Belmont in Europe – a mostly indirect influence

Søren Holm[1]

Abstract

This paper traces the reception of the Belmont Report in Europe and its influence on the development of European research ethics thinking and European research ethics systems. It is argued that it is very difficult to trace a clear, linear reception history because it is difficult to disentangle the influence of the Report from the influence of other concurrent development such as the 1975 revision of the World Medical Association Declaration of Helsinki, and the requirement for research ethics review in the Vancouver Group's 1978 "Uniform requirements for manuscript submission". It is argued that the Report's insistence that the focus of research ethics should be the rights and interests of the individual research subject, and the use of an ethical framework and not ethical theory as the basis of analysis and justification of recommendations, where never the less very important for the development of research ethics. The divergence between Europe and the USA in the governance of non-biomedical research is analysed and it is argued that it can, at least partly be explained by the absence of strong drivers for the introduction of research ethics committees outside of biomedicine in Europe and by the ability of non-biomedical researchers to mobilise effectively against the introduction of such committees.

When the Belmont Report was published in 1979 the European research ethics community was very small, even if we take this community to include everyone who was either working in research ethics academically or professionally; and the report itself made very little impact in European medical journals[2]. If we try to trace its later *wirkungsgeschicte* (reception history) in Europe and in much of the bioethics literature worldwide we find that it is most often quoted either 1) as a landmark in the history of research ethics, without any further explication of its actual content, 2) as a forerunner of the principle based approach to biomedical ethics developed by Tom Beauchamp and James Childress in "The Principles of Biomedical Ethics" (Beauchamp and Childress 1979), or 3) conflated with other outputs or recommendations from the National Commission, including the working papers commissioned by the Commission[3]. It is thus difficult to trace the direct influence of the Belmont Report as distinct from the influence of the principle based approach in general and the influence of the whole body of work of the National Commission.

Taking the Belmont Report as the capstone of the work of the National Commission and interpreting the remit of the analysis to include that work and not only the Report in a narrow sense there is,

[1] Søren Holm
Centre for Social Ethics and Policy, School of Law, University of Manchester, Manchester, UK
&
Center for Medical Ethics, University of Oslo, Oslo, Norway

[2] My linguistic limitations entail that I have only been able to read and fully understand the primary literature in the Scandinavian languages, German and English, but the paper is based on wider searches aimed at identifying any relevant Dutch, French, Italian, Spanish and Russian literature as well.

[3] The National Commission for the Protection of Human Subjects of Biomedical and Behavioural Research

however no doubt that the Report has played an important role in the development of research ethics and bioethics in general in Europe.

In this paper I will analyse and discuss three distinct areas of influence and one area of contention, before discussing what the lasting legacy of the Report is in Europe.

Principles, research ethics and informed consent

The report introduces three principles as the foundation for research ethics, i.e. Respect for Persons, Beneficence, and Justice. Tracing a distinct reception history of the three principles in the report after the publication of the first edition of "The Principles of Biomedical Ethics" in 1979 becomes difficult, and in Europe it becomes completely impossible after the publication of Raanan Gillon's series of articles in the British Medical Journal in 1985 and 1986 popularising the principle based approach which were also collected and published as the influential book "Philosophical Medical Ethics" in 1986 (Gillon 1986). After this the three principles in the report were firmly supplanted in European bioethics discourse by the four principles proposed by Beauchamp and Childress.

