



Newcastle University ePrints

Woods S, McCormack P. [Disputing the ethics of research: the challenge from bioethics and patient activism to the interpretation of the Declaration of Helsinki in clinical trials.](#) *Bioethics* 2013, 27(5), 243-250.

Copyright:

This is the pre-peer reviewed version of the above article, which has been published in final form at:

<http://dx.doi.org/10.1111/j.1467-8519.2011.01945.x>

Always use the definitive version when citing.

Further information on publisher website: <http://onlinelibrary.wiley.com>

Date deposited: 23rd July 2013



This work is licensed under a [Creative Commons Attribution-NonCommercial 3.0 Unported License](#)

ePrints – Newcastle University ePrints

<http://eprint.ncl.ac.uk>

Disputing the ethics of research: the challenge from bioethics and patient activism to the interpretation of the Declaration of Helsinki in clinical trials.

ABSTRACT

In this paper we argue that the consensus around normative standards for the ethics of research in clinical trials, strongly influenced by the Declaration of Helsinki, is perceived from various quarters as too conservative and potentially restrictive of research that is seen as urgent and necessary. We examine this problem from the perspective of various challengers who argue for alternative approaches to what ought or ought not to be permitted. Key themes within this analysis will examine these claims and argue they have implications for the interests of the research subject, research governance and regulation. Using our work with TREAT-NMD, the neuromuscular clinical trials network, we posit that there is a place for advancing the discourse of moral rights and moral duties in the context of research especially from the perspective of patients and their families, and for including the politics of patient activism and empowerment. At the same time we remain vigilant to the danger that the therapeutic misconception and other serious vulnerabilities for the patient population in clinical trials, are at risk of being overlooked.

177 words

BACKGROUND

TREAT-NMD is a European Network of Excellence which was formed to advance diagnosis and care and develop new treatments for neuromuscular disease (NMDs) – genetic conditions causing progressive muscle wasting and often, early death. There are over 60 neuromuscular conditions, most of which do not have a cure or an effective treatment¹. The severity of these diseases is highly variable and TREAT-NMD has initially focussed on two of the most severe, Spinal Muscular Atrophy (SMA) and Duchenne Muscular Dystrophy (DMD). Both are chronic, complex, rare conditions², normally diagnosed in childhood, which leave people fully dependent on care. With the severest form of SMA babies die in their first year and people with DMD have foreshortened lives, typically dying in their twenties. Although some studies report good quality of life among people with muscular dystrophy³, more often people with the

¹ M. Pohlschmidt & R. Meadowcroft. 2010. Muscle Disease: the impact. Incidence and prevalence of neuromuscular conditions in the UK. London: Muscular Dystrophy Campaign: 15.

² Incidence in Europe is: for SMA 1:10,000 live births; for DMD 1:3,500 live male births.

³ E. Longo-Araujo de Melo & M.T. Moreno-Valdes. [Evaluation of the quality of life of children with Duchenne's progressive muscular dystrophy]. *Rev Neurol* 2007; 45: 81-87, J. Rahbek, et al. Adult life with Duchenne Muscular Dystrophy (DMD). Observations among an emerging and unforeseen patient population. *Neuromuscular Disorders* 2005; 15: 743-743.

condition and their families report care burden and support issues, isolation, social inequality and psychological stress and depression⁴.

INTRODUCTION

In this paper we provide a brief outline of the foundation of contemporary research governance which takes as its focus the rights, interests and dignity of the research subject. We identify some of the challenges that have been made against this research governance approach, which is perceived as involving restrictive and overly paternalistic practices. These challenges emerge from the critical stances taken within bioethics, medicine and patient activism and we review some of the similarities and differences between these positions. With a particular focus on patient activism we examine its origins and relevance to these contemporary debates and consider the ways in which the neuromuscular patient community has taken on the strategies of the activist approach. We go on to argue that some of the activist approaches are themselves challengeable. We conclude with a call for greater collaboration in

⁴ J.E. Bothwell, et al. Duchenne muscular dystrophy - Parental perceptions. *Clinical Pediatrics* 2002; 41: 105-109, F. Boyer, et al. Factors relating to carer burden for families of persons with muscular dystrophy. *Journal of Rehabilitation Medicine* 2006; 38: 309-315, B.A. Gagliardi. The impact of Duchenne Muscular Dystrophy on families. *Orthopaedic Nursing* 1991; 10: 41-49, B. Natterlund, et al. The illness experience of adult persons with muscular dystrophy. *Disability and Rehabilitation* 2001; 23: 788-798.

research governance, to include patients, clinicians, scientists and regulators.

