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The Philosophy of doing Observational Medicines Safety Research

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Abstract

The safety of prescribed medicines is everyone's concern and we might expect that our healthcare systems would have systems in place to link prescribing with serious adverse effects. However, in general this does not happen often because of concerns over privacy of healthcare data. This article discusses the philosophical arguments for and against the use of anonymised healthcare data for the purposes of determining the safety of medicines. We favour the utilitarian argument that the greater good is served by using these data for this purpose without the consent of individual patients.

Safety of Medicines: Everyone's Concern

The safety of medicines has always been the paramount concern of clinicians. The core ethic of medicine remains primum non nocere - "first, do no harm". Clinicians understand that no efficacious drug is entirely without adverse effects. The role of the prescriber is to improve the benefit to risk balance by prescribing thoughtfully to maximise benefit and minimise risk. If avoiding risk comes before all else, the only option is not to treat patients at all. Clearly, this is not a reasonable response. Nonetheless, there is a clear imperative to understand better the determinants of the benefits and risks of medicines as they are used in the real world.

Defining Safety

In the past, 'absence of evidence of harm' associated with drug therapy was an acceptable standard of assessing safety. This has progressively been superseded by an 'evidence of absence of harm' standard together with more formal assessments of the benefit to harm balance in specific patient groups. In general, we know more about recently licensed medicines than older drugs that were licensed when standards were low. Unfortunately, we continue to discover significant toxicity issues with older and newer medicines.

Perfection versus Pragmatism

In a perfect world there would exist very large amounts of un-confounded data on the benefits and risks of drug therapy in the setting of normal care. Within the NHS such data might be got by randomly allocating practice formularies to new versus old treatments and tracking the outcome of subjects. Whilst an attractive idea that might eventually be adopted there are many practical and ethical arguments to be won before such a system could be implemented. These include changing treatments at the practice level without individual subject consent (although they can opt-out), tracking subjects to determine the outcome of treatment changes, gathering and validating adverse effects and outcomes and dealing with the issues that might arise when subjects are told their treatment is being changed. Progress in this direction is being made [1,2]. A practical if imperfect alternative is to observe the normal care use of medicines. The NHS has access to vast amounts of data on patients who were exposed to medicines and systems are already in place that could track the major outcomes such as hospitalisation and deaths. Since these data are already collected the incremental cost of linkage of records would be relatively small. Interrogated appropriately, such a data resource could provide important estimates of safety and effectiveness.

There are example anonymised UK datasets available to researchers [3-5]. A *Modus operandi* thus appears to exist that such anonymised data sets can be created. But even with quite large databases, exposures to treatments for less common diseases or for recently licensed drugs becomes sparse and cannot provide useful data. Given that the NHS (and other health care systems) could benefit patients by analysing 'the NHS' database, it begs the question; 'why not?'

Barriers

Consent issues

In the perfect world we would get consent from everyone to use their data. In practice this is not feasible, largely a result of apathy or time-constraints rather than outright hostility to the concept [6]. Opt-out systems would be similarly difficult to implement as it would require everyone in the UK to be made fully aware of what their data would be used for to allow them to make a judgement as to whether they should opt out. Even if we did get informed consent, this could introduce bias [7]. So what are the ownership and ethical issues of using patient data without consent? Nevertheless, consented prospective observational systems may be one way forward as was one such study of subjects vaccinated against H1N1 virus (swine flu) [8].

Data ownership

The ethical and legal aspects of collecting patient identifiable data without patient consent have been discussed [9]. Whilst patients may not own their identifiable medical records, they have a right that these are kept strictly confidential unless they give their consent to disclosure. For anonymised patient data, a letter in The Lancet in 1990 stated "Insofar as it is capable of being owned the intellectual property in anonymised NHS data may be regarded as a fund of knowledge which should be available to society at large" [10]. A legal ruling that anonymised health information can be provided without a breach of confidentiality has been criticised as a "betrayal of confidence"

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[11]. Nevertheless the legal situation appears to be that acceptably anonymised data appear not to be owned by patients.

