Do we need a wider view of autonomy in epidemiological research?

Review bodies put great importance on informed consent, but **Mats Hansson** argues that their narrow view of autonomy could be harming patients' interests

Ethical review boards and data controllers in several countries require explicit and specific informed consent from patients for observational and epidemiological studies as well as for interventional studies. However, evidence is emerging that such strict interpretation of consent is introducing selection bias and reducing response rates.[1-5] By diluting the strength of scientific studies, this approach is denying patients access to the best medical knowledge. Using a real case, I argue that review bodies should adopt a wider view of consent.

Current approach

Several ethical guidelines have been drawn up with the explicit purpose of making informed consent the general rule for all types of study. A recent example is the ethical guidelines from the Council for International Organizations of Medical Sciences, which states:

> "For all epidemiological research involving humans the investigator must obtain the voluntary informed consent of the prospective subject or, in the case of an individual who is not capable of giving informed consent, the permission of a legally authorized representative in accordance with applicable law. Waiver of individual informed consent is to be regarded as exceptional, and must in all cases be approved by an ethical review committee unless otherwise permitted under national legislation that conforms to the ethical principles in these Guidelines."[6]

However, strict interpretation of consent requirements is lowering the scientific value of studies, limiting their capacity to provide new medical knowledge that would be beneficial for patients. Iversen and colleagues report how requirement of informed consent for linkage to a cancer registry seriously hampered epidemiological research.[1] Ward and colleagues had a similar experience with a UK nested case-control study of Creutzfeldt-Jakob disease,[2] and the requirement to obtain informed consent for participation in a Canadian stroke registry led to important selection biases.[3] In the United States lengthy consent procedures required for centres participating in an international trial of thrombolysis after acute myocardial infarction may have even cost lives.[4]

A potential solution to the problem of getting informed consent for prospective epidemiological research that uses longitudinal population based biological repositories or databases is to provide general information about possible research at the time the samples or data are collected—that is, obtaining broad consent.[7] However, this solution has been resisted in the ethical and legal literature. Bernice Elger suggests that "any consent to future research projects that are not clearly described, is by definition invalid because it is not informed."[8] Others have suggested that allowing donors of samples to give a broad consent for future medical research on their samples and data would be a dilution of ethics.[9-11]

However, a more generous view is available that is less costly to patients' need for evidence based medical treatment, as the example of an oestrogen follow-up study below shows. After several procedural turns involving the Swedish Data Inspection Authority and the National Board of Health and Welfare, the study was rejected by the regional ethics committee at Karolinska Institute in December 1999 and by the research ethics committee of the Faculty of Medicine at the University of Gothenburg in April 2000. I was not part of the research team but became involved in the ethical discussions about the study in 2009. The study has still not been done.

Requirement for explicit consent: a case study

In Sweden during the 1960s to 1980s, some adolescent girls who were expected to be very tall as adults were treated with oestrogen. The oestrogen was used to close the growth plates in their bones and thereby reduce their adult height. As oestrogen was not approved for such an indication, the treatment was experimental. No adverse effects were reported at the time, but little is known about the long term effects. An increased risk of developing breast cancer is reported in women who have used combined oral contraceptives before the age of 25, but it is not clear whether this can be explained by long term exposure, high doses, or the increased susceptibility of younger people.

A study was therefore planned to evaluate the cancer risk in women who had been treated with oestrogen during adolescence.[12] Up to 25 years had lapsed between treatment and this evaluation of cancer risk. Data were to be gathered through the national cancer registry, the national death cause registry, and medical records; the researchers suggested that no consent be obtained, fearing that it might cause unjustified concern and worry and result in women dropping out. The women would presumably be interested in knowing their cancer risk, but an odds ratio expressing risk cannot be translated into an individual prognosis; furthermore, clinical importance would not be clear until the study was completed and its findings validated.[13]

