;1(1):184.

[4] National Cancer Institute: https://www.cancer.gov; Alzheimer Society of Canada: https://alzheimer.ca.

[5] Canadian Cancer Society. *Canadian Cancer Statistics 2019*. September 2019: http://cancer.ca/Canadian-Cancer-Statistics-2019-EN.

needs of the aging population. Governments need to think through cost-control measures that can alleviate the financial pressures on their health care budgets while still delivering essential patient care and novel therapeutics.

REIMBURSEMENT LANDSCAPE

In the past few years, we have seen the industry shift to leaner, more specialized drug pipelines. There has also been a surge in competition in some of the most high-burden, high-cost and complex disease areas like oncology. In parallel, it has become increasingly difficult for patients to obtain access to new drugs. The introduction of novel groundbreaking drugs now comes with higher treatment costs, which is raising concerns about affordability and how payers will finance these new treatments. Over the 10-year period from 2006 to 2015, the cost of new anti-cancer drugs increased more than five-fold.[6] As a result, payers are struggling to find efficiencies and methods to control costs in their budget allocations to ensure the sustainability of the health care system.

There are several significant factors also at play currently: 1) The Canadian pharmaceutical environment is tumultuous, with the pending Patented Medicine Prices Review Board (PMPRB) reforms regulating the prices of all patented medicines; 2) The possibility of a national pharmacare program, which is envisioned to make prescription drugs more affordable and accessible; and 3) A fragmented Canadian health care system, with misaligned priorities between payers and health ministries. Payers have a shorter-term view with a focus on drug acquisition costs, whereas ministries view health care consequences over the long term.

With regard to the latter, these contrasting viewpoints are difficult for industry to reconcile and navigate when trying to build a case for a drug's value proposition. Additionally, the current access and reimbursement landscape imposes burdensome obstacles for go-to-market implementation.

Well aware of the challenges on the horizon, payers understandably want assurances from industry. Specifically, payers need to know that what they pay for actually works so they can forecast budgets accurately and predictably. However, if the industry and payers continue to use the same tools and offerings to secure reimbursement, it is unreasonable to expect a different outcome that will shift the trajectory of disease management and treatment. They need new solutions.

Fortunately, we are entering a transformative stage with the strength of research and potential for disruptive technologies. The thirst for discovery and life-changing solutions must now expand into other areas of the care continuum, such as reimbursement decision-making. It is clear that there are unique properties and opportunities that AI and other disruptive technologies provide. As such, both payers and health technology assessment (HTA) bodies need to rethink and upgrade their assessment frameworks.

> *"I believe that payers and HTA bodies are intrigued by the potential of AI and how it could support their efforts in ensuring appropriate and cost-effective use of therapeutic products. Education of these decision-makers on the potential of AI will be a key success factor. In addition, presenting concrete and practical examples of how AI has been leveraged to improve health care delivery and/or support reimbursement decision-making, conditional listings that leverage RWE, etc., is important, as payers typically don't have the time or bandwidth to figure out how to leverage AI on their own, given their myriad of other responsibilities."*
>
> *Dr. Judith Glennie, Pharmaceutical Policy Consultant and former Associate Director, Drug Programs Branch, Ontario Ministry of Health*

Why Canada is the Ideal Market to Conduct AI Work

Canada is among the most culturally diverse places in the world with about one in five Canadians born outside the country.[7] Canada's rich multicultural population is a microcosm of the globe, making it opportune for AI research.

As an HTA country, we apply the same rigour to our clinical and economic assessments as many of the largest markets in the world, rendering them scalable

[6] Harding A. "As cancer drug prices climb, value not keeping pace." Reuters Health News, April 12, 2018.

[7] "Marketing across Canada's multicultural landscape? New research from MediaCom Canada reveals what you need to know." January 2, 2018: https://digitalmainstreet.ca/marketing-across-canadas-multicultural-landscape-new-research-mediacom-canada-reveals-need-know/; Statistics Canada: https://www12.statcan.gc.ca/.

to countries like the UK, Germany and France. Canada also has a favourable risk-to-benefit ratio, given that Canadian pharmaceutical subsidiaries typically account for approximately 2% of global headquarter revenues.[8] The upside to conducting this work in Canada is that it limits the overall company risk, particularly when applying AI as a use case in one specific therapeutic area and/or indication.

