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SPECIAL REPORT

Ethical considerations on the use of big data and artificial intelligence in kidney research from the ERA ethics committee

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ABSTRACT

In the current paper, we will focus on requirements to ensure big data can advance the outcomes of our patients suffering from kidney disease. The associated ethical question is whether and how we as a nephrology community can and should encourage the collection of big data of our patients. We identify some ethical reflections on the use of big data, and their importance and relevance. Furthermore, we balance advantages and pitfalls and discuss requirements to make legitimate and ethical use of big data possible.

The collection, organization, and curation of data come upfront in the pipeline before any analyses. Great care must therefore be taken to ensure quality of the data at this stage, to avoid the 'garbage in garbage out' problem and suboptimal patient care as a consequence of such analyses.

Access to the data should be organized so that correct and efficient use of data is possible. This means that data must be stored safely, so that only those entitled to do so can access them. At the same time, those who are entitled to access the data should be able to do so in an efficient way, so as not to hinder relevant research.

Analysis of observational data is itself prone to many errors and biases. Each of these biases can finally result in provision of low-quality medical care. Secure platforms should therefore also ensure correct methodology is used to interpret the available data. This requires close collaboration of a skilled workforce of experts in medical research and data scientists. Only then will our patients be able to benefit fully from the potential of AI and big data.

Keywords: artificial intelligence, big data, machine learning, observational trial, real world evidence

INTRODUCTION

Big data and artificial intelligence (AI) are becoming part of our everyday practice as nephrologists. Whereas this digital revolution holds a lot of promise, we should as a nephrology community also be aware of potential challenges arising at different stages. Data collection, data access, data analysis, communication of data-driven findings, and finally the implementation of findings in clinical practice are all separate steps with different ethical questions. Nevertheless, many of these aspects are interrelated, and biases introduced at one stage will lead to incorrect conclusions or bias in the next steps.

In this current paper, we focus on the ethical aspects of collection and storage of big data, of the fair and relevant access to big data, and of the appropriate analysis of big data.

We acknowledge there are also ethical considerations around communication of results based on big data research, and around their implementation in the clinical encounter and their impact on the interaction between the physician and the patient. As AI technology is evolving rapidly, for example the introduction of the foundation models such as Chat Generative Pre-Trained Transformer (Chat-GPT), we have opted to discuss general, abstract, ethical principles as starting points for reflection, rather

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Table 1: Minimal information for informed consent and patient approval of routinely collected data.

- What is the purpose and/or objective of the study? (well defined vs fishing trip?)
- How many people will be included?
- What type of individuals will be included?
- How long will data collection go on (timeline of study)?
- Who has originated the study? Where patients involved in setting up the research question?
- Who will own the data? (government, academic institution, insurance company, for profit organization)?
- Who decides on how the data will be used?
- Who will analyse and report the study? (academics, scientific body, patient organization, industry, governmental agency?)
- Why can data collection be relevant to me?
- Will the data collection and its analysis lead to actionable interventions (hypothesis testing) or is it basic science (enhance understanding)?
- Will this data collection be used to further underpin real world activity of an intervention that has already been evaluated in a randomized controlled trial?
- What are the potential limitations, pitfalls, and eventual dangers in using this data collection to answer the question at hand
- Is there an option for secondary use of my data for other yet undefined research?

than in-depth technological analysis. It is clear that the advent of chatbots and large language models, together with automated clinical decision support systems, will change the shared decision-making model, and probably also the trust between patient and physician. Although relevant, we will not discuss these in depth in the current paper. We will, however, discuss how the collection of data itself might hamper this trust. Collection of and access to patient data should be recognized as a privilege to be earned through trust, and cherished through respectful handling.

MAGNITUDE AND REACH OF BIG DATA

Sources of big data

Progressively more data are directly available in digital format. The electronic health record (EHR) contains patient data of all contacts with health care providers. Part of these data is collected for use in direct patient care, and a substantial part for administrative reasons (insurance), (direct) quality assurance, and contributions to larger databases, e.g. national audits and registries. Other data may be collected specifically for clinical research, e.g. prospective studies, or clinical trials. All these are considered primary use, as the data are used for the purpose they have been collected.