Current phase II trials for therapies which would significantly ameliorate DMD are showing promise of reaching patients. This promise has heightened the expectation of a “cure” and increased the sense of urgency for research and with it the challenge of reassessing the risks that research participants might be exposed to.

The person whose future is foreclosed by a progressive and incurable disease inspires a moral claim on human endeavour, to find a means of treating and ideally curing them, that few would dispute. The vulnerability which comes with the diagnosis of a chronic, progressive disease may combine with other vulnerabilities, such as the dependency of the child, or person with diminished capacity and these vulnerabilities may be used to justify a highly precautionary attitude to research governance⁵. With an eye to the history of the abuses within medical research, a level of paternalism would initially appear to be warranted. However, with potential life saving therapies for DMD now being tested in clinical trials, patients,

⁵ Here we are drawing upon a general ethical concept of vulnerability as being open to wounding or harming, however there are more technical uses of the concept in the context of research ethics. A more nuanced account of vulnerability is needed and we are conscious that judging groups as vulnerable per se is one of the presumptions of paternalism in the research context that patient activism is reacting against.

clinicians and scientists are asking “who decides what’s best for the patient”?

DISPUTING THE ETHICS OF RESEARCH

Articles on research ethics usually recite the 20th century history of ethics from the Nuremburg Code and World Medical Association’s Declaration of Helsinki⁶ through Pappworth and Beecher’s exposures of unethical medical research⁷, to the present day. It should be acknowledged that the present context of medical research is a long way from the time, context and mindset of the Nazi experimenters. Although some concerns remain about the application of research ethics to contemporary practice⁸ there is now a consensus around

⁶ Allied Control Council. 1949. Trials of War Criminals Before the Nuernberg Military Tribunals Under Control Council Law No. 10 Washington, DC: US Government Printing Office: 181-182, World Medical Association. 1964. World Medical Association Declaration of Helsinki. Ethical Principles for Medical Research Involving Human Subjects. The World Medical Association, ed.

⁷ H. Beecher. Ethics of clinical research. *New England Journal of Medicine* 1966; 274: 1354-1360, M.H. Pappworth. 1967. *Human Guinea Pigs: Experimentation on Man*. London: Routledge and Kegan Paul.

⁸ C. Levine. Has AIDS Changed the Ethics of Human Subjects Research? *The Journal of Law, Medicine & Ethics* 1988; 16: 167-173, D. Shalala. Protecting Research Subjects — What Must Be Done. *New England Journal of Medicine* 2000; 343: 808-810, R. Steinbrook. Protecting Research Subjects — The Crisis at Johns Hopkins. *New England Journal of Medicine* 2002; 346: 716-720.

the core principles of research ethics which can be read as a sign of progress⁹.

In the light of challenges from a number of groups, we consider whether The Declaration of Helsinki has become a reified dogma of research ethics, or remains an important and relevant foundation.

Whilst there have been revisions to the original version, the underlying principles remain the same. These principles presume the research subject is inherently vulnerable and that researchers have the potential to exploit subjects in the interest of science, thereby justifying a degree of paternalism in research governance.

The traditional, what we shall call Helsinki approach, assumes that priority ought to be given to the welfare of the research subject followed by respect for their personal autonomy, both of which are expressed through the freedom to participate or not, and the right to withdraw without prejudice.

⁹ Council for International Organizations of Medical Sciences (CIOMS). 2002. International Ethical Guidelines for Biomedical Research Involving Human Subjects. 3 edn: CIOMS: pp.63, Council of Europe. 1997. Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine. In *Oviedo, 4IV1997*. C.o. Europe, ed.: Council of Europe, World Medical Association. 2008. World Medical Association Declaration of Helsinki. Ethical Principles for Medical Research Involving Human Subjects. The World Medical Association, ed.

