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## RESEARCH ON ELDERLY SUBJECTS: STRIKING THE RIGHT BALANCE

### Abstract

Elderly patients stand to benefit, more than any other group, from research advances against chronic progressive diseases. Diseases such as Alzheimer's dementia. But research into diseases whose target is mostly an elderly population requires the participation of elderly patients who are suffering from the disease to serve as research subjects. This generates a moral dilemma. Dementing patients are also, *ipso facto*, highly vulnerable people. In general, their decision-making capacity is compromised, often seriously. In particular, their capacity to give valid consent to a request that they serve as research subjects is questionable, at best. The principle of informed consent has been described as "the first principle" of research with human subjects, but the ethical dilemma faced by patients and their families is that if such vulnerable patients are excluded from participation in clinical research, they will lose not only the opportunity to be altruistic but may also be denied the possibility of gaining access to new and potentially effective therapy. Moreover, future generations of elderly patients will be denied the opportunity of benefitting from scientific advancement in the diagnosis and treatment of disease. Arguments in favor of and against doing research on less-than-fully competent elderly patients will be canvassed, as will arguments in favor of and against allowing less-than-fully competent patients to give voluntary informed consent. The role of advance directives and surrogate decision-makers for the elderly will be discussed. Finally, justification will be offered for the view that it is often morally permissible for researchers to recruit as research subjects such vulnerable population as the demented elderly, though qualifications will be attached to such justification.

### The Central Dilemma

Many chronic and disabling diseases disproportionately or exclusively affect the elderly. Alzheimer's dementia would be an obvious illustrative example. Unless medical scientists are able to conduct research upon elderly human subjects, prospects for the development of effective therapies will be poor. In the search for reliable diagnostic tests and for effective therapies, animal models are helpful but, ultimately, not adequate.<sup>1</sup> Scientific progress in the diagnosis and treatment of such disease requires that procedures and drugs be tested on those who have the disease or who are at high risk of developing it.

Unfortunately, the very factors which make it imperative to conduct research upon the elderly also pose serious ethical obstacles to recruiting them as research subjects. Stereotypes of the elderly as necessarily possessing

diminished mental capacity ought to be rejected, of course. There is as much heterogeneity among the population of elderly people, as there is among the population of young or middle-aged people. Thus, for purposes of recruiting volunteers to become research subjects there is no reason automatically to discriminate between the old and others. It would, nevertheless, be naive to deny that among the population of those with special vulnerabilities one would expect to find that old people are present in disproportionate numbers. Old people who are, for example, disabled by stroke, or ill with Parkinson's disease, tend to be physically and mentally vulnerable. They are not just physically frail; they are, often, emotionally vulnerable and/or intellectually impaired. Frequently they are institutionalized, which circumstance poses its own special ethical challenge.

Thus, research on the elderly is both ethically required and ethically suspect. Scientific progress towards the effective diagnosis and treatment of such diseases as senile dementia, which many would regard as an ethical imperative, requires experimentation which uses demented subjects. But it is a fundamental requirement of research ethics that subjects should only be recruited from that class of volunteers who are competent to give valid consent. Almost by definition, those who are demented are not competent to give such consent. A genuine ethical dilemma.

#### The Case Against Using The Vulnerable Elderly As Research Subjects

The locus classicus for the case against experimentation on frail patients would have to be the highly influential and much-cited 1969 article by Hans Jonas: "Philosophical reflections on experimenting with human subjects".<sup>1</sup>

In this article, Jonas focuses attention on the vulnerability of very sick patients to exploitation, especially when those patients are dying or suffering from serious chronic illnesses. He doesn't specifically single out the frail elderly, but they would constitute a paradigm case of the kind of patient whose vulnerability to exploitation concerns him. "The afflicted should not be called upon to bear additional burden and risk [involved in clinical trials], ...they are society's special trust and the physician's particular trust - these are elementary responses of our moral sense."<sup>1</sup>

Jonas is a leading advocate of the principle that averting a disastrous outcome always carries greater moral weight than promoting a good one.<sup>1</sup> It follows from this principle that one ought always to assign a higher priority to the value of minimizing the risk of harm to research subjects than one assigns to the value of promoting their best interests or, a fortiori, promoting the best interests of others. Jonas recognizes, of course, that without medical experimentation on human subjects the prospects for advancing scientific knowledge of disease will be seriously hampered, if not utterly stifled. Nor would he deny that the burden of individual suffering and disease will be increased if such scientific progress does not occur, or occurs at a much reduced pace. It seems clear that for a community to eschew the benefits of modern medical research whenever such research poses risks or hazards to research subjects would impose a heavy burden of avoidable disease on its members.

Consider the implications for any society which would consider adopting a rigorous Jonas-type policy of prohibiting all risky experimentation on research subjects. Virtually every clinical trial exposes its research subjects to some risk. Even a seemingly innocuous experiment to determine the efficacy of mouth rinse in preventing tooth decay for seniors, such as the current T.E.E.T.H. multi-centered trial,<sup>1</sup> exposes subjects to the risk that the rinse may, for a few people, irritate the lining of the mouth. Moreover, this clinical trial requires that each subject undergo a panoramic X-ray both at the beginning and at the end of the trial, which exposes every volunteer to a low dose of radiation. There may be no known adverse side effects from such a low dose of radiation, but the potential for harm

cannot be said to be non-existent. What is true of a comparatively innocuous mouth wash experiment on elderly volunteers will, a fortiori, be true for trials involving powerful new drugs or innovative surgical techniques. The point to note here is that there will be very few experiments on human subjects about which it can be said confidently: "This experiment is entirely without risk of harm to any of its human research subjects."

Those who adopt a Jonas-type ethical stance to medical experimentation would, presumably, decry even such an apparently benign clinical trial as T.E.E.T.H., on the grounds that it is unethical to invite any person, and especially any vulnerable person, to volunteer for any experiment which involves any degree of risk of any level of harm. Moreover, for those clinical trials in which the likelihood of harm is high and from which the harm itself, should it occur, would be grave, even the "superlative good" of public health would not, according to Jonas, provide adequate justification for carrying out vitally important research.<sup>1</sup> By contrast, proponents of experimentation on human subjects will argue that the prevention of disease or its cure, for victims, actual or potential, will sometimes provide a sufficient warrant for carrying out research involving risks to human subjects. The value of the end which is to be promoted, relief of suffering, say, will sometimes justify the risk of harm to research subjects entailed by the means. Against such consequentialist reasoning, Jonas insists that the essentially melioristic goals of medical research must be subordinated to the sacrosanctity of the individual research subject. On Jonas' view, even when the potential benefits from research would be significant, would accrue to a large number of present and future sufferers, and would far outweigh the likely harms, the principle of absolute protection for the "dignity" of the individual remains inviolable.

The ethical position taken by Hans Jonas is not, however, quite as rigorously absolutist as it may at first sight appear to be. Even the ethically abstemious Jonas accepts that when a community is faced with the sort of "clear and present danger" which is posed by a raging epidemic it may be morally legitimate to seek and accept the submission of human subjects to research which is hazardous. Thus, given the urgency and vast social dimensions of the current AIDS pandemic, a randomized clinical trial intended to test an AIDS vaccine might offer the kind of "transcendent social sanction" which Jonas requires in order to justify human experimentation. Research on patients suffering from senile dementia, however, would likely not meet even Jonas' somewhat modified but still strict ethical standards if the research posed any risks whatsoever to cognitively impaired patients.

#### The Case Against Hans Jonas: The Right To Be Treated As a Person

There is an inescapable aura of paternalism about the approach to experimentation advocated by Jonas. Individuals must be protected against the hazards of medical experimentation, he insists, even when they voluntarily consent to participate as research subjects, in full knowledge of whatever hazards (and benefits) may flow from their decision. Thus, Jonas might be seen as targeting elderly potential research subjects for special protection on dubiously legitimate paternalistic grounds simply because they are more likely to be cognitively impaired.<sup>1</sup>

Against this kind of paternalistic approach, Benjamin Freedman has argued that "there does seem to exist a positive right of informed consent, which exists in both therapeutic and experimental settings".<sup>1</sup> In other words, to deny to a competent individual, of whatever age, the opportunity to give (or withhold) informed consent to participation in a clinical trial is to undermine that person's right to be treated as an autonomous person.

When old people are capable of giving valid consent to becoming research subjects, (that is, consent which

is both informed and voluntary), to deny them the right to make the decision to participate in medical experimentation is to attack their dignity as persons. It is to treat them objects rather than as rational agents. When well-meaning health care professionals or family members refuse permission for an elderly person to become a research subject, they typically believe that they are acting benevolently. Indeed, their refusal even to consult grandma or grandpa about becoming a research subject derives, most often, from their conviction that they are acting to promote the old person's long term best interests. The danger here is that well-meaning family may be guilty of underestimating the older person's capacities "to act with as much enlightened self-interest as any other adult citizen in deciding whether a particular research project is something which is desirable for him or her."<sup>1</sup>

Benevolent care-givers will often be correct in their calculations, on behalf of older patients, of the comparative benefits and harms likely to arise from participation. Nevertheless, the usurpation of the old person's right to make this decision for herself will often be experienced as a diminution of autonomy. This is a point of some moral importance. To act in such a way that one reduces further the already questionable autonomy of an elderly person carries its own considerable risks of harm.<sup>1</sup> It has, perhaps, been insufficiently noticed that old persons may suffer more inadvertent harm from the paternalistic interventions of those who care for them than they suffer deliberate harm from those with malice in their hearts.<sup>1</sup>

### Competence and the Elderly Subject

When competent older patients have their competence unrecognized or inappropriately denied they may be harmed in several important ways. The most important of these harms is, perhaps, the undermining of their dignity as autonomous persons when they are treated "as children". Of scarcely less importance is the harm which arises from losing what may, for them, count as an life-enhancing opportunity to exercise their generous impulses - to behave as an altruistic member of the community in a project which promises important benefits to others, as well as to oneself. It must be admitted, of course, that the decision to allow an elderly person of limited competence to participate, altruistically, as a volunteer subject for a research project is morally troubling. When there is a high risk of grave harm, when the research is not intended to be even partly therapeutic for the volunteer, and when the competence of the elderly person is seriously compromised, few would defend the "right" of the elderly to participate. By contrast, when the risk is low and the harm trivial, when the research is intended to be at least partly therapeutic for the volunteer, and when there are periods of clear-minded lucidity during which the elderly person expresses a wish to volunteer, then few would raise strong moral objections to participation as a research subject. Sharpest disagreement is likely to occur within the grey intermediate zone, when risk and stake are neither frightening high nor inconsequentially low, and when competence is difficult to ascertain or fluctuates wildly.

