TRAMES, 2004, **8**(**58**/**53**), 1/2, 46–62

https://doi.org/10.3176/tr.2004.1/2.04

SHOULD RESULTS FROM GENETIC RESEARCH BE RETURNED TO RESEARCH SUBJECTS AND THEIR BIOLOGICAL RELATIVES?

Stefan Eriksson

Uppsala University

Abstract. This paper addresses the question of whether to return information about disease and hereditary dispositions, resulting from research, including information that not only affects the research subjects but is also of interest to their biological relatives. An important prerequisite for a return is that results meet strong quality requirements. Moreover, the arguments in favor of a contact should outweigh those against it. When there is a moral demand to inform biological relatives, subjects themselves typically act as informants. If subjects are in doubt as to whether a contact is required, the investigators themselves must make a judgment. If they feel it is indeed necessary, they should try to strengthen subjects' autonomy and encourage them to take responsibility. It is argued that this is neither a paternalistic line of action, nor does it undermine the autonomy of research subjects and their relatives.

Keywords: ethics, research ethics, genetic testing, genetic information, genetic counselling non-directiveness, duty to recontact, disclosure of genetic information, family ethics, kinship and family

1. Introduction

Medical research focusing on genetic disorders and changes will occasionally generate knowledge about a research subject's possible carrier status and his or her current or future disease. Furthermore, the knowledge gained often pertains not only to the subjects but also to their biological relatives. In this paper, I address the question of how to treat personal information about disease and hereditary dispositions, resulting from research, including information that not only affects individuals, but can also be of interest to their biological relatives.

First, I ask whether results should be returned at all. Perhaps the best way to keep difficulties at bay would be to avoid the issue. Second, if a case can be made for the desirability of returning information to the individual, I will ask whether this individual's biological relatives have a right or duty to know about familial

information that may greatly affect their lives. How do we weigh the arguments? As Crouch and Elliott point out (1999:275), when it comes to "moral decisions about the family, the tools of moral philosophy and the law have not always served us well, particularly when the question involves exposing one family member to risks for the sake of the other." I discuss how family ethics and a certain conception of autonomy challenge the often-undisputed notion of non-directiveness.

In this paper, I map the ethical terrain and provide reminders about important features, both moral and factual, that should guide any assessment of policymaking in this area. I do not try to propose what any individual should do in any particular situation. We need to remember that no ethical deliberation of the kind offered here can replace the subject's responsibility for his or her own actions. Facing up to responsibility and interacting with family members are identity-shaping actions and are thus closely connected to a person's innermost being. In Margaret Walker's words, in doing such things a person exercises "strong moral self-definition" (Walker 1987).

2. Should research results be returned to subjects?

Those who answer this question in the negative do so on principle or because of misgivings concerning the results' usefulness. The first type of objection asserts that it is never *necessary* to return results to subjects, as this should not be the investigators' first priority. This argument merits discussion, and I will return to it below.

Discussions of usefulness point to the quality of results. There is a concern that different types of errors could have crucial consequences, as individuals may change their entire lives because of a test result. With genetic information, an error may also greatly affect family (see, e.g. Fost and Farrell 1989). In the case of predictive information, it may be a long time before an error or a misinterpretation is recognized. One must be aware of the risk of errors due to situations such as misidentification or contamination of samples, incorrect testing procedures or transcription errors. A research laboratory seldom meets the same expectations regarding quality control as would a diagnostic laboratory. Therefore, strong requirements must be placed on the quality of results. This serves the initial purpose of limiting the results that may be considered for a return.

Results from research are often very uncertain, difficult to interpret, or even not applicable to the individual. These shortcomings pertain to screening tests in general (Sasse 2002), not least since genetic prognostications apply mostly to the aggregate rather than individuals (Finkler et al. 2003:404). Hence, it can be said that information to be considered for disclosure must be such that is applicable to an individual, reasonably legible, and reliable – that it springs from a relatively certain research result (i.e., its sensitivity and specificity). To be a basis for information to be shared, knowledge should furthermore indicate that harm is

foreseeable (the subject is at risk), that it is likely (*e.g.*, penetrance), and that it is serious. Most genetic research will reveal susceptibility rather than offer diagnosis of a certain disease. Of course, risk and likelihood must be balanced against the magnitude of threat posed to the subject. Regarding genetic diseases, time is an important factor. Is it reasonable to let people worry about a 50% risk of developing a disorder at the age of seventy when they are still in their thirties? Furthermore, in most cases, results should have clinical implications in order to motivate disclosure. That is, the disease should be preventable, treatable, or it should at least be possible to reduce the risk of harm with early intervention. Of course, the risk implied by such an intervention should be acceptable when judged against the predictive value of the research result.

Since it might be difficult to evaluate results and there may be wishful thinking on the part of investigators, it is recommendable that results be subjected to peer review before research subjects are contacted. Only when the study has been replicated or accepted by peers in some other way should the fulfillment of the requirements (Fig. 1) imply that a return might be considered (see Clarke et al. 2001). A typical model for the requirements indicating the permissibility or duty to contact the subject can thus be summarized:

Research findings	*Harm*	*Disease*
applicable to the individual	foreseeable	preventable
legible	likely	treatable or
reliable	serious	risk reducible

Fig. 1. Contact requirements

Undoubtedly, terms such as ‘reliable’ and ‘serious’ are vague. Definitions and explicit criteria are needed, but these are not addressed here. Instead, before a study, investigators and the research ethics committee should decide upon the precise point at which each requirement is fulfilled. Through defining the requirements relative to the particular project, an instrument is created to guide subsequent decisions.