Some of the critics of the Helsinki approach discussed here (ourselves included) accept that the moral starting point for research ethics has been ratcheted up to such an extent, that there is now a secure foundation from which to consider further refinements, deviations even, from the traditional Helsinki view. The thrust of the critiques we consider place a particular emphasis upon personal autonomy, give a new account of the duty and responsibility of potential research subjects and play down the vulnerability of the research subject¹⁰. Indeed paternalistic constraints imposed upon research may actually contribute to the vulnerability of the research participant by preserving a power difference between the researcher and the researched upon thus denying the so-called “vulnerable” their rights to autonomy¹¹. Moreover, paternalistic approaches are evident in the documents which regulate and guide research governance often emphasising the duties of those conducting the research and the vulnerability of the research subjects¹². The Department of Health in the UK has encouraged greater co-operation

¹⁰ J. Harris. Scientific research is a moral duty. *Journal of Medical Ethics* 2005; 31: 242-248.

Harris argues that the vulnerability of the research subject should not be privileged over and above their duty to participate, or indeed over society’s interest in research taking place.

¹¹ D. DeBruin. Reflections on vulnerability. *Bioethics Examiner* 2001; 5: 1.

¹² CIOMS, *op. cit* note 9

between patients and researchers but patient groups are still frustrated at the lack of collaboration¹³.

Critiques of medical paternalism and implicitly, of the conservative Helsinki approach, come from several quarters, starting from the broad critique of medicine characterised by the development of the sociology of medicine in the period following the 2nd World War¹⁴, from within Bioethics¹⁵, and from the wider spectrum of activism that lies between civil rights movements and health related consumer groups¹⁶. Rose and Novas have characterised the latter in terms of the concept of biological citizenship¹⁷. Biological citizenship

¹³ H. Munn. A new pathway for the governance of health research. *New Scientist* 2011, J. Thompson, et al. Health researchers' attitudes towards public involvement in health research. *Health Expectations* 2009; 12: 209-220, Department of Health. 2011.

Governance arrangements for NHS Research Ethics Committees. D.o. Health, ed. London.

¹⁴ M. Foucault. 1973. *The Birth of the Clinic*. New York: Pantheon, E. Goffman. 1961.

Asylums: Essays on the Social Situation of Mental Patients and Other Inmates. . New York: Doubleday, T. Parsons. 1951. *The social system*. New York: Free Press.

¹⁵ J. Harris. 1985. *The Value of Life*. 1 edn. London: Routledge and Keegan Paul, I. Illich.

1976. *Medical Nemesis: The expropriation of health*. New York: Pantheon, R.M. Veatch.

1981. *A Theory of Medical Ethics*. New York: Basic Books.

¹⁶ S. Epstein. The Construction of Lay Expertise - AIDS Activism and the Forging of Credibility in the Reform of Clinical Trials. *Sci Technol Hum Values* 1995; 20: 408-437, R.

Hugman. 1994. *Ageing and the care of older people in Europe*. Basingstoke: Macmillan: x, 199.

¹⁷ N. Rose & C. Novas. 2005. Biological Citizenship. In *Global Assemblages: technology, politics and ethics as anthropological problems*. A.O.a.S.J. Collier, ed.: Blackwell, : 439-463.

describes the social conditions of citizenship in terms of biological responsibilities, with forces operating in two directions. One direction is from above, in terms of the way in which authorities regard individual citizens and impose responsibilities on them. The other direction is from below, whereby self-organised communities of citizens seeking a level of participation and influence in spheres of concern to them. The picture is complex and it would be too easy to make generalisations however, there are allegiances of common concern across medicine, bioethics and patient activism, but also differences.

In terms of allegiances, there is frequent expression of frustration from within medicine that the medical profession is prevented from doing what it has been sanctioned to do in relation to research¹⁸. In our work we see this sense of frustration is shared by citizen activists within disease communities who are advocating for their right to participate in decisions about care, treatment and research. The Academy of Medical Sciences report on research governance in the UK, emphasised both the rights and responsibilities of patients to participate in research and encouraged more extensive patient and public involvement in research¹⁹. This common interest has, in some

¹⁸ AMS. 2011. A new pathway for the regulation and governance of health research.

Academy of Medical Sciences.

¹⁹ AMS, *op. cit* note 18 at 3.2 ff. in addition, at 3.3.2 the report also notes that medical paternalism may also be preventing patients joining research.

instances, led to greater collaboration between the medical profession and patient organisations and this is evident within the neuromuscular disorders community²⁰. With collaboration comes a levelling of power between patients and researchers, with the consequence that some groups of patients are less vulnerable because they are less disadvantaged by a lack of knowledge about research.

