WHAT CONSENT MODEL IS ETHICALLY JUSTIFIABLE IN CANCER POPULATION RESEARCH?

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Abstract

The important role that explicit informed consent plays in the conduct of research cannot be denied. Inhumane medical research has prompted over many decades the articulation of guidelines, legislation, and codes to ensure that research participants are protected from the harms inherent in some forms of research. However, there are now certain kinds of research, such as large epidemiological studies or data linkage studies, which offer potentially great benefits for whole populations but which, at the same time pose minimal, if any, harms to those included. These forms of research should not be required to adhere to the traditional informed consent requirements for the reasons articulated in this paper. The paper focuses on consent options for cancer population studies and examines the ethical issues associated with each model.

'Treating research differently is harmful to public health because it slows progress on solving important problems. In this regard, our focus on privacy protection has become a hindrance to scientific progress, which cannot be justified on ethical grounds.'[1]

The number of newly diagnosed cancer cases in Australia increased from 66,393 in 1991 to 114,137 by 2009.[2] Predictive modelling for the period 2007 to 2036 suggests that the impact of cancer is expected to increase dramatically, with approximately 110% in cumulative incidence of cancer in New South Wales alone.[3] While such long-term predictions are tentative,[3] it would be imprudent not to use routinely collected cancer data in large epidemiological and data linkage studies to identify priorities, to better plan and evaluate treatment strategies and screening programs, as well as care outcomes.[4,5] Such large-scale research can also guide the development of more efficient and effective systems, and more effective evidence-based policies in a context where resources are limited.[4] A key consideration, however, is what consent model should be adopted in such research.

Facts and myths about informed consent

In any discussion about consent models, it is instructive to bear in mind important historical facts that influenced and prompted the regulation of research by ethics committees.[1,6] The inhumane Nazi experiments and the publicly funded Tuskegee Study (cdc.gov/tuskegee/timeline.htm) suffice to remind us that human experimentation was conducted over extensive periods without the ability for participants to choose whether or not to participate, without accurate information regarding the nature of the research, and with no regard for the devastating harms inflicted on human beings in the name of science.

The default position enabling participation in research is rightly explicit informed consent, as it confers numerous benefits on research participants. Protections arise from a participant's ability to decline to participate without penalty, as well as from the conditions that consent processes impose on the research, such as the provision of appropriate information and reporting requirements. Obtaining informed consent provides protections against infringements of people's privacy and ensures that the trust that must exist between the public and the research community is promoted and protected. In addition, obtaining informed consent from participants demonstrates researchers' respect for people's autonomy, thus enabling them to make the choices they consider appropriate for themselves. Gaining greater importance as vast amounts of information are gathered about us is the role that informed consent plays in providing greater levels of control over the uses to which our information will be put. Informed consent, however, is also sought to satisfy institutional or legislative requirements.[7] This is an important motivator for researchers to engage in consenting participants, but if it is the sole motivation, the spirit and effectiveness of the whole process is undermined and it simply becomes a procedural exercise underpinned by necessity rather than respect for research participants.

The importance of obtaining consent from research participants is undisputed. However, its role and function can sometimes be overstated. For example, some assert that informed consent enables participants to control the risk to which they are exposing themselves as a result of information received and their ability to withdraw from the research.[8] This sounds appealing but, in practice, may not be so clear-cut. How informed consent, the process of

which culminates in an informed decision to participate, can itself truly provide any protection against unforeseen and unintended harms is unclear. Participants in clinical trials, for example, may receive all the information required for them to make an informed choice about the level of risk they are willing to assume, but their consent does not and cannot protect them from harms that may arise during the course of the research, such as unexpected adverse events. O'Neill argues that seeking informed consent '… reduces the possibilities of deception and coercion'.[9] It may be that deception is reduced, but it is difficult to argue that coercive influences are completely eradicated through the provision of informed consent, given the impact that the framing of information can have on how information is received and understood. Potential participants may, in fact, still be coerced to participate during the consent process even if '…additional accurate information is reliably available as demanded…'[9] simply as a result of *how* it is presented.

Informed consent: not the right model for all research

The requirement for explicit informed consent arose in relation to unethical human experimentation and primarily aimed to ensure that no research participant was involuntarily included in harmful research, and that associated research risks were transparently made known so participants could determine their willingness to assume certain risks.[10] The same kinds of risks are not involved in large epidemiological studies and insistence on this model has significant ethical implications relating to the ability to conduct sound research and the appropriate use of limited research funds.

Numerous considerations support the view that explicit informed consent in certain kinds of research is both inappropriate and harmful.