Even when an investigator fulfils her responsibility to disclose all materially relevant facts about the experiment to a potential research subject, and even when the subject gives his consent voluntarily, let us suppose with no element whatsoever of coercion, the consent given by the subject will not be valid consent if the subject lacks competence. When that is the case, then either the incompetent individual should be excluded from participation in the experiment or (an alternative to be discussed later) a surrogate should be identified who can legitimately make this decision on behalf of the incompetent patient.

The questions of how competency is to be defined, how it is to be measured, and how much of it is required for a patient to be considered eligible for recruitment to a clinical trial, are all of them difficult and complex. Attempts to provide adequate answers have proliferated and now constitute a substantial body of literature in their own right. Despite this large body of literature, or because of it, there is still much controversy about what constitutes the most satisfactory answer to each of the questions posed above. The issues may appear so purely theoretical as to be of interest exclusively to professional philosophers but, in reality, much of practical importance

hinges on the answers which are accepted. If, for example, excessively stringent criteria are adopted in the process of ascertaining whether a potential research subject is competent, many patients who might benefit from participation will be excluded, to their disadvantage and to the disadvantage of society and future generations. Alternatively, if inappropriately lax standards of competency are put into place then highly vulnerable patients may be exploited and harmed in ways that cannot be morally justified by appeal to their (the patients') valid consent. Errors in either direction expose an investigator to moral criticism.

So, how competent is competent enough? James Drane offers a promising approach in our quest for a defensible answer to this difficult question. In the course of his discussion of what constitutes patient competency to give informed consent Drane proposes that: "[A]s the consequences flowing from the patient's decisions become more serious, competency standards for valid consent or refusal of consent [ought to] become more stringent."<sup>1</sup> Drane doesn't direct his attention specifically towards the issue of the competency of elderly prospective research subjects to give consent to participation in a clinical trial. It seems clear, however, that when such research poses serious risks to the subject, especially when these risks are not counter-balanced by proportionately high expected benefits, he would insist upon the presence of a high level of competency - "an understanding that is both technical and personal, intellectual and emotional".<sup>1</sup> Where the risk and stake for the research subject are low, advocates of variable competency, such as Drane, would accept a proportionately low level of comprehension from the prospective subject. Even patients/subjects who are mentally or emotionally disturbed, suffering from anxiety, pain or reactive depression might qualify as competent to volunteer for research which threatens them with no more than minor inconvenience and which holds out hope of producing some benefits to them personally or major benefits to society.

Once it is recognized that competence (or "decisional-capacity", as some prefer to label it) is not a matter of all or nothing-at-all but is, rather, a sliding scale of capacities with many shades and degrees in between the poles at each end of the spectrum, one is more likely also to recognize that from the fact that an elderly person is incompetent to live independently, it should not be inferred automatically that she is incompetent to perform such other tasks as giving informed consent to participation in a clinical trial. A patient in the early stages of dementia, for example, might be judged incompetent to decide whether to participate in a therapeutic trial which presented high risks of grave harm, but this same patient might nevertheless be judged to possess the modest level of competence required to decide whether to participate in a trial which posed only slight risks of negligible harm. The former decision requires of a prospective research subject, who has a lot to lose, that she possess a clear understanding of the risks and benefits involved, the ability to weigh and balance these risks and benefits against the risks and benefits of the available alternatives, and a clearly thought out understanding of her own attitudes and values to these risks and benefits. A patient with senile dementia, even in the early stages of the disease process, is unlikely to possess this kind of decisional capacity. The latter decision, by contrast, requires an altogether more modest level of decision-making capacity, such that even a moderately demented person might be found competent to choose whether or not to participate.

In sum, with respect to the issue of "experimentation on elderly prospective subjects of less-than-full mental competence" it seems more appropriate, morally-speaking, to adopt a nuanced and qualified view rather than to adopt a position of either total rejection or total acceptance. It is too simple to ask the question "Is this patient competent to give valid consent to become a research subject?" The ethically appropriate question would be, rather, "Is this patient competent to give valid consent to become a research subject for this particular experiment, given its risks and benefits and given the patient's capacities relative to the complexities of the decision involved?" A patient in the early or middle stages of senile dementia might, for example, be judged competent to participate in a low-risk clinical trial but incompetent to decide to participate in a trial which posed high risks of serious harm. When investigators attempt to balance the competing concerns of (a) protecting subjects from the harms that could befall them as a result of their impaired decision-making capacity and (b) permitting prospective subjects autonomously to determine the shape of their own lives, the adoption of a variable standard of competence seems likely to contribute

to the achievement of a morally defensible balance.

If an excessively restrictive standard of decisional competency were to be adopted and if, as a result, some frail elderly patients were wrongly denied the opportunity to become research volunteers, the mistake would not be a trivial one. For, as Freedman forcefully reminds us, the physician-experimenter faces ethical risks not just from one direction but, simultaneously, from two opposing directions:

When the consent [of the potential research subject] is of doubtful validity...the physician experiences a conflict between two duties. He will not be ethically well-protected by choosing not to experiment, for there exists the possibility...that he is violating a duty in so choosing.<sup>1</sup>

This reminder is important because, to this day, many scientists and regulators of scientific research appear to believe that there is what might be called a “fail-safe” position, viz., the position that when consent is of doubtful validity one is morally obliged not to recruit the patient as a subject for research. In other words, the preponderant view among the scientific and ethical communities is that the burden of proof rests on those investigators who seek to accrue subjects with questionable decision-making capacity. By contrast, the gravamen of Freedman’s argument is that there is no such burden of proof on the investigator, because researchers have an equally important duty to potential subjects not to deny them, wrongfully, the opportunity to participate in what may for them be a meaningful life project. If Freedman is correct, and I believe that he is, then those who follow a Jonas-like ultra-strict standard for the recruitment of patients as research subjects are vulnerable to serious moral criticisms, viz., the criticism that they are slighting the autonomy of patients and the additional criticism that they are neglecting the very real benefits which many patients derive from their participation in clinical trials.

In one of the earliest modern studies of the ethical issues raised by medical research on human subjects, Henry Beecher cites a survey of prison inmates who unashamedly admit that altruism rather than money was their primary motivation for participating in a study involving malaria.<sup>1</sup> I say “unashamedly” because in our cynical culture many people are reluctant to admit that they were moved to act by altruistic motives - perhaps for fear of being pejoratively labeled a “do-good-er” - perhaps for fear of being disbelieved by cynical listeners. Indeed, one would expect that prison inmates would be more reluctant than most to admit (except, perhaps, during a parole board hearing) to harboring generous impulses. This lends added credibility to Beecher’s findings. Other studies [for example, that done by Annas et al., 1977]<sup>1</sup> confirm that in addition to altruism, prisoner volunteers for research participation are motivated by hope for a variety of benefits, including self-respect, curiosity, and relief from boredom. A nursing home differs in some important respects from a prison, but many of these same benefits would seem plausibly to accrue to residents who choose to become research subjects. One could argue, of course, that just because life in such institutions as prisons and nursing homes is so often bleak, boring, and depressing, their inmates are vulnerable to illegitimate inducements, for example, the “excitement” of participation in medical experimentation. Their consent could, in consequence, be viewed as coerced rather than voluntary. Since the effect of such an argument would be effectively to disallow any choices which either prisoners or the institutionalized elderly might make in an effort to improve their lives, it smacks of unacceptable paternalism.

The claim, here defended, that researchers have an equal obligation to investigate both the potential harms and the potential benefits of participation in any particular research trial, and to communicate their findings of harm and benefit to prospective research subjects, would not be universally accepted. Wicclair, for example, contends that “the ethical obligation to make a conscientious effort to uncover unknown potential harms and burdens to [potential] subjects” is weightier than “the similar obligation with respect to potential benefits to [potential] subjects.”<sup>1</sup> He offers two main arguments in support of this conclusion.

The first argument appeals to the best interests of the prospective research subject. Wicclair claims that, from the point of view of the research subject, to experience unexpected harms and burdens is worse than to miss the

experience of correspondingly significant benefits. Those who are risk averse will likely agree with this conclusion. But not every elderly person will be risk averse, and if large numbers of the elderly would prefer to risk some degree of harm as a result of becoming research subjects, in return for gaining the opportunity for some degree of benefit, would it not be presumptuous of Wicclair or any other well-meaning protector of the elderly to foreclose that decision on their behalf?

Wicclair's second argument is that "when there was insufficient disclosure of risks by investigators, subjects can claim to have been inappropriately used as a means to benefit others", whereas "a similar charge cannot be made when subjects fail to volunteer because there was inadequate disclosure of potential benefits by investigators".<sup>1</sup> This point must, I think, be conceded. But does the charge of having "been inappropriately used as a means to benefit others" carry greater moral weight than the charge of having been denied the opportunity to benefit from participation as a research subject in this or that experiment? This is the key question, and Wicclair does not offer us any good reason to prefer his conclusion rather than its opposite.

There are, in addition, two ancillary arguments which Wicclair offers in support of his contention that it is better to err on the side of wrongful exclusion rather than on the side of wrongful inclusion. He asserts that when elderly persons claim the right to refuse to serve as research subjects this rights-claim has a weight and legitimacy not enjoyed by the opposite claim, viz., that they have a positive right to participate in research studies of their choosing.<sup>1</sup> Wicclair's contention seems plausible, since there would be near-universal agreement that no one has a positive right to participate in a study of her choosing, while equally strong agreement could be expected for the claim that everyone has a right not to participate.

If Wicclair's point is reformulated, however, it loses much of its plausibility. He's clearly correct to suggest that no one has an automatic right to participate in a study of her choosing. Resources for research are limited, after all, and only a small minority of those who might wish to be accommodated as subjects for certain popular studies - such as those studies which are testing some new anti-AIDS drugs, with a high expected benefit to participants - can realistically be enrolled. But if such a study is being undertaken, would there not be a strong moral consensus that every person whose particular circumstances fit the study's protocol has a right not to be illegitimately excluded from the opportunity to participate as a subject in the study? Would it not be a case of wrongful discrimination if someone were so excluded on discriminatory grounds of their race, their sex, or their presumed (but not demonstrated) incompetence? This is not to deny, of course, that race or sex or age may sometimes be legitimate criteria for inclusion/exclusion. But when such considerations are medically and morally irrelevant to the clinical trial, anyone who was denied the opportunity to become a research subject on untenable grounds could surely complain of wrongful discrimination.

