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PERSPECTIVE

Accelerating healthcare innovation: the role of Artificial intelligence and digital health technologies in critical path institute's public-private partnerships

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Artificial Intelligence (AI) and Digital Health Technologies (DHTs) are radically transforming drug development. The FDA and EMA have formulated guidance documents for their use in clinical trials. A pressing need exists for a harmonized approach to assess and implement AI and DHT methodologies as Drug Development Tools (DDTs). As a neutral entity leading public-private partnerships, The Critical Path Institute has the competencies and infrastructure to address AI and DHTs' pivotal roles in drug development.

PUBLIC-PRIVATE PARTNERSHIPS EMPOWERING IMPLEMENTATION OF AI IN DRUG DEVELOPMENT

The integration of multi-modal data and sophisticated analytics algorithms, such as AI, to propel advancements in drug development and support regulatory decision-making is experiencing a notable surge.[1] Both the US FDA and EMA have initiated the formulation of recommendations for best practices concerning the application of AI algorithms in regulatory submissions.[2] Adding to this landscape, the recent executive order on AI safety and security issued by the Biden administration is poised to significantly impact the utilization of AI in drug development.[3] This order specifically targets the establishment of standards for AI, safeguarding privacy, advancing equity, fostering innovation and competition, and strengthening American leadership globally.

Within the highly regulated realm of drug development, a clear and pressing need arises for a harmonized and actionable approach to rigorously assess and implement AI and DHT methodologies for DDTs. The emphasis should specifically address the use of AI in drug development, in distinction from its application in Software as a Medical Device (SaMD), 501(k) clearance of devices, Clinical Decision Support, and drug discovery. Public-private partnerships (PPPs) such as C-Path, Pharma IQ consortia, and other professional societies are uniquely positioned to empower the implementation of AI and DHT in drug development.

As such, C-Path emerges as a distinctive and well-equipped entity to meet the regulators' needs in the context of AI in drug development. C-Path has not only demonstrated a proven track record in developing regulatory-endorsed DDTs, such as clinical trial simulation/enrichment tools (https://t1d-cte.c-path.org/), but has also adeptly navigated the intricate landscape of regulatory processes and fostered collaboration between industry, academia, and regulatory agencies over the past 18 years.

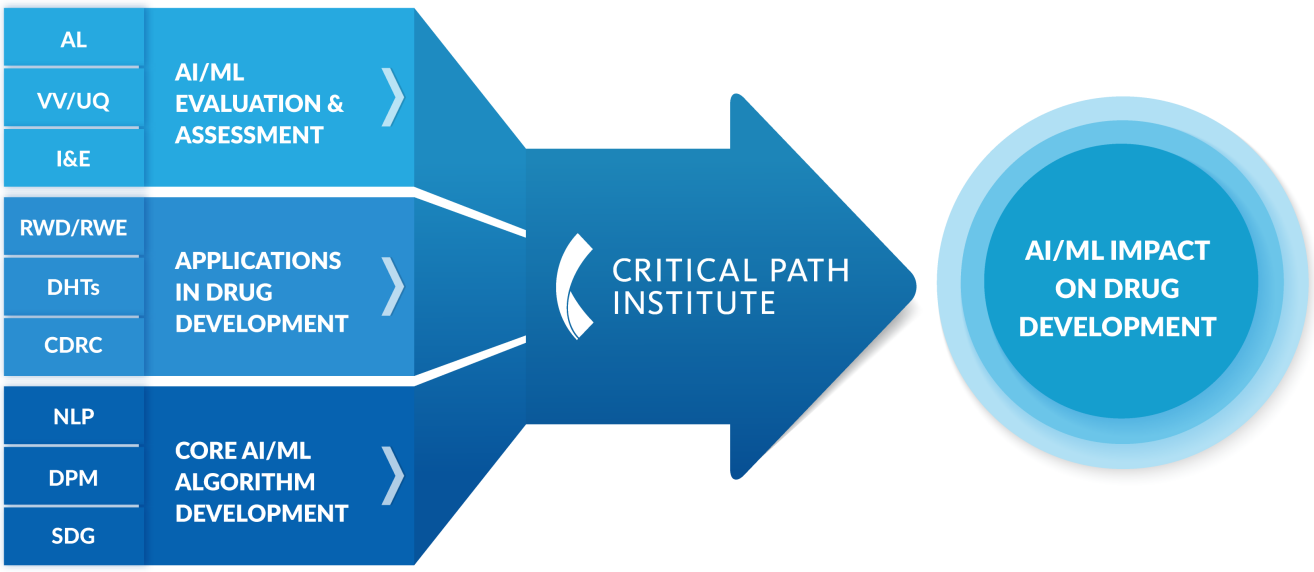
Positioned as a neutral entity that champions multi-stakeholder collaborations and public–private partnerships