AI Technology to Enhance Reimbursement Decision-Making

WHAT IS AI?

Artificial intelligence in computer science refers to the ability of a computer system to make a good prediction or a good decision on a specific task given context, which historically would have required human cognition.[9] Most of the capabilities available today can be categorized as artificial narrow intelligence (ANI), which assists with or takes over specific focused tasks but lacks the ability to tackle tasks outside of its training domain. Machine learning (ML) is an application of AI that provides systems the ability to automatically learn and improve without being explicitly programmed. It focuses on providing knowledge to computers through data, observations and interacting with the world such that they can use it to learn themselves. That acquired knowledge allows computers to correctly generalize to new settings that were not previously encountered as part of the training data.[10]

There are many ML approaches, called learning paradigms, which include supervised learning, unsupervised learning, reinforcement learning and others. These approaches can be used to train algorithms to perform specific tasks, including classification, cluster analysis, translation, regression, etc. This is conducted in a broad range of domains, such as vision, language and robotics, which depend on the underlying technology of neural networks. See Figure 1 for further information.

AI software can be applied to all stages of the care continuum including screening, diagnosis, treatment, prevention, monitoring and predictive capabilities.

Importantly, Canada is becoming world-renowned as one of the epicentres for AI.[11] The country is fortunate to have several high-profile Canadian AI institutes to support the health care industry with this important work. These include the Montreal-based Quebec Artificial Intelligence Institute (Mila), the Vector Institute in Toronto and the Alberta Machine Intelligence Institute (AMII).

POTENTIAL USES FOR AI IN HEALTH CARE

The potential uses for AI in health care are significant. The Canadian health care system is sitting on vast amounts of data gathered through electronic medical records, lab reports, genomics and clinical trials. However, much of it is dormant. AI technology can help extract value from the data by:

- Structuring the data and identifying links across the different datasets
- Further linking the data to clinical outcomes
- Providing key findings and actionable insights for health care providers[12]

AI software can be applied to all stages of the care continuum including screening, diagnosis, treatment, prevention, monitoring and predictive capabilities. The insights extracted can be used to assist with early identification of disease, appropriate diagnosis, and predicting the likely outcome or recurrence of a disease. There are valuable benefits for disease management as well, by providing information to help predict the likely patient response to treatment.[13]

In addition, AI-powered clinical decision-support systems and predictive analytics have the potential to help physicians make faster, less expensive and better data-driven care decisions to enable improved patient outcomes.

Looking at oncology as one promising area of AI application, cancer care teams could use prognostic data, clinical data and models to predict treatment response. This enables informed, patient-specific

[8] Government of Canada. Pharmaceutical industry profile: https://www.ic.gc.ca/eic/site/lsg-pdsv.nsf/eng/h_hn01703.html.

[9] Russell S and Norvig P. *Artificial Intelligence: A Modern Approach*, third edition: http://aima.cs.berkeley.edu/.

