

Vulnerable Adults in Research: A Tale of Two Regulations

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1. Introduction

Some scientific advances can become realities only with the help of vulnerable people who do not have legal capacity to consent to research. When dealing with legally non-competent adults, practitioners consider the patient's own wishes more than ever before, and so they have pioneered the practice of seeking what has become known as their 'assent' before treating them. Assent has been defined as a person's 'permission or affirmative agreement to something'. People who do not possess sufficient capacity to make a particular decision entirely on their own may nonetheless have certain psychological and cognitive abilities. Including such people in decisions that affect them directly, without necessarily handing the decision over completely, has certain intuitive appeal. Indeed, in many national and international guidelines on research using vulnerable populations, we see the widespread use of this new term, albeit one without the legal heritage of 'consent'. In common parlance, 'assent' can mean the same as 'consent' namely an expressed agreement to something. However, it has recently taken on a more technical, if not yet legal, meaning which appears to be distinct from consent in important ways. In particular, the term 'assent' now appears separately from 'consent' in certain national and international guidelines on how research. For example, assent has primarily and predominantly been used in guidance on research using children although in some documents, the term is applied to any patient lacking capacity including adults. For example, the World Medical Association's 2000 version of the Declaration of Helsinki states in Article 25:

"When a subject deemed legally incompetent, such as a minor child, is able to give assent to decisions about participation in research, the investigator must obtain that assent in addition to the consent of the legally authorized representative."

The rise of the notion of assent, at least in research, is an attempt to remedy the developmental and psychological error in the view that adults can be classed simply as either mentally competent or not.

The problem for those who govern research is how such involvement should be observed and how much weight should be attached to its outcome. There are particular difficulties identifying the values enshrined in the statutory requirements on how vulnerable adults can be used in research. In particular, the Mental Capacity Act 2005 (MCA), which is expected to be in force in England, Wales and Northern Ireland in April 2007, applies to any 'invasive' research, except clinical trials of drugs which fall under the Medicines for Human Use (Clinical Trials) Regulations 2004 (CTR), implementing the European Directive 2001/20/EC. The patient's wishes are important to the final decision regarding research entry but they carry different weights and seem relevant for different reasons.

In this paper, I seek first to identify the ways in which such patients in clinical trials are treated differently from other non-competent patients. Importantly, I will show that such patients do not have the same right to veto the research yet curiously may have more information upon which to base any objection. I will then seek to shed light on such differences by appealing to the rise of human rights, yet conclude that the rules relating to researching non-competent adults are open to legal challenge.

2. The Assessment of Mental Capacity

There are three main approaches to the assessment of capacity, namely by status, outcome, or function. In other words, a person could be viewed as lacking capacity by virtue of their status or state, the decision he makes, or an analysis of the components of the process he goes through to make this decision. Capacity also refers to the particular decision in question although a person will often be incapable of making certain types of decisions or may even be completely incapable, perhaps because unconscious, either permanently, temporarily or intermittently. The temptation could be to approach assessing capacity by looking at the status or medical condition of a person or the actual decisions he makes rather than the process through which he makes it.

Adults are presumed to be competent unless proven otherwise through a legal test, which was introduced in English common law and later clarified with advice from the Law Commission. This test relates to a particular decision at a particular time and was laid down by the *Re C* ruling in 1994. This case concerned a schizophrenic patient who refused to have his leg amputated when it became gangrenous. He was judged to be legally competent to refuse this treatment despite his delusional belief that he was a world class surgeon. The Mental Capacity Act 2005 now sets out a single statutory test for assessing capacity in adults, anyone over the age of 16 years, and applies to many types of decisions in finance and healthcare. This test is as follows:

A person is unable to make a decision for himself if he is unable:

- a) to understand the information relevant to the decision;
- b) to retain that information
- c) to use or weigh that information as part of the process of making the decision, or
- d) to communicate his decision (whether by talking, using sign language or any other means).

The last element is technically new to the Act although practitioners would probably manage a patient unable to convey any of his wishes as effectively non-competent and would treat him on that basis.

Also new to the Act is the requirement to take 'all practicable steps' to help the person make his own decision perhaps by using memory aids or different communication techniques. It remains to be seen how this will affect practice although advocacy groups may be used more frequently to facilitate decision-making where difficulties arise. At this point, I should also make the legal distinction between consent on the basis of a patient's 'broad understanding'

gleaned from *just* enough information to avoid the charge of battery, and consent on the basis of fuller detail required to avoid negligence. It is unclear whether the Act would encourage consent on the solely on the basis of the former.

