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Title: Assessing Individual Cost-Effectiveness Ratios (ICER) associated with health care using AI based-clinical decision support systems: which ethical issues?

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Abstract

We are interested here in the possibilities offered by Artificial intelligence (AI) technologies in the health care sector and in particular in supporting medical decisions. Combining AI technologies with clinical decision support systems enable to provide clinicians with new information that was impossible to generate instantly till now. Indeed, it make it possible to estimate the impact of patients' clinical and socio-demographic characteristics in terms of effectiveness (benefit/risk balance) and efficiency (incremental cost/effectiveness ratio (ICER)). For example, patients' age, their health histories and co-morbidities may have an impact on both the expected benefits of treatments (e.g., life expectancy and quality of life gains, risks of complications or adverse effects, etc.) and on costs (e.g., hospitalisation costs in case of serious health events, costs of adjuvant treatments, etc.). So far, economists have estimated average ICERs for target populations, also called "populations of indication" because the only available efficacy data are average efficiency data.

First, we address the question whether estimating individualized ICERs would be consistent with the classical utilitarian framework, as well as with Paretian welfare economics framework. Theoretically, estimating individualized ICERs would make it possible to better attain the objective of maximizing utility associated with health care under budgetary constraints.

Second, we address the question of the social acceptability of medical decisions based on an individualized ICERs. This would imply that a treatment for a given indication could be recommended for some individuals, but not for others. AI based-clinical decision support systems might reinforce implementation of utilitarian justice models by overcoming the current limitations pertaining to the information capacities of the actors. These avenues may therefore raise ethical controversies, that are maybe not unprecedented but certainly intensified. Thereby they make it even more necessary to organise institutional discussions on the ethical frameworks that must be favoured.

1. Introduction

1.1. Context

Artificial intelligence (AI) technologies offer new perspectives in many applied areas, especially because of their ability to combine different tools and resources. Innovation lies not so much in each of these tools and resources used in isolation. Instead, it follows from the possibility of employing them in a coordinated way according to user needs, through application programming interfaces (APIs).

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These programming interfaces make it possible, for example, to produce information from massive data on individual behaviour resulting both from the digitisation of exchanges between the actors and from the development of connected objects by means of adapted statistical techniques (data mining). This information can subsequently be restored to users in a natural language through the development of tools for using natural language (such as a conversational agent or "chatbot"). The tools for understanding natural language also allow the extraction of information from unstructured data.

We are interested here in the possibilities offered by these technologies in the health care sector and in particular in supporting medical decisions. The health sector is particularly conducive to the use of these technologies, notably because it is highly regulated, rather than being left to the free interplay of actors. The regulation of the health system by public authorities does indeed imply a need for producing and collecting reliable information about the quality and safety of care and the efficiency of practices. Consequently, such regulation of the health system results in a remarkable amount of public data, and a great potential for characterising healthcare pathways and patients' consumption of health goods and services, thanks to the information systems used for billing and reimbursement purposes (e.g. SNIIRAM and PMSI in France), as well as for the coordination between healthcare professionals using electronic health records (EHRs) and hospital information systems. These purposes have led to the creation of institutions responsible for defining methodological standards in the production of health-related information (ATIH in France). Such institutions are therefore well-placed to identify the value of new information technologies and to address the scientific, ethical and political issues they raise.