The Ethical Frameworks of Deontology and Consequentialism

Deontology

Discussions of medical ethics are often couched in the terms of 'duties' and 'obligations'. Such an approach is referred to as deontological. It is concerned with types of actions, and suggests that certain of these are permissible and others are not permissible. In the case of un-consented observational research, it is asserted that allowing researchers access to confidential patient records without explicit consent from the patient is morally wrong. Other considerations are irrelevant: the type of action in question is not permissible regardless of circumstances. In its simplistic sense this is the philosophical structure of Immanuel Kant [12].

Duty of care as a philosophy

Individual doctors and the health service as a whole operate under various duties to their patients. Arguably, the National Health Service (NHS) in the UK has a duty of care to the population it serves and to individual patients it cares for. The UK General Medical Council (GMC) guidance states: "Research involving people directly or indirectly is vital in improving care and reducing uncertainty for patients now and in the future, and improving the health of the population as a whole" [13]. In reality, even highly acclaimed management guidelines turn out to be about 50% opinion based rather than evidence based [14]. There is thus a strong argument that clinicians in general have a duty of care to participate in research and to improve the evidence base that underpins good medical care [15]. "Supporting this the GMC specifically mentions in section 14f of its Guidance for Good Practice, that physicians should; "help to resolve uncertainties about the effects of treatments" [16]. Certainly, when asked, the public are of the opinion that the NHS has such a duty of care to determine the safety and efficacy of the drugs it prescribes for its patients. In a survey of 1,040 representative adult members of the Scottish public carried out in 2010 97% of respondents agreed with the statement that "*The NHS has a duty to determine the safety and effectiveness of the drugs its doctors prescribe*" [1]. Interestingly the public thought that the NHS more than the regulatory bodies had this duty.

However, others judge that data captured in routine care for one purpose (such as the supply of prescription medicines) should not be used for other or secondary-use purposes [17].

Duty of confidentiality

The 'duty of confidentiality' ethic is often cited as a major reason for not constructing large patient databases. Patients consult with doctors under the assumption that such consultations are private, and that third parties will not be privy to information disclosed within them. A centralized database of patient information could, if compromised, be potentially damaging to patients and the duty of confidentiality might be breached. More significantly, to store such data, and allow researchers access to it, without the explicit informed consent of patients is regarded by some as itself a breach of confidentiality. The implementation of data security controls and patient de-identification techniques required to engender confidence that patient privacy is protected are significant but not insurmountable as various databases already exist that contain portions of NHS data. Nevertheless, these worries have impeded progress towards an integrated routine safety and effectiveness solution.

Consequentialism

There is an alternative way of evaluating permissibility and that is consequentialism. Perhaps the best known example of a consequentialist theory is utilitarianism (famously espoused by David Hume, Jeremy Bentham and John Stuart Mill), but any consequentialist position will share the same basic position [18]. What matters for moral permissibility to the consequentialist is not the type of action but the action's consequences. Again in the case of un-consented research, the question would be whether the overall benefit of performing un-consented research outweighed any costs (in terms of risks to the patient, and so on). If it did, it would be permissible; if not, it would be impermissible. There is nothing fundamentally 'wrong' with the proposal.

Consequentialism and public health

There are precedents for prioritising public health at the potential risk of harming individual patients. An example here might be Rubella vaccination. This is routinely administered to the entire population, yet individual recipients receive little to no direct benefit from it as Rubella is a mild illness. To that extent, recipients run only the risk of being harmed by the vaccination procedure, which could be regarded as a breach of the duty of care. However, such blanket vaccination has a large social benefit, in particular by protecting children yet to be conceived for whom the illness contracted *in utero* would be much more severe [19]. It seems that society has deemed that individuals cannot reasonably refuse the very small risk of receiving the vaccination, given the considerable benefits to others. Indeed, rubella vaccination is not even available as a single component vaccine in the UK but can only be given along with measles and mumps vaccination so patients cannot in practical terms opt out of rubella alone if they wish protection against these other infections. Indeed, women who are considering pregnancy who are not immune to rubella have to be given the combination measles, mumps and rubella vaccine as they cannot get rubella vaccination alone in the UK.