The Mental Capacity Act protects a person's valid and applicable 'advance decision' made before losing capacity, provided the person is over the age of 18 years when making it. These decisions usually relate to refusing certain treatments such as life prolonging measures but they could theoretically take the form of specifically refusing future research participation. A simple refusal at one point in time may not be an applicable advance decision unless the new circumstances are specifically foreseen. In all cases of advance decision-making, there are well-rehearsed philosophical and regulatory problems. For example, it is ethically legitimate in the standard case of an autonomous person to be able to change one's mind, although not where the evidence is that the change of mind was whimsical and not made with appropriate reflection. The Mental Capacity Act also speaks of 'advance statements' which give more general indication of the person's wishes and are less legally binding in specific cases.

The Mental Capacity Act 2005 thus provides a general approach to assessing mental capacity. For example, advance decisions regarding refusal of research participation would arguably include clinical trials of drugs. The Act however includes certain provisions for medical research which exclude clinical trials. I will discuss this exception, but first I will briefly describe how patients who are deemed non-competent are treated under the above Act.

3. Treatment of non-competent adults

In the absence of any advance decision, someone must judge what action would serve the 'best interests' of the patient. This decision rests with a previously appointed Attorney, if one is named and nominated by the person whilst still competent. Attorneys may be nominated jointly or severally and they cannot delegate the tasks to anyone else but retain the right to refuse or withdraw at a later date. If no one has been nominated, the person with the duty of care is then in a position to determine the patient's best interests. And in the event of disagreement, the ultimate arbiter would be the Court of Protection.

A legal analysis of best interests will identify a contestable concept of which one conception could take the longer term wishes of the patient into account such as in cases of donating an organ to a sibling. I submit that there are conceptions of 'best interests' that go much further and equate a person's best interests with the interests of others and society. Crucially, Article 3 of the Human Rights Act 1998 cannot be compromised in the public interest.

Section 4 of the Mental Capacity Act seeks to make the determination of best interests more explicit and hence open to analysis. 'Best interests' is supposed to be 'objective' test. The following list of considerations is presented in no particular order of priority.

The decision-maker should consider if and when the patient is likely to regain capacity, without giving any specific rules in this regard. The idea is that the patient's situation might somehow be suspended until such time as he can make his own decisions. Firstly, this is given no explicit priority within the criteria perhaps since in borderline cases of capacity, the patient's values may not change significantly over time and with slightly greater understanding. However, it is clearly a predication about capacity based on a person's condition. Secondly, the situation would then have changed and the decision to be made would therefore be a different one. Indeed, a patient's capacity may be regained *because* of a particular treatment given.

The next condition is negative in the sense that it confers duties on decision-makers to assess best interests but *not* on the basis of age, appearance or condition *alone*.

"(1) In determining for the purposes of this Act what is in a person's best interests, the person making the determination must not make it *merely* on the basis of-(a) the person's age or appearance, or (b) a condition of his, or an aspect of his behaviour, which might lead others to make *unjustified* assumptions about what might be in his best interests." (italics added)

However, this contradicts the first requirement to judge it is the patient's best interests to suspend treatment decisions on the basis that his *condition* may improve such that he may regain capacity. That is unless it is considered along with other factors I will discuss in a moment.

Before I do, it is worth noting that this section implies that age, appearance, and a patient's condition could be considered when determining best interests. It simply states that one *or* other would not be sufficient. The use of the conjunction 'or' suggests that it could be sufficient to determine best interests on the basis of the two characteristics *together*, e.g. the patient's age *and* medical condition.

In addition, are the relevant conditions referred to in (b), *only* those which lead to *unjustified* assumptions about best interests? If so, the requirement is tautologous: an *unjustified* way of determining best interests is to consider conditions which lead to *unjustified* assumptions about best interests.

However we choose to think about best interests, it is clear that getting the cooperation of the patient is less likely to be distressing for them and so would *prima facie* be in their best interests. The patient's current wishes and involvement are now an integral part of the determination of 'best interests'.