However, the idea that research ethics needs to be based in ethical principles, as distinct from being derivable directly from ethical theory or purely a matter of professional ethics or professionalism can plausibly be traced to the Belmont Report, as can the primary importance of two of the three principles developed in the Report i.e. Respect for Persons, and Beneficence (that contains both the positive and the negative aspects of the duty to do good); or after the establishment of the hegemony of four principles and the division of the original principle of Beneficence into its positive (Beneficence) and negative aspects (Non-maleficence), their replacements Respect for Autonomy and Non-maleficence. These principles are important in themselves, but they are also important because they focus on the rights and interests of persons in their role as (potential) research participants. This focus may seem obvious in retrospect, but it may be less obvious than it initially appears. There is an underlying tension between a focus on the interests and rights of the individual and a focus on the manifold public goods that well planned and conducted research produces. Our current research ethics resolves this tension decisively in favour of the individual. One of the main general principles enounced in the Helsinki Declaration since the 1975 revision (of which see more below) for instance states:

> "5. Every biomedical research project involving human subjects should be preceded by careful assessment of predictable risks in comparison with foreseeable benefits to the subject or to others. *Concern for the interests of the subject must always prevail over the interests of science and society.*" (my emphasis)

But, this principle that individual interests must always prevail of societal interests has been subject to trenchant criticism (Harris 2005). We could have developed a research ethics that put greater emphasis on the public good side of the equation, and less on individual rights and interests and this would have implications for our consent practices and perhaps especially for deciding when consent requirement can be waived. Recently this question of balancing of interests have been re-actualised in the overlapping discussions about biobanking, secondary research use of health data, big data and

the learning health system (for two very different analyses of these issues see Porsdam Mann et al 2016 and Ploug & Holm 2017).

Basing the discourse about research ethics in ethical principles, and not in ethical theory (e.g., utilitarianism, Kant's duty-based ethics or Aristotelean virtue theory) or conceptions of professionalism has two effects. First, it makes contributions to the discourse from outside the professions directly involved in conducting the research legitimate and opens up the field to 'outsiders' like philosophers, theologians and social scientists. Although these groups are not strictly 'strangers at the bedside' in relation to research ethics (Rothman 1991), their involvement became crucial to the future development of the field worldwide (Jonsen 1998). This can for instance be exemplified by the pivotal and enduring role played by Ruth Faden and Tom Beauchamp's 1986 book "A History and Theory of Informed Consent" in the international debate (Faden and Beauchamp 1986), or by the role played in Denmark by Peter Rossel's 1979 book Medicinsk Etik (Medical Ethics) which despite the title is primarily about research ethics and which was a major critique of and corrective to the 'research ethics is professional ethics' line taken by the Danish medical profession (Rossel 1979, Riis 1977 & 1983, see also Rossel 2017) . At the same time a principle based approach provides non-philosophers with a ready-made and accessible framework within which to develop their own ethical arguments.

Second, basing research ethics in ethical principles instead of in ethical theory, and the focus on the rights and interests of the research participants partly mitigates the risk of being rhetorically seduced by the most radical deductions from ideal ethical theory. A number of ethical theories are frequently deployed in bioethics. These include consequentialism and its most well-known variant utilitarianism, claiming that only the consequences of actions matter in ethical evaluation and that we should aim at maximising the net good consequences/utility. And, on the other end of the theoretical spectrum we see deontologists (adherents of a duty-based ethics) deploy an absolute prescription derived from one version of Kant's Categorial Imperative that we should "always treat others as ends in themselves, never merely as means". It is true that an argument based in consequentialism may tell us that cognitively competent research participants should be allowed to consent to any level of risk, perhaps even certain death, if the research promises great future benefits for other people and society. And, that those research ethics committees (RECs) that impose risk thresholds are therefore acting in ways that are paternalistic and unjustified (Edwards et al 2004). But the principle based approach gives us a reason to, at the very least, scrutinise such radical pronouncements from theory very carefully, since they seem to be breaching one or more of the principles at a very basic level. On the other hand the principle based approach also shields us from the more absolutist pronouncements of deontological fundamentalism, e.g. in relation to the impermissibility of research where potential participants cannot provide consent themselves (Woodward 1999). The claim made here is not that ethical theory has no role to play in criticising research ethics, or that a principle based approach always lead to the right conclusion, but that the principles may act as a buffer between the brilliant theoretical argument and the implementation of its conclusions in the messy world of actual research practice and multiple stakeholders.