1. 2. Objective

The issues most often discussed in the literature relate to the protection of personal data and to personal autonomy (Mittelstadt and Floridi, 2015). A general analysis of the ethical issues raised by artificial intelligence is given by Coeckelbergh (2020). While acknowledging the importance of these issues, we focus here on the normative issues raised by the production of new information with AI-based clinical decision support systems (CDSSs). A CDSS is software designed to be a direct aid to clinical decision-making with targeted clinical knowledge, patient information, and other health information (Sim, I., Gorman, P., Greenes, R. A., Haynes, R. B., et al. 2001; Sutton, R.T., Pincock, D., Baumgart, D.C. et al., 2020). Combining artificial intelligence methods with CDSSs helps to provide clinicians with new information that was impossible to generate instantly till now. We address the question whether, and to what extent, production and use of such information may change the normative framework supporting medical decisions. The notion of "normative issues" point to value judgments underlying evaluation criteria to determine the merit or worth of a treatment and decision criteria to determine actions. These value judgements involve, first and foremost, a particular conception of how to produce knowledge as the basis for action. They also assume a special view of social justice, in as far as medical decisions involve the consumption of collective resources, at least in countries where health care spending is socialised. Conceptual and practical interrelation between statistical tools and forms of governance have, in particular, been highlighted by Desrosières (2008) who emphasised the link between the epistemological models that underlie the production of statistical knowledge and the normative assumptions guiding the development of public action. *"As a speciality in mathematics, statistics is both a tool of proof, but also an instrument of government, which sets the pace and coordinates many social activities, and serves as a guide to public action (...) Drawing on various examples, it may be asked in what way do quantification and statistical algorithms contribute to the performance of the social world, in various configurations, and in arrangements whose parts are complementary to each other."*⁵ (Desrosières, chap.1).

2. Normative models underlying the tools presently used to help health professionals in decision-making

Instruments currently used by health professionals include: best practice recommendations, professional journals, prescription assistance software, mobile applications, peer groups, etc. These are based on two

⁵ Unofficial translation.

decision models: a model based on the efficacy criterion established on evidence-based medicine (EBM) and a model based on the economic efficiency criterion.

2.1. The efficacy criterion based on evidence-based medicine

The notion of EBM appears for the first time in the 1990s to point out a new paradigm for medical practice (Guyatt, 1991; Evidence-Based Medicine Working Group, 1992; Sackett, Rosenberg, Gray et al., 1996). It refers to a decision-making model in health care not only based on scientific evidence but also on the clinical experience of the practitioner and the preferences of the patient. *“Evidence based medicine is the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients. The practice of evidence-based medicine means integrating individual clinical expertise with the best available external clinical evidence from systematic research”* (Sackett, Rosenberg, Gray et al., 1996, p. 71). It should be distinguished from an older model of clinical decision-making exclusively based on clinical experience and knowledge of physiological mechanisms (Fagot-Largeault and Guillin, 2012). EBM stands for both a method of deliberation and the informational basis upon which the clinician should rely:⁶

- the kind of information that practitioners must take into account (scientific data resulting from systematic observation, such as that obtained from randomised controlled trials) (Bothwell and Scott, 2016; Parkkinen et al. 2018).);
- the confidence they can place in it (a hierarchy of evidence according to the methods used to produce it);
- the methods for synthesising these data (systematic review of literature).

More specifically, EBM is part of a positivist epistemological model: only observable facts are taken into account, and theoretical models are of interest only to the extent that they can in fact predict the occurrence of events (Djulgovic, Guyatt and Ashcroft 2009, Tröhler, 2000 and 2012)⁷. Finally EBM involves basing therapeutic decisions on an estimation of the benefit-risk balance faced by a patient or a group of patients.⁸ For a detailed description of the history of EBM and its methods see Goodman (2002). In this article, we refer to EBM solely to designate this informational basis upon which the clinician should rely and not the method of deliberation for clinical decision-making, which involves taking into account the practitioner's clinical experience and the preferences of the patient. However, in the Discussion section, we consider that the development of AI-based CDSSs may impact this deliberation process (see Section 5.3.2.).

2.2. The criterion of economic efficiency

The efficiency criterion is used by many health technology assessment agencies: to establish recommendations for good practice; to decide whether a particular technology should be covered by reimbursable care; and to decide on whether public health programs should be implemented (screening, prevention) (Dolan, 2001; Drummond et al. 2015). The efficiency criterion involves estimating the amount of additional resources that it must be agreed to pay in order to obtain an additional unit of a result, such as a year of life saved or a quality-adjusted life-year (QALY). In practice, this means estimating an incremental cost/effectiveness ratio (ICER) associated with the particular health treatment under study, compared to other available treatments. If a strategy is both cheaper and more effective, then there is no difficulty in interpreting the outcome of the assessment: it is efficient. But if it is both more costly and more effective, then its efficiency needs to be established. This means that society

⁶ We use the terms “informational basis” as suggested by Amartya Sen to designate “the informational basis the information on which the judgment is directly dependent” (Sen, 1990, p. 111)