Wicclair's second ancillary argument is that "since expected benefits provide an important inducement to prospective subjects, it is to be expected that investigators will conscientiously identify and disclose potential benefits."<sup>1</sup> His point is that no special encouragement is required to induce investigators to disclose potential benefits since they would do so enthusiastically in any event. This generalization about the motivation of clinical researchers has a certain common sense appeal. Why should it be necessary to reinforce the already strong inclination of researchers to communicate possible benefits to patients? It is, after all, the potential harms that they are most likely to feel tempted to conceal or down-play, and it is therefore their duty to disclose such harms that needs to be emphasized.

The duty to disclose potential harms does need to be stressed. That seems incontestable. But I would argue that the duty to disclose potential benefits also requires to be stressed. In a litigious society, when a certain class of people has been identified as less-eligible to participate in an important social activity, such as clinical research trials, a prudent researcher might well feel that it would be better to discourage such elderly volunteers by

minimizing or simply not disclosing potential benefits. In this way, she could avoid “the hassle” of ethics committees, suspicion from over-protective relatives, and possible litigation if things go badly for volunteers whose frailty puts their decision-making competence into question. Such an attitude on the part of researchers would be understandable, but not morally defensible. Every prospective research subject is entitled to decide for herself, after full disclosure of both potential benefits and potential burdens, whether or not she wishes to participate. The right of informed consent requires that the prospective subject make her decision in the light of all materially relevant information.

In sum, once we recognize that researchers have a moral duty to recognize valid as well as invalid consent, and that these moral duties are equally weighty, we are forced also to recognize that there is no fail-safe position. Whether any particular patient, however elderly or infirm, is capable of giving a valid consent to experimentation, is a question which can only be answered after careful examination of the circumstances of the case. Pace Jonas, it cannot be answered a priori.

### The Case Against Hans Jonas: Social Utility

Setting aside, for the moment, the anti-Jonas argument which supports recruitment of elderly patients for risky (to some degree) research by appealing either to the autonomy or to the overall best interests of the potential subject, we turn now to a different argument, one which appeals to the social utility of permitting at least some medical experimentation on elderly persons.

There is virtually unanimous consensus among demographers that an increasingly large number of people, especially in advanced industrial or post-industrial societies, will be surviving to very old age.<sup>1</sup> More of us will be living into old age, and more old people will live into old old age. As a concomitant to this phenomenon, popularly labeled “the ageing population”, more of us will live long enough to suffer from those disabling and chronic diseases that primarily or uniquely affect the aged. In order for scientists to improve their understanding of such diseases sufficiently to develop effective therapies or, better still, preventive strategies, it is necessary for society to promote and pursue a vigorous program of geriatric research.

Even with respect to those diseases (cancer and heart disease, for example, and stroke,) which affect some younger as well as many elderly people, if elderly patients are to receive proper medical treatment it is necessary that researchers acquire adequate knowledge concerning the safety and efficacy of drugs and of surgical treatments when used in the treatment of the old. As Bell and her colleagues observe:

Results of well-controlled clinical studies using healthy young or middle-aged adults who are not taking medications that might interfere with the research project cannot be generalized to persons in whom the aging process is coupled with multiple chronic illnesses and several concomitant medications.<sup>1</sup>

The important point to note here is that the ageing process itself together with some disease states more prevalent among the elderly make it unwise to extrapolate data acquired from research on younger study populations to older

populations.

The need for extensive research on the elderly becomes even more exigent when one takes into account the great diversity to be found within the category of “the elderly”, some of whom enjoy robust good health and mental acuity while others are acutely ill and mental compromised. Many elderly people are dependent upon a great range of drugs for a variety of serious conditions, but some elderly people live medication-free lives. Stereotypes of the elderly as physically frail and mentally incompetent disguise the heterogeneity to be found within this group. In consequence, research on the elderly will have to be equally sensitive to diversity and will need to focus on many sub-populations within the general category of “the old”. Urinary incontinence, for example, is a problem from which many old people suffer. But because there are several types of urinary incontinence, which differentially affect particular sub-groups of the elderly, and because this condition will often co-exist in the elderly with such other conditions as diabetes mellitus, congestive heart failure, or symptomatic arthritis, clinical trials which seek to ascertain the efficacy of experimental drug therapy will face special difficulties not usually encountered with drug trials on younger populations.<sup>1</sup>

Research in geriatric medicine thus poses some unique problems. For example, “scientists must consider the importance of cohort effects, the need to separate age-related effects from the effects of disease and psychosocial factors.”<sup>1</sup> Norms and clinical practices developed by research on general populations will not necessarily serve older patients well.<sup>1</sup>

Moreover, this requirement for research on elderly patients themselves arises not only within the realm of geriatric medicine but, much more broadly, within the realm of all gerontological research and gerontological policy-formation. The elderly, it should be noted, require services from a range of professionals other than physicians and nurses. The same empirical argument which establishes that geriatric research is necessary if we are to develop effective medical treatments for the elderly also establishes that gerontological research on elderly subjects is necessary if we are to develop effective social and psychological programs and sound gerontological social policy. If we desire to live in a society in which elderly patients and clients are well-served by social workers, clinical psychologists and policy planners, as well as by doctors and nurses, we have no choice, pace Jonas, but to accept the necessity of research on the elderly.

Jonas’ argument affirms that society has no right to demand of its members that they make significant personal sacrifices on behalf of the public good. Fair enough. Nevertheless, it is widely accepted in many western societies that society also has an obligation to provide at least minimally decent medical care for everyone. This obligation could plausibly be interpreted to entail that society has an obligation to promote the development of effective treatments. To forego medical experimentation involving some non-trivial level of risk would be functionally equivalent to abandoning most medical research. To forego medical research in this dramatic fashion would be to deprive ourselves and future generations of the benefits of new diagnostic tests, new treatments, new potential cures for dreadful diseases and crippling disabilities. Such moral reasoning, when offered in criticism of Jonas’ position, leads directly to the conclusion that every member of society has an assignable *prima facie* obligation to promote health through a willingness to volunteer for research. There would not appear to be any obvious reason why the elderly, considered as a group, would be exempt from such a basic social obligation. Indeed, for any individual, young or old, to accept the benefits of others’ volunteer efforts of this sort, without being willing to make similar efforts herself, smacks of what we might label “moral parasitism”. We are here dealing with that familiar game theoretic issue: the problem of the free rider. Old people are no more exempt from moral strictures, in particular the stricture to contribute to the collective good, from which they in turn benefit, than any other group in society.

Thus, one might argue, against Jonas, that there is a significant ethical cost attached to not doing research on vulnerable potential research subjects. As one physician expresses the moral point:

In the discussion of ethical considerations relating to clinical research, the rights of the unborn generations to benefit from the fruits of research must also be weighed. It can be debated that no man today has the free and moral right to condemn his grandchildren to the same perils of disease to which he is exposed by virtue of the present lack of effective scientific information, and his failure to participate in a search for it.<sup>1</sup>

Without extensive scientific research, employing elderly human volunteers as subjects, we not only forego the opportunity to acquire new and more effective treatments for the present generation of old people and for future generations, but we risk allowing actual harm to older people as a result of their treatment with insufficiently tested therapies. Moreover, it is worth keeping in mind that even when inadequately tested therapies turn out not to be actively harmful they may be inefficacious. Given the fact of scarce medical resources, one person's provision is, so to say, another person's deprivation. Thus, the issue of cost-effectiveness carries with it a moral dimension which, when combined with the imperative of promoting health, tends to add further support to the conclusion that we would be ethically remiss if we were to abstain from medical research which is likely to yield beneficial knowledge.

Suppose, however, for the sake of argument, that one were to concede to Jonas that self-sacrifice, in non-emergency situations, is supererogatory, and that "our descendants have the right to be left an un plundered planet; they do not have a right to new miracle cures."<sup>1</sup> Let us also concede that, after all, Jonas may be right when he insists that neither present social welfare nor concern for future social welfare obligates individuals to participate in clinical trials as research subjects. Accept that neither of these important goals could justify society in demanding of individuals that they accept the personal sacrifices associated with becoming a volunteer for hazardous experimentation. Having made all these concessions, however, one might nevertheless question why it would be wrong for society to accept the voluntary informed enrolment as research subjects of those who are motivated to participate, whether by altruism, by a sense of moral obligation, or by perceived self-interest.

One could also question the a-historical and asocial conception of the self which is presupposed by Jonas' extreme individualism, with its concomitant near-exclusive focus on individual rights. As Alasdair MacIntyre has reminded us, the process by which individuals construct their identity and achieve the status of autonomous beings is one which necessarily takes place through community membership.<sup>1</sup> Once the reciprocal ties of the individual to his or her community have been understood and their importance recognized, one may feel that what is needed is less an exclusive stress on protecting the rights of the individual and more a stress on finding the correct balance between the rights of individuals and the needs of the community from which individuals derive their identities and draw their strength. A patient-centred ethos, or a research-subject-centered ethos requires to be counterbalanced by the morally legitimate claims of the wider society.<sup>1</sup> Rights need to be counterbalanced by responsibilities. At the very least, community needs and the individual's responsibility to promote the satisfaction of those needs should not be slighted or ignored. The communitarian perspective is one which deserves to be considered and to be assigned some moral weight in policy deliberations.<sup>1</sup>

### Morally Coercive Appeals for Voluntary Self-sacrifice

Jonas argues against the moral permissibility of any appeal to members of society that they volunteer to become

research subjects. He opposes such appeals on the grounds that the mere issuing of the appeal, the calling for volunteers, inevitably exerts moral and social pressures on potential subjects.<sup>1</sup> This argument has special force when the appeal is directed towards frail elderly patients by their personal physicians, nurses, or nursing home care-givers. Many of the factors which make such patients highly desirable as research subjects, for example, their continuous presence in an institution where their health can be easily monitored and their progress tracked, also render them highly vulnerable to exploitation. This is especially true for patients with cognitive deficits who, according to some estimates, constitute almost one half the population of most nursing homes.<sup>1</sup> Moreover, even for those frail elderly patients who are cognitively intact, serious moral problems arise when attempts are made to recruit them as research subjects, some of which are discussed below.