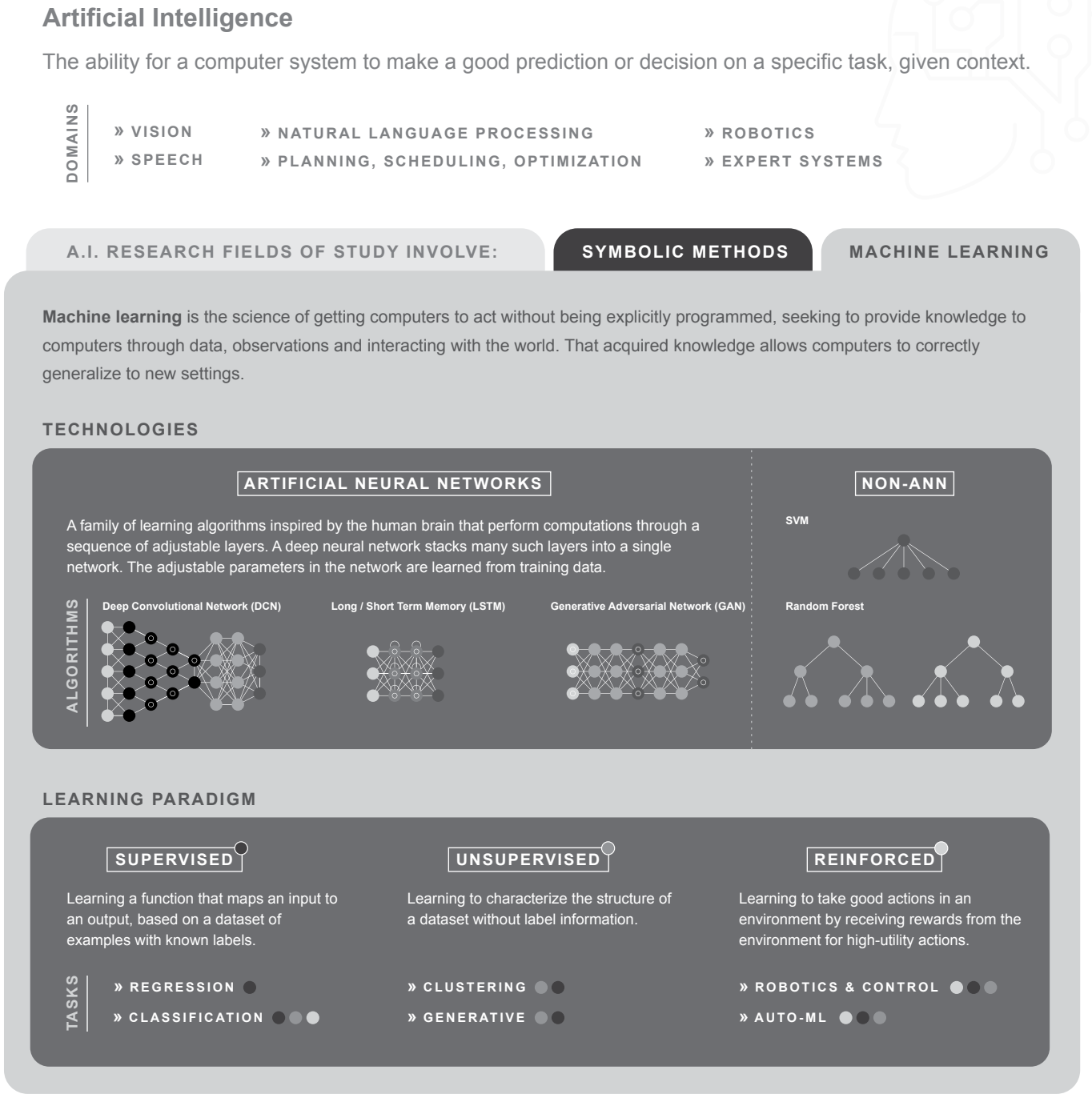
[10] Stephens et al. Frontiers of Oncology. 3.2020.

[11] "How Canada got so smart on artificial intelligence." *Globe and Mail*. April 7, 2019: https://www.theglobeandmail.com/opinion/editorials/article-how-canada-got-so-smart-on-artificial-intelligence/.

[12] Price, W Nicholson. Artificial intelligence in healthcare: applications and legal issues. 14 SciTech Lawyer 10 (2017).

[13] Ibid.

Figure 1: Machine Learning



Source: Imagia

treatment decisions that reduce manpower and resource waste in the health care system and empower value-based care.

AI represents an opportunity to experiment with different strategies and mechanisms to more closely align the costs and treatment benefits.[14] The outputs can be used to model budget impact analysis and identify potential avenues to offset and/or avoid certain costs earlier in the patient journey. This is done by applying real-world data and using AI to

[14] Harding A. "As cancer drug prices climb, value not keeping pace." Reuters Health News, April 12, 2018.

predict treatment response and outcomes. Overall, this will lead to operational, clinical and health care efficiencies that will aid in reimbursement decision-making by allowing for timely, appropriate therapy and preventative procedures.