⁷ *“For example, the drug erythropoietin is shown to improve fatigue in cancer patients (observed by patients reporting that they feel better). From these observations, we can predict that future patients (who are yet to be observed) will also feel better after administration of this drug. We can speculate about the underlying mechanism of the drug (i.e., whether it produces its effects by increasing the level of hemoglobin or binding to hypothetical erythropoietin “fatigue” receptors) and its effects on patients (subjective feelings of fatigue). But direct evidence of the true effect of erythropoietin will remain unobservable.”* (Djulgovic, Guyatt and Ashcroft, 2009, p. 161)

⁸ The positivist epistemological model of EBM is consistent with the principle of maximising benefits with respect to risks and with the utilitarian principle of the greatest happiness for the greatest number. This second principle was put forward by Helvetius, followed by Beccaria and Bentham, in order to provide legal and political sciences a with positive base.

values the health benefits provided by the technology at least as much as it values the results achieved by using the same amount of resources elsewhere in the health sector or in other public services (i.e., it involves establishing the opportunity cost). To make such a judgment, health economists and institutional actors often put forward a “cost-effectiveness threshold value”. This value represents the maximum amount that society is willing to spend in order to gain an additional year of life in good health. In Great Britain, for example, it is considered that society is willing to pay €36,000 to produce a year of life saved in good health.⁹

This efficiency criterion requires that society adheres to a utilitarian model of justice. On the one hand, the most frequently-used tool to assess the efficiency of health treatments are QALYs. They allow the impact of treatments on individual patients’ lifespan be taken into account, and also to account for the utility associated with various states of health linked to this lifespan (Brazier et al. 2007; North et al., 2009). On the other hand, the ICER estimate implies that the goal is to maximise the production of health gains, under budgetary constraint. All individual gains or benefits have the same weight and the unit result is equal to the average benefit. Everyone has the right to be treated, provided that it has been shown that the resources consumed cannot be better used elsewhere by producing more health benefits. Health resources are therefore allocated according to the “*ability to benefit individuals*” (Culyer and Wagstaff, 1992).

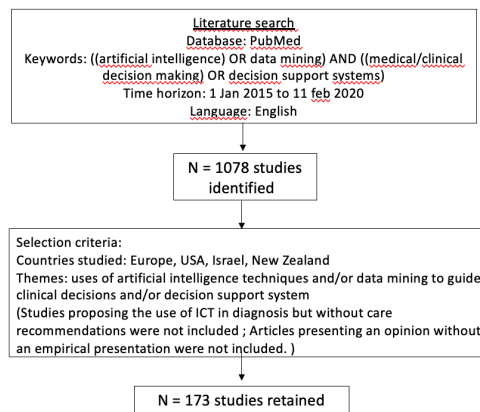
These two decision models (the model using the efficacy criterion based on EBM and the model based on the economic efficiency criterion) are complementary. In order to estimate a cost-effectiveness ratio, the risk-benefit balance needs first to be estimated. Moreover, the methods of producing evidence are common: both models rely on a positivist approach that involves the production of experimental data and/or systematic observations. However, the efficiency criterion is more restrictive than the efficacy criterion. It means not only seeking to maximise benefits relative to risk, but also seeking to maximise collective welfare. A particular treatment may therefore be recommended from the point of view of the efficacy criterion and not from the point of view of the efficiency criterion. These two frameworks are particularly visible in Cochrane (1972).

3. Method

The method is based on two steps. Firstly, a scoping literature review was carried out, intended to assess the availability of AI based-CDSSs. The search strategy and the flowchart is summarised in Table 1. The aim of this literature review was not to evaluate the pertinence of the clinical decision support systems (CDSSs) presented, but only to examine their main characteristics: the area of treatment in question; the nature of information sent to the practitioner (prediction of events, treatment recommendations, etc.); and the data sources used to define algorithms. To this end, all relevant articles were included, regardless their methodology. Second, these new tools were analysed in order to examine whether they involved changing decision-making models: i.e. whether they are based on decision-making models other than those previously described. From this we identify a series of ethical controversies in the discussion.

⁹ However, exceptions to this decision-making rule are possible, for particular populations of patients or because of the uncertainty which surrounds this estimate (see NICE, 2008).