"(4) He [The person making the determination of best interests] must, so far as reasonably practicable, permit and encourage the person to participate, or to improve his ability to participate, as fully as possible in any act done for him and any decision affecting him... (6) He must consider, so far as is reasonably ascertainable- (a) the person's past and present wishes and feelings (and, in particular, any relevant written statement made by him when he had capacity), (b) the beliefs and values that would be likely to influence his decision if he

had capacity, and (c) the other factors that he would be likely to consider if he were able to do so.”

The person making the determination of best interests is also required to consult a number of key people to inform this determination.

“(7) He must take into account, if it is practicable and appropriate to consult them, the views of-(a) anyone named by the person as someone to be consulted on the matter in question or on matters of that kind, (b) anyone engaged in caring for the person or interested in his welfare, (c) any donee of a lasting power of attorney granted by the person, and (d) any deputy appointed for the person by the court, as to what would be in the person's best interests and, in particular, as to the matters mentioned in subsection (6).”

4. Research provisions under MCA

Any decision made on behalf of a non-competent adult must be made in the patient's best interests under the Mental Capacity Act 2005. The expected benefits of research must be thought to outweigh the risks such that the research is ‘therapeutic’.

“(a) have the potential to benefit P without imposing on P a burden that is disproportionate to the potential benefit to P”

There are provisions for doing non-therapeutic research using such people although the degree of risk is capped to ‘negligible’ such that the ‘best interests’ standard is not obviously compromised. ‘Non-therapeutic’ research could be compatible with a person's best interests as it is now described widely by the Act although whether it is in a person's best interests to contribute to medical knowledge is currently contentious.

“(b) be intended to provide knowledge of the causes or treatment of, or of the care of persons affected by, the same or a similar condition....(a) that the risk to P from taking part in the project is likely to be negligible, and (b) that anything done to, or in relation to, P will not- (i) interfere with P's freedom of action or privacy in a significant way, or (ii) be unduly invasive or restrictive.”

The Act expressly permits an adult to continue to participate in a study in the event of losing the capacity necessary to give consent. Conversely, it is reasonable to suppose that a person could at first refuse while competent but then relent once capacity is lost and assent to further research proceedings. Either way, the less capacitated a person becomes, the less reliable the test. The moral weight should *prima facie* be given to the ‘most autonomous’ decision.

Legislators have sought to avoid the charge that a patient's agreement was mere compliance with what had already been deemed to be in their best interests. Despite including the patient's wishes in this determination, assent effectively means merely complying with what the real decision-maker considers ‘necessary’. However, despite non-competent patients

being encouraged to 'participate' in the decision-making, there is still a real possibility that the patient may not have any proper information, knowledge or understanding of their situation. I think that there should be a louder echo of consent here at least in terms of what information patients are given, a point we will return to in relation to clinical trials.

Strangely, much weight is given to any dissent (opposite of assent), even when the research is generally thought to be 'therapeutic' and the patient has little or no ability to understand the situation. Section 33 clearly indicates that any objection is a veto and yet lays down no conditions such as informing the patient according to their level of understanding as in clinical trials.

"(2) Nothing may be done to, or in relation to, him in the course of the research- (a) to which he appears to object (whether by showing signs of resistance or otherwise) except where what is being done is intended to protect him from harm or to reduce or prevent pain or discomfort... (4) If he indicates (in any way) that he wishes to be withdrawn from the project he must be withdrawn without delay." (italics added)

Notice that 'assent' is the mere absence of an objection. Interestingly, the European Convention on Human Rights and Biomedicine (which the UK has not ratified) does not use the language of 'assent' but does give an non-competent person a similar veto power without the need to provide appropriate information, require any understanding on his part, or obtain an active endorsement of the project.

"Research on a person without the capacity to consent...may be undertaken only if all the following conditions are met... and the person concerned *does not object*." (italics inserted)

This veto, we will see, is in sharp contrast to the rules relating to drug trials where a patient's wishes need only be *considered*, yet at least these wishes must be informed to a greater or lesser extent.

The exception to respecting a dissent under the Act is relevant only to preventing pain or discomfort rather than actively benefiting the person. Apart from these circumstances, any dissent seems to trump even the judgement of a nominated Attorney, any advance decisions in this regard, and/or an initial consent to participate before capacity is lost. This clearly makes the difference between research and routine practice fundamentally important. A person making the judgement of best interests may have potentially conflicting interests although must not importantly be connected with the research. It is at least clear whose interests should come first and the decision-maker must consult a range of interested parties. No one view must take priority. But what is lost in transparency of process is gained in the scope and depth of the evidence sought.