Increasingly, however, data are used for secondary purposes that go beyond the original reasons they were collected, and potentially go beyond what a person receiving care may reasonably expect their data would be used for. For example, EHRs could be searched for presence of indicators of progressive kidney disease and be linked to a database of community pharmacies to explore real world relation between adherence to certain drugs and kidney health. This would require linking of data from (re-)identified individuals. There is big debate on the circumstances when informed consent is needed for such secondary use of data. Different criteria should be met before one can reasonably assume patients are capable to actually provide informed consent (Table 1). Different criteria should be met before one can reasonably assume patients are sufficiently empowered to provide informed consent (Table 1). It is obvious that in the context of secondary use of data, it is often not very feasible to obtain informed consent. Accordingly, many have advocated waiving the need for informed consent for use of secondary data (e.g. from an EHR). Most authors refer to the duty of easy rescue or the common interest to justify such a deviation from respecting patient autonomy. Even if one accepts this rule as a justification, which not all ethicists do, it should be clear that doing so comes with ethical obligations. First, the 'rescue' should be easy. This implies that the eventual risk to the person providing his/her data should be very low, either because anonymity is guaranteed or because the sensitivity of the content of the provided information is considered low. For example, extracting an anonymous data set to link blood pressure readings from an EHR to evolution of kidney function over time would qualify as 'easy' because the risk to the individual is low: data are anonymous, and 'blood pressure' is not a sensitive issue. By contrast, linking a dataset with genetic information from patients with a rare kidney disease with life style data and outcome would be problematic. Indeed, risk of re-identification of individual patients is high in this setting, and lifestyle is a sensitive issue. Furthermore, invoking the rule of easy rescue presumes there is 'rescue' involved in the action. This implies that the research question is relevant, and the methodology and design of the study using these secondary data robust. Clearly, even if informed consent is waived, there should be an ethics board that investigates whether these criteria at least have been met. As this assessment requires knowledge and skills in ethics, methodology, and nephrology, the ethics committee members should be appropriately qualified. There should indeed be additional concern about the methodological issues involved when using secondary data. As described further, and depicted in Tables 2 and 3, there are many sources of methodological defaults, all of which may lead to incorrect or false conclusions. Translation of these (false) conclusions into clinical practice can seriously damage patient care. Therefore, secondary use of data can only be allowed when sufficient effort is done to secure a high level of quality of analysis of the data. Making health data solely available within trusted research environments (TREs or 'safe havens') as they are currently launched in the UK [1] would certainly be a substantial progress. Such TREs are platforms that are open to all researchers provided they have appropriate accreditations. They only allow analysis of the data within the secure environment of the data servers and incorporate strict layers of control on the outputs generated with regard to methodological scrutiny of the analysis done and the conclusions drawn. There is an opportunity for such environments, by design, to encourage the use of open, transparent, and reproducible practices. TREs should not only protect privacy, they should also ensure that available data are 'research ready' and thus well curated for errors or unreliable inputs. Data curation might also include ensuring that all data for a certain parameter use the same metric unit and are adjusted for differences in

Table 2: The impact of timing of data collection and study design on type of question that can be answered.

Answer	Question	Delivery of study treatment	Study purpose	Timing of data collection	Type of study design
Descriptive	To what extend is treatment A being used as treatment for condition X	Observational	Exploratory	Start of data collection predates start of study	Epidemiological study
	What are symptoms in patients with condition X?	Observational	Exploratory	Start of data collection predates start of study	
Association	What has been the impact of introducing drug A on the outcome of condition X?	Observational	Exploratory	Start of data collection after start of study	Pragmatic trial
	What has been the impact of introducing drug A on the outcome of condition X?	Observational	Hypothesis Generating	Start of data collection before start of study	Target trial emulation
Causal	Is treatment A better than B in terms of improving a given outcome	Interventional	Hypothesis testing	After start of study	Traditional RCT Pragmatic trial
	Is an alternative dosing schedule of A as effective as the standard dosing regime of A	Interventional	Hypothesis testing	After start of study	Traditional RCT Pragmatic trial

underlying methodology. For example, a national dataset containing serum creatinine from all laboratories in the country might imply that units need to be standardized [2], and eventual transformations are done to adjust for different methods used to measure creatinine. Such data curation is often time consuming, and needs input from different specialties. As TREs can serve as 'single point of entry', they can not only provide the necessary skills and manpower to perform such data curation, but also do this in an efficient and consistent manner. There is a great need for such initiatives if we want to keep the trust of the public and use the data provided by them for the greater good.

Furthermore, there is a tsunami of data originating from social media, on-line shopping, internet searches, positioning systems, etc. Although these data are not directly health related, they can easily be coupled to available health data [3]. This enormous datafication of our society and lives and the secondary use of these data poses opportunities but also ethical concerns.

Trust and privacy

Regulatory frameworks such as General Data Protection Regulation (GDPR), theoretically protect privacy by requesting informed consent and/or anonymization of data. In the case of the Deep Mind app Streams, it became apparent the hospital had not done enough to protect the privacy of patients when it shared data with Google [4]. However, even if data are completely de-identified, personal privacy can be endangered as algorithms can easily re-identify people [5]. Potential breaches of privacy, be it at individual or group level, might also make patients refrain from revealing all factors potentially affecting their health situation clearly and honestly to their treating physician. When setting up data collections it is thus of utmost importance to safeguard the patient-physician trust relationship. Again, establishing TREs might help preserve this trust.