Table 1 Documentary Research Flow Chart



4. Results

4.1. Key features of tools to support medical decisions that mobilise artificial intelligence technologies

The results of this scoping literature review are synthesised in the Table 1 below, and a detailed description is included in the Appendix. Most studies may be seen as pilot studies, at early stages of technology development, since underlying algorithms were built from samples of limited size ($n < 1000$), and not from massive data. In most cases, authors built algorithms using historical patient records from healthcare institutions ($n=58$) or from cohorts ($n=12$). Only one study put forward an algorithm based on national data (Lopez-de-Andres A, 2016). It should also be noted that the authors did not systematically specify which parameters algorithms were based upon, in particular the socio-economic parameters. These parameters were only specified in 18 studies and mainly included: age, gender and tobacco consumption. The other studies did not specify whether these parameters were included or not.

The literature shows that all AI-based CDSSs (those which have been tested and with published results) seek to guide the practitioner by predicting the expected efficacy of the various treatment options. Given patients' characteristics, most experimental studies ($n=48$) were on technologies predicting the likelihood of events (adverse events, intervention outcomes, survival, death rates, remissions, etc.). Some other studies ($n=20$) presented technologies used for defining care recommendations (drugs, surgery and patient follow-up). A majority of these AI-based CDSSs take into account patient characteristics to predict the occurrence of events (57 articles) and to make recommendations (21 articles out of these 57 articles). In 18 articles, they integrate some socio-economic characteristics of patients (such as age, gender, sedentary lifestyle, tobacco, body mass index), in addition to clinical characteristics.

It was noted that a significant number ($n=70$) of the articles presented the use of new technologies for diagnostic purposes and not for clinical decision support purposes. These articles were considered irrelevant to our study.^[3]

Table 1

Year of publication (n=number of articles)
2015 (n=34), 2016 (n= 10), 2017 (n= 33), 2018 (n=33), 2019 (n=54), 2020 (n=10)
Category of article (n= number of articles)¹⁰
Studies showing the relevance of clinical decision support software using AI and/or data mining (n=121)
Literature reviews (n=32)
Theoretical and/or empirical articles on the development of tools used by software in decision support (n=16)
Therapeutic areas (n=number of articles)
Various (n=65), Cancer (n=23), Cardiovascular (n=19), Psychiatry (n=7), Nephrology (n=6), Surgery (n=9), Diabetes (n=7), Emergency care (n=5), Ophthalmology (n=1), Paediatrics (n=2), Dentistry (n=1), Hepatology (n=3), Nephrology (n=6), Intensive care (n=2), Haematology (n=1), Neurology (n=1), Palliative care (n=2), Rheumatology (n=2), Nursing (n=1), Gerontology (n=1), Gynaecology (n=4), ORL (n=1), Public health (n=1)
Outcomes of decision support software presented in the articles
Prediction of events given the personal characteristics of patients (occurrence of adverse events, intervention results, survival, mortality rate, remissions, etc.) (n=48)
Care recommendations (drug treatment, surgery, follow-up) (n=20)
Verification of drug interaction (n=1)
Summary of available clinical data and adjustment according to patient characteristics (n=2)
Sources of data used to define algorithms
Historical patient records in institution (n=58)
Epidemiological cohorts (n=12)
Samples of patients in clinical trials (n=4)
Databank of diagnostic tests (n=2)
National health database (n=1)

4.2. Normative Frameworks Underpinning AI-based clinical decision support systems

4.2.1. A decision-making model based on the effectiveness criterion based on EBM enhanced thanks to individualised evaluation of the benefit-risk balance

Far from deviating from the normative framework of the EBM, the new possibilities offered by artificial intelligence technologies may instead reinforce it. Thanks to these new technologies, available scientific data are at the same time ‘bigger’ and more accessible to practitioners. These technologies should indeed allow the search for information about available scientific data to be facilitated. They should also make it possible to estimate the results expected from the various treatment options given patients' personal characteristics (age, gender, medical history, co-morbidities, biological and clinical variables), much more than ever before, and as Hamet and Tremblay (2017) as well as Krittanawong et al. (2017) have emphasised. Recommendations of good practice to date are currently limited to offering

¹⁰ Categories are not exclusive.