The Clinical Trials Regulations 2004

Drug trials are exempt from the Mental Capacity Act 2005 as they are covered by the Clinical Trials Regulations 2004.

11. The clinical trial relates directly to a life-threatening or debilitating clinical condition from which the subject suffers.

Unlike the Act, the CTRs do not distinguish explicitly between therapeutic and non-therapeutic research.

9. There are grounds for expecting that administering the medicinal product to be tested in the trial will produce a benefit to the subject outweighing the risks or produce no risk at all.

And rather than to try to put a cap on risk, the regulations speak of 'minimising' it.

13. The clinical trial has been designed to minimise pain, discomfort, fear and any other foreseeable risk in relation to the disease and the cognitive abilities of the patient.

Despite using the notion of assent, the treatment of non-competent adults is approached differently by the CTR. While not referring to the term 'assent' explicitly, the CTRs certainly use the concept under section 5 of schedule 1 on non-capacitated adults.

6. The subject has received information according to his capacity of understanding regarding the trial, its risks and its benefits.

Assent appears to be much more active and explicit than under the Mental Capacity Act.

7. The explicit wish of a subject who is capable of forming an opinion and assessing the information ...to refuse participation in, or to be withdrawn from, the clinical trial at any time is *considered* by the investigator.

Notice that any 'assent', while appropriately informed accordingly to the person's ability to understand, must merely be *considered* by the principal investigator. It does not have to be respected in the sense of ultimately deciding the matter. The result is an unsatisfactory merger of this test of assent (not 'full' consent) and evidence that the test has been met (the genuine 'considered' opinion that the patient has assented).

While the CTRs seem to protect the person's current wishes less vigorously than the MCA, despite requiring more information giving and more active endorsement, there is the added protection against incentives.

8. No incentives or financial inducements are given to the subject or their legal representative, except provision for compensation in the event of injury or loss.

A 'legal representative' must make a decision over what a person would have wanted had they the capacity to choose for themselves. In other research, however, a person if already nominated by the subject whilst competent should be consulted not to make a 'substituted judgement', but to help determine their 'best interests', despite there being more emphasis under the Act's research provisions for determining the patient's hypothetical wishes.

"P's wishes and feelings about taking part in the project would be likely to be *if P had capacity* in relation to the matter."

The participation of non-capacitated people in drug trials requires a 'substituted judgement' which, rather than relying on the determination of best interests, does so by a form of constructive consent which attempts to respect the incompetent patient's hypothetical autonomy which could theoretically put their best interests at risk. There are further difficulties with the idea of substituted judgement designed to construct some form of autonomy from a hypothetical will.

For clinical trials, 'legal representatives' of adult patients must also make a decision about the participation of people without capacity and they need only *consider*, not necessarily respect, the patient's actual wishes on the day, even if they dissent. Such representatives are legally charged with representing the 'presumed will' of the patient and, as this is drafted separately from the non-competent patient's *actual* wishes, it must be their *hypothetical* will.

"The informed consent of the legal representative has been obtained; consent must represent the person's presumed will and may be revoked at any time, without detriment to the person...."

This requirement is crucially not a determination of 'best interests' in any objective sense and it is unclear how the legal representative can 'presume' someone else's will. We suggest that it requires a judgement of what the patient would have wanted had he the full capacity to make up his own mind and is thus a form of 'substituted judgement'.

A substituted judgement makes most sense when there is some information about the patient concerned but this information could fall well short of an advance decision or statement about a specific event or when there is knowledge of the patient's dispositions whilst competent. An inference however may be made about what he would have wanted in a particular situation now arising. A close relative or friend is usually in the best epistemological position to make this judgement usually having inside information about the patient's likes, dislikes, personality and life-style. Such representatives are called 'personal representatives' under the Regulations. In the famous American end-of-life case, *re Quinlan* (1976), there was some 'evidence' of the patient's wishes when competent although apparently not sufficiently objective and specific to be a formal 'advance directive'. Then in a subsequent case *re Spring* (1980), from which the term substituted judgement comes, there were no specific advance discussions with the patient when he was competent and so the relatives had to make inferences from knowing his other preferences under different conditions. However, substituted judgements have well-documented limitations. The use of such judgements falls down principally because of practical difficulties in obtaining sufficient knowledge or evidence of *actual* preferences while competent in any given situation especially when a person has not yet gained, and may never gain, full or sufficient capacity.