For some it seems natural to return results that meet the contact requirements (Hannig et al. 1993, Feinleib 1991), while others present arguments to the contrary (e.g. the Danish Council of Ethics 1993). One of the main objections is that it would be too time-consuming and costly to contact research subjects, and that this cost may even inhibit important research. This objection considers the research as more important than any possible individual benefit. The idea is that too many resources are spent on information and counseling activities that in the end may have relatively insignificant results on people’s health. Another objection makes an argument about justice or good stewardship. Curtis Naser points out “[R]esearchers owe a fiduciary obligation to their funding sources which make the

research possible." (1998:174) Thus, it would not be responsible to use a great deal of funding for activities other than research. These are sound arguments, but the obstacles in no way pertain to all studies. It is not always time-consuming or costly to contact subjects when this is clinically relevant, and even very large studies may find time- and cost-effective strategies. Further, it is possible already at the funding stage to make clear that return of results may be part of the research project. Therefore, the funding sources will already have approved that some funding be used for this purpose.

3. Beneficence and respect

So, although these arguments may show that contact is not necessary, and is in some cases clearly undesirable, there may nevertheless be good reasons for it when the contact requirements are met. First, we have the general principle that we should *do good* and *prevent harm*. In some instances, even small changes in life-style may prevent disability and early death, as is the case with autosomal dominant polycystic kidney disease, hereditary hypercholesterolaemia, or α_1 anti-trypsin deficiency (Wilcke 1998). Such cases present researchers with a palpable obligation to establish contact.

One could take a further argumentative step concerning a subject's *right* to important health information. Investigators would then have a corresponding *duty* to disseminate information. But Naser has a point in stating, "clinical benefits to individual research subjects are not *positive* rights…" (Naser, 166). We cannot claim to have an individual benefit from research. We may give provisos regarding participation in a research project, thus exercising our negative right to decide whether or not to participate, but the research as such is not aimed at giving benefits to the individual. The benefits of research redound to "future unknown patients, society in general, or the common good" (Naser, 168).

Even if there is no positive right, a duty does not have to depend on a corresponding right. This has been pointed out by Mary Ann Cutter:

> *To show respect for persons is to value persons by* refraining *from eliminating the necessary conditions of personhood, which include life, bodily integrity, and freedom to make choices and to act upon them, and so on. In addition it means* acting to promote *the presence of such conditions. Respect involves, then, a negative and positive duty to others. On this view, respect is not dependent on the consent or rights of another. The obligation to show respect for persons is not an obligation to the person in question. It is an obligation to act in certain ways toward that person or persons. And so, on this analysis, respect is owed to the innocent and vulnerable, to communities of persons, as well as to rational agents* (Cutter 1998:150).

I believe Cutter makes a relevant point, and that project managers should show respect for research subjects by considering a return of information that may be beneficial to them. It is not always a good experience receiving such news, however. There is a possibility of quite adverse reactions to news that one may carry a

latent genetic defect. Such information could cause emotional distress, lead to drug abuse or even attempted suicide. If subjects are to be contacted only when specific contact requirements are met, strong reactions are possible, as the case would then most likely be serious.

By no means is good news exempt from these considerations. In a study, it was shown that 10% of people who learned they did not carry the gene disposing for Huntington's disease had problems adjusting to their new status as non-carriers (Wiggins et al. 1992, see also Peters et al. 1999:21). Another example would be a negative test result bringing the realization that the people believed to be one's biological parents were in fact not the biological parents. Thoughts on the possibility of seeking one's "real" birth parents may be upsetting. Last, consider that so-called preselected individuals (children who are singled out by their families as the ones who "will eventually develop" a disease that "runs in the family") who test negative may be ostracized from the family as a result (Richards 1996:266).

Researchers contacting people about supposedly important results, without having the skill or time to provide appropriate counseling, might not be beneficial or respectful. There is a need to carefully explain to affected subjects that the penetration of diseases varies, that, likewise, the age of onset and speed of progression vary, and finally that the clinical expression may differ, sometimes greatly. The probabilistic nature of genetic knowledge must be made explicit in light of the deterministic views often spread to the public. Contrary to intuition, a negative test (e.g. for breast cancer) may nevertheless imply that one continues to have the same risk for future disease as the rest of the population does. The difference between being a carrier and having a disease is another distinction that is hard to understand. Subjects usually have a hard time grasping the intricacies of probabilities; even health professionals sometimes find this difficult (Thomson 1997). For example, Giardiello et al. (1997) report that in a study of physicians who ordered a genetic test for colon cancer, the test results were misunderstood 31.6% of the time. Sankar (2003:400–401) cites many other studies with similar results. Thus, great caution should be taken in weighing the pros and cons of a decision to inform. Availability of appropriate counseling can therefore be considered a plus in the consideration.

To conclude, the most important prerequisite for a return is that results meet well-defined contact requirements. Moreover, the arguments in favor of contact should outweigh those against it, and *a plan and organization* for supplying information and dealing with its consequences should be in place. Then, and only then, will the duty to establish contact follow from the fact that the contact will be beneficial to, and show respect for, participants.