Of course, it would be quite wrong to suggest that all or even most elderly persons are “frail”, either physically or intellectually. Rather, the suggestion is merely that various kinds of frailty are increasingly present with advancing age. Ageing patients are typically in a weakened physical state and often experience emotional upset. Many are likely to feel both dependent upon and submissive towards those who are responsible for their care and treatment. It is well-established by empirical research that patients who are ill tend to suffer a concomitant diminution of their autonomy.<sup>1</sup> The problem becomes more serious still when the patient is gravely ill and/or institutionalized. To be removed from one’s familiar surroundings and one’s familiar routines is inevitably a disorienting experience, and when this deracinating process is accompanied by a significant loss of privacy and the substitution of unfamiliar care-givers for friends and family, the effects on autonomy can be marked. It seems unreasonable, therefore, to expect that an elderly patient (or any patient, for that matter) who is gravely ill and/or suffering significantly from pain, discomfort, emotional fatigue or distress, perhaps living in an institution and heavily dependent upon its staff, will nevertheless be able to attend to the subtleties of a complex research project, much less possess the capacity freely and rationally to assess potential risks and benefits.

This line of reasoning has led to the proposal that patients who are in a seriously weakened or otherwise vulnerable position be assigned (or, at an earlier stage, be encouraged to designate) an “advocate”, someone whose obligation it would be to represent their wishes or needs. To some authors, the family seems the appropriate place to look for such an advocate. Others, suspicious of family dynamics, argue that when a patient requires either an advocate or even a surrogate decision-maker the person chosen should be independent of the family system.<sup>1</sup>

### Physician-Researcher Conflicts of Interest

Many commentators have observed that patients have traditionally tended to think and behave towards their doctors in a submissive manner - admiring and obedient in the manner of good children responding to parental commands.<sup>1</sup> This observation is much less true today, at least in most Western societies, than it would have been prior to the advent of the consumers’ and women’s movements of the 1960s. Even so, it is still likely to be true for many geriatric patients. Given that many elderly patients grew to maturity in an era marked by a higher degree of deference to authority than that which prevails in contemporary society, it will often be the case that they manifest a submissive deference towards their care-givers which can be easily exploited (consciously or unconsciously) by physician-researchers who solicit their own patients to participate in a clinical trial.

The role of personal physician diverges significantly from that of scientific investigator, though the same person often takes both roles. Thus, it seems potentially exploitative, and therefore ethically dubious, to use the trust accumulated by physicians in their traditional role as healers for purposes related to their distinct role as scientific investigators.<sup>1</sup> The performance of dual roles raises the specter of potential conflict-of-interest, viz., conflict of

interest between the duty of undivided loyalty to an individual patient, which inheres in the physician role, and the duty of advancing medical knowledge, which is the primary goal of medical research.

Since each of these roles - that of scientific investigator, on the one hand, and personal physician, on the other - defines itself by reference to a different primary purpose, the possibility of conflict of interest is an ever-present danger. Because physicians have a plurality of responsibilities, they must attempt to reconcile and balance a plurality of value commitments. The Hippocratic Oath, in all of its many versions may insist that for a physician "the life and health of my patient shall be my first consideration", but most modern physicians would acknowledge that they have such additional moral responsibilities as an obligation to safeguard public health, to protect the interests of future generations, to promote the well-being of society, to obey the law. These multiple responsibilities and obligations will occasionally come into conflict with each other. Even when there is no outright conflict, there may be tensions between competing values which are difficult to reconcile.

This worrying problem is not confined, of course, exclusively to geriatric research. All patients, and certainly all acutely ill patients, are vulnerable to implicit coercion when their personal physician invites them to participate in clinical research. As Berkowitz rightly observes, "[i]t is difficult to imagine that an institutionalized subject or a subject dependent upon his or her physician for treatment and/or relief from suffering, would not be influenced by the care-giver's desire for patient participation in any research proposed."<sup>1</sup> Wherever possible, therefore, the invitation to participate in clinical research should come not from the patient's personal physician or care-giver but from some entirely independent person who exercises no power over the patient. In this way, those whose primary role is to serve as physician care-givers would be distinct from those whose primary role is to serve as researchers. Explicit assurances to patients - that no untoward consequences whatsoever will follow from a refusal to volunteer for research - should also be mandatory. Where credible evidence exists that patients nevertheless feel intimidated, it may be necessary to withdraw the invitation, unless the element of coercion can somehow be successfully counter-acted.

To re-iterate: the primary purpose of research is to contribute to knowledge; the primary purpose of medical treatment is to benefit the individual patient undergoing the treatment. In the case of what is often labeled "non-therapeutic research", the fact that it may be carried out by a medical doctor upon a research subject who happens to be, simultaneously, his/her patient, is coincidental and should be treated as morally irrelevant, for the doctor deals with the subject exclusively in her (the doctor's) role as a scientist.

Unfortunately, in some situations it is exceedingly difficult or even impossible to eliminate role conflicts between the "physician-as-healer" and the "physician-as-researcher". The difficulty is generated partly by the fact that the distinction between therapy and research is often in practice quite blurred. The distinction is less clear-cut than one might wish because of the large number of gradations which exist between the experimental and the therapeutic ends of the medical spectrum. It is sometimes not easy to say confidently whether a particular clinical trial is more accurately to be labeled as "therapy" or as "research". For example, much medical research is explicitly intended to be of direct benefit to the patient, as when a promising new experimental drug is given to cancer patients under controlled conditions with the aim of discovering whether it is more beneficial, overall, than some older drug. Thus, elderly patients who are in the early stages of a dementing process may gain access to a new but promising drug by agreeing to become subjects in a clinical trial of a new therapy designed to slow mental deterioration. Alternatively, or additionally, the elderly patient may benefit indirectly by receiving especially careful medical attention from highly trained specialists.

This activity sounds as if it could properly be labeled “therapeutic”. However, one needs to keep in mind that one of the essential purposes underlying so-called therapeutic experimentation is to contribute to medical knowledge. Procedures may be undertaken, in pursuit of this objective, which are not strictly necessary for the treatment of the patient. When treatment is combined with research systems of treatment are chosen partly with a view to curing the patient but partly, also with a view to testing new procedures or comparing the efficacy of various established procedures. The patient who is also a research subject may thereby be exposed to added hazards, discomforts, or inconveniences. Despite these negative aspects of research, it will sometimes be to the direct and immediate benefit of a patient to become a research subject. (As outlined in the previous paragraph.) The key point to note, however, is that patients who are potential research subjects, especially when they are physically or mentally frail, will typically need assistance in weighing and balancing the competing values involved in any decision to volunteer as a subject. Wherever possible, that assistance should be given by persons whose professional orientation does not put them into a conflict of interest situation.

### The Institutionalized Elderly

When elderly patients become institutionalized, perhaps because of chronic illness or physical frailty, the mere fact of institutionalization should be considered as a liberty-limiting factor: “For example, an individual [who has been institutionalized] may not believe that he is free to refuse participation or withdraw because of fear of subtle discriminatory practices or attitudes among the care-givers.”<sup>1</sup> If some elderly patients do harbor such fears and if, in consequence, their consent to become research subjects is more reflective of a desire to avoid possible untoward consequences than it is reflective of a genuine wish to participate, one would have to say that their consent was coerced rather than voluntary.

There is also a legitimate worry, on the part of those concerned to protect the elderly from exploitation, that the experience of institutional life is likely, for many nursing home residents, to have reduced still further their already compromised ability to engage in autonomous decision-making. Once individuals become acculturated to allowing nurses or attendants to make personal decisions on their behalf, there is a marked deterioration in their sense of efficacy and independence. Thus it comes about that those old people whose physical or mentality frailty has led to their being institutionalized in the first place then suffer from a further reduction in their capacity to function autonomously as a result of paternalistic control from their institutional care-givers. The experience of dependency (on institutional care-givers or family) together with the experience of interdependency (via the peer pressure towards conformity from fellow institutional residents) combine to generate serious doubts about whether they are capable of giving voluntary consent to become research subjects.<sup>1</sup>

On the other hand, participation as a subject for scientific research can be a highly beneficial experience for nursing home residents, even when the research is not intended to be therapeutic for its volunteers. Those who live within such institutions not uncommonly find their lives marked by loneliness, with few opportunities for significant social interaction. Most people, young or old, require such social interactions to thrive, and this is no less true for the institutionalized elderly than for others. Indeed, because the richness of their lives has inevitably suffered as a result of their constrained living circumstances, it is likely to be more true for them than for others. People seem to need involvement with some larger social project or purpose in order to give meaning to their lives. As noted above, the willing participation in a scientific project the goal of which is to advance medical knowledge can be a source of great emotional satisfaction to those who make the choice to become research subjects. For reasons such as these,

there is some weight to the claim that it would be wrong to deny such a potentially worthwhile activity to elderly people solely on the grounds that their lives are lived within a care institution.

Thus, if we keep in mind Freedman's warning that there is a moral cost to over-protectiveness which counter-balances the more commonly noted moral cost attaching to under-protection of vulnerable subjects, we will not automatically conclude that nursing home residents ought to be entirely excluded from the opportunity to decide whether or not to become research subjects. Once the opposing dangers are both recognized, one is compelled to admit that experimentation on elderly nursing home residents cannot be accepted or rejected *uberhaupt*. Some kind of discretionary balancing in each individual case of the likely benefits and harms appears to be unavoidable. But, of course, if it is decided to permit institutionalized elderly prospective subjects to participate in research as volunteers, it might be morally required to set careful limitations to such research.