practitioners indications for subsets of patients corresponding to typical clinical situations (e.g., 60-year-old individuals with essential hypertension). It is necessary for practitioners to question their relevance of these recommendations for each patient, given her or his clinical situation and environment.¹¹ In contrast, the production of information about the expected efficiency at the individual level is now possible, thanks to the ability of APIs to identify the clinical and socio-demographic characteristics of each patient from the data contained in patients' medical records. These shall also include unstructured data contained in textual content (operation reports, biological checkups, clinical notes, letters, etc.). AI-based CDSSs could then incorporate these individual characteristics in their management recommendations by adjusting expected efficiency results accordingly, as soon as robust evidence data is available. Subgroup data from clinical trials, for example, allow measurement of the impact of certain clinical characteristics (previous medical conditions, co-morbidities, age, stage of disease progression, etc.) on the efficacy of treatment. Evaluating the effectiveness and tolerance of treatments in an individualised way should allow a better targeting among patients those who will benefit from those who won't.

3.2.2. The efficiency criterion is not taken into account by these new clinical decision support tools, despite the new possibilities of estimated individualised ICERs

However, we notice that none of these AI-based CDSSs took into account a criterion of economic efficiency to support practitioners' choices, excepted Bremer V, Becker D, Kolovos S, Funk B, van Breda W, Hoogendoorn et al. 2018. The fact that almost none of these CDSSs considers the criterion of economic efficiency is all the more remarkable as the combination of AI methods with CDSSs makes it possible to generate new types of information in this area. Indeed, AI-based CDSSs could estimate the impact of patients' clinical and socio-demographic characteristics on both the numerator and the denominator of the incremental cost-effectiveness ratio (ICER). For example, patients' age, their health histories and co-morbidities may have an impact on both the expected benefits of treatments (e.g., life expectancy and quality of life gains, risks of complications or adverse effects, etc.) and on costs (e.g., hospitalisation costs in case of serious health events, costs of adjuvant treatments, etc.).¹² Some socio-demographic characteristics may be associated with a greater or lesser adherence to treatments and thus may alter their actual effectiveness, just as geographical environment may have an impact on the consumption of care. So far, economists have estimated average ICERs for target populations, also called "populations of indication" because the only available efficacy data are average efficiency data. However, estimating average ICERs may be considered as a default choice. HTA agencies recommend estimating ICERs for subpopulations when the conclusions of assessments are susceptible to vary significantly as a result of a heterogeneity of health outcomes or costs (Espinoza, Manca, Claxton, Sculpher, 2014; NICE, 2013; HAS, 2012). The interest in estimating individual ICERs is discussed by Gestel, Grutters, Schouten, Webers, Beckers, Joore (2012), Padula, Millis, Worku, Pronovost, Bridges and Meltzer (2016) and Olchanski, Cohen, Neumann, Wong, and Kent (2018). The authors do not hold that this approach should depart from the normative framework in which traditional cost-effectiveness analysis is embedded. On the contrary, it would make it possible to better attain the objective of maximizing the production of health gains under constraints, by informing the actors about situations of inefficiency of treatments which would not have been identified in the population approach. To estimate individual ICERs and to provide this information to practitioners would therefore be consistent both from the point of view of the classical utilitarian framework and of the new Paretian welfare economics. The first utilitarians proposed evaluating a policy with the aim of maximising the sum of cardinal utilities. This implies in fact measuring the quantity of pleasure and pain which each action may produce, for each individual, and taking into account circumstances as much as is possible. Evaluating this public policy from the perspective of Pareto's unanimity also implies estimating its consequences on the level of well-being of all persons likely to be affected. *"The ingredients of CBA (cost-benefit analysis) include identifying the scope of the policy being evaluated, its effect on resource allocation and price, the consequences for welfare of individuals affected, and a global measure of*

¹¹ "To be sure, rationality (not to mention the evidence-based canon) demands that the best evidence be used in patient care. But what has been called the 'evidence gap' between clinical trials and individual patients (Mant 1999) afflicts us everywhere we turn. We must draw from the general and apply to the particular" (Goodman, 2002, p. 100).