4. Information to biological relatives

If the primary research subject is given crucial health information, biological relatives may also have an interest in the information. Should they, then, be involved from the outset by being given information and perhaps being asked to

consent to future contact? A strong principle of this kind has been put forth by the Swedish Medical Research Council. It states that the research ethics committee "must also carefully consider situations such as when gene markers may have individual or group interest for concerned relatives of the person who has submitted the sample. In such cases informed consent should be obtained from anyone who could be directly affected by research results" (Medical Research Council 1999). In favor of this position, we may argue that to conduct research on the sample of one person is at times in effect to simultaneously do research on another person. We must also view biological relatives as patients (or as human subjects participating in a study). Clearly, however, in order for someone to be a patient he or she must be conscious of this fact. But relatives to a patient, *X*, are neither aware of being patients (given their awareness of being relatives to *X*), nor may they want to become patients when given the genetic information originating from *X* (Goldworth 1999:397). To this counter-argument, it might be replied that in order to be the subject of *research* such awareness is not necessary. Research on people not aware of being subjects is often performed. To conclude, then, it seems unclear whether biological relatives may be properly considered subjects in the way this argument presupposes.

More important, for investigators to be required to give information to, and acquire consent from, every biological relative who may possibly be affected by the research result is not feasible, except in rare cases involving very small studies. To contact every person possibly affected beforehand would be outrageously time- and cost-consuming. As noted above, this would be poor stewardship. Further, it does not seem reasonable to give the relatives such veto power over whether or not the research subject should be able to participate in research. This, presumably, would put an unreasonable limit on personal decision making in matters of health and participation in research. Thus, contact with biological relatives should only be made when there *are results* that meet contact requirements, and when investigators are *morally required* to make contact.

Let us, then, examine why such a moral requirement may exist; certain international organizations believe that it does. For example, the Hugo Ethics Committee (1998) noted that genetic research might yield genetic information that is important to biological relatives, and that respect for families should be facilitated. The committee concluded that special considerations should be made for access by biological relatives (see also, e.g. World Health Organisation 1997). I will address three possible reasons why a duty to contact biological relatives may exist:

First, it is sometimes a question of *justice* regarding whether biological relatives should be given the offer of having results returned. In clinical genetics research, the use of "detailed medical and family histories over three or more generations about siblings, parents, children, cousins, aunts and uncles, and more distantly related family members… Complete individual and family social, reproductive, and health history… are all essential components" (Pergament 1997: 92f.) Is it not reasonable to suggest that biological relatives, by sharing information and submitting samples along with a great deal of their time – and thereby

making successful research possible – are entitled to receive information springing from that research that may be very important, if available? This argument carries some weight, but only if it would be considered a *good* thing to receive such information, and if the receiving party *wants* it. This consideration brings us to the two main arguments found:

Second, I stated above that health professionals have a duty, or obligation, to benefit their patients and to prevent harm from coming to them – the so-called principles of beneficence and nonmaleficence. These principles should govern a professional's behavior toward the whole of community. If harm can be avoided by a certain action of the professional, he or she is obliged to try to act as such unless there are obstacles preventing it. There is such a duty on investigators to rescue as well. This is why, for example, we expect physicians and investigators in medicine to inform the community as a whole about potential health problems and to instruct on how to avoid health hazards. Therefore, relatives should be informed when the benefit of a disclosure outweighs possible harm.

Third, and last: Suppose a person *A* learns she has late-stage cancer. She also learns that her relative, *B*, tested positive for this disease ten years ago in a research project. From that test, it would have been very easy to predict that *A* had a 50% risk of contracting the disease in the near future. The physician directing the research, as well as *B*, knew this. Nevertheless, neither of them contacted *A*. The disease could have been cured at an early stage, but now it is too late. *A* feels betrayed and tells them she had "*a right* to know!" It does not seem an unreasonable thing to say. Whatever we theoretically make of rights, this seems as good an example as any of where talk of rights is appropriate. We may not have a positive right to research results, but when the relative and his physician have the information in their hands, our claim to being informed carries much more weight.

5. Harms, rights and duties

Even when the affected relative and his physician have an obligation to disseminate information, they may be reluctant to proceed. What if possible harm speaks against giving information? What if there are uncertainties as to whether the unwitting relative would actually want to exercise his or her right to information? Glass et al. have pointed out that a contact in itself may have unwanted consequences for the parties concerned.

To begin with, family members may be ignorant of facts that could prove embarrassing. "Facts such as adoption, incest, artificial insemination, nonpaternity, pregnancies, or permanent institutionalization because of mental illness are frequently hidden from at least some family members" (Glass et al. 1996:6). It is not difficult to agree with the conclusion that participation in research should not extract "secrets from those unwilling to share them" (ibid.). As is the case with research subjects, relatives may react with fear, anger, survivor guilt, despair and the like when confronted with both positive and negative test results (Taswell and Sholtes

1999). For these reasons, some people do not welcome being contacted and receiving knowledge about their health status. They may decline any information about their own risk for disease; questions asked about relationships and diseases might revive memories of actions or events thought to be long forgotten. If this happens, the right *not to know* and the right *to privacy* are discarded. Accordingly, the Swedish government concludes, "no-one should have to receive knowledge about their future diseases if they do not wish to do so" (Swedish Government 1989:19).

The problem is that a right not to know may clash with the right to know as discussed above. This conflict is sometimes evident in official documents, such as the Convention on Biomedicine by the Council of Europe (1997: Chapter 3, article 10:2): "Everyone is entitled to know any information collected about his or her health. However, the wishes of individuals not to be so informed shall be observed." How does one comply with both these demands when even asking for the willingness to receive information might let the cat out of the bag? If you are asked whether you want to be tested for a particular disease, the question in itself reveals that you are at risk.