The idea that participant consent is an important component of research ethics, and especially biomedical research ethics can be traced back to the very origins of research ethics and can be found long before it was enunciated as Principle 1 in the Nuremberg Code in 1947 (e.g. Sass 1983, Hattix 2018). It has both ethical and legal roots and it would be highly problematic to claim that any

particular document, including the Belmont Report was crucial for its development after Nuremberg. However, in the Report we find one of the first clearly enunciated and widely publicised accounts basing a recognisable version of informed consent in an ethical principle of Respect for Persons. Today it would be difficult to find a healthcare professional in Europe or North America who if asked 'why should we seek informed consent for research?' would not answer something like 'because we need to respect peoples' autonomy'.

The principle of Justice has played a much more prominent role in US research ethics than it has in Europe, especially in relation to discussions about and regulation of recruitment practices. This is probably not because European ethicists and regulators do not take formal and distributive justice seriously, I have myself argued that they may take it more seriously than some US bioethicists (Holm 1995), but because the context was and is different. After mentioning the Nazi atrocities and the Tuskegee study The Report rightly states that:

> "Against this historical background, it can be seen how conceptions of justice are relevant to research involving human subjects. For example, the selection of research subjects needs to be scrutinized in order to determine whether some classes (e.g., welfare patients, particular racial and ethnic minorities, or persons confined to institutions) are being systematically selected simply because of their easy availability, their compromised position, or their manipulability, rather than for reasons directly related to the problem being studied. Finally, whenever research supported by public funds leads to the development of therapeutic devices and procedures, justice demands both that these not provide advantages only to those who can afford them and that such research should not unduly involve persons from groups unlikely to be among the beneficiaries of subsequent applications of the research."

However, the concern about racial and ethnic minorities emerged much later as a significant social concern in Europe. Most European countries have robust tax or mutual insurance based public health care systems and this entails that the concerns about the distribution of the fruits of medical research according to ability to pay are much less relevant in the European context. However, Justice has been making a comeback in research ethics in Europe first in discussions about the inclusion of women in clinical research, and later in relation to the need to do more pediatric clinical research (Nuffield Council on Bioethics 2015).

The first revision of the Declaration of Helsinki

The Declaration of Helsinki was originally promulgated by the World Medical Association (WMA) in 1964 and it was comprehensively revised in 1975. The revision process was led by the Scandinavian medical associations and the draft text of the 1975 revision was prepared by three Scandinavian doctors, Clarence Blomquist from Sweden, Povl Riis from Denmark, and Erik Enger from Norway (Riis 2003, Lahlum and Ruyter 2012). It was passed unamended with only one vote against and one abstention at the World Medical Assembly in Tokyo, 1975 (Solbakk 2010). The 1975 revision, sometimes called 'Helsinki II' introduced a number of changes, of which two were aimed at ensuring better compliance with the Declaration. In the late 1960s and early 1970s it had become evident that neither the Nuremberg Code from 1947 nor the 1964 WMA Helsinki Declaration had had any appreciable impact on research practice, and the root cause of the problem was identified as relying

exclusively on researchers themselves in relation to the implementation of the Code and Declaration in their research projects. The two compliance inducing innovations in Helsinki II were 1) prior review by "a specially appointed independent committee" (Article 2) and 2) a requirement that "Reports of experimentation not in accordance with the principles laid down in the Declaration should not be accepted for publication" (Article 8).

The second of these innovations was primarily the brain child of Povl Riis, who was editor in chief of Ugeskrift for Læger (the Danish Medical Journal) and the Danish Medical Bulletin at the time. He was a few years later to become a co-founder and leading light in the Vancouver Group formed in 1978, the group that later became the International Council of Medical Journal Editors. The Vancouver Group's acceptance of this rule from Helsinki II on behalf of prominent journals in general medicine[4] and its inclusion in the Group's "Uniform requirements for manuscript submission" had a massive impact. The uniform requirements were rapidly adopted by journals outside the Group. They were already accepted by 130 journals in 1981 and more than 400 in 1991 (Huth 1981, International Council of Medical Journal Editors 1991). This meant that the bar on publication of research that was not conducted in conformity with the Helsinki Declaration became a very effective enforcement mechanism across the globe.