Though there may be an allegiance to a biomedical research agenda between medicine, bioethics and patient organisations, there are differences. For example there is a discernable difference of emphasis regarding responsibility. From some in bioethics there is talk of duty²¹, but the significant point about a duty is that it can be a form of obligation that may be insisted upon by others and in that sense can be viewed as a reversal of the traditional Helsinki approach. The traditional approach emphasises that the interests of

²⁰ F. Muntoni, et al. 149th ENMC International Workshop and 1st TREAT-NMD Workshop on: "planning phase i/ii clinical trials using systemically delivered antisense oligonucleotides in duchenne muscular dystrophy". *Neuromuscul Disord* 2008; 18: 268-275.

²¹ H.M. Evans. Should patients be allowed to veto their participation in clinical research? *Journal of Medical Ethics* 2004; 30: 198-203, M.G. Hansson & M. Hakama. Ulysses contracts for the doctor and for the patient. *Contemporary Clinical Trials* 2010; 31: 202-206, J. Harris. Scientific research is a moral duty. *J Med Ethics* 2005; 31: 242 - 248, J. Harris & S. Holm. Should we presume moral turpitude in our children? - Small children and consent to medical research. *Theor Med Bioeth* 2003; 24: 121-129.

the research subject are above all other interests and that the subject's participation is based upon both free and informed consent and a lack of coercion²². There is no mention of duty as a consideration. In contrast the emphasis placed by patient organisations is upon the *right* to participate in research. Rights are powers that accrue to citizens and such powers impose obligations upon others and can be insisted upon by those whose rights they are.

THE CHALLENGE TO HELSINKI FROM BIOETHICS

Contemporary medical ethics regards the principle of respect for autonomy as foundational. It is against this reassuring background that some have begun to argue that autonomy ought to be balanced against other important responsibilities of the citizen, such as the obligations of beneficence. It has become regarded as legitimate to argue that the precautionary approach of Helsinki not only limits autonomy, but also prevents citizens from fulfilling their moral duty to do good by participating in beneficial medical research²³. Harris and Holm²⁴ have argued that there ought to be a change in attitude, even with regard to children, from the highly conservative position usually

²² WMA, *op. cit.* note 9.

²³ Harris & Holm, *op. cit.* note 21; Hansson & Hakama, *op. cit.* note 21; R. Rhodes.

Rethinking Research Ethics. *Am J Bioeth* 2010; 10: 19-36.

²⁴ *ibid.*

adopted²⁵. To adopt this cautious approach is to 'presume the moral turpitude of children'²⁶ rather than consider that they are burgeoning moral citizens who should be encouraged to do what is right. From this bioethical perspective, citizenship is extended to include children who should be regarded as substantially wronged if they are prevented from fulfilling the obligations of a 'good' citizen.

THE CHALLENGE TO HELSINKI FROM CONSUMERISM AND PATIENT EMPOWERMENT

A similar claim to the idea that citizens have a moral duty to enter research, albeit with a different emphasis, has emerged from the domain of citizen activism. Dating from around the 1960s against a background of civil rights there are several strands to citizen activism, one related to political consumerism and another to civil liberties. Both are concerned more broadly with the provision and governance of social goods. Health and access to health care became a contested subject in this era as citizens began to challenge the presumption that the medical professions' power to work in the patients' best interests, meant the authority to decide *for* patients²⁷. A presumption roundly rejected by women's and disability

²⁵ S.D. Edwards & M.J. McNamee. Ethical concerns regarding guidelines for the conduct of clinical research on children. *Journal of Medical Ethics* 2005; 31: 351-354.

²⁶ Harris & Holm, *op. cit.* note 21, p. 121.

²⁷ D. Lupton, et al. Caveat emptor or blissful ignorance? Patients and the consumerist ethos. *Social Science and Medicine* 1991; 33: 559 -568.

groups, which began to insist upon the right to participate in health care decisions made about them²⁸.

It is clear that consumer activism on health falls within the bounds of biological citizenship as described by Rose and Novas except that the obligations of the citizen are reconfigured as consumer rights²⁹.

The consumer analogy remains a good one, since in the contemporary context of biomedical research there has been an increasing recognition that there are commodities of biovalue used in negotiation and exchange³⁰. Human tissue, genetic information, and access to cohorts of patients have become the basis for a kind of commerce and at times a bargaining tool, between patients and professionals³¹.