The value of privacy (here, the ways and circumstances under which other people access information from a person or give information to a person) may be based on the view of privacy as an intrinsic human good or as a means to fostering flourishing and autonomous individuals (Allen 1997:35). In either case, it is something that should be respected. On the other hand, access to relevant and important information makes an autonomous and flourishing individual life possible. By receiving information, the individual becomes equipped to make a truly informed decision. One may even see disclosure of information as a much-needed tool for important genetics education in contemporary society. Hence, to decide that someone should not receive possibly distressful information is as paternalistic an act as is revealing the information. Accordingly, an unrestricted right to privacy (interpreted as an absolute right not to be informed of matters concerning health, regardless of circumstances) must be avoided. Moreover, we need to keep in mind that a diagnosis does not necessarily lead to a diminishing quality of life or emotional malfunction; on the contrary, improvement often follows (Bozcuk 2002, Broadstock et al. 2000, Wiggins et al.). The distress of a relative, due to the suspicion that there is something to be revealed, may be remedied by a disclosure. For some, a positive test result will confirm suspicion and establish a sense of control. Hence, the therapeutic privilege (to withhold information that may damage the patient's health) should not be used lightly.

Here, one can introduce the possibility of a *duty* to know. If someone, by knowing, has an opportunity to take preventative measures and if the choice of action makes a definitive impact on the well-being of others, it seems reasonable to say that he or she *should* choose to know. This seems particularly important when it comes to reproductive choices (we may even be obligated to return results about incurable diseases in such circumstances). When you choose to have or not to have a child with a severe genetic disorder, your decision will have an impact on your own situation, your ability to care for your spouse, possible (even future)

siblings, as well as for the society (*e.g.*, costs). This is not to say that only one conclusion is possible, but that it is an inherently good thing to make such decisions knowingly and responsibly. People *do* feel that they have such a duty (see, for example, the case of Anita M in Kielstein 1998:136f.), therefore the right *not to* know, which in some circumstances may seem justified, should be properly counter-balanced by a duty *to* know in other circumstances. No general conclusion is possible; each case with its particular circumstances must be considered.

When a research subject agrees that a disclosure of research results should take place, the standard procedure is that the subject him- or herself informs the biological relatives. The subject is the best judge of whether the benefits outweigh the harm, and is in the best position to decide when, how, and how much to tell. The subject also knows if embarrassing facts have presented themselves, and is the only person with the moral right to decide whether to disclose them or keep them secret. Many participants in the debate are satisfied with this and leave the rest to each individual to decide. If someone chooses not to tell the biological relatives, it is his or her own decision. The autonomy of the patient or research subject is seen as the prime value to safeguard. In the next section, I will challenge this standpoint.

6. Family ethics and autonomy

A research subject may feel free to reveal just as much information to biological relatives as he or she finds convenient. But what if the stakes are high for relatives and there truly *are* good reasons for a return of results? The Nuffield Council on Bioethics (1993:42) has given this example:

> *A man diagnosed with a mild form of adrenoleukodystrophy (ALD), an X-linked condition that can be carried by healthy females, did not wish his diagnosis or the genetic implications to be discussed with his family. Seven years later, his niece gave birth to two successive boys who have a more severe form of ALD. The illness only came to light in them when the elder boy started to display symptoms. The mother's sister, the man's other niece, has also given birth to a son subsequently diagnosed with ALD. Both families are bitterly resentful that the medical services did not warn them of their genetic risk.*

There is something troubling with the notion that a person's autonomy should trump the biological relatives' well-being and opportunity to make an informed and autonomous choice in, for instance, reproductive matters. The core question is whether one relative is right in withholding information that may greatly affect the future well-being of other relatives. We may need to realize that we "are too genetically intertwined to really be autonomous individuals anymore. My decisions about studies of my genome, or those of my as yet unburied ancestors, can affect not only my living relatives, but those yet to be conceived" (Lawrence 1998:134). The paradigm of research ethics and healthcare is the free, autonomous agent. This reflects an earlier shift from prescriptive courses of action toward an enchantment of patient autonomy. However, genetic research may need the

cooperation of family members to succeed, and, more importantly, by its very nature concerns whole families (Glass et al., 5, Finkler et al., 410). This shows that the picture of an autonomous agent is a construct suited to a certain time and place, and that the time may have come to challenge this construct.

John Hardwig is one ethicist who has proposed that more weight should be given to families in healthcare decisions. He states that families also have interests, and plain justice demands that we listen to what they say. The interests of family members are sometimes more important than are those of the patient, and so the former should override the latter. Basically, Hardwig gives two arguments in favor of this conclusion. First, because ”the lives of those who are close are not separable, to be close is to no longer have a life entirely as you choose. To be part of a family is to be morally required to make decisions on the basis of thinking about what is best for all concerned, not simply what is best for yourself” (Hardwig 1990:6). Second, if we treat every patient as if only his or her own wishes and interests were of importance, we will strengthen an individualistic medical ethic and thereby actually undermine close relationships, something that will both have grave consequences and threaten something we perhaps value for its own sake (Hardwig, 7).

Today it is often assumed that as “personal autonomy deserves respect” one should not try to “influence the decisions” of subjects. This is known as the dogma of *non-directiveness*. Would not the line of action proposed by Hardwig abandon this dogma, and hence undermine respect for autonomy? However, to give equal weight to the family does not necessarily mean to neglect autonomy. According to Hardwig, autonomy is not solely a right to choose what is best for oneself, but rather a *responsible* use of freedom that is diminished whenever one ”ignores, evades, or slights one’s responsibilities” (Hardwig, 8).