within drug development, C-Path operates based on five core competencies that form the bedrock of its impactful contributions to the field. Firstly, data management and standards play a pivotal role in ensuring the quality, integrity, and interoperability of data, facilitating effective collaboration and informed decision-making (https://c-path.org/programs/dcc/). As a result, C-Path has seen a significant growth in total data contributed over the last few years. C-Path currently has 694,401 subject-level clinical records from 425 studies and 13,190 subject-level nonclinical records from 153 studies. Secondly, modeling and analytics contribute to the institute's ability to harness the power of computational approaches, enabling predictive modeling and data-driven insights (https://c-path.org/programs/quantmed/). Thirdly, biomarkers, a cornerstone competency, involve the identification and validation of biological indicators that aid in understanding disease mechanisms, optimizing clinical trial design, and enhancing patient stratification (https://c-path.org/programs/bmdr/). Fourth, clinical outcome assessments focus on evaluating the impact of interventions from the patient's perspective, providing valuable insights into treatment efficacy and patient-reported outcomes (https://c-path.org/programs/proc/). Lastly, regulatory science encompasses the expertise required to navigate the complex regulatory landscape, ensuring that C-Path's initiatives align seamlessly with evolving regulatory standards (https://c-path.org/programs/regsci/).

Within C-Path's Quantitative Medicine (QuantMed) Program, which embodies the Model-Informed Drug Development (MIDD) and quantitative analytics core competency, C-Path has developed a range of internal lines of expertise, including unique approaches to real-world data (RWD) and DHTs such as algorithmic literacy. This solid foundation uniquely equips C-Path to respond to the call for action. This perspective paper aims to illuminate how C-Path's distinctive position and core competencies can be harnessed effectively to employ AI in drug development (Figure 1). The organization's extensive experience in building trust among diverse stakeholders, spanning industry, government, academia, and patient advocacy groups, underscores its capability to drive impactful and collaborative advancements in the field.

IMPACT OF AI IN DRUG DEVELOPMENT

AI is positioned to transform the drug development lifecycle, bringing forth enhanced efficiency, accuracy, and innovation. Concurrently, DHTs contribute to real-time patient monitoring, enriching the understanding of drug



AL = Algorithmic Literacy
VV/UQ = Verification, Validation and Uncertainty Quantification
I&E = Interpretability and Explainability
RWD/RWE = Real World Data, Real World Evidence
DHT = Digital Health Technology
CDRC = Cure Drug Repurposing Collaboratory
NLP = Natural Language Processing
DPM = Disease Progression Models
SDG = Synthetic Data Generation

FIGURE 1 Illustration of C-Path efforts to expand AI/ML impact in drug development.

responses. C-Path, particularly through its QuantMed Program, has been actively engaged in the field of AI in drug development and clinical pharmacology since 2017. The organization has cultivated expertise in evaluating model and algorithm performance and assessing the credibility of AI methods across diverse application domains.[4] Demonstrating ongoing leadership, C-Path continues to drive AI implementation in drug development through initiatives in education, training, and mentorship while pressing for the need for strong oversight and safety measures in such implementation into the drug development lifecycle.[5]