Impact of stringent consent requirements on population research

The constraints that stringent consent requirements impose on large-scale population research have been articulated in the literature at length.[4,11] In addition to leading to lower participation rates, the opt-in consent model also results in biased samples.[12,13] An example of the dire consequences on epidemiological cancer research is seen in Europe. The impact of additional protections imposed on registry data to align with the European data protection directive (95/46/EC) was crippling, as research and other key functions of cancer registries were severely impacted or halted in some jurisdictions.[4] Having considered the impact on epidemiological research and other key areas such as quality control, the European Commission is now in the process of replacing the directive.[4]

Protections surrounding uses of data

The articulation of multiple protections afforded to individuals' data in large epidemiological or data linkage research has also been extensive.[4,11,14] Such protections are greater guarantees for research participants than any consent process could provide and include, but are not limited to: legislation and regulation; ethics committee oversight; technical, physical and personal security protections the data are subject to; as well as the broader data sharing systems developed, all of which ensure that participants are exposed to minimal risks.[4,11,14] Participants in an Australia-wide study indicated that they had a strong preference for opt-in consent for any secondary use of their health information (92%).[15] Interestingly, this finding was not linked to concerns about privacy, as 89% of these individuals indicated. It was also shown however, that the greater the assurances about the de-identification of data, the greater the support for use of health information in research.

Benefits arising from population research

Examples of the benefits of large population studies abound, and some of these have been mentioned in the above sections.[16-20] Roder and colleagues provide a detailed account of the traditional, recent, and emerging role that cancer registries play in producing wide ranging benefits, including when these are employed in research.[19]

Harms of not using routinely collected data to benefit large populations

Cancer alone will burden communities significantly in years to come and healthcare systems will increasingly be functioning under greater constraints due to increased demands for treatments.[3] Additional resources will go towards caring for increased numbers of cancer survivors and at the same time there will be an impact from lost productivity.[3] Often not considered is the fact that our attempts to provide the best consent process results in poor quality research, poor quality outcomes from the application of biased findings, an inability to conduct certain research, and ultimately a waste of precious resources which should be used to address pressing emerging health needs.

Our difficulty seems to lie in shifting consent paradigms, not only to match the new research capabilities and the multiplicity of safeguards applied in such research, but also to respond to the new demands on health systems around the world. This paradigm shift from our excessive commitment to individual rights, to the exclusion of other important values, to a more balanced consideration of communal benefits has not yet fully occurred, despite clear statements from highly regarded research declarations and guidelines.

There may be exceptional situations where consent would be impossible or impracticable to obtain for such research

i.e. medical research using identifiable human material or data. In such situations the research may be done only after consideration and approval of a research ethics committee.

Declaration of Helsinki, Article 32, 2013 [21]

However, when the research design involves no more than minimal risk and a requirement of individual informed consent would make the conduct of the research impracticable (for example, where the research involves only excerpting data from subjects' records), the ethical review committee may waive some or all of the elements of informed consent.

CIOMS [22]

Opt-out consent model

Refusal to consent is not necessarily an indication of people's objection to the research or concern about the risks involved. In fact, one study has shown that non-involvement was primarily a result of recipients of research information failing to understand key research facts, even though the initial reason provided was a lack of interest in the study.[23] Reasons for non-participation relate to disinterest, which was by far the most prominent reason in another study, feeling too ill or too old, or simply being too busy.[24] The defining features of the opt-out consent model relate to a) people not having to take action to be part of the study; b) the fact that some participants may be missed because of change of address and are therefore included without their knowledge; and c) the fact that people are unlikely to take action not to be involved unless they have strong objections to participating. Therefore, the fact that the opt-out consent model increases research participation compared to the opt-in consent model is not surprising.[12] Opt-out consent is viewed as an ethically appropriate consent model where the risks from participation are negligible, because it appears to better balance the need for information provision to potential participants and the ability to decline, but also enables important research to proceed when complete and representative samples are required. For this reason population studies rely on this model for appropriate sample sizes that will ultimately lead to reliable research findings.

The Prostate Cancer Registry, for example, was established in Victoria in 2009 in recognition of the rising incidence in prostate cancer in Australia and the human and economic impact of this.[25] The registry uses an opt-out consent model to increase recruitment capability and aims to 'monitor quality, benchmark outcomes and to assist clinical research'[25]. The opt-out consent model has also applied to research using registry data, such as a study that enrolled men diagnosed with prostate cancer, which aimed to evaluate patterns of care.[26] Likewise, the Victorian Lung Cancer Registry was also set up in recent years using the opt-out consent model and, while not set up primarily for research, it will nevertheless enable research to be conducted using the same opt-out consent process.[27] A large UK study on prostate cancer reported on the difficulties they encountered in the conduct of their low risk research,[28] which was delayed by almost two years while approvals were being sought. Faced with these difficulties, the research group concluded that an opt-out consent process would be suitable for public health research.[28]

Numerous studies in other areas of health research have also acknowledged the need to use the opt-out consent model. For example, it was both argued for and used successfully in a study examining the link between the prescription of antibiotics and antibiotic resistance of E. coli urinary tract infection.[29] This study achieved a participation rate of 85.5% and an opt-out rate of 14.5%,[29] which may be higher than usual opt-out rates as a result of urine samples being submitted not by participants, but by the participating practices.