Would not such a line of reasoning put great restrictions on personal liberty? For example, Hallowell et al. argue that women’s choice to undergo testing for BRCA1/2 mutation (a mutation predisposing to breast cancer) out of a perceived obligation to care for their relatives constrained their choices, since they felt they had “no real choice” (2003:76). Does this make their act of choosing “more chimerical than real”? Certainly, one is emotionally *tied* to other persons through being part of a family and it is true that we are *bonded* by love, but to repudiate those relationships will not make us freer (Crouch and Elliott, 277). Jacquelyn Kegley puts it succinctly: “[A] necessary condition of one’s being a person is being-with-others” (Kegley 1998:56). Autonomy and freedom are not concepts with defined meaning outside particular situations and social settings; instead, they take on a new meaning by being put in such genetic contexts as discussed here. To say that I “have no choice” may be interpreted as an expression of an autonomous decision to face up to the present situation. Compare this to a mother who is asked why she persists in caring for her criminal son, and answers “I have no choice; after all, he is my son”. Not having a choice expresses a fundamental attitude that most of us find admirable. This attitude must be kept separate from cases in which people are coerced against their better judgment.

Given the definition of autonomy proposed by Hardwig, we might come to realize that there exists a temptation to evade one's responsibility *in the name of* autonomy and freedom. Hence, the individual should be encouraged to assume not only decisional responsibility, but also to consider the welfare of biological relatives. As soon as a person donates a biological sample for research, relationships with relatives come to the forefront. The act entails giving something that in this respect is not private, and therefore he or she should assume responsibility for the fact that what is done may affect close kin (genetically close, if not always socially). Given that true autonomy involves responsible deliberation over the needs of others, the professional (or investigator) should sometimes try to strengthen such autonomy, even if the first reaction of the subject is to avoid all responsibility for his or her biological relatives. This is in line with how health professionals seldom hesitate in being directive about medically beneficial behaviors, tests and therapies. In fact, even the professionals who are most affirmative of non-directiveness often testify to the impossibility of carrying it out in real-life situations (Cunningham-Burley and Kerr 1999, Williams et al. 2002). We may even ask whether counselors ever have intended to be non-influential on a correct analysis of 'non-directiveness' (Lietaer 1992).

This discussion also casts light on whether giving information to biological relatives should be considered paternalism. We can now differentiate between a) an autonomous decision *to face* a problem, and b) *deciding upon* the problem autonomously. Even if disclosing information to someone who has not asked for it disallows an autonomous choice in the former sense, it makes an autonomous choice possible in the latter. According to the notion of autonomy deliberated above, in order to enhance a person's autonomy it is of greater importance to promote the possibility of the latter than to give in to the former. Thus, by denying a person the choice of facing the problem or not, one is in reality promoting the things that make the first principle important in the first place: promoting the individuals' dignity, the possibility to think and choose for oneself. It may be said that one has a duty to determine one's own actions on such an account, something that must be done through thoughtful and informed deliberation of possibilities.

The fact that the autonomy principle has greater weight in the latter sense can be brought out in another way. In order to deny someone autonomy in this sense, we usually demand a very strong justification. People can be forced to receive care, for example, when their actions may put themselves or others at great risk. On the contrary, people receive information almost daily that is neither anticipated nor asked for. Constantly, when we open the newspaper or listen to the radio, a piece of information may come through that can greatly affect our lives. Of course, there is a difference between intentionally giving someone specific information that will affect him or her, and publicly announcing information that may affect individuals. The point is that in both instances, the person receiving information cannot control when and what will be learned. To receive information we do not anticipate is one of the contingencies of life. However, our ability to choose how to react when faced with such information is often thought to be the hallmark of humans.

Of course, the decisions to be made must not be *results* of autonomy in the first sense being overridden. This would mean that someone else formulates and forces the problem on you. The problem must be factual, independent of the disclosure of information. My view is that a person objectively has a problem, whether or not he or she knows of it yet, when health information exists together with different options for actions that would significantly change the life of the affected person if disclosed. I suggest that the contact requirements given above function as a "first test" for deciding when someone *objectively* has a problem of such multitude as to require a denial of autonomy in the first sense.

7. The moral obligation to inform

In real-world situations, an obligation to inform biological relatives is dependent on the quality of the relationship. Individuals are more likely to discuss disorders with close relatives (Peterson et al. 2003:84, Claes et al. 2003, d'Agincourt-Canning 2001). Very few acknowledge having an unrestricted obligation to biological relatives that they may not even know. Hence, the strength of Hardwig's two arguments above is dependent on obligations that exist within relatively close social relationships. It is paramount that we keep in mind the difference between the social family and biological relatives. Hardwig and others argue for an ethic of families (in the social sense), but this ethic cannot automatically be applied to relationships between biological relatives. Few would accept the idea of owing moral considerations to a stranger with a closely matching DNA profile out of this fact *alone*. Obviously, the moral demand on subjects to contact biological relatives will be a function of how well the contact requirements are met, the benefit/harm ratio, and perceived closeness to concerned relatives (see Fig. *2*).