However, individual privacy might no longer be the most relevant concern [6]. Who will collect the data for what purpose (context of use) is more of relevance. When asked, patients are more willing to provide data for academic basic research than for research funded by administrative or industrial sponsors [7]. Anonymized data collections can have scientific value to better understand patterns of risk, or can help to focus on certain populations who might benefit most from an intervention. For example, in elderly patients with eGFR < 20 ml, the EQUAL study identified an association between nutritional status, poor physical performance, mental status, and decline in eGFR. However, data collections may also jeopardize solidarity within health care insurance [8] when used to differentiate insurance fares for individuals on the basis of risk profiles identified. An estimate of risk can be derived from data from biomarkers, or genetic background, but also from indicators of risk-taking behaviour (e.g. interdialytic weight gain in patients on haemodialysis). The former are clearly unjust arguments on which to base an insurance premium, as they are non-modifiable factors. For the latter, one could argue that they are modifiable and thus personal choice of the patient, who should then bear the consequences of his actions. It can even be considered unjust towards those trying to decrease their health-related risk to have them pay the same fee as those who do not. Of note, the existence of such technology gives people no other reasonable choice than to share their data. If they are not willing to share their data, they simply will be considered 'high risk' and have to pay the highest premium. Accordingly, this problem cannot be solved by better data protection measures.

GDPR also includes the right to be forgotten. In times of automated searches of EHR by large language models (LLMs) this principle can, however, be very difficult to achieve in practice, as these LLMs will always find back the deleted information in old letters, and 'correct' updated patient files with pre-existing data.

Equity

Data collection can re-enforce existing health disparities, as some health-related risk factors might hit harder in people with psychosocial vulnerability. For example, low-income families might not have the necessary budget to buy healthy food or decent housing: factors associated with kidney disease in observational data sets [9]. Penalizing them by asking higher health insurance fees because big data analysis indicates they exhibit unhealthy behaviour would further add insult to the injury.

Table 3: Data quality requirements.

	What does it mean?	Examples
Completeness		
Missing data topics	Are relevant data topics missing for the whole dataset?	• age at inclusion in an analysis of mortality • urinary output in an AKI dataset
Informative missing data	Is there potential information in the fact that data are missing vs present for some patients for a certain data topic (metadata)?	creatinine only available in patients at risk for AKI and not inpatients at low risk
Selective data/selection bias	Is the dataset biased for some important confounder?	social deprivation status missing in a dataset linking crime rates with race and neighbourhood
Representativeness for the population	Is the distribution of the parameters included a in the dataset representative for the distribution of these parameters in the population?	underrepresentation of females, elderly, or people of colour
Representativeness for the problem/disease	Are the parameters included and their distribution in the dataset representative for the distribution of these parameters in this condition?	a study on impact of diet on outcomes of patients with diabetic kidney disease includes only a small portion of people with high social deprivation
Robustness	Can we be certain about the reliability of the source of the data? (e.g. are all measurements for a certain parameter done using the same, well-established technique?)	a dataset in which it is unclear whether all serum creatinines have been determined using the same laboratory method
Correctness	Have the data been scrutinized and verified?	
Relevance	Is each data topic relevant for the question at hand, or are there parameters that do not have a realistic relation with the question at hand?	including many irrelevant parameters increases the algorithm 'memorizes' the data to produce shortcuts rather than finding a generalizable relation
Granularity	Are the included data points sufficient to answer the question in a reliable way?	a dataset in which age is defined as below or above 65 would not have sufficient granularity to correct for age in a mortality analysis
Description of data labels	Is it clear and distinct what exactly is understood by each of the data labels. Can the same data label represent different definitions of a condition? Can different data labels represent the same condition?	• acute kidney injury can be defined according to different criteria, e.g. KDIGO, AKIN, or RIFLE • each definition can be implemented in different ways (e.g. with or without urinary output)