The rights discourse can thus be seen as a substantive claim for both negative and positive rights. Negative rights understood as freedom from the interference of paternalistic doctors and regulators. Positive

²⁸ Hugman, *op. cit.* note 16; M.A. Rodwin. Patient Accountability and Quality of Care: Lessons from Medical Consumerism and the Patients' Rights, Women's Health and Disability Rights Movements. *American Journal of Law and Medicine*, Vol 20, p 147, 1994
1994, S. Ruzek. Transforming doctor-patient relationships. *J Health Serv Res Policy* 2007; 12: 181-182.

²⁹ Rose and Novas, *op. cit.* note 17

³⁰ C. Waldby. Stem cells, tissue cultures and the production of biovalue
Health, An Interdisciplinary Journal for the Social Study of Health, Illness and Medicine
2002; 6: 305-323.

³¹ D. Dickenson. 2008. *Body Shopping*. Oxford: Oneworld.

rights understood as rights to goods and services including the right to be involved in research at all stages and the right to demonstrate one's responsible citizenship.

Throughout the 1960s and 70s and using models of civil rights patients came together to form organisations to advance their own health interests and to set the research agenda. In clinical trials in particular, the HIV/AIDS activism is a powerful exemplar which, in its time, radically changed the trial landscape³². HIV/AIDS activists resented their exclusion from debates about treatment and research and challenged the restrictions on access to promising drugs, merely because they were the subject of randomised, controlled trials. In particular they thought the "paternalistic" policies of drug regulation were perceived to rob patients of the right to assume the risk of experimental treatment³³.

Thus, the vulnerability of HIV/AIDS patients was arguably a construct of these exclusions and activists sought to redress the balance in a number of ways. First, by learning to speak the language of biomedicine in order to dispute with biomedicine on equal terms. Second, by becoming activist consumers and developing a parallel market, forming buyers clubs to gain access to the most promising

³² Epstein, *op. cit.* note 16; R. Dresser. Patient Advocates in Research: New Possibilities, New Problems. *11 Wash U JL & Pol'y* 2003: 237-248.

³³ Epstein, *op. cit.* note 16, p. 146.

therapeutic agents. Third, by effective political lobbying, questioning the regulation and governance of drug development. This combination of rights activism, political consumerism, and expression of personal autonomy through collective action, is the legacy left to contemporary patient groups.

THE CASE OF NEUROMUSCULAR DISORDERS

This legacy can be discerned in the evolution of organisations representing people with neuromuscular disorders (NMDs). Within the field of muscular dystrophy, patient organisations were formed as a reaction to the “no help, no hope” approach of physicians, termed therapeutic nihilism³⁴. From the formation of Association Francaise contre les Myopathies (AFM) in France in the 1960s onwards, patients and their families started to organise, self-educate, raise money and make contacts with sympathetic scientists and clinicians. Parents were spurred on by the shock that not only was there no cure, but no treatment at all and went about creating a research infrastructure and engaging the interest of policymakers³⁵.

³⁴ P. Furlong. 2010. Advocating for Children. In *Goldlab Inaugural Symposium*. University of Colorado: Goldlab.

³⁵ V. Rabeharisoa. The struggle against neuromuscular diseases in France and the emergence of the "partnership model" of patient organisation. *Soc Sci Med* 2003; 57: 2127-2136.

A consequence of this activism is that patients and their families have assured their credibility by becoming knowledgeable about their diseases, raising funds and developing research programmes. To give an indication of scale and significance AFM, one of the biggest muscular dystrophy charities, funded the establishment of a centre for genetics research, Genethon in 1991. In addition to making a major contribution to the mapping of the human genome, Genethon has become a leading research centre for rare genetic disease³⁶. Lobbying and awareness raising about clinical trials by the HIV/AIDS activists of the 1980s highlighted how progress could be accelerated by engaging politicians, healthcare providers and the pharmaceutical industry³⁷. NMD patient organisations have been equally successful in these areas and a combination of self-organisation, self-education, lobbying, financial leverage and ability to set the research agenda, is characteristic of NMD activism now. For such active patients and parents it is clear that there is less information asymmetry between them and medical professionals, than one might find with patients with newly acquired disease or acting without the support of a patient organisation.

SOCIAL AND ETHICAL COMPLEXITY IN PATIENT ACTIVISM

³⁶ Genethon. 2011. Homepage.

³⁷ Epstein, *op. cit.* note 16; V. Rabeharisoa & M. Callon. The involvement of patients' associations in research. *International Social Science Journal* 2002; 54: 57-65.