That is, one might propose that, since cognitive impairment and/or institutionalization increase(s) vulnerability to exploitation, it would be morally desirable, perhaps even morally mandatory, that special restrictions be applied to research carried out using individuals who already suffer with such significant burdens. Hans Jonas, for example, proposes that if it is decided to carry out research using vulnerable people as subjects - something of which he disapproves in any event - then the research carried out must be specific to the disease or disability from which the volunteer is herself suffering.<sup>1</sup> This requirement - that research on vulnerable subjects be "patient-specific" - has now been incorporated into the National Commission's Report and Recommendations in Research Involving Those Institutionalized as Mentally Infirm.<sup>1</sup>

Jonas also proposes a sliding scale of eligibility for recruitment as a research subject. Those who are most knowledgeable about the research, viz., those with membership in the research community itself, should be regarded as the first and most eligible for accrual to clinical trials. Of the entire pool of possible research subjects, physicians are typically the best informed, healthiest, and least vulnerable to coercion from fellow researchers. Thus, they ought to be viewed as the prime group from whom subjects should be drawn. As Jonas rightly notes, there is a long and honourable history of self-experimentation among physicians.<sup>1</sup> If members of the medical community should properly be regarded as the first and the most highly preferred candidates for recruitment as research subjects, the last to be considered for recruitment should be those who are physically or intellectually frail. Those who are highly vulnerable - owing to such factors as their illness, their diminished comprehension or their institutional captivity - are, in consequence, least able to give valid consent and should, therefore, be regarded as the least preferred candidates for recruitment. As Jonas puts the point:

The poorer in knowledge, motivation, and freedom of decision (and that, alas, means the more readily available in terms of numbers and possible manipulation), the more sparingly and indeed reluctantly should the reservoir be used, and the more compelling must therefore become the countervailing justification.<sup>1</sup>

The research ethics policy to which this argument points might be formulated as follows: recruit first among those who are least vulnerable to exploitation; recruit last, and only when absolutely necessary, among those who are most vulnerable.

Moreover, as a matter of general policy, one's reluctance to allow participation by the frail elderly in a clinical trial should increase as the risks to research subjects increase. When research involves high risks of serious harm then one would want to insist with special vigor that the most vulnerable prospective research subjects be placed at the very back of the queue rather than at the front. There is a clear and obvious moral distinction to be drawn between research which involves no more than minimal risks of no more than trivial harms, on the one hand,

and research which is likely to be outright hazardous to many or all of those who participate, on the other.<sup>1</sup> One would also view the accrual of vulnerable patients to clinical research trials with greater sympathy when the research is intended, to a significant degree, to be therapeutic for the patient, and when the patient's non-participation as a research subject carries risks of harm (from the disease) that are of the same order of magnitude as those posed by the research itself. To put the matter crudely, a patient suffering from advanced senile dementia or rapidly metastasizing cancer has "very little to lose" when standard therapy offers virtually no hope of remission or decent quality of life. This is not to suggest that patients suffering from otherwise "hopeless" medical conditions have nothing to lose because of their severe dementia or their imminent death. Participation as a research subject may expose them to such additional burdens, for example, as the discomfort of being poked, prodded and tested. Even the least invasive medical experiments is likely to involve some degree of discomfort or inconvenience, if not the risk or actuality of harm.

Nevertheless, while recognizing the virtue of the sort of carefully restrictive policy advocated by, among others, Jonas and The National Commission, it must be acknowledged, in practice, that for certain kinds of medical research, the only suitable or the only available prospective subjects may be individuals who rank high on the vulnerability scale. That is, for reasons explained earlier, there may be no way to achieve some supremely important advances in scientific knowledge without conducting clinical trials on those whose lives are already heavily burdened by illness and disability. If society is concerned, for example, about the plight of patients whose lives are blighted by senile dementia, or concerned about the fate of long term nursing home residents, it must find ways of facilitating research into both dementia and the quality of care delivered in such institutions. When the research is intended to be therapeutic, then it also holds out the possibility of real benefits to those who voluntarily participate, as well as to future generations of patients. But even when the research has little or no therapeutic potential for its subjects, it may nevertheless produce a significantly favorable surplus of good over bad consequences. Those attracted to the consequentialist approach to ethical decision-making will find such considerations to be of considerable moral significance.

## Informed Consent

Individuals who are considering whether to volunteer as subjects for medical research have to confront what for many is a difficult and complex task: evaluation of the comparative risks and benefits associated with each option. Each person must decide what she stands to gain and what she stands to lose by agreeing or refusing to participate. Physicians are also required to make such case-by-case calculations as a basis for the recommendations they make to patients who are also potential research subjects. But those patients who contemplate becoming research subjects are entitled, legally as well as morally, to undertake their own evaluation of the risks and benefits, and to bring their own attitudes and values to bear in reaching a decision. Individuals who choose to become research subjects ought never to be viewed simply as experimental "raw material". Rather, they are entitled to view themselves and to be viewed by the experimenter as "joint adventurers" or "partners" in the enterprise. Consent makes this relationship possible, and represents the duty of fidelity and loyalty between researcher and subject.<sup>1</sup> The doctrine of informed consent has been accepted widely as a, and perhaps as the, fundamentally important moral requirement for every kind of research on every kind of human subject.

Consent is important, but it must be consent based upon adequate information, communicated in a form which patients can understand. If people agree to become research subjects without having been given adequate

information in a form which they can understand, then they have not really had an opportunity to decide their own fate.

Is there any reason to think that the generally accepted moral standards or principles governing experimentation on human subjects - including the principle requiring that informed consent be obtained from potential research subjects - should be any different for older than for younger people? E.W.D. Young answers this question negatively: "While it is true that the aged have special needs, it is not clear that special ethical principles are needed to respond to the moral dilemmas raised by health care and biomedical research in the aged."<sup>1</sup> Sachs and Cassel agree with this view, claiming that: [T]here are no a priori reasons to treat differently the research participation of older people."<sup>1</sup> They argue that since the vast majority of older people are cognitively unimpaired and live outside controlling institutions, the elderly should not be considered as a special category for purposes of research ethics. The fear is, of course, that if the elderly are classified as a special group in this context, the process of so classifying them may perpetuate, in an ethically undesirable manner, their segregation from general society.

Even if Young, Sachs and Cassel are correct, that is, even if the same moral standards and principles which obtain for research on people of middle age also apply to those who are old, might it nevertheless be true that special regulations are necessary when applying these standards and principles to the elderly? Given that special regulations exist to protect the institutionalized mentally disabled, prisoners, pregnant women, foetuses and children, it would not be a surprise to discover that we also need special regulations to protect elderly research subjects, as a group.

It is acknowledged, of course, that people of whatever age who are cognitively impaired or who are institutionalized or both are especially vulnerable to exploitation. Accordingly, members of these groups require special regulatory protection and special moral consideration. The same is true for such populations as children, or the mentally ill. But, since the category of "elderly people" encompasses a full spectrum of the human condition - from the robustly healthy to the physically frail, from the mentally acute to the mentally confused, and from the living-independently to the institutionalized-dependent - individuals who fall within this category of "elderly" are sufficiently heterogeneous that regulatory bodies are justified in deciding not to treat them as a separate population,<sup>1</sup> or so it is argued.

The appeal of this position derives some of its force from the fact that no one, in these enlightened times, wants to be guilty of the sin of discriminatory stereotyping. Thus, since the majority of older people are cognitively intact and live independently, age may be a factor but it will generally not be the most important factor when, for example, discussing issues of capacity to give informed consent. We could label this "the assimilationist" position, since it insists that no special criteria are needed for the protection of experimental subjects who happen to be old.

A very different answer to our question - "Do we need special ethical guidelines for research on the elderly?" - is offered by Richard Ratzan, who argues in favor of the conclusion that "being old makes you different".<sup>1</sup> The cluster of physiological and psychological changes that are a normal concomitant of the ageing process may well be relevant to the process of obtaining informed consent from elderly people. We could label this view the "special category" position. Ratzan claims that the elderly have different values and weaknesses from the young (and perhaps different strengths, as well). He further claims that when the elderly are invited to participate as research subjects, it is morally wrong not to take special precautions to safeguard their dignity and their autonomy. Empirical evidence is cited in support of the claim that the cognitive abilities of elderly research subjects decline with normal ageing and are often different from those of younger subjects. Comprehension by any elderly subject of the proposed research ought to be viewed as problematic. Memory declines, as does learning ability, when compared

to that of younger subjects.<sup>1</sup> Impaired hearing and vision are also much more common among the elderly than among the young, which can easily result in communication difficulties if researchers do not take special measures, such as large-type print and increased voice volume, when seeking informed consent from potential research subjects who are elderly. Since informed consent forms are notoriously convoluted and legalistic in their language, not to mention esoteric in the vocabulary they employ, and since elderly people have generally had fewer opportunities to undertake higher education and may, in consequence, have a less well-developed ability to comprehend such obfuscatory forms, specially designed forms may be required.<sup>1</sup>

This makes the problem-solving process of informed consent a slower and more arduous process for many elderly subjects than it would be for their younger counterparts. Ratzan concedes that although the problem-solving abilities of elderly people often involve deterioration, at least some of these differences may be regarded as adaptations rather than as impairments. Even so, if researchers are to obtain valid informed consent from apparently competent elderly research volunteers, the researchers must attend carefully to ageing-induced differences and must ensure that the process by which consent is obtained takes proper account of the strengths but also of the weaknesses which old age typically produces in the quality of decision-making.

Strategies which might be employed to facilitate properly informed consent among prospective subjects who are elderly include, for example, having family present at the interview, presenting relevant materials in both written and oral form, and perhaps on video as well, so that it can be replayed later at leisure, simplifying information so that it can be easily comprehended by those with lower educational attainments, ensuring that printed materials employ large print and that voice communications are loud enough to be audible to the hearing impaired, where these are necessary for hearing or sight-impaired individuals and, perhaps most important of all, ensuring, by means of follow-up questions or questionnaires, that the relevant information has been successfully comprehended.<sup>1</sup> One researcher has proposed that it may be necessary, in order effectively to protect the rights of elderly individuals, to employ comprehension tests before participation in research investigations.<sup>1</sup> Of course, such special consideration should be given to all prospective research subjects who suffer from special disabilities, but since the prevalence of such disabilities increases with age, it seems only prudent to emphasize their importance when dealing with an ageing population.

In addition to such potentially important physiological differences between elderly and middle aged populations, there is some reason to think that the old may have an age-distinctive point of view as to what counts as a potentially significant harm, a harm worth taking into consideration when deciding whether to become a research subject. Berkowitz warns, for example, that since concerns about vision and mobility loss typically loom much larger in the minds of most older people than they do in the minds of others, for the obvious reasons, “even a minuscule [sic] risk of vision or mobility impairment may become a material consideration affecting consent and therefore requiring disclosure to this particular population.”<sup>1</sup> In other words, when deciding which risks are materially irrelevant and, therefore, need not be communicated, investigators must take care not to project their own sense of priorities upon elderly potential research subjects. A risk which seems trivial to younger persons may seem significant to the elderly.