Furthermore, such individuals or groups might be less well represented in a dataset, resulting in bias if an algorithm is applied to them [10]. Because not all health care facilities use EHRs, datasets will not contain data for certain populations. Accordingly, algorithms trained on the available data will perform less well in these populations, probably leading to lower quality of care. Correct application of algorithms based on secondary data also requires adaptation to local circumstances and practices, which requires input from data scientists. The lack of availability of data scientists might exacerbate existing health inequity in underserved regions or populations. Missing data from individuals are often determined on the basis of the available data of others in the dataset in a process called profiling. In this process, people are automatically attributed the characteristics for the missing data (e.g. units of alcohol/day) of those of the group they were classified in based on the available data (e.g. gender, age, postal code, on-line shopping behaviour, use of public transport). This may result in confirmation bias [11]. For example, patients with diabetes and proteinuria will often be considered to have diabetic nephropathy, whereas a substantial proportion will have another cause identified when biopsied [12]. Equally, it is well conceivable that in neighbourhoods with higher social status, more frequent screening is done for kidney disease and its risk factors than in more socio-economically deprived areas. As a result, the impression might be created that kidney disease and its risk factors are more prevalent in high socio-economic areas, and thus that accordingly, more kidney-oriented healthcare should be provided in those regions. Profiling also results in uniformization rather than individualization of health care [13].

Justice and power

Systematic and broad collection of health care data also results in power asymmetry between those who own the data (mostly large AI companies, insurance companies, and telecom providers) and those providing the data [14]. Training the new foundation models, the backbone of generative AI, requires enormous amounts of training data [15], which can only be assembled by a limited number of big tech companies, providing them a monopoly position. Alongside Deep Mind [4], several other big tech companies have obtained access to and ownership of large files of patient data from EHRs [16, 17]. In none of these cases have patients been informed about the fate of their data or received rewards for their use. Most big tech companies might have other priorities than the health of the patient [17]. Therefore, ethical and legal guidelines should not only focus on individual rights but also on public

benefit, societal equity, sustainability, and accountability [18]. As a nephrology community, we should be cautious of the inherent ethical and societal risks associated with collection of data from our patients to ensure the data is really used to benefit patients with kidney disease.

The concentration of data in large institutions and tech companies also has consequences for research. The monopoly position provides them the power to decide who gets funding or not, and which topics are going to be researched or not. Furthermore, they decide how the results of the research will (not) be presented, interpreted, and/or translated into clinical practice (or not) [19].

A power asymmetry also exists between the physician and the organization. Management is increasingly controlling physicians' time and workflow by collecting quantitative and qualitative data about physician activities and performance. This may limit the flexibility for the physician to tailor treatment to the actual needs of the individual patient, further contributing to a uniformization, rather than individualization of treatment. Clinicians might be reluctant to write down their true ideas and perceptions in the EHR for fear these might be used against them or their patient at a later stage, or spend unnecessary time in overdocumentation of their clinical reasoning. This might also induce overconsumption of investigations to exclude unicorns.

The special case of genetic data

The complex field of genomic data raises specific ethical, technical and privacy concerns. An in-depth analysis is therefore beyond the scope of the current paper.

In recent years, groundbreaking technologies have emerged in the field of genomics, enabling scientists to describe genetic variability and link this with oncology, neurology, inflammation, and rare diseases. Genetic information is, however, literally, at the core of our existence. Datasets with detailed genetic and epigenetic information, while extremely valuable, are therefore also not without risk. A high risk for re-identification of persons in a database with single cell RNA data was recently demonstrated when these data were linked with phenotype data [20]. Besides individual privacy, there is also a risk of profiling and potential stigmatization of persons based on their genetic traits. In addition, while the combination of powerful machine learning and genetic datasets can lead to unexpected discoveries of potential biological pathways, there is also a high risk that some of these discoveries might be spurious, and in fact do not represent real entities [21]. Datasets involving genetic data therefore deserve special scrutiny.

COLLECTION AND SHARING OF PATIENT DATA: MINIMAL REQUIREMENTS FOR ETHICAL IMPLEMENTATION

Some general broad requirements are fundamental when setting up data collections. These requirements are essential in the sense that if they are not met, data collection cannot be considered ethically justifiable. They are, however, not sufficient in themselves, and further evaluation of the data collection is needed (Tables 2 and 3).

Purpose of the data collection

Collection of data should have a clear and well-defined goal. Ideally, there should be a clear rationale and justification why and how collection of data will potentially contribute to an improvement of the health of the population the data are collected from. There should be a good balance between potential benefits and harms, not only for the individual but also for the (kidney) community. Relevant questions at this stage can be 'will collection of these data help us to take better care of our patients?', 'will collection of these data make it easier for physicians to provide care?', or 'will the knowledge we derive from the analysis of these data lead to better outcomes for our patients?'. Some potential applications of big data sets within the field of clinical nephrology are depicted in Fig. 1, with for each an example of an existing study based on the dataset [22–28].