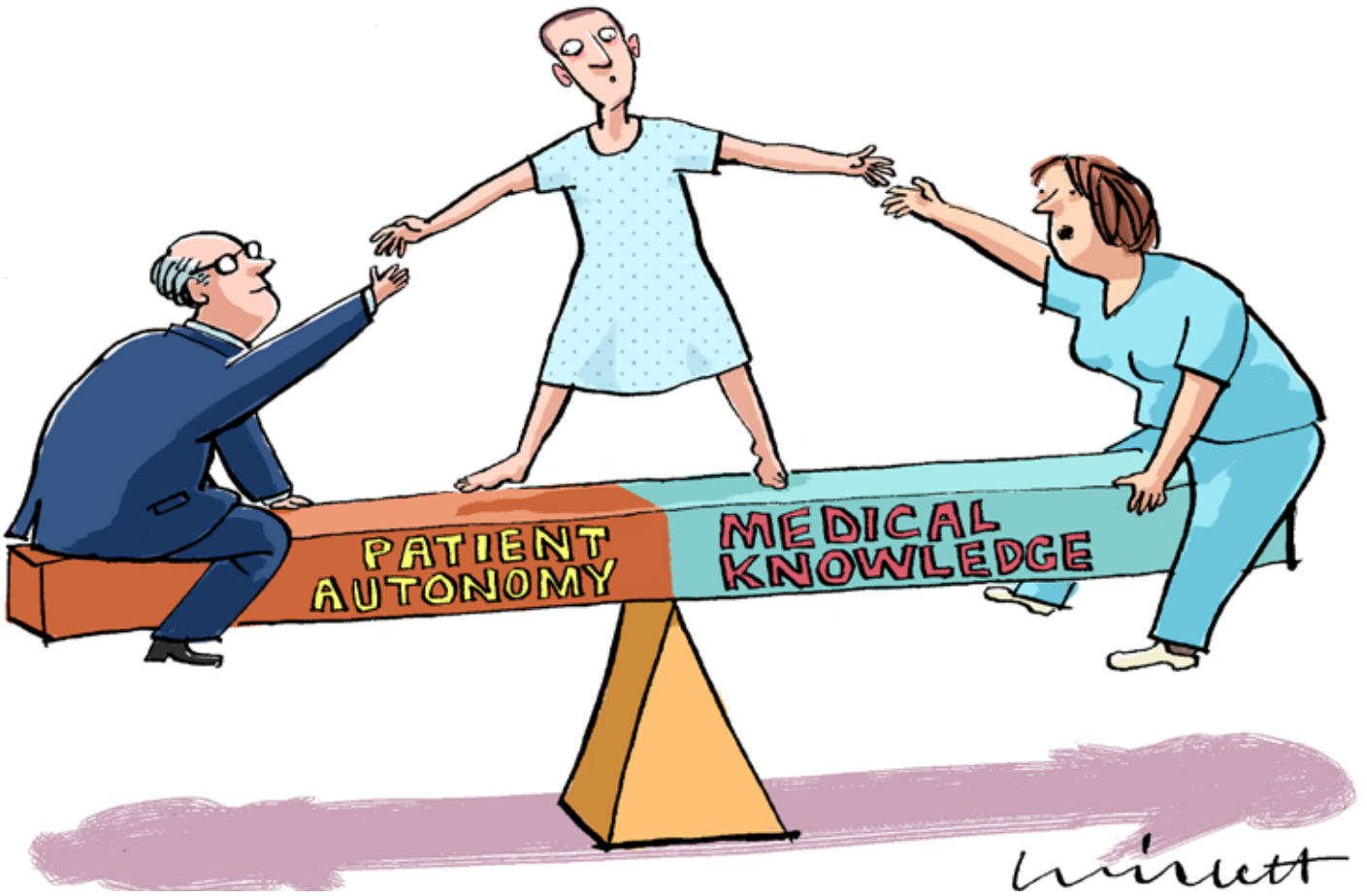
However, the ethical review board decided that this study could not be carried out unless there was specific and explicit consent from each woman. Dissatisfied with this decision, the research group conducted a qualitative study with semi-structured telephone interviews in 22 women.[12] The women expressed frustration over the fact that this research had not started earlier; they wanted to know how many of the women had got breast cancer, as well as their own risk. Their views about informed consent differed. Some wanted to be able to give consent while others were content to be simply offered the chance to refuse. Some of the participants were concerned about missing data: "Yes, it's really good that they ask beforehand, but at the same time, well, what if everyone said no. Then you would never know."

In fact, just a few women saying no may be sufficient to jeopardise the interest in knowing, depending on the statistical power required in the study.

What type of autonomy is at stake?

We do not know how the ethical review board reasoned but it appears that it focused on an individual's interest in having a say. The board, in line with the guidelines described above, may have rejected the study out of respect for the women's autonomy. The research concerned the women directly; it involved their bodies and their lives, even if the decisions about the treatment were made by their parents. They should have a say.

This is what I call a restricted view of autonomy. It disregards the risks in the sense that even when



there is only limited risk of harm the research participants will still have a say. It also disregards the scientific value in the sense that participants are given a say even if the resulting drop-out rate makes it unlikely that the study will be able to draw any scientifically valid conclusions. Accordingly, this view also implies a disrespect of individuals' interest in enjoying benefits—such as medical knowledge—that are not attainable unless others collaborate.