In an earlier section of this paper [“Physician-Researcher Conflicts of Interest”], the potentially coercive effect of physicians recruiting their own geriatric patients was discussed. It was noted that valid consent to become a research subject must not only be informed, it must also be voluntary, that is, uncoerced. This entails that those doing geriatric research should pay careful heed to the fact that the lives of elderly people are not infrequently lived within a “pervasive web of dependence”.<sup>1</sup> The dependence of many elderly patients - those living independently but even more so those who have been institutionalized - on their families, friends, neighbors, and on government agencies - to provide them with assistance in living, can easily lead to an attitude on their part of passive acceptance, resignation and compliance.<sup>1</sup> If such an attitude of complaisant passivity is a normal concomitant of the ageing process, then it may often be the case that the consent given by older people to participate in medical

research is not truly voluntary consent. Moreover, as Strain and Chappell note, when compared to younger prospective subjects, the elderly may not be as aware of what is entailed in volunteering to become a research subject, and they may not appreciate fully that they have a right to refuse.<sup>1</sup>

Without falling into the trap of discriminatory stereotyping of old people as a group, it should be possible to recognize that when the old, and especially the very old, are to be recruited for scientific experimentation, it behooves those inviting such participation to take those steps necessary to ensure that the volunteers are truly volunteers and not simply human raw material for the progress of science. If the research community is properly sensitized to those processes of ageing which are most likely to affect an elderly patient's capacity to give valid consent, then those elderly patients who require special protection are most likely to receive it. It is not a bad thing that scientists engaged in geriatric research should receive periodic reminders of the danger that some of the elderly who "volunteer" to participate in medical research may, for one or another of the reasons discussed above, be merely acquiescing rather than properly volunteering to participate. Unless special safeguards are in place, the quality of the consent given by elderly patients must be regarded with some scepticism. This line of argument reinforces the position of those who, like Hans Jonas, wish to eschew the recruitment of old people as research subjects, or at the least accept their participation only after rigorously ascertaining that their consent is fully informed and properly voluntary. On the other hand, it is equally important to stress that those who view the participation of elderly subjects in research as a potential boon to subjects, society, and future generations will not view these objections as insuperable.

When the risks to research subjects are low, and when the harm, should it occur, is trivial, and when the possible benefits to elderly potential research subjects are considerable, many will feel inclined to accept a weak standard of decision-making capacity as adequate to the situation.<sup>1</sup> Thus, an elderly person whose cognitive impairment nevertheless permits some minimal awareness of what is transpiring might nevertheless be judged to possess sufficient decision-making capacity to enable her to assent to participation in a low-risk/high benefit clinical trial, even when the direct benefits accrue to others. [On this point, see also the earlier discussion, in the section titled: "Competence and the Elderly Subject.]

Some may feel that, when proper consent is beyond an impaired patient's capacity, the acceptance of mere "assent" puts us on a slippery slope to ethical danger and degradation. However, the possibility of therapeutic benefit to the individual subject should go at least some distance to offset this moral concern, as would evidence (from family members, say) that the individual, when competent, expressed such values or desires as might count as authorization for participation in low-risk research. The availability of an advance directive giving explicit instructions would, of course, carry more weight still. How much additional weight one ought to assign to such advance directives, with respect to the recruitment of individuals as research subjects, is discussed below.

### Informed Consent by Advance Authorization

If the topic of research on elderly subjects occasions much controversy, the sub-topic of research on incompetent elderly subject generates greater controversy still. The arguments of Hans Jonas, discussed at the outset of this paper, are directed generally against the recruitment for research purposes of patients who are vulnerable to abuse or exploitation. They weigh most heavily, however, against the enrollment of patients who are totally incompetent to give valid consent, patients such as the seriously demented elderly. It seems clear that Jonas would favor a virtually absolute ban on the use of incompetent elderly patients as research subjects. That is to say, on his view, if an

individual, as a result of Alzheimer's disease, stroke or multi-infarct dementia, becomes cognitively impaired to such a degree that she loses the capacity to give or withhold informed consent, then it becomes ethically impermissible to use her as a research subject. Impermissible, full stop. Similar arguments are offered by Paul Ramsey against the use of children for non-therapeutic research,<sup>1</sup> and apply with equal force to patients of any age who are incompetent to give informed consent.

There is no denying the moral appeal of such a blanket restriction. As a result of illness, the incompetent may have lost their autonomy, but this loss, so far from rendering them prime material for exploitation by the rest of society, ought to lead us to respect absolutely such dignity as remains to them. Because the incompetent elderly are typically institutionalized, at least in most advanced western industrial societies, it is often both convenient and efficient to enrol them in clinical trials. But convenience and efficiency, however much such considerations may weigh with harried researchers scrambling to enlist statistically adequate numbers of research subjects, ought to be subordinated to the moral requirement of offering maximal protection to vulnerable populations.

On reflection, however, a blanket prohibition of the sort defended by Jonas and Ramsey seems difficult to defend. As discussed earlier, participation in a clinical trial sometimes offers the possibility of significant health (or other) benefits to research subjects. If we were to prohibit, tout court, the participation of both young children and the incompetent elderly from clinical research, because they lack competence to give valid consent, we would sometimes be denying to them the opportunity to gain important health benefits. It is not impossible, as discussed previously, that participation in a clinical trial could provide subjects with access to some new and highly effective drug treatment - one with the potential to restore a significant level of cognitive functioning to seriously demented patients.

For this reason, even philosophers who strongly agree with a Jonas-like approach to human experimentation, are inclined to permit the enrolment of incompetent patients in those clinical trials which reasonably offer to the patient/subject substantially more benefit than harm.<sup>1</sup> With respect to research having therapeutic potential, it would be unfair to incompetent patients never to allow them to participate. The objective of protecting such patients from harm or exploitation can be achieved by other means, such as allowing a surrogate decision-maker to give or withhold consent on their behalf. Even if society were to adopt an outright prohibition against the participation of incompetent elderly patients as experimental subjects, concern for the interests and well-being of such incompetent patients would require that an exception be made, at least for those clinical trials whose prospective benefits significantly outweigh their likely harms, compared to other alternatives available to the patient. In short, research with therapeutic potential ought not to be ruled out *a priori*.

There is a second reason, closely related to the first, why one should hesitate before endorsing any absolute prohibition against using the incompetent elderly as research subjects. Imagine this situation. A physician-investigator who is treating a patient with early-stage Alzheimer's dementia asks the patient whether she would be willing to give advance authorization to be enrolled later in a clinical trial of a new drug therapy with potential to reverse the dementing process from which she is suffering. That is to say, she is being invited now, while still competent, to give valid consent to her participation at a later time, at which later time her dementia will have progressed to the point that she will then have become mentally incompetent to give valid consent. If the patient refuses to give such advance consent then, of course, it would be a clear violation of research ethics subsequently to enrol her as a subject in such a trial. But if the patient agrees to give such advance authorization, then it would seem to violate both the principle of benevolence and the principle of patient autonomy to refuse to honor such a directive.<sup>1</sup>

The most obvious motive for an elderly patient to give advance authorization to becoming a research

subject would be a present desire to gain future access to potentially effective treatment. But some patients suffering with degenerative diseases which cause progressive cognitive impairment may wish to give advance authorization to their becoming research subjects even when there is little or no prospect of future therapeutic benefits for themselves. They may do so from other motive, such as a desire to benefit future generations or to advance scientific knowledge. If the elderly patient is presently competent to give voluntary informed consent to becoming a research subject, if the patient understands the potential benefits of the research for others and the possible risks of harm to herself, and if the patient wishes now to authorize her future participation in a clinical research trial from such motives as altruism or a sense of social obligation, would it not be a case of unwarranted paternalism to deny the patient this right?

Ronald Dworkin has argued, persuasively in my view, that respect for the personhood of currently-competent patient requires that we continue to respect their autonomously-chosen values even after they have lost their rational decision-making capacity.<sup>1</sup> If, therefore, at a time when I am still capable of formulating a plan for my life as a whole, I give advance authorization for my future participation as a research subject in a clinical trial, others have a moral obligation to respect my current values as an autonomous person by acting upon those desires, even after I have, through cognitive deterioration, lost both my autonomy and my decision-making capacity. In other words, what happens to me after I have lost competence should be governed by the attitudes and values which I have explicitly expressed before losing competence.

However, not everyone accepts the moral legitimacy of this position. Rebecca Dresser, for example, argues that one becomes a quite different person as a result of severe cognitive deterioration. If the demented person is viewed as having become a different person from the person she was when competent, then care-givers of the demented person are bound to consider only her current needs and wishes.<sup>1</sup> The patient has ceased to be the person with the values she once held. She has, instead, become a different person who, although incompetent, has a quite different set of needs and desires from those previously felt and expressed (by the person she used to be). On this view, care givers and researchers are morally bound to assign decisive priority to the fulfilment of these current needs when they are inconsistent with those previously expressed.

Any attempted adjudication of the complex metaphysical issues of personal identity - when does a person cease to be "the same" person? - would be much beyond the scope of this paper. Those who feel the force of Dworkin's appeal to the weight of autonomously-chosen values, will insist that it is obligatory for society to adhere to the demented patient's earlier wishes, at least when the patient's current (demented) preferences do not explicitly conflict with those earlier expressed. The most difficult situations, however, and the ones posing the greatest ethical tension, will be those in which a competent patient has expressed a wish to be treated in a certain manner which that "same" patient, now demented, actively opposes.

Here is one possible example of such a situation. A person, when still competent, exercises her right to autonomous decision-making by directing that she should be enrolled (or continued) in a clinical trial even after her dementia progresses. That person, now demented and no longer capable of rational decision-making, protests strongly against some features of participation in the trial (the need for a daily injection, let us say). This discordance between previous (competently-expressed) and current (incompetent) wishes puts the researchers into an extremely awkward dilemma. If they regard the advance directive of the patient as a kind of Ulysses-contract, instructing them to disregard any later (non-autonomous) changes-of-mind in favor of respecting her current (autonomous) values, then they will feel justified in disregarding the demented research subject's later protests.

The knowledge that one's advance directive will be later respected is likely to provide some degree of comfort to patients, which comfort provides a consequentialist argument in favor of privileging advance directives.