Necessity for data collection

Furthermore, it should be necessary to collect the data, meaning that the collection of the data is the best way to answer the question, and that each data item in the dataset contributes in an essential way. As described before, the mere collection of data in itself might pose serious risks for privacy, equity, solidarity, and justice. Therefore, collection of data that are not necessary to achieve the intended goal cannot be ethically justifiable. It is a widespread conviction that randomized controlled trials (RCT) are the gold standard to create evidence. Whereas this is true in principle, RCT methodology is also fraught with inherent problems. They take time to set up and be completed, especially for patient relevant outcomes such as mortality or development of comorbidities. Results are thus not always timely. Using routinely collected data can substantially reduce the time needed to answer certain questions [29]. Recently, Fu *et al.* [30] used a nationwide observational cohort to answer the question of timing of start of chronic kidney replacement therapy. Using appropriate statistical modelling, their results showed high congruency with those obtained within the IDEAL RCT [31]. RCTs are notoriously expensive, creating a bias in topics selected for investigation by RCT. Trials based on routinely collected data are much cheaper and can thus be done to answer questions industry or funding agencies have no interest in. RCTs also have very strict in and exclusion criteria, and interventions are mostly highly specific and strictly controlled. Therefore, results from an RCT mostly apply poorly to the population in an everyday clinical practice, this in contrast to registries with routinely collected data or pragmatic trials [32]. For some questions, it is difficult or impossible to get an answer by an RCT. Clinical questions involving many (continuous) decision points, or many potential combinations of decision parameters, so-called dynamic treatment regimes, cannot be answered by RCTs as the number of potential treatment arms increases exponentially [33]. A good example here is timing of start of start of kidney replacement therapy in AKI [28]. Routinely collected data may help to identify combinations of criteria likely to be most successful, and which can be consecutively tested in an RCT. Some questions cannot be explored by an RCT because this would involve unethical interventions, for example the effect of smoking. In such a setting, routinely collected data to perform natural experiments can be of high value.

Methodological and epistemological approach

For routinely collected data to have added value to create evidence on justifiable medical interventions [34], correct methodology and rigour should be applied [35] (Table 2).

Before data collection begins, a detailed analysis plan with an appropriate methodological approach to address the questions posed, should be provided. There is growing evidence on how inferences from big data can go wrong [36]. Ideally, methodologists