RELEVANCE FOR PAYERS AND REIMBURSEMENT DECISION-MAKING

In the past few years, payers have shifted their focus to value-based health care. They want to pay for medications that work optimally for the appropriate patient at the correct time of intervention. This is the value that AI can bring to the equation.

Consider the implications for access and reimbursement and, more specifically, discussions with HTA bodies and the pan-Canadian Pharmaceutical Alliance (pCPA) on a drug's value proposition and the potential to save unnecessary costs, time and procedures. AI can boost evidence-based decision-making to select the most appropriate medications with optimal efficacy for a given patient or subpopulation at treatment initiation rather than through trial and error. This can certainly aid in bringing more specificity to discussions on coverage criteria for new medications or alternatively enhancing coverage criteria for existing medications to better serve the patient population. This is where the applications of AI start to get interesting – not only for patients and health care providers, but also for payers looking for areas where costs can be mitigated or potentially redirected to garner more value.

Physicians will be able to garner the insights to discern whether a drug will prove efficacious or not, as well as how to dose appropriately.

Many people think about AI in its most basic functionality – as a productivity tool used to augment and automate human capabilities. Once you start getting into the more transformational aspects of disruptive technology, like virtual testing, the insights become interesting to payers. Having the ability to predict a test result in real time during the procedure allows health care providers and decision-makers to choose optimal care pathways. As one example, during a procedure AI can predict within milliseconds whether a detected polyp is cancerous or benign and the type of processing it requires. A physician will know whether or not they must escalate testing to a more advanced or more expensive test, and whether pathology is required. This is transformational.

Some of the more advanced properties of AI are the principles of probability and predictability based on medical information (i.e. "big data") to support enhanced decision-making. AI can uncover information and testing gaps that may have significant repercussions for patient care, disease management and treatment guidelines.

The benefits of this can be significant for patients, health care professionals and reimbursement bodies. Physicians will be able to garner the insights to discern whether a drug will prove efficacious or not, as well as how to dose appropriately. As a result, when a patient is prescribed a particular medication, there will be a higher probability of success. This will have far-reaching ramifications for the health care industry. Faster, more accurate and more successful diagnosis and treatment will translate into significant medical cost mitigation. This is due to a decreased likelihood of adverse events, reduced physician visits for additional testing, as well as less time spent conducting trial and error treatment with other medications.[15]

NAVIGATING THE CHALLENGES OF AI

Creating data-related value while preserving patient privacy is the most significant challenge in the health care and life sciences sectors. Developing robust AI-driven health care solutions requires access to large data sets, accessed across multiple institutions and countries, to create meaningful insights. Although much has been written about AI as one of the possible solutions in health care decision-making, AI must overcome its own set of challenges, including the following.[16]

- **Data not being set up for AI breakthroughs at scale.** There is a wealth of unstructured health care data from fragmented sources that sits siloed within hospitals, administrative systems and device databases. The dormant data is trapped in these

[15] Ziad Obermeyer, et al. Predicting the future - big data, machine learning, and clinical medicine. *N Engl J Med*. 2016;375:1216-1219; Kriwet C. "Here are 3 ways AI will change healthcare by 2030." January 7, 2020: https://www.weforum.org/agenda/2020/01/future-of-artificial-intelligence-healthcare-delivery/.

[16] "Healthcare big data and the promise of value-based care." *NEJM Catalyst*. January 1, 2018: https://catalyst.nejm.org/doi/full/10.1056/CAT.18.0290.

systems. We need to find mechanisms to extract the valuable insights from the data that can be shared across health care networks to accelerate discoveries and medical advancements.

- **Health care data is organized for routine clinical access, not for outcomes-based investigation.** Information is organized to allow for a quick overview of a single patient across different data sources – labs, pathology, imaging, history, etc. – which enables clinical decisions at the point of care. For example, a clinical encounter is dictated as a story with patient context in text format. This is not structured to be AI-friendly and is difficult to understand when "ingested" by these types of technologies. Rather, the data needs to be formatted for ML purposes (i.e. statistical learning).
- **AI systems require a significant amount of data to produce robust findings.** Single hospital and industry datasets are simply not sufficient on their own to allow AI-driven discovery processes in precision medicine. That is why the concept of federated learning (i.e. sharing learnings and algorithms that travel across institutions while maintaining institutional data privacy) is critical to help solve this challenge.
- **Maintaining the privacy and security of patient data are significant concerns that need to be addressed.** There is robust legislation that rightfully prohibits sharing private health care records across institutions, provinces and country borders. Ensuring adherence to patient data privacy and institutional privacy are key concerns.[17]