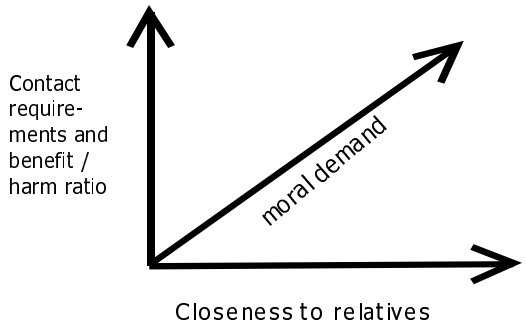

Fig. 2. The affected relative's moral obligation to inform as a function of contact requirements, benefit ratio and closeness to the biological relatives.

The closer the relationship is from genetic (contact requirements) and social (closeness to relatives) aspects, respectively, the more that speaks in favor of a contact. Therefore, relatives considered for a contact will typically be easy to find. That is, the principle above also answers questions of how to set limits regarding what counts as "family" and whether distant relatives should be contacted.

8. Is this strategy workable?

An obvious concern is that only a small number of people will consent to being subjects in a study that is carried out on the premise that one must accept responsibility for the dissemination of information to biological relatives. After all, to be faced with the "messenger dilemma" of informing one's relatives is typically perceived as bad news or a burden (Adelswärd and Sachs 2003, Bonadona et al. 2002, d'Agincourt-Canning, Hallowell et al.). Is this concern well-founded?

First, note that re-contact will be unusual in a research setting, given the strong contact requirements outlined. On the rare occasions that this becomes an issue, research suggests that individuals conceive of themselves as selves in relation, with a prime responsibility to care for other family members by providing them with important information (Hallowell et al.). Note that women tend to bear a greater responsibility for the health of their families than men do; therefore, we need to be observant of gender aspects. Of course, the fact that women shoulder responsibility might show that they are "active moral agents", but it can also be interpreted as women assuming a "disproportionate responsibility", perhaps going too far in efforts to contact people they do not even know (d'Agincourt-Canning, 244–245). If the burden to establish contact is disproportionately assigned to women, perhaps an injustice is done. Gender aspects aside, the idea that men and women do feel a responsibility to care for other family members finds support in other studies. Commonly, people do think they have a responsibility to disclose genetic and hereditary information to family members (Applebaum-Shapiro et al. 2001, Bonadona, d'Agincourt-Canning, Decruyenaere et al. 1993, Lapham et al. 1996, Lehmann et al. 2000, Peterson et al. 2003, Plantinga et al. 2003, Wilcke et al. 1999). This supports the idea that we should encourage subjects to face up to responsibility.

To summarize, a strategy for addressing these problems should be presented already in the informed consent phase. Often, research subjects will agree that research results should be disclosed. Doing so will nevertheless be an exception to the rule, since there are strong demands on the quality of results, and since arguments in favor of disclosure must carry greater weight than arguments against it. As argued before, the most important prerequisite for a return of results is that the contact requirements be met (Fig. 1). Typically, when contacting the biological relatives is a moral demand; the subjects inform them (Fig. 2). If subjects are in doubt about a contact, the investigators must themselves judge whether it is required. If they believe it is, they should try to strengthen the subjects' autonomy

and encourage them to take responsibility. This strategy, empirical research suggests, will not be a major obstacle to the recruitment of research subjects. Rather, it will be in line with the practices already adopted by health professionals, and will be congenial with public morals.

Acknowledgement

I am grateful to Gert Helgesson, Josepine Fernow, and an anonymous referee for their sympathetic readings of an earlier draft, resulting in a number of valuable suggestions for improvements.

Address:
Stefan Eriksson
Biomedical Ethics
Uppsala Science Park
S-751 85 Uppsala
Sweden
Tel.: +46 18 6112287
E-mail: Stefan.Eriksson@bioethics.uu.se

References

Adelswärd, Viveka, and Lisbeth Sachs (2003) "The Messenger's Dilemmas – Giving and Getting Information in Genealogical Mapping for Hereditary Cancer". *Health, Risk & Society* 5, 2, 125–138.

Applebaum-Shapiro Suzanne E., J. Peters, J. O'Connell, C. E. Aston, and D. C. Whitcomb (2001) "Motivations and Concerns of Patients with Access to Genetic Testing for Hereditary Pancreatitis". *The American Journal of Gastroenterology* 96, 5, 1610–1617.

Allen, Anita L. (1997) "Genetic Privacy: Emerging Concepts and Values". In *Genetic Secrets: Protecting Privacy and Confidentiality in the Genetic Era*. Mark A. Rothstein, ed. 31–59, New Haven & London: Yale University Press.

Bonadona, Valérie, Pierre Saltel, Françoise Desseigne, Hervé Mignotte, Jean-Christophe Saurin, Quing Wang, Olga Sinilnikova, Sophie Giraud, Gilles Freyer, Henri Plauchu, Alain Puisieux, and Christine Lasset (2002) "Cancer Patients Who Experienced Diagnostic Genetic Testing for Cancer Susceptibility: Reactions and Behavior after the Disclosure of a Positive Test Result". *Cancer Epidemiology, Biomarkers & Prevention* 11, 1, 97–104.

Bozcuk, Hakan Sat, V. Erdogan, C. Eken, E. Ciplak, M. Samur, M. Özdogan, and B. Savas (2002) "Does Awareness of Diagnosis Make Any Difference to Quality of Life? Determinants of Emotional Functioning in a Group of Cancer Patients in Turkey". *Supportive Care in Cancer* 10, 1, 51–57.