¹² Furthermore, just as it is possible to adjust a health outcome observed in a clinical trial on individual characteristics, so the gain in quality of life, measured in QALYs, may be adjusted according to these same characteristics.

welfare changes that aggregates individual welfare changes.” (Bodway, 2016). However, the social acceptability of medical decisions based on an individualised ICER is not guaranteed. To estimate individual ICERs would imply that a treatment for a given indication could be recommended for some individuals, but not for others. This is because the costs incurred collectively would be judged too high for too limited benefits of a treatment in some given circumstances. Such decisions are justified from the point of view of utilitarian and Paretian models of justice. But it is not clear whether societies would be willing to apply these models of justice in such a systematic manner. The production of new information generated by CDSSs, in particular the individualised estimation of efficiency of the different treatment options, could reopen old debates about the principles of justice. So far, these have been largely theoretical, but they will soon be present in a practical way.

5. Discussion

The analysis of the recent literature and of the avenues currently explored by the different actors to mobilise AI in decision support systems suggest that these technologies do not so far involve changes in the normative frameworks which underpin the instruments currently in use to support medical decision-making. On the contrary, AI-based CDSSs might reinforce normative frameworks by overcoming the current limitations due to the information capacities of the actors. These avenues may therefore raise ethical controversies, that are maybe not unprecedented but that are certainly intensified.

5.1. New medical, AI-based CDSSs have led to a re-opening of the controversy between deontological and consequential morality

CDSSs based on EBM effectiveness criteria, or on efficiency criteria both assume acceptance of consequentialist morality or consequentialism, which assesses the justness of an action based on its consequences for the individual concerned and for society as a whole (Kerridge et al. 1998). The right or just option is that which produces the best consequences, from what is commonly accepted as objective: for example, the greatest happiness of the greatest number if one follows a utilitarian model of justice. This consequentialist morality may be challenged in the name of deontological principles that judge the morality of action by principle, regardless of its consequences. Those who advocate deontological morality consider that certain acts are absolutely mandatory (e.g., for a healthcare professional this means using all possible means to care for the patient) and that actions themselves are good or bad (e.g., killing, stealing, lying, etc.) (Berten, 2004 (1996)).

Until now, the ability of actors to assess the consequences of their actions was limited by their informational capabilities: lack of time to keep abreast with the latest scientific evidence, lack of computational skills to infer from this evidence an estimate of the expected consequences, in a particular decision-making context. New clinical decision support tools should overcome some of these difficulties and increase actors’ ability to measure the consequences of different medical options, by individually estimating effectiveness and efficiency. As a result, these technologies should enable consequentialist principles of justice to be implemented in a much more systematic way. This, however, raises the question of the acceptability of a systemic application of consequentialist principles in medical decision-making. For example, some variables, such as age, gender or socioeconomic group, may have an impact on the effectiveness of a treatment and therefore on its efficiency. From the point of view of a consequentialist morality such as utilitarianism, this may lead to not recommending certain health treatments for some patients when these have high ICER values. Such practices, however, could be considered as unjust on the basis of an deontological morality that recommends providing the same treatment to all patients with similar diseases, regardless of personal characteristics, according to the principle of equal access to care (Lepri et al. (2016) and Mittelstadt and Floridi (2015)). These ethical dilemmas could arise particularly in the context of CDS technologies using unsupervised machine learning techniques (Coeckelbergh, 2020, Ch. 6).

We believe that, so far, the fact that it has not been possible to assess the efficiency of treatments individually has helped in part to avoid these dilemmas. The inability to “calculate” the consequences at an individual level used to leave a space of uncertainty in which ethical stands were not necessarily formalised and so allowed the physician to follow her or his values. Now however, the dilemma between being “consequentialist” and being “deontological” could resurface with new clinical decision support tools.

