Artificial intelligence in pharmacovigilance

Proposal to form a CIOMS Expert Working Group

February 2, 2022

Consensus action proposed

An Expert Working Group managed by the Council for International Organizations of Medical Sciences (CIOMS) is proposed. The objective of this Working Group would be to establish and promote principles and guidance for the use of artificial intelligence or intelligence augmentation in the field of pharmacovigilance. While general guidance and regulation is being developed for the use of methods seeking to achieve artificial intelligence across other technical and scientific disciplines, the aim of the proposed CIOMS Expert Working Group would be to address its use, opportunities, and challenges specifically within the field of pharmacovigilance. As such, the CIOMS Expert Working Group would build on and complement the broader initiatives underway.

Background

Since the early 2000s, the ability of computer algorithms to solve pre-specified tasks previously performed by human specialists has rapidly evolved. This falls within a field of research referred to as Artificial Intelligence born in the 1950's and dedicated to the study of intelligent agents – systems that can perceive their environment, act autonomously to achieve certain goals and adapt their behavior over time. Intelligence augmentation is the combination of artificial and human intelligence seeking to complement and enhance human specialist performance.

Today, artificial intelligent agents are approaching human-level performance at specific tasks such as speech and image recognition, vehicle navigation and protein structure prediction. On, for example, breast cancer prediction [1] and strategic board games like chess and Go, algorithms outperform human experts. In other domains, humans supported by computers provide the best possible performance. Computer algorithms have the advantage of being able to work relentlessly unaffected by external factors like emotions and cognitive biases, and processing extremely large amounts of data. At the same time, algorithms so far perform well only on tasks that are narrow in scope and have clearly defined target functions. They require access to reliable and relevant training data (or in the case of reinforcement learning, hard and fast policies for evaluation), which are usually not available for more ambiguous tasks.

[1] https://www.nature.com/articles/s41586-019-1799-6

Furthermore, each algorithm is dedicated to a single task – an artificial *general* intelligence able to perform higher level cognitive functions and ultimately learn any intellectual task that humans can master, is not yet in sight.

Even so, methods for artificial intelligence and intelligence augmentation will have a major impact on the processes and practice of pharmacovigilance. Already, well-resourced regulatory authorities and biopharmaceutical companies are adopting automated or semi-automated approaches to data management and analysis – a digital transformation catalyzed by the unprecedented volumes of incoming individual case reports to process and assess during the COVID-19 vaccination campaigns.

Artificial intelligent agents can free human experts from tedious and repetitive tasks in pharmacovigilance, allowing them to dedicate their time and efforts to analyses requiring the full breadth and depth of their expertise, such as differential diagnosis or causality assessment. Moreover, intelligent agents can distil and compile information from vast and diverse data sources, enabling human specialists to make better-informed decisions and highlight patterns that they may miss.

In contrast, misguided automation efforts focused exclusively on efficiency and financial targets, risk eliminating the value added by humans in the loop and could ultimately compromise the unique strength of the pharmacovigilance system which has been designed to capture data specifically for the purpose of causality assessment in the individual case.

Issues to be addressed

Algorithms seeking to achieve artificial intelligence present several unique challenges. These challenges affect regulatory agencies, public health institutions and biopharmaceutical companies alike, and they lack geographical boundaries.

Modern artificial intelligence methods rely largely on complex statistical machine learning methods such as deep neural networks, that have intricate architectures and millions of tunable parameters making it impossible for human experts to directly survey and comprehend their inner workings. The lack of transparency makes it difficult to assess how algorithms will generalize unseen data, and if there are specific domains in which they should not be used. It calls for guidance on how to validate, communicate and safeguard the continued performance of complex algorithms.

Lack of transparency presents specific challenges to intelligence augmentation where humans need to interact effectively with the computer algorithms and account for their recommendations in their own decision-making. Evaluation of such hybrid systems presents unique challenges as well, related to the variability within and between human specialists and their interactions with the computers.

The reliance on training data is pronounced in developing and deploying the machine learning algorithms supporting many artificial intelligence initiatives. Complex algorithms require large amounts of data and in many cases, there is no (or not enough) training data available. In other cases, the training data is not fully representative of the problem to be addressed, and the

resulting algorithm may be similarly misaligned. Machine learning algorithms may also perpetuate historical systematic errors present in training data. When the algorithms themselves cannot easily be understood, it is even more important that the training data on which they are optimized is transparently communicated.

Equally important as the training data is the choice of target against which to optimize performance. If certain errors are more severe than others, this needs to be accounted for in training and evaluating the algorithms.

The capability of machine learning algorithms to adapt over time and learn from new experiences and data is an important strength and requisite for their continued relevance and accuracy in evolving environments. At the same time, continual change makes auditing and inspection difficult. Special steps may need to be taken to ensure that earlier results and predictions can be recreated and understood. For example, if a relevant signal was missed because adverse events had been incorrectly encoded by a machine learning algorithm, we will need to be able to assess the version of the algorithm in use at the time that the incorrect encodings were made.

Different processes in pharmacovigilance carry different risks and may need separate consideration.

Specifics

Composition of group

Senior scientists with expertise in pharmacovigilance and/or artificial intelligence will be invited from drug regulatory authorities, biopharmaceutical companies, non-commercial research organizations, academia and WHO. Patient and healthcare representatives and bioethical experts will also be engaged. Preferably, there should be representatives from all six WHO regions.

Deliverables

- Scoping review
- Consensus report
- Template for assessment of initiatives seeking to develop and/or deploy methods for artificial intelligence in pharmacovigilance.

Timing

The project would run for three years. During this period, there will be on average one to two face-to-face meetings per year (depending on the epidemiological situation) supplemented with remote meetings and digital collaboration.