At C-Path, there are multiple ongoing projects across several diseases that are employing AI to address unmet needs. Within the CDRC, as depicted in Figure 1, in a PPP model we leverage RWD to evaluate the off-label use of drugs for new indications, an end-to-end data and analytics pipeline has been constructed through an Amazon Web Services (AWS) cloud architecture that includes a natural language processing (NLP), with Large Language Models (LLMs), pipeline for structuring free-text data and clustering analysis to search for treatment patterns within the CURE-ID platform. In the type 1 diabetes (T1D) consortium, C-Path' QuantMed program has developed a Clinical Trial Enrichment Graphical User Interface (https://t1d-cte.c-path.org/). The user or sponsor can utilize the interactive dashboard to define the characteristics of trial participants, enabling the prediction of the mean probability of a T1D diagnosis within that specific trial group. To safeguard data privacy and facilitate open-source accessibility, a generative model based on deep learning was employed to create a cohort of synthetic subjects. Within Parkinson's disease, C-Path's Digital Drug Development Tools (3DT) consortium seeks to better interpret and utilize DHTs in a variety of scenarios through studies such as WATCH-PD.[6] These initiatives entail the proficient handling of large volumes of DHT data. The process includes skillfully managing data deidentification and transfer capabilities while the study is in progress, ensuring patient privacy and security. This holistic approach underscores the present integration of AI and DHTs to advance understanding and treatment strategies for Parkinson's disease. However, while these examples demonstrate C-Path's expertise, there are a multitude of challenges and applications the drug industry faces concerning AI/ML and DHTs.

DEVELOPING COMPETITIVE ADVANTAGES IN AI AND DHT

C-Path's unique position provides significant value to the realm of AI and DHTs, leveraging the pre-competitive, collaborative, and interdisciplinary approaches necessary to understand the proper use of these tools at various stages in the drug development pipeline. This is achieved through the development of transparent and comprehensive evidentiary support frameworks designed to harness the maximum potential of these technologies while emphasizing clarity for the nuances and implications of their use, including safety, ethics, and appropriate usage. These frameworks include the metadata-based decision tool for identifying opportunities for DHT use and existing evidentiary support levels, the activity identification and verification framework for developing human activity recognition algorithms to assess data quality, and the algorithmic literacy framework for comprehending and assessing algorithm usage with respect to the intended context of use.[7,8] An example of where these tools have been leveraged was as a part of Critical Path for Parkinson's (CPP's) consortium's 3DT initiative, where the role of wearable sensors for measuring motor symptoms of Parkinson's Disease was assessed and documented.

Furthermore, C-Path is an optimal collaborator for future endeavors in AI and health care due to their extensive datasets and technical proficiency in both disease and regulatory domains. Functioning as a trusted partner and platform provider, C-Path actively facilitates consortia, respecting patient safety and security through meticulous data management practices. With a demonstrated history of creating open-source and user-friendly software, exemplified by the FDA-funded Rare Disease Cures Accelerator-Data and Analytics Platform (RDCA-DAP) initiative, C-Path emerges as a reliable and innovative player in shaping the future landscape of AI in health care.

SCALABILITY OF C-PATH'S INNOVATIONS AND PREPARING FOR THE FUTURE

C-Path's endeavors in innovation and future-focused strategies are encapsulated in the scalable technologies and solutions developed by our team. They support the entire spectrum of algorithm development and assessment, emphasizing process validation, algorithmic literacy, and adherence to regulatory guidance. This approach creates a dynamic sandbox for responsible, safe, and rapid AI development. Algorithms are crafted using a risk-based approach with clearly defined optimization objectives with strict adherence to good development practices (GDP). Leveraging a library of basic functionality, we facilitate the rapid assembly of data analysis pipelines, promoting the generation of RWE. The use of dashboards will aid in the collection and documentation of validation.

Looking forward, C-Path envisions broader integration of AI in healthcare workflows, enhancing productivity with automated tasks and interconnected data pipelines, with scalability reaching beyond our organization, magnified by open-source dissemination. This evolution ensures continuous validation of data pipelines for reliability in light of new scientific insights. The future of AI in drug development is characterized by diverse model complexities and input-data modalities. Transparency and explainability remain core principles, supported by interpretability modules affirming AI's validated state across privacy, security, and data domains. Assembling validated AI pipelines will become increasingly seamless, illustrated by optical character recognition translating doctor's notes for database querying using natural language processing and retrieval augmented generation algorithms.

CONCLUSION

In summary, this perspective paper underscores C-Path's crucial role in advancing AI/ML and DHTs in drug development. There is an urgent call for a unified approach to assess and implement these methodologies for DDTs, and C-Path is uniquely positioned to address this need. Through collaboration and innovation, C-Path pioneers the application of AI/ML and DHTs in health care, emphasizing privacy and security. Stakeholders are encouraged to continue partnering with C-Path for ongoing progress and innovation at the intersection of AI/ML, DHTs, and health care.

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CONFLICT OF INTEREST STATEMENT

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DISCLAIMER

AI tools were employed for drafting assistance and improving overall readability and language.

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