The Power of Data-Driven Insights through Federated Learning

Conventional ML is performed on data aggregated in one location, at one site, through centralized learning. In contrast, federated learning systems enable the collaborative training of ML models on data distributed among multiple organizations (e.g. multiple sites within a province, across countries), providing more diverse patient data.

Federated learning is an important practical solution in health care AI, because the data remains onsite with its respective owners and is not centralized, aggregated or directly shared. Since the data is sitting in different locations, the ML models travel and aggregate the learnings in a central server (Figure 2), retaining data privacy and governance. Using these systems, health institutions and technology companies can achieve best practices in terms of data access while ensuring security. For example, the data can remain within the firewalls of individual hospitals and also remain de-identified for use in the larger cohorts needed to optimize algorithms to enhance the overall patient experience.

Federated learning is an important practical solution in health care AI, because the data remains onsite with its respective owners and is not centralized, aggregated or directly shared.

Federated learning enables the training of a model that accounts for all the data from the different sources, combining or harmonizing learnings from different sources, and making them suitable for mega- and meta-analyses.

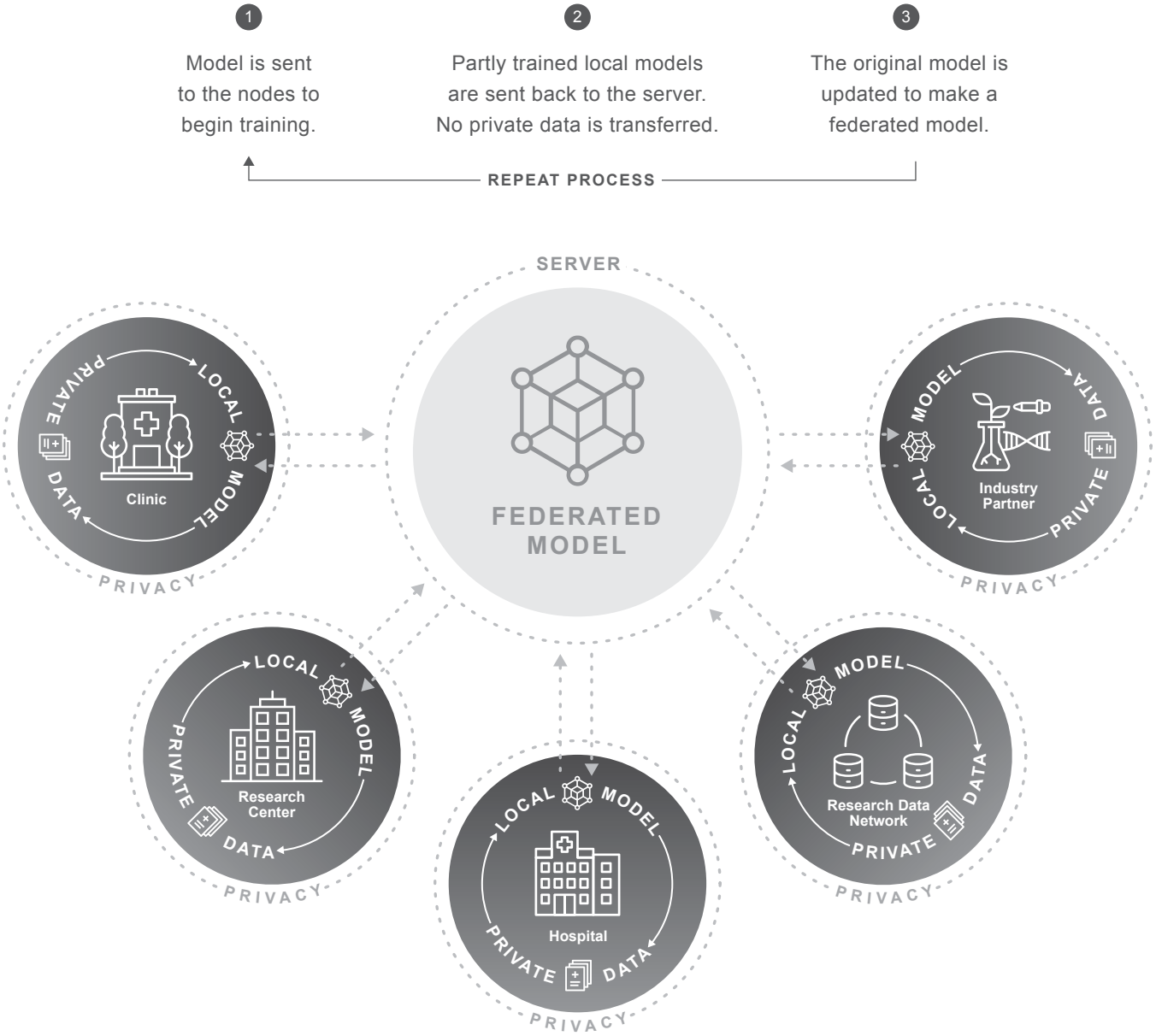
Imagia's EVIDENS™ AI discovery platform and clinical collaboration ecosystem enables federated learning on patient data across multiple hospitals and unites creative minds in both AI and health care to power discovery at scale. The platform empowers clinical researchers from different pan-Canadian institutions and beyond to derive outcomes-based insights from real-world evidence (RWE) and collaborate on AI biomarkers and clinical decision-support systems. Imagia's unique health care AI ecosystem gives hospitals, medical device makers, pharmaceutical companies and diagnostics manufacturers the opportunity to benefit from a vast AI clinical solutions innovation pipeline to make advances in personalized health care.