The other innovation, the "independent committee" was inspired by the US Institutional Review Boards (IRBs). In many institutions in the USA these pre-dated the National Commission, but the Commission's work led to a more uniform approach to the composition and function of IRBs (National Commission 1978). In Europe Research Ethics Committees (RECs), as they came to be known in most countries, were almost non-existent before 1975, but the new requirement in Helsinki II led to a rapid introduction of RECs in Western Europe. It is not clear whether this would have happened if conformity to Helsinki II had not been policed through the journals that signed up to the Vancouver Group's uniform requirements. Even though some of these journals may not actually have checked whether the requirement for IRB or REC review had been fulfilled, the standard requirement to state in the published papers that the research had received prior review or approval had a powerful effect in itself. The need to conform to the Declaration in order to be able to publish created strong institutional pressures to establish the structures, i.e. RECs that were necessary to claim conformity. In many European countries RECs were established in a fairly haphazard manner with each institution having its own procedures for membership and working practices (as an example see the descriptions of the situation in the UK in Neuberger 1992, Foster et al 1995), but in a few countries the establishment of RECs was centrally lead and those countries often ended up with a system of uniformly constituted regional RECs that were not bound to one specific institution (e.g. Denmark and Norway) (Riis 1983, Holm 1992). It was only in the late 1980s and early 1990s that more uniformity was imposed on RECs in most European jurisdictions as part of a general trend towards formal, legal regulation of biomedical research ethics. This trend towards more formal regulation continued throughout the 1990s and had a number of underlying international drivers. One important driver was the International Council on Harmonisation's Good Clinical Practice (GCP) guidelines issued in 1996 and their later implementation in European Union

[4] The founding members were Annals of Internal Medicine, Medical Journal of Australia, British Medical Journal, Journal of the American Medical Association, Lancet, Tidsskrift for den Norske Lægeforening, Index Medicus, New England Journal of Medicine, Ugeskrift for Læger & Danish Medical Bulletin, New Zealand Medical Journal, Canadian Medical Association Journal, Western Journal of Medicine.

law by the GCP Directive in 2001 (International Council on Harmonisation 1996, European Union 2001). GCP mandates the approval of clinical trials of investigational medicinal products by formally constituted RECs. The other important driver was the work in preparation of what eventually became the Council of Europe's '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'. This preparatory work was ongoing in various Council of Europe bodies from the early 1990s and alerted governments to the need for regulation in this area (Council of Europe 1997).

The curious loss of 'and Behavioral Research' in the European reception history

Institutionalised research ethics in most European countries has followed a different trajectory than in the USA. Following the 1975 revision of the Declaration of Helsinki many countries introduced research ethics committees for biomedical research. In some countries this was a planned process, and in some it was initially more locally driven by the need to have committee approval in order to publish in the best journals (see above). However, almost nowhere in Europe were committees introduced to scrutinise and approve non-medical research, except that some countries defined the scope of REC approval to include all research taking place within a health care institution, including medical sociology research and other non-biomedical research in this setting.

When in the 1990s research ethics was legally regulated in most countries in Europe and the Council of Europe issued a legally binding human rights convention dealing *inter alia* with issues of research ethics, this was again restricted to the biomedical field.

Some European countries, including the UK, have seen the introduction of non-biomedical RECs in the last decade and a half, but these are completely distinct from the biomedical RECs and not legally regulated in the same way, if at all. There are still many European countries that do not have mandatory or even voluntary approval systems for non-biomedical research, including countries with long-standing and well-functioning biomedical REC systems and significant non-biomedical research activity, such as Norway and Denmark.