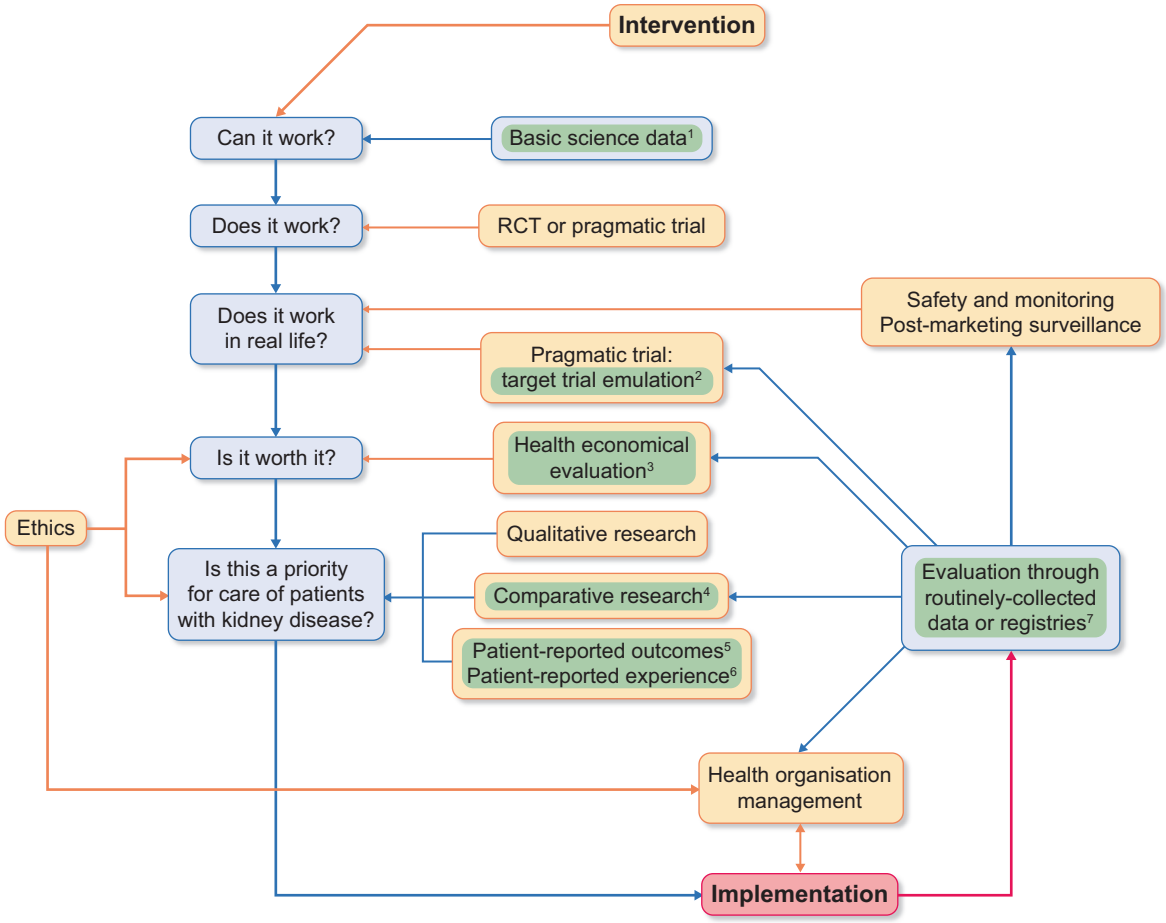

Figure 1: Potential uses of big data collections to progress nephrology. A knowledge development cascade within kidney disease. Different levels at which big data and routinely collected data can contribute to improved care for patients with kidney disease are highlighted in green. Superscripts indicate an example of a registry or a study set up to provide an answer to the question at hand. (1) El-Achkar *et al.* [24]. This project will integrate different datasets to establish evolving, spatially anchored, cellular, and molecular atlases of the cell types, states, and niches of the kidney in health and disease. To final aim is to identify subtypes of disease that are not readily apparent but through advanced clinical phenotyping, pathomic, transcriptomic, proteomic, epigenomic, and metabolomic interrogation of kidney biopsy samples. (2) Morzywolek *et al.* [28]. This study used target trial emulation on a large ICU database to optimize criteria for starting renal replacement therapy in patients with AKI at ICU. (3) Griffiths *et al.* [27]**.** This study used a dataset of patients undergoing percutaneous coronary intervention derived from Medicare toe explore the real-world performance of predicted contrast induced acute kidney injury. (4) Suzuki *et al.* [25]. This study used a subset of patients starting with SGLT2i vs DPP4i from a nationwide claims database to make a comparative analysis for kidney outcomes. (5) Oberdhan *et al.* [26]. This study used data from the ADPKD Registry, a secure, HIPAA-compliant, online platform (IQVIA, oc-meridian.com/pkdcure) hosted by the US based Polycystic Kidney Disease Foundation (PKDF). (6) Hawkins *et al.* [22]. This study used three UK national data collections to develop a Kidney PREM Short Form for more frequent measurement of patient experience to inform local service improvements. (7) van de Luijtgaarden *et al.* [23]. This analysis demonstrated the real-world performance of peritoneal dialysis and haemodialysis in Europe as represented in the ERA data registry.

with expertise in causal inference and data science should thus be involved in the development of the dataset [37]. Analysis is only possible after data are carefully shaped, checked, and curated. Data can be misinformative or plainly harmful when these preparatory steps are inadequate, or performed with intentional corner cutting. Results should only be presented with full consideration of limitations of the data and the analysis, and communicated with careful consideration of decisions that were taken along the whole data pipeline. General anthems of 'old school epidemiology' remain valid even in the era of big data. It is essential to understand that just having 'more data' does not solve problems with underlying issues of study design nor improves the quality of the data. Even in times of causal machine learning, one should be cautious of basic errors in epidemiological reasoning when interpreting observational data. In some situations, the best solution may be to acknowledge that the data sources cannot be used to answer the question of interest (Tables 2 and 3). Data quality is therefore crucial (Table 3). Data should be verifiably accurate and timely. Definitions of items should be distinct and uniform, to avoid semantic opacity [38] or creep in the data. The label 'acute kidney injury' for example covers a whole range of potential conditions [39], even after harmonization by KDIGO. All these different conditions have a different clinical and prognostic meaning [40], even though in publications they all are labelled as 'AKI according to KDIGO' This creates bias and confusion. This is especially problematic when data have been primarily collected for administrative rather than clinical use [41]. Preferentially, data are complete and contain all relevant items necessary for answering the question at hand. Methods used for data curation and analyses should be completely reported. Also, key limitations of data sources should be emphasized in their reporting. If not, results are not trustworthy nor reproducible [42]. A move towards TREs,