In developing organisations that are: major funders of research; effective political lobbyists; and founders of strategic alliances, patients and their families have demonstrated a challenge to the presumption of vulnerability. At the level of the collective the patient organisations and “credible” individuals within them are not vulnerable subjects requiring protection from the potential exploitation of researchers.

Section 6 of the Declaration of Helsinki states that, ‘In medical research involving human subjects, the well-being of the individual research subject must take precedence over all other interests’³⁸. This implies that well-being is separable from all other interests. However, some activists in the NMD field claim their well-being may depend on them being able to take part in clinical trials and they therefore demand participation as a positive right. From the patient perspective the moral duty argued for by Harris and Holm³⁹ becomes a moral right. We see this shift as significant in two ways; first, as a rejection of medical professionals as the arbiters of patients’ best interests. Second, as an assertion of a direct link between patient welfare and activism, including the right to participate in research.

This latter aspect can be distinguished from the argument that there is a moral duty to participate in medical research. The moral duty

³⁸ WMA, *op. cit.* note 9.

³⁹ Harris & Holm, *op. cit.* note 21.

argument is a claim about how a duty to do a greater good may take priority over personal autonomy and welfare. Moreover, the moral duty is something impersonal; it applies to everyone, and in principle may be imposed on others. However, we suggest that the activists' claim is radical in a different way because it claims that the right to participate in research is not only an assertion of autonomy, but also a condition of their welfare and not in conflict with it. The latter is a complex point, and suggests at least that autonomy and welfare interests are much more closely related than other analyses have suggested⁴⁰. For these patients the very notion of being "active" is embedded within their conception of self, self-worth and autonomy. Thus the welfare of the individual is contingent, at least in part, upon the opportunities afforded to the person to act autonomously and in a way that affirms their value as a moral agent. The act of participating in research is both for one's own interests and in the interests of similar others and as such is a form of conditional altruism. The point is captured well by Gordon McClurg, a businessman with DMD who sees no problem in patients having multiple reasons for entering a trial: 'Is there an inherent conflict between, on the one hand an aspiration to benefit personally at as early a stage as possible from a treatment that may restore physical capacity, improve quality of life or even extend it, and on the other, the desire to be part of a clinical trial to establish the efficacy of an experimental treatment, a process

⁴⁰ R. Dworkin. 1994. *Life's dominion : an argument about abortion, euthanasia, and individual freedom*. 1st Vintage Books edn. New York: Vintage Books: xiii, 273.

which may well advance the interests and wellbeing of other or all sufferers?⁴¹.

The challenge that this landscape of patient activism presents to the Helsinki tradition is significant. The idea that the research subject is also someone who insists upon their right to participate in research, is an active ally of the researcher and someone who sees their interests as intimately bound up with the possibility that research happens, departs from the idea of the vulnerable and potentially exploitable research subject inherent in the Helsinki approach. If we give credence to this new relationship between the researchers and the researched upon then the next question is surely, how should we be interpreting notions of patient interests as contained in the Helsinki declaration? Whilst we are sympathetic to the need for revision to Helsinki and the research regulation it has inspired we are also concerned that it should not be abandoned completely for reasons we now explore.

PUSHING THE RIGHTS AGENDA

In our empirical work we have seen that a strong insistence upon the right to participate is not without its problems. We can see the acceptability or otherwise of risks associated with research, as a

⁴¹ S. Woods, et al. The therapeutic misconception, decision making and informed consent: the ethics of trial participation for neuromuscular disorders. *in preparation* 2011.

territory of dispute between activists and professionals⁴². For example, some patients with life limiting disease seem prepared to take risks over and above those which are deemed acceptable both by the medical professions, ethics committees and by wider society⁴³. There are men with DMD, nearing or beyond the mean age of death for their disease group, who declare they would, 'rather die trying [an experimental therapy], than die from the disease itself'⁴⁴. These men take the idea of altruism to another level, that of sacrificial altruism. A minority of patient advocates see ethical safeguards as a restriction on what they are permitted to do with their own body and that this has a negative effect on their well-being and limits their self-determination. The claim is repeatedly made by patient activists that no-one is better placed than the person with the condition, or their family, to make a judgement about the level of risk that is worthwhile.