It would then be possible to draw on Rawls's work to justify the limitations of applying consequential principles. Rawls indeed argued that the goal of maximising collective well-being is secondary to the respect for fundamental rights. From this perspective, Rawls identifies a series of goods that must be guaranteed to everyone. These primary goods are what everyone rationally wishes for, whatever their desires and tastes, and which everyone must have in order to be truly free to make choices and fulfil their life project. Rawls argues that it is imperative to ensure the fair distribution of these primary social goods, even if this leads to a decline in overall welfare output at the collective level. While Rawls did not discuss the place of health among this list of primary social goods, several authors have studied the application of these Rawlsian principles of justice in the field of health policy (Fleurbaey 2007; Sen 2002; Daniels 2009). Concretely reconciling consequentialist and deontological moralities, based on a Rawlsian approach, could therefore lead deliberately to "censoring" certain variables or results in the algorithms used in these CDS tools (Berendt and Preibusch, 2014; Floridi, 2016; Berendt and Preibusch, 2014). As Sen suggests, this means that respect for fundamental rights "*set constraints within which a social choice is made*" (Sen 1993, in Bertin, 2004 (1996)).

5.2. The new medical, clinical decision support tools used should reopen discussions on the rules for weighting health benefits

A second set of questions arises about the value systems used by algorithms to summarise information about the benefits and risks of different treatments. This is particularly so when the CDSS recommends specific treatments. A particular treatment may, for example, have a positive impact on pain reduction, while having a negative impact on mobility or functional abilities. Similarly, a treatment may increase length of life, yet degrade its quality, or vice versa. How are these different consequences to be weighted together? As a function of individual preferences or socio-cultural contexts, some dimensions have more value than others. Until now, the weighting of the consequences of interventions on different dimensions (quality of life, life expectancy, tolerance, etc.) are carried out by expert groups when good practice recommendations exist and by practitioners while they are drafting prescriptions as part of a joint decision with patients. In health technology assessments, it is usual to distinguish between assessment and appraisal phases. In the assessment phase, the consequences of treatments are measured, while in the appraisal phase the advantages and disadvantages of treatments are evaluated and compared so that an overall judgment can be reached.¹³ It is during this appraisal phase that ethical value judgments can be incorporated, alongside scientifically established facts.

The question therefore arises as to how these AI-based CDSSs will weight all the consequences of treatments on the different dimensions of individuals' lives and how these weighting matrices are being built and justified in the context of pluralistic societies. Some instruments have been developed in health economics (e.g. QALYs) to guide public decision-makers in this exercise of assessing the balance of advantages and disadvantages of different treatments. These instruments use the results of general population surveys to assess individual preferences for different dimensions of quality of life. However, they have been designed to guide the allocation of health resources at the collective level. They allow the average value to be assessed which individuals in the general population place on each of the dimensions of quality of life (Dolan, 2001). Nonetheless, these instruments are designed to guide the allocation of health resources and not to guide individual decisions on the choice of treatments. Moreover, the results of the economic evaluation serve to inform the deliberations and not to replace them. It is therefore necessary to see how a margin of appreciation for practitioners and patients may be preserved.

5.3. The use of new AI-based CDSSs requires the reopening of discussions about utilitarianism and the consideration of redistributive principles.

Assuming that AI-based clinical decision support tools take into account economic efficiency, particularly through individualised ICER, this would mean strengthening the utilitarian justice model and increasing the controversies that it has traditionally raised. The utilitarian justice model proposes to base public choices on an objective of maximising the sum of individual utilities. Health economists

¹³ Tools such as those used in economic evaluation help guide this work of comparative assessment by summarising the effects of treatments on individuals' health (thanks to QALYs, for example). However, the results of economic evaluation inform deliberation and are not a substitute for it.

adapt this utilitarian framework by evaluating health treatments with a goal of maximising the sum of years of life gained, weighted by utility scores associated with quality of life (QALY). There are many criticisms of the utilitarian justice model in general, and of its adaptation within health-care economics (North Daniels and Kamlet, 2009; Hausman, 2015). The main criticism concerns the lack of a redistributive principle within the utilitarian justice model. Indeed, unlike the models of justice that were developed subsequently, particularly as a result of Rawls's work, utilitarianism does not account for the distribution of the *outcome* of interest – utility – in the population. Public resources are allocated to maximise the total amount of this *outcome*, regardless of how it is distributed among the population. Yet, health inequalities are particularly unacceptable because health is a fundamental condition of well-being, as it allows individuals to lead the lives they want, and to have activities that are sources of pleasure (Anand and Peter, 2004). Thus, Rawls's liberal-egalitarian models of justice propose to allocate resources in a way that will maximise the situation of the most disadvantaged (maximin). Discussions then focus on the assessment criterion used to assess the situation of individuals. Are the most disadvantaged individuals persons with the lowest life expectancy (Harris, 1995; Williams, 1997); those who have suffered from life-long economic inequalities; persons with the lowest range of capabilities (Sen, 1987); or those who have no responsibility for their illness (Dworkin, 2002)? Following these discussions, new methods have been developed to assess the efficiency of treatments by integrating a goal of equalising health outcomes (Coast *et al.* 2008; Fleurbaey 2007; Asaria *et al.* 2015; Cookson *et al.* 2017; Samson *et al.* 2018). These methods are part of the more general literature on theories of social choice (Adler and Fleurbaey 2016). The possibility of mobilising these types of methods in medical decision support should be explored.