An alternative reasoning would have been to regard autonomy as the primary concern but balance the interest of the individuals having a say against the risks they are exposed to through this research and the potential benefits from the results—in this case an accurate estimate of the general cancer risk associated with oestrogen treatment during adolescence. The review board may have considered the risk that the women might have learnt about the study in other ways, but this risk should then be balanced against their interest in knowing about their cancer risk. This is what I call an expanded view of autonomy.

Being autonomous is a matter of deciding for oneself, but not in isolation from others. If the ethical review boards apply the consent norm strictly in accordance with a restricted view of autonomy, as they did in this case, and demand that each participant is asked regardless of risks and scientific value, the participant may feel respected. However, if asking the women in the oestrogen follow-up study will substantially decrease the possibility of fulfilling their desire to know their cancer risk, and to take precautionary actions to minimise this risk, the decision by the review board in fact implies doing harm. The result of the ethical review thus represents a contradiction in terms since the boards' primary motive is to prevent harm to patients in medical research. To ask for consent also undermines the possibility of participating in the development of medical science, and if this is one interest at stake the participant is more likely to experience a lack of respect from being asked.

Exercising autonomy through trustworthy democratic institutions

According to an expanded view of autonomy where different interests must be balanced the women should have access to indirect means of influencing the decision. This is attainable through the construction of various social structures and institutions in a democracy. Two examples of indirect means are of particular interest for observational and epidemiological research. Firstly, the government or parliament can decide on behalf of the citizens. Several established medical registries use this view of autonomy—for example, national cancer registries and national cause of death registries. There is no consent, but the individual has the right to know what type of information is in the registry. Secondly, individual citizens can exercise moral and legal authority through an ethical review board when the representatives take their different interests into account. The board will have different information and consent procedures to select between.[14]

One objection to the expanded view of autonomy is that it implies a kind of paternalism that is not compatible with a respect for the moral authority of individual citizens. In order to avoid this accusation decisions need to be transparent. When society's system of rules and institutions are being shaped, individuals must be able to see that attention is being paid to their interests but also appreciate why these interests are sometimes subordinated to other people's interests or to the public interest.

The public must understand, and have the possibility of influencing, how the balance between different interests is struck. The legitimacy of the decision, which is made by the representatives of the general public, is based on the fact that people are able to follow the chain of argument in all its relevant detail. They should be able to see that all relevant circumstances and arguments have been taken into account in a way that is reasonable with regard to the importance of the balancing process and its consequences.[15] Adoption of

an expanded view of autonomy would therefore require more insight into the reasoning of the ethical review boards than is always provided today.

Conclusion

Respect for autonomy implies that research participants should also have access to indirect means of exercising insight and influence on decision making—for example, through institutions such as ethical review boards or through instructions to these boards laid down by legislators. This does not entail a disrespect of the individual; on the contrary, vital interests of the individual will not be fulfilled without such a perspective. If ethical review boards and data controllers continue to apply a restricted view of autonomy, legislatures should enact laws to help ethical review boards reach better decisions.

Mats G Hansson professor of biomedical ethics, Centre for Research Ethics and Bioethics, Uppsala University, Department of Public Health and Caring Sciences, PO Box 563, SE-751 22 Uppsala, Sweden

Mats.Hansson@crb.uu.se

Accepted: 11 April 2010

The work for this paper was supported by the EU programmes Cancer Control using Population-based Registries and Biobanks and AutoCure.

Competing interests: None declared.

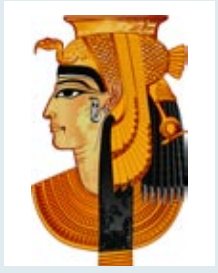
Provenance and peer review: Not commissioned; externally peer reviewed.

