MACHINE LEARNING AND THE VALUE OF HEALTH TECHNOLOGIES
Face-to-face with machine learning

“Because you watched *The Crown.*” This simple statement gets us to keep browsing and watching Netflix, despite us often not knowing that the suggested films and documentaries even existed. Yet what underlies this simple statement is remarkably complex – it is generated by a sophisticated algorithm trying to predict what we are likely to enjoy watching based on our previous actions. That’s the elegance of Netflix’s algorithm. Complexity presented as simplicity, effectively and with finesse. Netflix represents a relatively new example of what machine learning can achieve, and may serve as illustration to future generations of how machine learning entered our daily lives. But Netflix is only one example among many. Machine learning can estimate road traffic for Google Maps, recognise our speech, and can even identify the location of a failure in a city’s piping system by considering water flow data.

Machine learning can be applied through the development of algorithms that can unravel or ‘learn’ complex associations in large datasets with limited human input.¹,²

*These algorithms are capable of making predictions that go beyond our capabilities as humans as they can process and analyse more possibilities than we can. And that’s where – perhaps – the greatest potential of machine learning lies.*¹,²

The uptake of these state-of-the-art methods in healthcare has not been as quick as in other fields; still, some examples exist of machine learning algorithms being used for the prevention, diagnosis and risk stratification of patients in a number of disease areas.²,³ The application of machine learning for demonstrating the value of health technologies is at an even earlier stage, although the increase in research papers and abstracts on this topic in the last few years suggests uptake may be gathering momentum. The implementation of these methods, however, will require considerable effort as expert knowledge and particular skillsets need to be developed. Is this extra effort really worth it?
How can machine learning be used to demonstrate or add value?

New technologies and ever-increasing computational power enable us to gather and store large amounts of data. We often do not make the most of these data because such datasets are not easy to interpret, or because they come from different sources and in various formats. Cleaning and manipulating these large datasets can be a monumental task. For this reason, it’s more important than ever to provide decision-makers with tools that can facilitate their work and optimise the allocation of resources in the healthcare system.

So, how can machine learning help us?

Treatment pathway optimisation. The likelihood of a health technology being available to patients will increase if the target population is appropriately defined, i.e., if the health technology is placed in the treatment pathway where its greatest benefit can be realised and demonstrated. Machine learning algorithms can help determine patient subgroups with a significant treatment benefit, thereby establishing where in the treatment pathway a product will maximise patients’ outcomes. Researchers have tried, for example, to understand which metastatic melanoma patients can be cured by a particular treatment. This type of information can, according to the researchers, enable a better assessment of the cost-effectiveness and budget impact of new technologies, optimising the use of resources available in the healthcare system. Other examples in the recent literature include the prediction of treatment benefit in multiple myeloma and gastric cancer.

Decode complex associations. With the increasing availability of extensive datasets containing large numbers of variables, machine learning methods represent our best choice for deciphering intricate data patterns. This can lead to, for example, the development of disease models that can be used for cost-effectiveness and budget impact modelling. Chronic obstructive pulmonary disease (COPD) and systemic lupus erythematosus (SLE) are two diseases for which health economic models have been developed based on mathematical equations describing complex relationships between biochemical factors, clinical indicators and patient outcomes. In SLE, data from clinical trials and a comprehensive registry were used to predict and compare patients’ costs and outcomes with belimumab compared with the standard of care. This model structure was accepted by health technology assessment (HTA) agencies such as the National Institute for Health and Care Excellence (NICE); the manufacturer’s submission resulted in a recommendation for belimumab in a particular SLE population.
Software that strengthens a product’s value proposition. We can use machine learning algorithms to develop software that can go hand-in-hand with health technologies, leading to a synergistic increase in the value of the combination. For example, Zhao et al. explored several machine algorithms to predict the duration of robot-assisted surgeries (RAS) in a hospital. RAS requires a large investment and, therefore, when a hospital acquires such technology, hospital managers need to make sure that its use is maximised. In this case, the authors demonstrated that machine learning algorithms made better predictions of case durations compared with traditional estimation procedures (i.e., previous case duration averages and surgeon adjustments). If implemented in the real world, these algorithms would help optimise the resources available in the hospital, increasing the value of RAS.

Shared decision-making. There is an increasing interest and need to promote patient-centric policies in our healthcare systems. Wouldn’t it be great to be able to identify the likely outcomes of a particular patient treated with a particular treatment? For instance, we could try to predict whether a patient is likely to advance to a progressed cancer stage with a given treatment, considering a set of baseline clinical and genetic characteristics. This is what is meant by personalised medicine, and machine learning methods will undoubtedly help us achieve this.