The regulation of 'Behavioural Research' and more broadly the social and behavioural sciences has thus fallen by the wayside in most of Europe as a concern for official, state intervention. What explains this divergence in approach between the US and Europe? Seen from a European perspective there are, at least three interrelated factors at play:

1. The lack of a 'European Commission' on research ethics established early enough to influence the basic institutional design of the research ethics system
2. The Helsinki Declaration and later the International Council for Harmonisation (ICH) Good Clinical Practice (GCP) Guidelines being the main drivers for research ethics institutionalisation
3. 1 and 2 making it possible for groups outside of biomedicine to organise and provide effective resistance against what they see as the imposition of a biomedical model of research ethics on their distinct research practices

At the time in the 1990s when the Council of Europe became seriously engaged in drafting a human rights convention covering research ethics the basic structure and scope of the 'research ethics system' was already fixed in most European countries (Council of Europe 1997). The structure through which research ethics was implemented and policed was the REC and the scope was in most countries only biomedical research or the slightly wider scope of all research taking place within the health care system. This was a result of the drivers for setting up such systems being initially the Helsinki Declaration and later the GCP guidelines and their eventual implementation in legal instruments such as the EU Clinical Trials Directive (European Union 2001). This lead to an instance of path dependent development were the features of the already existing non-legally regulated research ethics system came to determine the features of the legal regulations as they were introduced in the 1990s.

The long latency period between the first introduction of RECs in the 1970s and their official regulation in most European countries in the 1990s also meant that social scientists could mobilise effective resistance against attempts to extend formal research ethics scrutiny to their disciplines. They could follow their American colleagues in labelling RECs and the research ethics principles that they policed as 'biomedical' and alien to the social sciences, and could label any attempt to extend the scope of REC approval as 'medical imperialism' (Schrag 2010). In their resistance they could also draw on the descriptions in the literature of negative experiences with IRB oversight of social science in the USA and Research Ethics Board oversight in Canada (Seiler and Murtha 1980, Ceci et al 1985, van den Hoonaard 2001 & 2002, Haggerty 2004), and on their own national examples of how social science projects within the health care system had been mishandled by the REC system. A common complaint was and is, for instance that RECs only understand positivist, quantitative research methodologies and that they impose the methodological standards for quantitative methodologies on interpretivist, qualitative research where they make little sense (Høyer et al 2005). This resistance is ongoing and has been successful in most of Europe and where research ethics oversight systems for the social sciences have been introduced they are almost always completely distinct from the legally regulated biomedical RECs.

What would have had to be different for the European developments of research ethics governance outside of biomedicine to be more like the US developments? Some generally acknowledged and widely publicised research scandals in social science or experimental psychology early on might have helped (although see Hedgecoe's recent analysis of the limited role of scandals in driving biomedical research ethics, Hedgecoe 2017). But, even though experimental psychologists in Europe conducted similar types of studies as Milgram and Zimbardo, and social scientists employed deception in similar ways as Laud Humphreys none of the European studies ever created more than brief and localised negative interest. In the writings of Maurice Pappworth, Peter Rossel and others the ethical problems in biomedical research was exposed in the 1960s and 1970s, but nothing with the same kind of impact happened outside of medicine (Pappworth 1967, Rossel 1979). Never the less, the development of a robust REC system for non-biomedical research might have come about if there had been a social science equivalent of the ICMJE and if that body had made REC review and approval a pre-condition for publication. As discussed above such a requirement is a strong jurisdiction independent driver for the development of RECs in a particular area of research. But, such a body was not established in the 1970s when RECs started to be established in Europe, it still does not exist, and there is currently no general consensus that REC approval should be required in

the social sciences, see for instance 'Wiley's Best Practice Guidelines on Publishing Ethics - Research Ethics in Journal Articles (Wiley 2014).

A basic ethical distinction between therapeutic and non-therapeutic research?