Those prepared to act as sacrificial altruists might argue that, even if they personally come to harm through clinical trial participation, the NMD community, their biosocial group, might benefit⁴⁵. It can be

⁴² F.G. Miller & S. Joffe. Limits to research risks. *Journal of Medical Ethics* 2009; 35: 445-449.; M.P. Slevin, H; Lynch, D; Drinkwater, J; Gregory, WM;. Who should measure the quality of life, the doctor or the patient? *British Journal of Cancer* 1988; 57: 109-112.

⁴³ Miller & Joffee, *op. cit.* note 42.

⁴⁴ P. McCormack. 2009. Notes from Action Duchenne conference. personal communication.

⁴⁵ Waldby, *op. cit.* note 30.

seen that in the case of chronic, progressive, disease the potential therapeutic benefit of taking part in a trial can weigh heavily on the scales for some patients and at the same time, as they lose function and get closer to the age at which death is expected, risk can seem less threatening⁴⁶. The combination of the lack of separation between therapy and experiment and the hope for therapeutic benefit for both themselves and the disease community, can lead some patients to develop a “nothing left to lose attitude”, which drives them to challenge the boundaries of what others see as acceptable risk. Such opinions might well be bolstered by an appeal to consumer autonomy, that research ought to be a laissez faire market in which the only precautionary principle is that of caveat emptor. In our view this would be an extreme shift. Whilst there are legitimate reasons for arguing that the Helsinki approach is too paternalistic, these are reasons for a revision of the approach rather than wholesale abandonment.

It should be recognised that this is not a dispute about personal autonomy but rather a dispute about what *respect for autonomy* is an entitlement to. There is a clear need to take seriously the claim that autonomous individuals should be permitted to assert positive rights and make choices at some risk to themselves. However, the potential for autonomous rights to fly in the face of widely sanctioned

⁴⁶ L. Baker. 2008. The views of young men living with Duchenne Muscular Dystrophy. London.

concerns about, and responsibility for the welfare, safety and dignity of others must also be given credence. Such responsibilities are shared equally and generally by patients, parents, researchers, clinicians, in fact all citizens. This is not an excuse to merely dismiss the claims of patients but is rather a call to find a means to establish the extent of patient rights that ought to be sanctioned and thus render meaningful the moral responsibility enshrined in the Declaration of Helsinki 'to protect the life, health, dignity, integrity, right to self-determination...'⁴⁷.

There is a common interest in establishing and protecting standards of dignity and respect which reflect the shared societal concern for all of its members. The TREAT-NMD network provides a good example of how such a collective approach can work in practice and of the kinds of mechanisms that can successfully allow different groups to exchange ideas and explore each others' points of view in depth. 20% of the EC-funded partners in ANONYMOUS are patient organisations, 2 of them umbrella group, together representing almost 500 rare disease patient organisations across Europe. The network is immediately mutually beneficial as it situates the patient organisations within a wider club of interest which includes scientists, clinicians and researchers, and vice versa.

⁴⁷ WMA, *op. cit.* note 9.

The network uses a number of mechanisms to encourage exchange between the different groups. One is appointment on committees and most have upwards of a third of members who are patients or their representatives. These committees do regular empirical work together⁴⁸ and the network has a general commitment to transparency and open debate. One example of a practical outcome of this deep and close collaboration was a workshop organised by TREAT-NMD and the European Medicines Agency (EMA) to discuss how regulation might work for a potential personalised therapy for NMD. The meeting discussed the usual clinical and pharmacological issues but began with the patient perspective and concluded with a presentation on ethical issues⁴⁹

Recent wider recognition of the value of encouraging collaboration between different groups involved in clinical trials can be seen in EURORDIS' Clinical Trials Charter for use between sponsors and patient organisations, as well as Patient Partner's publications on Patient Involvement in Clinical Research⁵⁰.

⁴⁸ A. Aartsma-Rus, et al. The risks of therapeutic misconception and individual patient (n = 1) "trials" in rare diseases such as Duchenne dystrophy. *Neuromuscular Disorders* 2011; 21.

⁴⁹ F. Muntoni. 2009. The Development of Antisense Oligonucleotide Therapies for Duchenne Muscular Dystrophy - report on a TREAT-NMD meeting hosted by European Medicines Agency, 25 September 2009. TREAT-NMD Network.