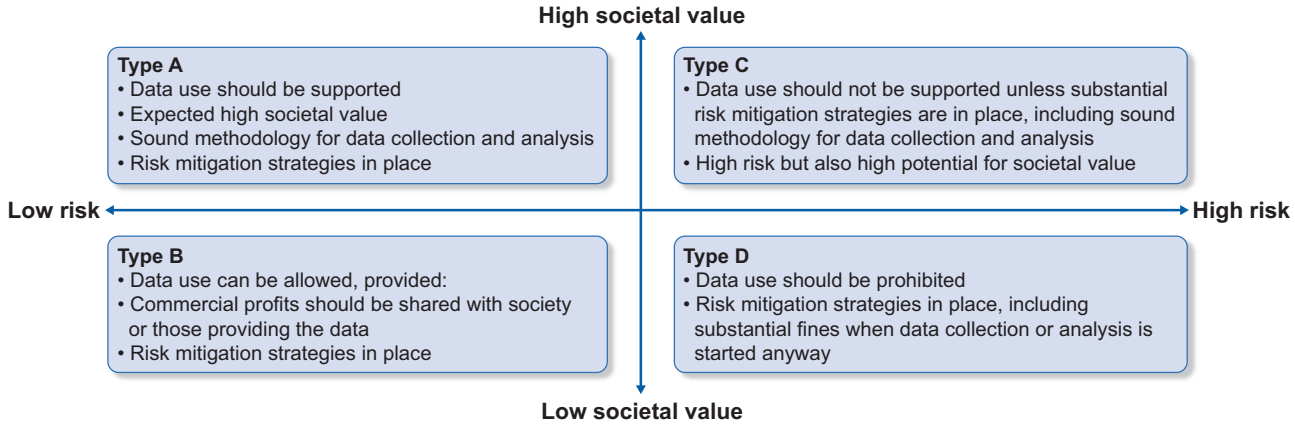

Figure 2: Classification of ethical appreciation of data collection. Type A data collection: a national registry collects pseudonymized data of patients with CKD stage 4 and 5 in a strictly protected server. The scientific advisory board consists of experts in nephrology, epidemiologists, and patient representatives. Using state-of-the-art causal inference and dynamic treatment modelling they intend to optimize criteria and decision points to start kidney replacement therapy to achieve optimal survival and quality of life. The societal value of this question is high, as kidney replacement therapy comes at a high personal and societal cost. The associated risk is low and mitigated by the fact that data are pseudonymized, and governed by a trustworthy advisory board. The question cannot be truly answered by a randomized controlled trial, as many different decision points need to be explored. Type B data collection: national collection of dialysis catheter related infections in all units, including patient demographics, data of cultures (germs and microbial sensitivity), type of catheter, location, operator, type of catheter lock used, and response to antibiotic treatment. Data are stored on a central protected server using RedCap. Data analysis (descriptive epidemiology only) is supervised by an advisory board of the National Renal Society. All centres can themselves retrieve data from their own patients and obtain analysis of their results as compared to all other centres. The risk of this data collection technique is low, as data are pseudonymized. The risk is mitigated as data are securely stored on a dedicated server using trustworthy technology (Redcap) and supervised by a trustworthy party. Results will indirectly benefit patients as they inform their treating physicians about local epidemiology. Value is limited as only descriptive analysis can be performed. Type C data collection: a tertiary referral academic centre intends to set up a biobank for a rare genetic kidney disease, with the intention to use AI and -omics technology to identify potential new targets for a drug. As the disease is highly prevalent in a poor underserved area in Africa, they plan to include also this region in their dataset through the local hospitals. There is a potential for societal benefit (identification of new treatments for a rare disease), however there are also many substantial risks involved. Risks relate to methodological issues (proper collection, storing and shipping of biomaterials, data collection), as well as to ethical issues (risk of detracting time and money to care of this subgroup of patients at the expense of more general health issues in the region). Most important, there is a high risk that the population who provided the data will never be able to benefit itself from the to-be-developed treatment, as they cannot afford it; a mitigation strategy could be that part of the (financial) profit derived from the biobank flows back to local health care programmes. Type D data collection: a commercial company wants to collect data from the EHR and the HLA typing laboratory of patients waitlisted for kidney transplantation, so they can send them personalized advertisements for well-matched paid living donation from international donors. This data collection should not be pursued as it can be used to facilitate illegal commercial organ trafficking.

the hosting of well-curated data with clear documentation of provenance and data dictionaries, and an emphasis on reproducibility across the full analytic pipeline will help.

Weighing of risks and benefits of data collection

Risks of data collection should be carefully weighed against expected benefits. This weighing should ideally not be evaluated by the people setting up the data collection, but preferentially by an independent multidisciplinary panel of content experts, ethicists, and social scientists. As most important stakeholders, patient representatives should also be involved, although they might need additional training to understand peculiarities of data research [43]. As potential harms not only affect individuals, but also society as a whole; the societal impact of the data collection and its intended use should be clear and receive public support. Individuals or groups who could eventually be harmed by the data collection should have the means to defend themselves and receive compensation. Ideally, data collection should not be in single hands but rather in so-called TREs, data trusts, or conglomerates of the different stakeholders involved. These TREs should have a clear mission and vision, and a legal structure and constitution. They should have a clear and transparent model for decision making on sharing and analysing the data. Such TREs should have a sustainable, independent, source of funding, and clear description of how benefits of the data collection are shared among stakeholders [1, 44].