5.3.4. New clinical decision support tools using AI should reopen epistemological discussions on the model for producing clinical evidence

We have previously indicated that these new decision support tools do not imply a change in the decision model from the traditional EBM model. However, the methods used by these new CDS tools to generate evidence, which rely on specific statistical techniques, raise important questions. These statistical techniques are based on an epistemological framework which is distinct from that on which EBM is traditionally based. Data mining methods make predictions based on statistical associations between the different variables. But they do not identify an underlying theoretical model (Mullainathan and Spiess, 2017). They are therefore different from the traditional randomised controlled trial methodology that aims to demonstrate the causal relationship between health care and health improvement based on experimentation. Data mining methods are also different from econometric methods based on a structural approach. However, these distinctions need to be qualified. Some current good practice recommendations are also based on the demonstration of associations, without a causal relationship being established: for example, risk scores for cardiovascular ailments (Giroux, 2010). In addition, clinical data from randomised control trials (RCTs) have for decades been supplemented by non-causal statistical analyses: for example to identify the efficacy of treatments for sub-populations, results are extrapolated beyond the duration of trials, or indirect comparisons can be made. At the same time, several authors have discussed the possibility of estimating causal inferences using data mining methods (Grimmer, 2015, Shiffirin, 2015).¹⁴ Controversies about the value of scientific proofs according to the statistical methods used are not new: they have existed for as long as the principle of a scientific medicine has been put forward (Fagot-Largeault and Guillin, 2012). Yet they have been renewed by these new data analysis techniques and require reconsideration (Kitchin, 2014).

6. Conclusion

The analysis presented here has documented the dissemination of AI-based clinical decision support systems (CDSSs) based on a scoping review of the literature. We have seen that these new technologies should generally lead to strengthen the normative frameworks underpinning existing clinical decision support systems by overmultiplying the information capacities of the actors, but should not necessarily lead to a change of the underlying normative frameworks. By reinforcing these normative frameworks,

¹⁴ http://www.nasonline.org/programs/sackler-colloquia/completed_colloquia/Big-data.html

the ethical questions they raise gain new topicality. The limitations that actors have faced until now while striving to estimate the consequences of their actions led to a restricted application of consequentialist principles. As a result, in a context of uncertainty, these limitations allowed a space of the indeterminacy of values to be preserved and left open a space for everyone to decide on a case-by-case basis. It is possible that these AI-based CDSSs may make value systems more explicit, univocal and mutually exclusive, as one will need to be chosen which is nested in the underlying inferences or weights systems, thereby making it even more necessary to organise institutional discussions on the ethical frameworks that must be favoured.

In addition, the development of these AI-based CDSSs raises questions about the roles of clinical expertise and HTA agencies. The production of best practice recommendations, based on typical cases, may be made less necessary than it has been previously, as AI-based CDSSs may directly aggregate the information from different clinical trials and adjust the expected results for patients on their individual characteristics. It is likely that expertise is moving towards a validation of the information technology and of the source-data used, although evaluation models of these technologies remain to be defined.

We hope that this article will draw the attention of health economists to the possibilities offered by AI-based CDSSs to estimate individual ICERs. It seems essential to us to encourage this scientific community to discuss whether these individual ICERs are consistent with the theoretical framework of welfare economics. This question has rarely been discussed except by the authors mentioned above. We also hope to draw the attention to the actors involved in the design of AI-based CDSSs to the ethical controversies which could be raised by introducing cost parameters in algorithms.

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