⁵⁰ Patient Partner. 2011. Patient involvement in clinical research. A guide for patient organisations and patient representatives. P. Partner, ed. Soest: Patient Partner, Patient

THE CASE OF CHILDREN

In addition to the issues already covered, when considering the impact of rare disease upon children, there are other and specific concerns. Some parents are prepared to take decisions that put the family welfare at stake, through personal and financial sacrifice, in order to increase the chances of entering their child into research. So, talk of: moving to another country in the hope of accessing a clinical trial; issuing legal challenges to companies who do not release the results of drug trials as quickly as families hoped; building research facilities in countries with weak jurisdiction to avoid regulation; and buying into biotech companies to influence research priorities which will favour their child's condition, are all examples of the type of conversations which regularly take place in the patient community. Such discussions are difficult to capture as they do not usually take place within the public arena and are open to criticism from other members of the patient groups and the medical profession. One public case, which illustrates the extreme motivations behind some actions by patients, was the Gunvalson trial where the mother of a boy with DMD issued a lawsuit against a

biotech company to argue for access to a therapy which was still in phase II trials⁵¹.

Evident in these examples is the passion and desperation of parents seeking the best for their child. Also evident are the circumstances in which a misleading conflation of ideas is made easy. First, the belief that a clinical trial means treatment, the therapeutic misconception, which drives some parents to go to extreme lengths to chase a “cure” for their child⁵². Second, driven by the therapeutic misconception, is the conflation between the right that research happens, a legitimate and reasonable expectation, and the right to participate in research, which, per se, is not a reasonable expectation⁵³. The effectiveness of collective action in raising awareness, and setting and resourcing the research agenda may play a role in fostering these confusions, especially if a family have been particularly involved in such activities. There may be a notion that their child deserves to be

⁵¹ Nature Biotechnology. Gunvalson decision sends shockwaves through industry. *Nature Biotechnology* 2008; 26: 1201-1201.; Author. 2008. Jacob Gunvalson, Terminally Ill, Can't Demand Experimental Drug: Court *Huffington Post* 16 December 2008.

⁵² P.S. Appelbaum, et al. The Therapeutic Misconception - informed consent in psychiatric research. *International Journal of Law and Psychiatry* 1982; 5: 319-329.

⁵³ In addition, neither of these confusions acknowledge the fact that over 80% of clinical trials are unsuccessful, R. Greville. 2010. Cost and Affordability of Medicines. Bevan Foundation.

included in the trial in return for the family having given of their own resources, a point emphasised in the Gunvalson case⁵⁴.

CONCLUSIONS

It is clear that solutions to the complex social and ethical issues we have described lie neither in fettering patient activism nor abandoning ethical governance. Patient activism can be effectively expressed within collaborative networks as an alliance of peers, rather than as a reactionary force.

At the same time it is necessary to be vigilant that the positive gains that have been made through patient activism do not become a springboard to therapeutic misconception and unacceptable risk taking. A balanced view of the activism that pushed the boundaries for HIV/AIDS and other disease groups will recognise that some of the activism was ultimately self-defeating⁵⁵. There is still a place for the precepts and concerns enshrined within the Helsinki approach but it is legitimate to question the way in which those precepts and concerns are interpreted and applied. This is a collective responsibility and not the sole prerogative of a professional elite. Patient organisations want their voices heard but they also want responsible, timely and ethical research into the conditions that afflict

⁵⁴ R. Abelson. 2008. Advocating a treatment, but Denied Access to It. In *The New York Times*. New York: New York Times.

⁵⁵ Dresser, *op. cit.* note 32.

them. In the ethical governance of research there needs to be a balance between the science orientated, professional, approach to research governance and a social and emotional one, which recognises that having a chronic progressive disease is as great a threat to dignity and well-being as participation in a clinical trial has the potential to be. Research ethics committees and Institutional review boards could place greater emphasis on the issue of patient involvement than is currently the case⁵⁶. However real collaboration needs to happen much further upstream from the point of ethical approval and will require academic researchers and pharmaceutical companies to be open to patient involvement from the earliest phase of research design. If but one aspect of the Helsinki approach could change then it should be that the normative prescriptions are developed within a collaborative dialogue between professionals and patients, their families and advocates.

So, working alongside researchers and clinicians and engaging with regulators would give patient organisations the opportunity to substantially determine what constitutes ethical research and would add legitimacy to the necessary sanctions and controls imposed by research governance.

⁵⁶ The NHS ethics review application form asks for evidence of patient involvement but it is not compulsory to have patient involvement.

Acknowledgement: TREAT-NMD is funded by the EU via FP6 under contract number LSHM-CT-2006-036825.

We would like to thank the anonymous reviewers who made very helpful comments on a first draft of this paper.