Thought experiment

It is useful to test intuitions in the realm of the thought experiment. It is possible that a 'deontologist' might favour un-consented observational research, or that a 'consequentialist' might oppose it. In general, however, the strongest arguments in favour of such research come from the consequentialist perspective, while the strongest oppositions come from the deontological. In teasing out these opposing ethics it is useful to consider a hypothetical situation where un-consented research is carried out, to see how the various lines of argument run.

Suppose that there exists a universal database of all the patient information gathered in the course of routine practice. Suppose that appropriately vetted researchers can gain access to this information at will, and conduct research using it. Finally, suppose that all of the information is perfectly anonymised – no specific individual can be identified by the researchers – and that there is perfect data security – nobody can gain access to the information illicitly. In this case, there is no additional risk to patients from having their data stored in this way. Furthermore, as this is observational and not interventional research, there is no additional risk in terms of treatment received: patients are treated as part of normal practice, exactly as they would have been were they not the subjects of research.

The deontologist might well agree that no material harm is being done in this case. But to the deontologist, that may not be the point. The point is that doctors make a binding commitment not to disclose any information acquired in consultation to third parties, except in circumstances such as referral to a specialist. Yet here, the data is made available outside of the bond of trust between doctors and patients. This breach of confidentiality is impermissible, regardless of whether material harm results or not. At root, the objection to un-consented observational research is that individual patients are being required to participate in a social project without their permission. Immanuel Kant discusses the idea that individuals must not be treated as means to an end, but as ends in them selves. In this case, patients – or more specifically the information held about them – are being used as means to pursue the goal of drug safety. Objectors feel that this violates their rights as individuals: it is immoral to *require* people to engage in a social project, however admirable it would be if they volunteered.

The consequentialist, on the other hand, should have no qualms with this thought experiment. By assumption, the data cannot be used malevolently against the patients: it is perfectly secured and perfectly anonymised. As such, the very worst case that could arise is that the research being carried out would yield no benefits, in which case the net benefit of the system would be zero. This, then, is a morally permissible system: it is, at least, no worse than the alternative of no such system. Of course, research is likely to yield benefits, which immediately tips the argument further in favour of allowing such research.

The Present Situation

Anonymisation is not, in reality, a perfect process. But it can be done extremely thoroughly, so that in the majority of cases it is simply not possible to identify the source individual, while in the remainder it is at least extremely difficult. In addition, researchers can be made to face severe penalties (such as dismissal) for attempting de-anonymisation. Thus, acceptable standards of data security can be achieved [20]. If this is the case, it is not unreasonable to conclude that inclusion is a violation of privacy?

Negotiating the Moral Maze

Recently, the Academy of Medical Sciences report entitled: 'A new pathway for the regulation and governance of health research' has concluded that 'research should be embedded as a core NHS activity and that ways need to be found of providing access to patient data that protects individual interests and allows approved research to proceed effectively' [21]. Thus there is a need to re-examine the way that we deal with this issue.

Conclusions

The risks of any meaningfully private information being disclosed in a properly regulated system are extremely small. But the risks from not undertaking observational research are significant. If safety and effectiveness of medicines (and indeed other healthcare interventions) are to improve and if new drugs are to be assessed early in their clinical use, then it is essential that a new framework for observational research be established. The alternative is to fail in the duty of care to everyone.

Competing Interests Statement

David Rutherford has no competing interest. Li Wei, Thomas MacDonald and Isla Mackenzie declare that they have an academic interest in analyzing observational data for public health research. Thomas MacDonald and Li Wei have done commissioned observational research for the pharmaceutical industry on behalf of the University of Dundee.

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