Making Progress

During the past two years, we have seen several progressive steps that signal change. Health Canada, the Canadian Agency for Drugs and Technologies in Health (CADTH) and Quebec's Institut national d'excellence en santé et en services sociaux (INESSS) are taking notice that disruptive technologies are here to stay and realize that the current evaluation processes and systems must evolve. Below are a few examples of progress made to date.

[17] Office of the Privacy Commissioner of Canada. PIPEDA in brief: https://www.priv.gc.ca/en/privacy-topics/privacy-laws-in-canada/the-personal-information-protection-and-electronic-documents-act-pipeda/pipeda_brief/.

Figure 2: Collaborative and Transfer Learning Across Institutes



Source: Imagia

- In 2018, a formalized aligned review process among Health Canada, CADTH and INESSS was implemented for eligible submissions, including new drugs and new indications. Heather Logan, CADTH Vice-President (Acting) of Pharmaceutical Reviews at the time, said "We share a common goal of helping ensure that all Canadians have access to effective therapies that bring value to patients and our health systems."[18]
- The same year, CADTH introduced its life cycle strategy, with a focus on anticipating health system and technology trends to develop agile management strategies.[19]
- In 2019, Health Canada embarked on a consultation regarding software as a medical device, including the criteria and clinical interpretations to regulate software products in Canada. This consultation

[18] CADTH news. June 22, 2018: https://www.cadth.ca/news/health-canada-cadth-and-inesss-collaborate-align-drug-review-processes.

[19] CADTH 2018-2021 Strategic Plan, Overview. April 16, 2018.

included feedback from disruptive technology companies to ensure the guidance accounted for properties that may be unique to disruptive technologies like AI.[20]

- In January 2020, the Office of the Privacy Commissioner of Canada launched a consultation specific to AI in relation to the *Personal Information Protection and Electronic Documents Act* (PIPEDA). In particular, it focused on how privacy principles should be applied or enhanced in the development and deployment of health care AI systems in order to eliminate and/or reduce privacy risks as well as unlawful bias and discrimination.[21]

In order to stay relevant, the Canadian health care system will need to adapt and take "disruptive" steps in this increasingly challenging environment.