When asking research participants about their preferences in a study relating to vaccine safety surveillance (n=1129),[30] there was evidence that participants were not as committed to the opt-in model as might have been expected. Support for opt-out consent and no consent were favoured in this study, with 40% of participants preferring opt-out consent and 30% preferring no consent for the linkage of their child's vaccination records with their hospital records in the context of vaccine safety surveillance.[30] Other studies have shown that even if people do not believe that explicit consent is required, they often prefer to have some knowledge about how their information is used for research purposes.[31-33]

Justification for a no consent model

The opt-out consent model is generally preferred in large epidemiological research, but there are ethical issues relating to opt-out consent that have not been explored. Firstly, most researchers and ethics committees that approve research employing the opt-out consent model do not view as ethically questionable the fact that information about such studies may never reach a large proportion of the intended research participants,[34] who are therefore simply included in the research without their knowledge. The fact that some of the intended participants are aware of the research while others are not, and that some have the opportunity to decline to participate while others do not, introduces a level of inequity in research. The opt-out consent model may therefore be regarded as superficially functioning as an ethically appropriate model but, in fact, may be a model that simply aims to appease our concerns about consent. Secondly, it has been argued that applying the opt-in consent model for uses of medical records in research may undermine the principle of fairness, as it is unfair for some to refuse to participate yet reap the benefits of such research.[35] This same argument also applies to the use of data in large data sets for any

consent process that enables non-participation. Those reluctant to provide consent (whether opt-in or opt-out) may not fully appreciate at the time of refusal that in the future they or their loved ones may well be beneficiaries of research conducted. In addition to the above issues, the extensive amounts of research time and funding used to engage in prolonged consent processes given the large cohorts is not a mere inconvenience to researchers, but more worryingly, a poor use of limited public research funds, which, if used more efficiently, could yield greater benefits for the public.

Numerous studies have identified that the public lack an understanding of research processes and the multiple safeguards ensuring that research participants are protected, as shown in a systematic review of public opinion to secondary uses of existing health records.[36] The same study conducted two focus groups comprising 19 men with prostate cancer. These men also lacked considerable knowledge about research and safeguards. They became even more accepting of their information being used without consent after considering the effects of stringent consent requirements on the quality of research due to selection bias. Those men who continued to support the view that consent was required, despite the clarifications provided, were satisfied that an opt-out consent model was appropriate.[36]

Another study focusing on lay people's consent preferences relating to data linkage revealed that when people are provided with adequate information regarding both research process and safeguards, and are made aware of the impact of inflexible consent requirements, they weigh up the potential risks (including, for example, loss of privacy, loss of control over uses of their information, as well as not being respected) against the public benefits arising from large data linkage studies.[37] Most participants supported the non-consensual use of their information and none of these participants were concerned about the initial use of identifying information, as they were satisfied that the best practice processes involved provided adequate safeguards.[37] Some felt that information no longer identifying them did not have the same moral dimension as identifying information and should therefore be used without consent, provided safeguards are in place.[37]

With regard to cancer research specifically, a large scale UK study (n=2872) found that members of the British public show strong support for the confidential use of identifiable data by the National Cancer Registry for purposes other than treatment, including research.[38] Research has shown that there appear to be differences in views on sharing information for research purposes depending on the health status of those asked. For example, a 2011 US study showed that people affected by cancer are more willing to have their personal data accessed for research purposes, ranging from 59.4% to 70.4% depending on their status at the time of the study, as being survivors on treatment, living with cancer as a chronic illness, post-treatment survivors than those not affected by cancer and the general population, 55.9% and 32.4% respectively.[39]

The vast amounts of data available should be viewed as a valuable resource which can yield immeasurable benefits to large populations. Even though individual controls, such as consent, are not exercised in large scale research using existing data, increased external controls in the form of numerous safeguards are in place to ensure that harm is avoided.[40] Such protections are central to research where consent is not sought, precisely because the protection of individual privacy and minimisation of harm to individuals are regarded as being critically important.[11]

It is nevertheless also crucially important for the public to be aware of the kinds of research being conducted and the manner with which data are used. Transparency in this regard will ensure that the research community remains a trusted partner in finding solutions to the ever challenging health landscape now and into the future. Information regarding uses of health data can and should be provided at the point of collection of such data for treatment purposes, if not for any other reason, because this is a demonstration of respect towards those whose information may be used in research. Researchers and governments alike have a responsibility to educate the public about future health needs, the role that population research plays in finding solutions, the numerous safeguards that apply, the great contribution that each cancer patient makes to the development of cancer treatments and cancer care, and how information on advances can be accessed. Only when the public is armed with such insight can there be a shift away from the focus on individual needs and desires.

Conclusion

All consent models currently used have an important role to play in the conduct of research. However, discerning the correct model for the kind of research involved has proved challenging, as evidenced by the extensive literature over many decades. Our commitment to seeking consent, whether opt-in or opt-out is, in part, a result of important historical facts that must be borne in mind by researchers. However, current pressing health challenges, of which cancer is only one of many, urge us to use large population data sets wisely for the benefit of all, while ensuring that the highest levels of protection are available to all those whose information is used for secondary purposes such as population research.

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