The more unusual cases further underline the fundamental philosophical problem with 'substituted judgement' which become increasingly hypothetical and arbitrary the more 'distant' the decision maker. Here, effectively a complete stranger must choose on his behalf

according to the so-called 'reasonable person standard'. Indeed, in a further American end-of-life case, *Superintendent of Belchertown State School v. Saikewicz* (1977), the patient had never been competent and the decision was therefore based on the relatives 'best guess'. Under the Clinical Trial Regulations, where a personal representative cannot be found, a 'professional' representative may step in and this person, usually a doctor at the same hospital, may know nothing about the patient concerned. It may thus be possible to justify any number of choices on the grounds that a 'reasonable person' could have made them, including crucially some sacrifice for the public good. It is not clear what 'reasonable' limits might be imposed on such judgements.

Along with epistemological difficulties, there are similar problems associated with the legal representative having potentially conflicting interests. The very reason why a legal representative was introduced was to try to solve the problem of the doctor-researcher alone making this decision and his having potentially conflicting interests to his patient and to his science. The way to resolve such a potential conflict is to get an *independent* view, although enlisting the help of a personal or professional legal representative is unlikely to achieve this in practice. While relatives may know the patient personally, they may have ulterior motives and, when a personal representative cannot be found, a professional representative, who may be the doctor with the duty of care towards the patient or someone else from the health service, may also have the economic interests of the research institution at heart.¹ Research may not be in the best interests of the patient and simply asking a legal representative may not adequately protect them. The Mental Capacity legislation seeks to address this problem by putting the patient's best interests at the centre of their care whether in routine treatment or research and gives weight to a decision by someone already nominated and trusted by the patient.

5. Human rights and research regulation

It is not enough to identify the apparent differences in approach to non-competent adults. We must also seek to explain where these differences spring from and what their implications are for future policy and practice. I suggest that the human rights movement can both explain the mere fact that there are differences and maybe offer clarity and coherence in the longer term.

The Human Rights Act 1998 explicitly incorporated the European Convention for the Protection of Human Rights and Freedoms into domestic law, despite the UK having been a signatory of it since 1951. The delay, it is claimed, was due to the fact that common law already offered the requisite protections and hence statute was unnecessary. However, now the Act has taken effect, it certainly offers new challenges for legislators and judges and is both a fundamental and overarching statute having no less a status than as part of the English constitution itself. Domestic law must at least be 'compatible' with the Human Rights Act 1998 although Parliament is still the supreme power and the courts can only declare an incompatibility where one arises in the normal expectation that the legislature will affect a remedy by changing offending domestic practice. The language of human rights has been couched and debated in both moral and legal terms and certainly heralds a new yet evolving

culture. In short, while individual members of society have enjoyed certain rights for a long time, since 1998 these rights have become more explicit and enhanced.

Individuals thus have certain legal rights simply by virtue of being human. This means that vulnerable populations have the same rights as everyone else, of which some are absolute while others limited or qualified. It is in this context that we must attend to the moral and legal status of the patient who lacks legal capacity to make decisions for him or herself. The common law defence of 'consent' in circumstances of medical treatment and research is thought to rest within this Article 8 on liberty. However, in order to give consent, the patient must have further legal status and be recognised as a 'legal person' who is the paradigmatic legal actor who can 'sue or be sued'. This longstanding legal and culturally entrenched notion of a 'person' presupposes that s/he has moral status in the sense that s/he can carry full rights and responsibilities and is fully autonomous. Moral philosophers have traditionally ignored the issue of incapacity preferring instead to examine the 'standard case' of the perfectly rational and reflective agent, although they might disagree on the precise conditions which need to be met in order to reach a genuinely autonomous decision. This omission has had a lasting legacy.

In order not to set the benchmark too high and so exclude most of the population, the mental faculties needed to count as a full legal person in practice are not onerous. This benchmark is laid down by domestic law and, while it is 'functional' in the sense that it looks only at abilities relating to a particular decision and not at biological, social or political status, it certainly rests absolutely on moral status which itself is contentious. 'Personhood' remains hotly debated, as does the notion of 'potential' person.