Assess the perception of a product. When trying to demonstrate or understand the value of a health technology, either before or after entering the market, it is crucial to evaluate different stakeholders’ perceptions and get answers to questions such as: is this technology providing the benefit you expected? What do you or don’t you like about the technology? Machine learning algorithms can be used to analyse social networking sites or interviews and help improve a product’s value proposition or better define the product’s target population. This is what is known as sentiment analysis. For instance, Roccetti et al. extracted and analysed the data posted on Facebook by Crohn’s disease patients to understand their opinions on the treatment with infliximab. Also, Korkontzelos et al. assessed the value of sentiment analysis for the identification of adverse events expressed by patients in social media, highlighting the potential of machine learning in pharmacovigilance. These examples show that sentiment analysis could be used to, among other applications, inform a product’s value proposition and positioning in the treatment pathway; however, its full potential in healthcare has not yet been demonstrated.
Machine learning algorithms have the potential to deal with various data analysis problems, with many different objectives. Data scientists can choose from a wide array of algorithms with different levels of complexity, from commonly used decision trees to cutting-edge neural networks and deep learning, to address the problem they are considering (Figure 1).1,2

**Figure 1. Examples of machine learning algorithms and their applications**

- **Random forests**
  Identification of clinical factors contributing to disease progression in patients with gastric cancer after nivolumab treatment12 *(example of treatment pathway optimisation)*

- **Simulated treatment learning**
  Estimation of benefit in multiple myeloma patients not treated with the therapy of interest5 *(example of treatment pathway optimisation)*

- **Gradient boosting**
  Prediction of the probability of being cured with a particular treatment in metastatic melanoma patients4 *(example of treatment pathway optimisation)*

- **Neural networks**
  Prediction of the duration of RAS for each particular patient in a hospital to optimise the use of resources9 *(example of software that adds value)*
The examples discussed in Figure 1 illustrate the potential of machine learning in healthcare and, in particular, for demonstrating and adding value to health technologies. However, the field is advancing rapidly, with new methods and potential applications coming to light every day.

**Machine learning may help us find answers to questions that we didn’t even think of in the past, revealing evidence previously hidden among the data. We can use these methods to dig up imperceptible patterns and allow health technologies to be used at the right time and in the correct patient population.**

There is plenty of room for innovative thinking that might challenge our previous expectations of how data can help inform decision-making around healthcare technologies.

**What are the challenges with machine learning?**

The application of machine learning is not, however, free of challenges, and some of them may not be straightforward to handle. Each approach has its own technical difficulties that expert data scientists can help to handle. Other challenges include:

**Choice of algorithm.** There is a wide variety of algorithms available, so which one should we use? Due to the relative infancy of machine learning application in healthcare, and, therefore, a lack of robust experience, it’s not obvious whether certain algorithms perform better than others in given situations. That’s why many researchers implement a range of models and compare their performance in order to choose the best. Issues such as over- or under-fitting and bias also need to be considered when choosing between various well-performing algorithms.

**Acceptability.** Machine learning algorithms often outperform classic statistical models; but, on the contrary, machine learning models tend to be less intuitive than classic statistical models. For this reason, the acceptability of these algorithms among key stakeholders, such as clinicians, represents a considerable challenge that must be overcome. But we must be clear: the objective should be to assist experts in making a decision rather than the algorithm making the decision.
Ethics. There are ethical considerations that may come into play. For example, what would happen if a model incorrectly predicted that a person is not sick? Who would be responsible for the error? Challenges related to data security and privacy may also be prominent. With regard to privacy and equity, for instance, researchers have shown that insurance companies could use machine learning methods to identify unprofitable enrollees, highlighting that vulnerable patients may require special protection from regulators to avoid being subjected to unfair policies.

With machine learning becoming increasingly important in our everyday lives, it’s only a matter of time before its application in healthcare is more commonplace. Now is the time for open discussion to understand how machine learning can help us make the “right” healthcare choices. For the patient, the “right” choices allows them access to best available technologies for their condition and circumstances; for payers, the “right” choices enable them to deliver the best healthcare to a population given the resources available. Machine learning might help ease the tensions that exist between these viewpoints by helping us better understand in which patients and in what application the greatest benefits of a health technology might be realised. Through this, machine learning has the potential to improve the healthcare of our societies as a whole, and all of us have the ability to shape it by embracing what is coming.
References