Contrariwise, if they regard the current interests of demented patients as morally decisive, and if they construe those interests as accurately expressed by the patient's protest against participation in the clinical trial, then they will feel obliged to ignore the patient's advance directive in favor of respecting the patient's current experiential wishes. There is, however, an additional factor, of some moral relevance, one which militates against privileging an advance directive over a currently expressed wish. The non-therapeutic treatment of non-co-operative or even actively resisting demented patients, as part of a research protocol, may have difficult-to-measure effects on the morale and well-being of health-care personnel, not to mention possible effects on the family and friends of the incompetent patient who witness or learn of what is happening. If the practice of allowing an advance directive to over-ride currently expressed wishes were to produce distress or lowered-morale for care-givers, family, friends, researchers, then this would provide a consequentialist argument against following the instructions of the advance directive.

To recapitulate. There are several competing ways of conceptualizing this moral conflict. It could be viewed as a conflict between the values of two distinct persons: the autonomous desires expressed by the competent patient while she was still competent, and the current desires expressed by the patient now that she has entirely lost decision-making competence. Conceived in this way, it might seem sensible to ignore the values and wishes of the autonomous person since that person no longer exists and, instead, to respect the current wishes of the demented person.

Alternatively, the moral conflict could be viewed as a clash between the sometimes-competing values of autonomy and benevolence. Conceived in this way, one would have to choose between respecting the (previous) autonomous values of the patient even when following those wishes would cause suffering or distress to the incompetent person she has become, or assigning a higher value to the minimization of present pain and distress, thereby sacrificing her interest in having her autonomous wishes respected even after she has lost autonomy. For a person who cares deeply about making something morally significant out of her progressive dementia and who believes that the best way to do this is to bind her future self, Ulysses-like, to participate in a non-therapeutic clinical trial of a new anti-Alzheimer's drug, the inability to bind herself in this way could seem disrespectful of her autonomy. Moreover, if she now suffers from or feels distressed by the knowledge that her wishes may not be respected after she has ceased to be competent, this suffering/distress would itself count as a consequentialist reason to accept an obligation to respect her autonomy. In other words, if the principle of benevolence is allowed invariably to trump that of autonomy, one consequence could be that additional suffering would be caused to those who feel strongly committed to controlling what happens to them in their post-competent life. Thus, such a policy, although aiming to minimize patient suffering, could be counter-productive.

In the light of such considerations, we might wish to re-conceptualize the conflict as one between two competing assessments of how best to minimize suffering and distress. The problem for care-givers and researchers would then be a practical one: how to assess, consequentially, the comparative benefits and harms of adopting one policy rather than another. It seems likely, however, that there exist wide divergences among individual patients concerning the value they would assign, respectively, to controlling the overall shape of their post-competent lives via advance directives and the value they would assign to promoting their comfort and experiential interest once they have lost competence. This is a seriously complicating factor, since any blanket policy of always assigning a higher priority to one or the other would be guaranteed to run afoul of the value priorities of some individuals. On the other hand, a policy of assigning weight to one or other value on a case-by-case basis, which would take individual differences of value priority into account, would face the possibly insuperable difficulty of discovering for each patient just what they value and how much they value it in various actual and hypothetical situations. This would require eliciting from them information both about the respective weight they assign to the sometimes competing values of autonomy and beneficence and the respective weight they assign to minimizing different kinds of distress.

Jaworska attempts to navigate a passage out of this difficult-to-resolve clash of values (between autonomy and beneficence) by arguing, against Dworkin, that we ought to respect the current interests of demented patients, not because (as Dresser claims) they are different persons from the persons they once were but, rather, because “many of these patients may still be capable of autonomy to a significant degree and that they may still have authority concerning their well-being”.<sup>1</sup> For Jaworska, in contrast to Dworkin, the salient question for those wishing to show respect for an Alzheimer’s patient becomes neither, “Can this patient reason thoroughly and come to a rational decision?” nor “Does he grasp his life as a whole?” but rather “Does this patient still value?”<sup>1</sup>

By “the capacity to value”, she means “the capacity to originate the appropriate bases for one’s decisions.”<sup>1</sup> Consider, for example, how an Alzheimer’s patient might value listening to music “as a way of holding on, as a way to still lead a recognizably human existence despite his disease.”<sup>1</sup> A demented patient is said to be capable of valuing (a critical interest), and not simply of desiring (an experiential interest), if she can give some rationale for choosing the activities she in fact chooses.<sup>1</sup> If, as Jaworska argues, the capacity to value is not completely lost in dementia, then to the extent that it is retained, “respect for the immediate interests of a demented person is contrary neither to his well-being nor to the respect for his autonomy.”<sup>1</sup>

Although Jaworska seems to be advancing a position much different from Dworkin’s, the differences in the end may amount to little more than nuance and subtle shading. Dworkin is concerned primarily with patients who are suffering from late-stage Alzheimer’s disease, patients who invariably lack not only a sense of their own lives as a whole, but lack also what Jaworska calls the capacity to value. Moreover, Dworkin and Jaworska both agree that in the early stages of dementia, a person will still be capable of autonomous decision-making, which capacity imposes on their care-givers an obligation to respect their wishes. Such differences as do exist between their approaches manifest themselves, if at all, only in the middle-stages of dementia, when a patient might possess what Jaworska calls the “capacity to value”, but lack the capacity to formulate a plan for her life taken as a whole, which latter capacity Dworkin associates closely with being an autonomous agent. Even in this middle-zone of dementia, however, the differences between them are, on close inspection, less striking than one might at first expect. Dworkin argues, in the name of patient autonomy, that we should be willing to override the patient’s current preferences when those current preferences conflict with the patient’s previously expressed autonomous life-plan. But, perhaps surprisingly, Jaworska, too, appears to be willing, where appropriate, to allow the demented person’s earlier autonomous wishes to override her current preferences: “The caregiver must learn to pay attention to the person’s values rather than to her concrete, yet perhaps ill-informed selection of options.”<sup>1</sup>

Where they differ, Dworkin and Jaworska, is in this: that Dworkin wishes to privilege the values of a person at that point in time when she possesses sufficient autonomy to lead her life according to her own life-plan, whereas Jaworska wishes to privilege the values of a person at that point in time (presumably much later in the course of the dementing process) when she is capable of self-governance only in the rather more limited sense of possessing some sort of rationale for her preferences. We may, then, she concedes, set aside the expressed preferences in favour of those which more closely fit the underlying value which the patient is seeking to promote.

As between these two conceptions of autonomous decision-making, the traditional one (Dworkin’s) and the revisionist one (Jaworska’s), which is the more defensible? On Dworkin’s conception, we are entitled to ignore Ulysses’ plea to be unbound from the mast, safe in the knowledge that by so doing we are nevertheless respecting his autonomy. We should ignore Ulysses’ currently expressed desire, despite the force and passion with which he both feels and expresses it, and despite the present suffering to him which our refusal entails, because we know that his overall life-plan, formulated in a reflective moment, includes the desire both to hear the Sirens sing and to survive the experience without being lured by siren-song into the whirlpool of Scylla or smashed on the rock of

Charybdis. It would appear, however, that on Jaworska's rather "thin" conception of autonomous decision-making the plea of Ulysses to be unbound would count as autonomous and deserving of our respect so long as he can give us some rationale for his wish to be released.

Well, there is no doubt that Ulysses bound to the mast of his ship, could provide us with reasons or a rationale for his wishes, so Jaworska would, presumably, advocate that we release him to pursue his fatal passion, despite his stringent earlier instructions to do no such thing. For many, this will seem a telling objection to Jaworska's position. The judgement of Ulysses' men - who chose to ignore his current wishes in favor of what they took to his authentic/real/objective/critical/long-term wishes - somehow seems more genuinely respectful of his autonomy than would be the alternative of acceding to his present suicidal pleadings. Conceding, however, that there is some appeal to Jaworska's thin conception of autonomy, at least when one is confronted by an elderly demented patient, one could adopt a policy of allowing individual patients, while they are still competent, to choose for themselves the circumstances in which they would prefer to have their contemporaneous interests set aside in favor of their more reflective (fat-autonomy) interests. That is, those who have begun to suffer from cognitive deterioration but who still qualify as autonomous in the full or strong sense could decide to instruct others whether or not to privilege their subsequent weakly autonomous wishes. Ulysses clearly instructed his men to ignore his subsequent wishes, at least during the period of time when he was under the potentially fatal attraction of the Sirens. But others might wish to instruct their care-givers that they desire to have their choices respected so long as they are capable of giving any sort of reason or rationale for those choices at the time they are made.

Keeping in mind the ethical requirement that research subjects retain the right to withdraw from a clinical trial at any time, each approach would offer a somewhat different answer to the question: at what point does a dementing research subject lose her right to change her mind? For Dworkin, the die will be cast once the subject is no longer capable of formulating a life-plan; for Jaworska it would be when the subject is no longer capable of giving some sort of rationale for her wishes. Deciding when either of these points has been reached in the life of any dementing patient will be a difficult challenge.

Which still leaves unaddressed the question: how should care-givers proceed, with respect to enrolling a currently demented patient as a research subject in a clinical trial when the patient has not given explicit advance instructions, while competent, as to their wishes?

### Surrogate Informed Consent

People who are suffering from a progressive diminution of their cognitive abilities frequently designate a member of their family or a close friend to become their surrogate decision-maker at that point in time when they have lost competence. They may do so formally by vesting durable power of attorney in this person, or informally by indicating to the treating physicians and nurses that so-and-so is the person to whom the medical team should refer when a decision must be made. When a patient's cognitive impairment has advanced to such a point that she no longer seems competent to make important decisions, and when an important health care decision has to be made, it has now become customary for the medical care-givers to seek instructions from a designated surrogate, when one exists. It doesn't seem a very big stretch to assign to a proxy decision-maker the further role of deciding whether to

consent to the patient's participation in research with therapeutic potential, for this continues to fall under the rubric of "health care decision-making". When, however, the question to be decided is whether the incompetent patient should participate in research with hazards for the patient but with little or no therapeutic potential, reluctance to accept a proxy decision is likely to be much increased.