The defence against a charge of violating Article 3 during medical treatment and research for a person who lacks such capacity is one of 'medical necessity' and hence best interests. However, Article 14 of the Human Rights Act 1998 prohibits discrimination on any ground such as sex, race or any other status and, when used in conjunction with Article 3 on prohibiting torture, there may speculatively be a future challenge to the way people with marginal, borderline, or fluctuating capacity are viewed by the courts especially where potential capacity can be established. And freedom from discrimination is a significant step towards achieving equality of respect for all, although discrimination may be difficult, and arguably unnecessary, to prove when there are no obvious comparative groups. The vision of human rights goes further and includes ideas such as 'dignity', an idea I will revisit later.

As human rights become more embedded into practice and the courts look further to external treaties and good practice guidelines, the interpretation of rights means they can still 'grow' albeit slowly and incrementally. For example, the Convention on the Rights of the Child may be particularly influential in terms of giving children an articulated and public voice and including them in all decisions that affect them. The really interesting arguments will thus be in the implementation of the Act by the courts. Indeed, we have already seen that the longstanding notion of a legal person was reborn in the ruling over transsexuals changing their birth certificate and adopting new legal relationships as a result such as marriage. I argue that people lacking mental capacity should be offered greater involvement in decisions about medical research and this argument provides moral coherence with the substance of

Conventions and treaties external to the Human Rights Act 1998. However, we have seen that there are difficulties in placing the new idea of 'assent' within the traditional ethical notions of 'autonomy' or 'best interests' although it categorises more agreeably with an emphasis on the moral rights of the person. Assent originates from less formal and legal research guidelines which in turn reflect what is currently seen as 'good practice'. Now allied with human rights, assent is arguably more a matter of protecting 'dignity' than respecting autonomy. The concept of dignity has been used in a variety of ways but is always taken to be a characteristic of humans as a species.

"Dignity...is...an expression of an attitude to life which we as humans should value when we see it in others as an expression of something which gives particular point and poignancy to the human condition. By its nature, dignity can be neither pursued nor used, but only lived, fostered, enhanced and admired."

There is a sense in which dignity is universal and objective and became legally important, particularly in continental Europe, following World War II. The law seeks to identify a 'circle' of rights which may help to protect such life underlining its importance.

"True it is the phrase [human dignity] is not used in the Convention but it is surely immanent in Article 8, indeed in almost every one of the Convention's provisions. The recognition and protection of human dignity is one of the core values – in truth, *the* core value – of our society...

People who lack the capacity to make decisions for themselves nevertheless possess human dignity in this sense. We might argue that simply respecting a person's current wishes by seeking their assent does not adequately protect their dignity and that respecting advance decisions and protecting their best interests are also important. The differences we have described in moral and legal approaches to incapacitated people should serve to emphasise the problems in viewing the ethics of research in terms of promoting human dignity with a protective circle of rights. While there is a wide consensus that everyone has dignity, it is less clear how individual human rights could and should be used to protect it.

Culturally and politically, we have seen movement in the way people lacking legal capacity are viewed,² and this should create more philosophical, psychological and public policy interest in the decision-making abilities of people with limited or fluctuating capacity and motivation in developing ways of facilitating or even sharing decisions. Ultimately, however, it will be left to the courts to rule when current regulation is challenged on the grounds on human rights.

6. Conclusion

In conclusion, while legislators, the courts, and policy-makers have attempted to place research using people lacking capacity in line with practice, there are significant differences in regulatory approach which seem to belie different values. The desire to get 'consent' is very strong in practice and, when a person is not able to give it, practitioners naturally look

for the next best thing. However, the emerging notion of assent does not fit neatly with the traditional notions of autonomy and best interests and will need illuminating in the future when the existing rules are challenged. Importantly, I have shown that non-competent adults have the power of veto in non-trial research yet may not have adequate information upon which to base this decision. In contrast, any objection in a clinical trial may not be decisive yet may be better informed. I have argued that there should be a louder echo of consent here at least in terms of information giving according to the patient's level of understanding.

Additionally, there are different people who make the decision about research participation in trials and non-trial research respectively. In trials, personal or professional legal representatives try to construct an incompetent patient's 'autonomous' wish and this is problematic not least because such a wish is hypothetical and also because they may have potentially conflicting interests. In non-trial research, the person with the duty of care must make a judgement of best interests although it is by no means clear what this really means.

Such differences in regulation may be explained by a desire to promote human dignity and to protect it with a circle of human rights. However, there remain many questions over how this can be achieved, if at all, and we now wait for the courts to make their judgements and lead the way.

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