Broadstock, Marita, Susan Michie, and Theresa Marteau (2000) "Psychological Consequences of Predictive Genetic Testing: A Systematic Review". *European Journal of Human Genetics* 8, 10, 731–738.

Claes, Erna, Gerry Evers-Kiebooms, Andrea Boogaerts, Marleen Decruyenaere, Lieve Denayer, and Eric Legius (2003) "Communication with Close and Distant Relatives in the Context of Genetic Testing for Hereditary Breast and Ovarian Cancer in Cancer Patients". *American Journal of Medical Genetics* 116A, 1, 11–19.

Clarke, Angus, Veronica English, Hilary Harris, and Frank Wells (2001) "Ethical Considerations [Pharmacogenetics Working Party Report]". *International Journal of Pharmaceutical Medicine* 15, 2, 89–94.

Council of Europe (1997) *Convention for the protection of human rights and dignity of the human being with regard to the application of biology and medicine: Convention on Human Rights and Biomedicine*. ETS no. 164. Oviedo: Council of Europe.

Crouch, Robert A., and Carl Elliott (1999) "Moral Agency and the Family: The Case of Living Related Organ Transplantation". *Cambridge Quarterly of Healthcare Ethics* 8, 3, 275–287.

Cunningham-Burley, Sarah, and Anne Kerr (1999) "Defining the 'Social': Towards an Understanding of Scientific and Medical Discourses on the Social Aspects of the New Genetics". *Sociology of Health and Illness*, 21, 5, 647–668.

Cutter, Mary Ann G. (1998) "Negotiating Diverse Values in a Pluralist Society: Limiting Access to Genetic Information". In *Stored Tissue Samples. Ethical, Legal, and Public Policy Implications*. Robert F. Weir, ed. 143–159, Iowa City: University of Iowa Press.

d'Agincourt-Canning, Lori (2001) "Experiences of Genetic Risk: Disclosure and the Gendering of Responsibility". *Bioethics* 15, 3, 231–247.

Danish Council of Ethics (1993) *Ethics and the Mapping of the Human Genome*. Copenhagen: Danish Council of Ethics.

Decruyenaere, Marleen, Gerry Evers-Kiebooms, and Herman Van den Berghe (1993) "Perceptions of Predictive Testing for Huntington's disease by Young Women: Preferring Uncertainty to Certainty?" *Journal of Medical Genetics* 30, 7, 557–561.

Feinleib, Manning (1991) "The Epidemiologist's Responsibilities to Study Participants". *Journal of Clinical Epidemiology* 44, Suppl. 1, 73s–79s.

Finkler, Kaja, Cécile Skrzynia, and James P. Evans (2003) "The New Genetics and its Consequences for Family, Kinship, Medicine and Medical Genetics". *Social Science & Medicine* 57, 3, 403–412.

Fost, Norman, and Philip M. Farrell (1989) "A Prospective Randomized Trial of Early Diagnosis and Treatment of Cystic Fibrosis: A Unique Ethical Dilemma". *Clinical Research* 37, 3, 495–500.

Giardiello, Francis M., Jill D. Brensinger, Gloria M. Petersen, Michael C. Luce, Linda M. Hylind, Judith A. Bacon, Susan V. Booker, Rodger D. Parker, and Stanley R. Hamilton (1997) "The Use and Interpretation of Commercial *APC* Gene Testing for Familial Adenomatous Polyposis". *The New England Journal of Medicine* 336, 12, 823–827.

Glass, Kathleen Cranley, Charles Weijer, Roberta M. Palmour, Stanley H. Shapiro, Trudo M. Lemmens, and Karen Lebacqz (1996) "Structuring the Review of Human Genetics Protocols: Gene Localization and Identification Studies". *IRB, A Review of Human Subjects Research* 18, 4, 1–9.

Goldworth, Amnon (1999) "Informed Consent in the Genetic Age". *Cambridge Quarterly of Healthcare Ethics* 8, 3, 393–400.

Hallowell, Nina, C. Foster, R. Eeles, A. Ardern-Jones, V. Murday, and M. Watson (2003) "Balancing Autonomy and Responsibility: The Ethics of Generating and Disclosing Genetic Information". *Journal of Medical Ethics* 29, 2, 74–83.

Hannig, Vickie L., Ellen Wright Clayton, and Kathryn M. Edwards (1993) "Whose DNA Is It Anyway? Relationships between Families and Researchers". *American Journal of Medical Genetics* 47, 2, 257–260.

Hardwig, John (1990) "What about the Family – The Role of Family Interests in Medical Decision Making". *Hastings Center Report* 20, March/April, 5–10.

Hugo Ethics Committee (1998) "Statement on DNA Sampling: Control and Access". *Eubios Journal of Asian and International Bioethics* 8, 2, 56–57.

Kegley, Jacquelyn Ann K. (1998) "Genetic Information and Genetic Essentialism: Will We Betray Science, the Individual, and the Community?" In *Genetic Knowledge. Human Values & Responsibility*. Jacquelyn Ann K. Kegley, ed. 41–66, Lexington, Kentucky: ICUS.

Kielstein, Rita (1998) "Genetic Knowledge and Human Values: A Clinician's View". In *Genetic Knowledge. Human Values & Responsibility*. Jacquelyn Ann K. Kegley, ed. 131–143, Lexington, Kentucky: ICUS.

Lapham, E. Virginia, Chahira Kozma, and Joan O. Weiss (1996) "Genetic Discrimination: Perspectives of Consumers". *Science* 274, 5287 (25 October), 621–624.