Regardless of whether the decision to be made by a surrogate involves consent to therapy or consent to participation in research with therapeutic potential or consent to become a research subject for a trial which is not intended to be therapeutic for its participants, the key question to be answered is: to what standard should the surrogate appeal in making his decision? The most widely canvassed decision-making standard is one labeled "substituted judgement". On this standard, the role of the surrogate is first to determine what the incompetent patient would herself have wanted and then to instruct the health care providers or researchers accordingly. Suppose, for example, that a surrogate must decide, on behalf of an incompetent elderly patient, whether or not to consent to her participation in a non-therapeutic clinical trial. According to the substituted judgement standard the surrogate should ask himself: What would she (the patient), given her attitudes and values before she became incompetent, have wanted to do in this kind of situation? In this way, the decision which issues from the proxy decision-maker, whether to approve participation or to withhold consent, will be one which seeks to respect the autonomous values of the patient, even though disease has now robbed the patient of the ability to inform us herself about what these values were.

A surrogate decision-maker will sometimes have enjoyed opportunities to discuss with the patient, before her impairment, such issues as the patient's attitude towards participating in clinical trials, with or without therapeutic potential. Such explicit advance discussions are, alas, comparatively rare but, when they occur, they give a surrogate decision-maker confidence that he will be able successfully to represent the wishes of the patient at a time when the patient can no longer represent herself. Much more often, however, there will have been no antecedent discussion between the proxy and the patient about the matter upon which a decision must now be made. The patient herself may not have given much thought to the general question of becoming a research subject, and it is even less likely that she will have given serious consideration to the question of whether she wishes to be enrolled in a clinical trial at a time in her life when she is suffering from advanced dementia. If she has thought about the matter, she may not have reached any clear-cut decision. And even if she has reached such a decision, she is unlikely, as mentioned above, to have communicated it clearly to those close to her.

Thus, although substituted judgement may be widely accepted as the ideal to which health care proxies should aspire, as a practical matter it seems unlikely that proxies will very often possess sufficient evidence to be confident that their decisions on behalf of the patient do indeed approximate closely to the ones which the patient would have made for herself. Empirical research tends to confirm the worrying extent to which surrogate decision-making fails closely to track the decisions that the incompetent elderly would have made for themselves.<sup>1</sup> For example, when a series of hypothetical clinical scenarios concerned with life-sustaining treatment decisions is presented to older adults and their potential proxies, the lack of correspondence between the choices made by the old people and the choices made on their behalf by their potential proxies was significant.<sup>1</sup>

Part of the difficulty, though only part, appears to rest with the kind of question which is, all too often, posed by the physician to the surrogate. The wrong questions to ask are questions such as "What do you want us to do for the patient?" or "What is your recommendation?" Such vague questions focus the surrogates' attention on their own preferences rather than on the patients' previously expressed attitudes and values. They tend, thereby, to elicit answers which diverge significantly from what the patient would have wanted. By contrast, recent empirical research indicates that when proxy decision-makers are explicitly asked to make the choice which they believe the elderly person would have wanted for herself, their answers are not only more accurate, they also have the ancillary benefit of reducing "animosity and discord between family members and physicians".<sup>1</sup>

Because of the difficulties facing surrogate decision-makers in their efforts to ascertain what the patient would have wanted had the patient been competent to decide for herself, the American College of Physicians [ACP], has concluded that the only proper role for the substituted judgement standard is a negative one: surrogates ought not to consent to the enlistment of an incompetent person as a subject for experimentation if there is evidence that the subject herself would have refused.<sup>1</sup> Absent such evidence, surrogates should base their decision to give or withhold consent for participation in research based solely upon what they understand to be in the best interests of the patient. Thus, if a proxy decision-maker knows from prior discussions with the patient that she would have wanted to participate in research, including non-therapeutic research, but the patient is now incompetent and the proxy believes that participation would not be in the patient's best interests, then the proxy ought to ignore the patient's prior wishes and should refuse permission. At least, according to the American College of Physicians.

The strictures of Hans Jonas, discussed at the outset of this paper, exhort us to view incompetent as the least eligible candidates for recruitment as research subjects. Especially when a research project is not intended to be directly therapeutic for its subjects. When the subjects to be recruited are incompetent elderly patients, the moral objection to such recruitment is, indeed, weighty. Wherever and whenever feasible, non-therapeutic research, especially that which involves more-than-minimal risks, should recruit its subjects from within the group of those who are competent to give valid consent to their own participation. The American College of Physicians, in its position paper cited above, adopts a stance which seems on the face of it to be only marginally more permissive than that advocated by Jonas. It declares flatly that surrogates should not consent to non-therapeutic research "which presents more than a minimal risk of harm or discomfort".<sup>1</sup> But the ACP also advocates that a national review body be established "to evaluate and make a final determination on research protocols involving incompetent persons that may not otherwise be allowed under the guidelines set forth here, such as non-therapeutic research which poses more than a minimal risk of harm or discomfort to cognitively impaired subjects."<sup>1</sup>

Critics might want to object that the ACP position on non-therapeutic research involving incompetent elderly patients manages, simultaneously, to be too restrictive and too permissive. It is too restrictive because it prevents a surrogate decision-maker from following the advance instructions of a competent elderly patient who clearly expresses the wish to participate in future non-therapeutic research, notwithstanding the risks which such participation may carry. Since there are significant potential benefits [as discussed above] accruing to individuals who agree altruistically, to participate as research subjects even when the research is not intended to be therapeutic the exclusively negative role which the ACP assigns to the substituted judgement standard could be viewed as a diminution of patient autonomy. The ACP guideline seems less than adequate because the purely negative role it allocates to substituted judgement results in a difficult-to-defend slighting of the earlier attitudes and values of the now-demented patient. In this regard, the guidelines for non-therapeutic research, as proposed by Wicclair, seem ethically more satisfactory: "For research without therapeutic potential, surrogates should be instructed that they may consent if ...considering the nature of the proposed study, the potential benefits and harms to subjects, and what is known about the cognitively impaired person, they can reasonably conclude that the person would have consented..."<sup>1</sup> As a safeguard, Wicclair sensibly proposes that "the reasoning of surrogates should be scrutinized by persons who do not have a vested interest in recruiting subjects."<sup>1</sup>

A further ethical doubt about the ACP proposed guidelines for non-therapeutic research on incompetent patients arises when one considers the scope for abuse inherent in their proposal that a national review body be established which would have very broad decision-making powers. It is more than a little worrying, for example, that the national review body would have the power to approve the recruitment of incompetent elderly patients for highly risky clinical trials absent any strong evidence that the patients, while still competent, gave explicit authorization for such participation. Where the research is not intended to provide health benefits to the patients

who become subjects, and where the risks of harm or discomfort to vulnerable subjects are more-than-minimal, it would seem ethically mandatory to eschew the recruitment of such incompetent patients unless one had solid evidence that they had given advance authorization for such participation. Guidelines which do not absolutely require such advance authorization run the risk of undermining the social contract between citizens and society, and raise the possible specter of vulnerable patients being unjustly exploited as “guinea pigs” solely for the benefit of others.

## Conclusion

As this *tour d’horizon* has made clear, it is no easy matter to chart an ethically defensible course through the minefield of problems which fit under the label “the ethics of research on elderly subjects”. Striking the right balance between such competing objectives as promoting socially important medical research, on the one hand, and protecting the dignity and the interests of vulnerable elderly patients, on the other, requires that each god being given his or her proper due. If our sole objective were to encourage the most rapid possible development of effective therapies for the diseases which afflict an ageing population, we would view restrictive guidelines as “bureaucratic red tape”, and would favor maximal de-regulation. We would favor a policy of loosening or eliminating governmental “fetters” so that the medical/scientific research community could “get on with the job”. If, on the other hand, our sole objective were to provide maximal protection against harm to elderly patients, especially those who are vulnerable because cognitively impaired, we would favor total exclusion of such patients from the pool of those eligible for non-therapeutic research.

Simplicity has its attractions, but both of these positions, when stated in such an over-simplified way, become self-defeating. A society which stressed the importance of research but which neglected to stress the rights and interests of potential research subjects would be one in which the research enterprise itself would fall into such disrepute that the stream of both volunteers and financial support on which it crucially relies would dwindle markedly. However much the public might cheer new research advances, public confidence in the moral integrity of the research process is a frail plant which could easily sustain damage if the research process came to be seen as exploitative of the most vulnerable members of society. On the other hand, the protection of potential research subjects, especially those who are most vulnerable to harm because of their cognitive impairments, could easily mutate into the sort of paternalistic over-protectiveness which destroys the very autonomy it seeks to respect and thereby undermines the best interest of the elderly it purports to defend.

The task of negotiating the right balance between such competing foundational values is almost certain to be an ongoing process. Solutions which elicit broad public support at one historical juncture may require to be modified in the light of changing public attitudes and values. Shifts and modest changes of emphasis are to be expected and should be welcomed as part of healthy social evolution. What can be confidently concluded is that any social policy which pursued either objective - promotion of research or protection of research subjects - without serious regard to the other, would be self-defeating. A society which eschewed medical advance in the fight against debilitating disease would be as unappealing as one which set no moral bounds on the pursuit of such advance.

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71. Uhlmann, R. F., R. A. Pearlman, & K. Cain. "Physicians' and spouses' predictions of elderly patients' resuscitation preferences." *Journal of Gerontology* 43. 1988.
72. Zweibel, N.R., C.K. Cassel. "Treatment choices at the end of life: A comparison of decisions by older patients and their physician-selected proxies," *The Gerontologist* 29. 1986. See also Uhlmann, *op. cit.*
73. Tomlison, Tom, Kenneth Howe, Mark Notman & Diane Rossmiller." "An Empirical Study of Proxy Consent for Elderly Persons." *The Gerontologist* 30, no.1.1990.60
74. American College of Physicians, "Cognitively Impaired Subjects," *Annals of Internal Medicine* 111, no. 10. 1989. The policy advocated in this position paper would cover such cases as those reported by Warren *et al* [Warren, J. W., J. Sobal, J.H. Tenney et al, "Informed Consent by proxy: An issue in research with elderly patients." *New England Journal of Medicine* 315. 1986], in which proxies gave consent for their relatives to participate in research despite their belief that the relatives would not themselves have consented when competent.
- preclude a proxy from giving consent to participation in research when the proxy believes that the patient would, when competent, have refused to participate. It would

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75. American College of Physicians, *op. cit.*, p. 844-845.

76. *Op. cit.*, p. 846.

77. Wicclair, *op. cit.*, p. 182.

78. *Loc. cit.*