Recommendations

While progress has been made, there is still more to do. In order to stay relevant, the Canadian health care system will need to adapt and take "disruptive" steps in this increasingly challenging environment. Payers and HTA bodies need to increase their readiness level to support dossiers that include AI as a clinical solution. Some of the more immediate steps that must be embraced include: 1) developing risk tolerance; 2) expanding the appetite for collaboration, potentially with stakeholders that have not been on their radar previously; and 3) actively seeking diversity in the talent pool.

Disruptive technologies have the ability to bring significant value to the care pathway from the preclinical stage to patient management. However, the health care industry, including HTA bodies and payers, will need to become more risk tolerant if they are serious about uncovering transformational insights that have the potential to change the trajectory of patient outcomes.

The health care industry, more so than most, has an enormous amount of data at its disposal. To extract optimal value, companies need to apply disruptive technologies, open up these data vaults and incorporate the beneficial insights therein within their reimbursement dossiers. This will facilitate meaningful discussions with payers on how these insights can translate into incremental patient benefits that bring value to the overall health care system.

Consider failed clinical trials as an example of the rich information that ends up locked away. In a failed trial, there is still a subset of patients for whom a medication has worked. Consider the possibilities if organizations were to apply AI to extract advanced insights to help refine the patient population for future studies. Moving forward, consider the possibility of expediting confirmatory trials to secure regulatory approvals. Imagine extracting advanced insights to secure patient access to a new product, conditional reimbursement, and the potential to improve coverage criteria. AI can help identify a narrower patient population that may be more responsive to a particular medication or mitigate adverse events, which could help expedite reimbursement decision-making.

Most single institutions and industry players do not have enough data on their own to make the big discoveries that will profoundly impact health care. That is why collaborative ecosystems are essential. It allows for multi-institution and industry collaborations where the insights and learnings that are extracted can be federated, i.e. shared across institutions. This is really about getting partners to trust each other and work together across pharma and biotech, academia, and research partners.

Lastly, we need to take a close look at the talent pool. Not only do pharma and biotech need to start considering dual-domain expertise, but payers have to consider incorporating this expertise on their review panels. It is an opportunity to tap into different skill sets and backgrounds. Consider sourcing talent from technology companies and including data scientists and physicians on staff together. If we continue looking to the same sources and talent pools, we cannot expect transformational change to occur. This new reality requires us to break out of this mold and be open to divergence in thought.

[20] Health Canada. Guidance Document: Software as a Medical Device (SaMD): Definition and Classification. 2019: https://www.canada.ca/en/health-canada/services/drugs-health-products/medical-devices/application-information/guidance-documents/software-medical-device-guidance-document.html.

[21] Consultation on the OPC's Proposals for ensuring appropriate regulation of artificial intelligence: https://www.priv.gc.ca/en/about-the-opc/what-we-do/consultations/consultation-ai/pos_ai_202001/.

Conclusion

Value-based agreements that include disruptive technologies need to gain more traction if we want to see them as value creators.[22] The upside is evident: entire value-chains poised to reinvent disease detection, diagnosis and prediction, with the potential to save lives.

These changes require bold moves. Technologies will continue to evolve and make significant advancements throughout the entire health care pathway. Research will continue to be augmented by disruptive technologies like AI on both the academic and industry fronts. Industry players, regulatory bodies, HTA bodies and payers will need to align around a common framework that recognizes the value and unique properties that AI will bring to reimbursement decision-making.

Payers must evolve from a static one-size-fits-all approach to a more flexible and dynamic operating model that is aligned with disruptive technologies. This new approach will require open minds, education, a willingness to execute "pilot" use cases, and potentially ongoing technological assessments to ensure that we are moving in the right direction.

It is imperative that industry, policy-makers and payers come together to champion these ground-breaking, forward-thinking and high-impact technological opportunities. The potential is there to uncover health care efficiencies, mitigate unnecessary costs and, above all, improve patient outcomes. This will transform health care as we know it today for the benefit of patients. PRA

Shelley Epstein is a business leader with extensive commercial experience in global health care, honing her expertise over 20 years at Merck and Co. At Imagia, where she is the Vice President of Corporate and Public Affairs, Shelley shapes and implements initiatives to advance government and non-government organization strategic partnerships that support global AI in health care development.

[22] "Key trends for payers and providers." Healthcare Dive, January 17, 2020.