1 Iversen A, Liddell K, Fear N, Hotopf M, Wessely S. Consent, confidentiality and the Data Protection Act. *BMJ* 2006;332:165-9.
2 Ward HJ, Cousens SN, Smith-Bathgate B, Leitch M, Everington D, Will RG, et al. Obstacles to conducting epidemiological research in the UK general population. *BMJ* 2004;329:277-9.
3 Tu JV, Willison DJ, Silver FL, Fang J, Richards JA, Laupacis A, et al. Impracticability of informed consent in the registry of the Canadian stroke network. *N Engl J Med* 2004;350:1414-21.
4 Collins R, Doll R, Peto R. Ethics of clinical trials. In: Williams CJ, ed. Introducing new treatments for cancer: practical, ethical, and legal problems. Wiley, 1992:54.
5 Coleman MP, Evans BG, Barrett G. Confidentiality and the public interest in medical research—will we ever get it right? *Clin Med* 2003;3:219-28.
6 Council for International Organizations of Medical Sciences. *International ethical guidelines for epidemiological studies*. CIOMS, 2009.
7 Hansson MG, Dillner J, Bartram CR, Carlsson J, Helgesson G. Should donors be allowed to give broad consent to future biobank research? *Lancet Oncol* 2006;7:266-9.
8 Elger B. Consent and use of samples. In: Elger B, Biller-Andorno N, Mauron A, Capron AM, eds. *Ethical issues in governing biobanks. Global perspectives*. Ashgate Publishing, 2008:57.
9 Hofmann B. Broadening consent—and diluting ethics? *J Med Ethics* 2009;35:125-9.
10 Árnason V. Coding and consent: moral challenges of the database project in Iceland. *Bioethics* 2004;18:27-49.
11 Caulfield T. Biobanks and blanket consent: the proper place of the public good and public perception rationales. *Kings Law J* 2007;18:209-26.
12 Hultman CM, Lindgren A-C, Hansson MG, Carlstedt-Duke J, Ritzen M, Persson I, et al. Ethical issues in cancer register follow-up of hormone treatment in adolescence. *Pub Health Ethics* 2009;2:30-6.
13 Helgesson G, Dillner J, Carlson J, Bartram CR, Hansson MG. Ethical framework for previously collected biobank samples. *Nat Biotech* 2007;25:973-6.
14 Hansson MG. Balancing the quality of consent. *J Med Ethics* 1998;24:182-7.
15 Tushnet M. Legal conventionalism in the US constitutional law of privacy. In: Paul EF, Miller FD Jr, Paul J, eds. *The right to privacy*. Cambridge University Press, 2000:141-64.

Cite this as: *BMJ* 2010;340:c2335

FROM BMJ.COM

Where are the women leaders?



Richard Smith writes: "At the end of my class on leadership at Warwick Medical School comes a dreadful moment. I've enjoyed myself and am packing up, when the only student left, a woman, says to me: "Why were no women leaders mentioned?"

I don't panic, but I at once recognise that we've discussed many male leaders and not one woman. The student helps me: "We tried to think of a woman leader but couldn't. Girls make up more than half the class, but they haven't come up with anybody either. We thought you would, but you didn't. I'm not blaming you, but what does it mean? Can't I be a leader if I'm a woman?"

What does it mean? I know you can be a leader if you're a woman, but why haven't we come up with any examples? We've discussed Mahatma Gandhi, Winston Churchill, Barack Obama, Marcus Aurelius, Jesus, Mustafa Kemal Atatürk, Joseph Stalin, Gordon Brown, Tony Blair, Nelson Mandela, Adolf Hitler, Henry V, and even Simon Cowell, but nobody has mentioned a woman.

The student and I start trying to think of examples. Mother Teresa? Something flakey about her. Margaret Thatcher? Not a great model for a medical student. Joan of Arc? Too crazy, too much of a victim. Benazir Bhutto? The student is of Pakistani origin and not impressed. Indira Gandhi? A despot. Boudiccea? More legend than real woman. The Queen? Perhaps, but too odd a form of leadership. Hillary Clinton? Something uncomfortable there. Cleopatra? It seems a problem that much of her power is remembered as sexual. Elizabeth I? Maybe, but didn't she have all her rivals assassinated?

BMJ readers will, I hope, be able to come up with a compelling example of a well known woman leader whom the Warwick medical student can feel good about, but I've failed.

The student hypothesised that good women leaders were forgotten. Or perhaps it's a problem of scale: we've been thinking of "mega leaders," and so much of history up until now has been men's business. Maybe women eschew that level of leadership. Or perhaps we, particularly an aging white male like me, always feel ambivalent about female leaders. My list and comments might illustrate that point. Or could it be that some unacknowledged and unrecognised prejudice inside me thinks that women should be home suckling their young not transforming the world or its institutions?

Whatever the problem, I need to think of a well known and effective woman leader before I teach my next class. Please help me."

Readers of Richard's blog had plenty to say on the subject—here are just a few soundbites.

Courtenay writes: "You've thought of many but seem to discount them all for reasons of discomfort or somehow not being quite right, yet the men on your list (Stalin, Hitler, Simon Cowell, even Tony Blair) don't seem to receive the same sort of appraisal. Perhaps it is this instant damning of intelligent and powerful women that is the problem."

Shefaly agrees, saying that it is "interesting to observe that somehow women leaders' names are only associated with negative traits."

Penelope Else thinks we should forget what we think we know about these women: "Let's see what they achieved."

Abdul Jaleel thinks it depends on how one defines a "leader."

Read Richard's blog and others at http://blogs.bmj.com/bmj
Can you think of any other women leaders?

Have your say on doc2doc, BMJ Group's global online clinical community, at http://bit.ly/9M7rPI