Value of a data set

Initiatives for data collection are often described as 'advancing health care' or 'developing innovative technology'. Such positive rhetoric is mostly taken for granted by those setting up the data collection, but is not ethically neutral, as it creates justification of investment of money, time, and effort, and suggests a kind of moral duty for the patient and their physicians to contribute to the endeavour. This is especially so when put forward by famous researchers with long track records of publications, or when lobby groups use a mascot case to mollify the general public. The value of each data collection should be considerately explored. It is highly dependent upon the context of use (by whom, for what purpose), the quality and representativeness of the data (accessibility and interoperability, semantic transparency, and presence of metadata) and the methodology used for analysis.

It should be clear who will really benefit and how [45]. The valuation of a data collection can be different for those doing the data collection, the patient or society. Measures of value may be financial units, mortality or morbidity rates, well-being, general health indices, or scales, but also academic prestige. Ultimately, researchers making use of data, are incentivized to produce publications and impact. All these can lead to protective behaviour and perverse incentives. Similarly, large (academic) institutions may consider datasets as assets to be protected. This can result in resistance to sharing data that patients may have agreed to contribute with the understanding of sharing for the greater good.

As data collections are often done by large tech companies, financial drivers cannot be excluded. From the start, it should be documented how eventual commercial or other profits will flow back to those providing the data or to the community they belong to.

For patients involved, the potential to achieve or maintain a better health status is an important factor in the valuation of the data set. Therefore, it is of utmost importance that the informed consent letter is clear, distinct, complete, and honest about what can realistically be expected as a result from the data collection.

Value for society is harder to judge. A data collection potentially resulting in successful development of an innovative treatment might be of high (financial) value for a company, and the patients providing the data (increase in health), but can have detrimental consequences for society, e.g. by generating opportunity costs or by further enhancing inequity as only the wealthy will be able to afford the treatment. The societal value of a dataset also depends on the purpose it is going to be used for. The same data can be used to identify an underserved population to focus care, or to identify individuals at risk, so they can be denied a job or a loan.

Data solidarity

There is much ongoing debate on whether people have a moral duty to contribute their health-related data. Individuals cannot have a moral obligation to contribute if the abovementioned criteria are not met. An independent ethical review board, including ethicists, content specialists, data scientists, and representatives from patients and socio-political bodies should decide whether these criteria are met.

TOWARDS A CONCEPTUAL FRAMEWORK

A recent white paper [46] provides a good decision support tool to evaluate whether data collection is ethically acceptable, can be coercive (informed or not), requires consent, or should be discouraged or even prohibited (see Fig. 2). The evaluation is based on the value of the data collection for the patient and the society, and the associated risks, and places standards for (financial) compensation of those providing the data to make up differences in value creation for the parties involved. Involvement of data scientists and epidemiologists should be imperative to classify questions as descriptive, association or causal. As a consequence, there are limits as to what type of questions can reasonably be answered by certain types of data collection and methodological approaches [37, 47].

The white paper advises that, to make this framework sustainable and practically workable, administrative requirements can be tailored to specific settings (for example, a small academic research project vs a large-scale international data collection by a pharmaceutical or tech company). However, while we appreciate the concern for feasibility, we would caution for such an approach, as we believe that all research, even when small or limited in scale, should comply with minimal ethical and methodological standards.

CONCLUSION

AI and big data are promising tools to advance the outcome of our patients with kidney disease. However, as for most other medical inventions, the gap between potential benefit and potential harm might be small. The factual impossibility to escape data collection, and the high risk of monopolization of power would not be problematic in themselves if they would result in better or more individualized healthcare. However, in reality, many applications are available but few have been validated or incorporated in the clinical work flow [48, 49], and most result in regression to the average rather than individualization of care. We should also advocate to clarify legal issues related to litigations of nephrologists because of malpractice related to data donation itself (e.g. a patient who lost her job because her need for dialysis was leaked to social media because of a study) but also of decisions based on the clinical decision tools constructed on the collected data [50].

Therefore, as a nephrology community, we have to ensure that data collections can be constructed according to well-defined criteria, to maximize potential benefits and reduce potential risks.

We have described the minimal requirements such big data collections should have to avoid harming individuals or groups, society, or the nephrology community itself. While awaiting a clear and established legal framework, this reflection might provide guidance. Initiatives such as TREs should be encouraged not just to maintain public trust in the use of data, but maintain trust in sharing decisions at the level of the individual clinician patient relationship.

CONFLICT OF INTEREST STATEMENT

None declared.

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