Lawrence, Susan C. (1998) "Beyond the Grave – The Use and Meaning of Human Body Parts: A Historical Introduction". In *Stored Tissue Samples. Ethical, Legal, and Public Policy Implications*. Robert F. Weir, ed. 111–142, Iowa City: University of Iowa Press.

Lehmann, Lisa Soleymani, Jane C. Weeks, Neil Klar, Lois Biener, and Judy E. Garber (2000) "Disclosure of Familial Genetic Information: Perceptions of the Duty to Inform". *American Journal of Medicine* 109, 9, 705–711.

Lietaer, Germain (1992) "Von „nicht-direktiv" zu „erfahrungsorientiert": Über die zentrale Bedeutung eines Kernkonzepts". In *Neue Handlungskonzepte der Klientenzentrierten Psychotherapie. Eine grundlegende Neuorientierung*. Germain Lietaer, Rainer Sachse, and William B. Stiles, eds. 11–21, Heidelberg: Roland Asanger.

Medical Research Council (1999) *Research Ethics Guidelines for Using Biobanks, Especially Projects Involving Genome Research*. Stockholm: Medical Research Council, Dnr 1999–570.

Naser, Curtis R. (1998) "Researcher Obligations to Tissue and DNA Sample Sources". In *Stored Tissue Samples. Ethical, Legal, and Public Policy Implications*. Robert F. Weir, ed. 160–181, Iowa City: University of Iowa Press.

Nuffield Council on Bioethics (1993) *Genetic Screening – Ethical Issues*. London: Nuffield Council on Bioethics.

Pergament, Eugene (1997) "A Clinical Geneticist Perspective of the Patient-Physician Relationship". In *Genetic Secrets: Protecting Privacy and Confidentiality in the Genetic Era*. Mark A. Rothstein, ed. 92–107, New Haven & London: Yale University Press.

Peters, June A., Luba Djurdjinovic, and Diane Baker (1999) "The Genetic Self: The Human Genome Project, Genetic Counseling, and Family Therapy". *Families, Systems & Health* 17, 1, 5–25.

Peterson, Susan K., Beatty G. Watts, Laura M. Koehly, Sally W. Vernon, Walter F. Baile, Wendy K. Kohlmann, and Ellen R. Gritz (2003) "How Families Communicate About HNPCC Genetic Testing: Findings from a Qualitative Study". *American Journal of Medical Genetics Part C*. 119C, 1, 78–86.

Plantinga, Laura, Marvin R. Natowicz, Nancy E. Kass, Sara Chandros Hull, Lawrence O. Gostin, and Ruth R. Faden (2003) "Disclosure, Confidentiality, and Families: Experiences and Attitudes of Those With Genetic Versus Nongenetic Medical Conditions". *American Journal of Medical Genetics Part C*. 119C, 1, 51–59.

Richards, Martin (1996) "Families, Kinship and Genetics". In *The Troubled Helix. Social and Psychological Implications of the New Human Genetics*. Theresa Marteau, and Martin Richards, eds. 249–273, Cambridge: Cambridge University Press.

Sankar, Pamela (2003) "Genetic Privacy". *Annual Review of Medicine* 54, 393–407.

Sasse, Edward A. (2002) "Objective Evaluation of Data in Screening for Disease". *Clinica Chimica Acta* 315, 1–2, 17–30.

Swedish Government (1989) *Genetisk integritet [Genetic Integrity]*. Written communication to the Parliament, Skr. 1998/99:136. Stockholm: The Swedish Government. [http://social.regeringen.se/propositionermm/skrivelser/pdf/skr9899_136.pdf]

Taswell, Howard F., and Susan K. Sholtes (1999) "Predictive Genetic Testing: A Story of One Family". *Families, Systems & Health* 17, 1, 111–121.

Thomson, Elizabeth J. (1997) "Ethical, Legal, Social, and Policy Issues in Genetics". In *The Genetics Revolution: Implications for Nursing*. Felissa R. Lashley, ed. 15–25, Washington, DC: American Academy of Nursing.

Walker, Margaret (1987) "Moral Particularity". *Metaphilosophy* 18, 3-4, 171–185.

Wiggins, S., P. Whyte, M. Huggins, S. Adam, J. Theilmann, M. Bloch, S. B. Sheps, M. T. Schechter, and M. R. Hayden (1992) "The Psychological Consequences of Predictive Testing for Huntington's Disease. Canadian Collaborative Study of Predictive Testing". *New England Journal of Medicine* 327, 20, 1401–1405.

Wilcke, Jon Torgny R. (1998) “Late Onset Genetic Disease: Where Ignorance is Bliss, is it Folly to Inform Relatives?” *BMJ* 317, September 12, 744–47.

Wilcke, Jon Torgny R., N. Seersholm, A. Kok-Jensen, and A. Dirksen (1999) “Transmitting Genetic Risk Information in Families: Attitudes about Disclosing the Identity of Relatives”. *The American Journal of Human Genetics* 65, 3, 902–909.

Williams, Clare, Priscilla Alderson, and Bobbie Farsides (2002) “Is Non-Directiveness Possible within the Context of Antenatal Screening and Testing?” *Social Science & Medicine* 54, 3, 339–347.

World Health Organisation (1997) *Proposed International Guidelines on Ethical Issues in Medical Genetics and Genetic Services. Report of a WHO Meeting on Ethical Issues in Medical Genetics*. Geneva: WHO.