The 1964 and the 1975 versions of the Helsinki Declaration both contain a basic distinction between on the one side, using the phrasing of the headings in the 1975 version, 'Medical Research Combined With Professional Care (Clinical Research)' and on the other side 'Non-Therapeutic Biomedical Research Involving Human Subjects (Non-Clinical Biomedical Research)'. This distinction is made less prominent in the 2000 version and is only completely relinquished as a matter of headings in the 2013 revision. In relation to the first of these two categories the 1975 version specified that:

> "5. If the doctor considers it essential not to obtain informed consent, the specific reasons for this proposal should be stated in the experimental protocol for transmission to the independent committee (I, 2).
>
> 6. The doctor can combine medical research with professional care, the objective being the acquisition of new medical knowledge, only to the extent that medical research is justified by its potential diagnostic or therapeutic value for the patient."

Both of these articles and the distinction upon which they rest between therapeutic and non-therapeutic research were almost immediately criticised by Robert Levine (Levine 1979), who had been commissioned by the National Commission to write four preliminary, extensive papers on different aspects of research ethics, including a 44 page paper on "The Boundaries Between Biomedical or Behavioural Research and the Accepted and Routine Practice of Medicine" delivered to the Commission in July 1975 (Levine 1979).

Levine summarises his critique of the distinction in the following way in a paper commenting on the draft of the 2000 revision of the Declaration:

> "The Declaration of Helsinki requires revision because it is defective in two important respects.
> First, it relies on a distinction between therapeutic and nontherapeutic research; all documents that rely on this spurious distinction contain errors not intended by their authors.
>
> […]
>
> The nature of the errors that arise from a reliance on the distinction between therapeutic and nontherapeutic research is made clear by placing one of the document's provisions for therapeutic research (article II.6) next to one for nontherapeutic research (article III.2).
>
> > II.6. The doctor can combine medical research with professional care, the objective being the acquisition of new medical knowledge, only to the extent that medical research is justified by its potential diagnostic or therapeutic value for the patient.

> III.2. The subjects should be volunteers — either healthy persons or patients for whom the experimental design is not related to the patient's illness.
>
> This pair of articles rules out all rational research on the causes of diseases or on their pathogenesis or pathophysiology. Consider, for example, research designed to explore the role of neurotransmitters in the pathogenesis of depression. Since this research cannot be justified on the basis of its therapeutic benefit for the patient, as required by article II.6, it must be considered nontherapeutic. Therefore, as required by article III.2, the subjects of the research must be either normal volunteers or patients who have diseases other than depression. This is what I mean by unintended errors.
> The class of activities covered by the term "therapeutic research" is also problematic because all clinical trials of therapeutic agents include some components that may be therapeutic (or at least are so intended) and others that are clearly nontherapeutic. Those who rely on the distinction between therapeutic and nontherapeutic research usually categorize research protocols with one or more components that are intended to be therapeutic as therapeutic research. Thus, all components of such protocols, both therapeutic and nontherapeutic, are justified according to the relatively permissive standards for therapeutic research. Among the nontherapeutic interventions that have been justified on this basis are placebos, some of which have been administered by catheterization of the coronary artery, and repeated coronary angiography and endoscopy in patients who would not have undergone such procedures if they had been treated outside a research protocol. I refer to this phenomenon as the "fallacy of the package deal." It is because of such errors that in the 1970s, policy-making agencies in the United States and Canada rejected the distinction between therapeutic and nontherapeutic research. In his review of the major conceptual achievements of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research in the 1970s, Jonsen gives pride of place to the repudiation of the false distinction between therapeutic and nontherapeutic research." (Levine 1999, p. 531, references removed)

What explains the long historical persistence in the Helsinki Declaration of a distinction that Levine and the Commission had both thought was fatally undermined by argument already in the 1970s?

One factor is probably what could be called the phenomenology of research. Health care professionals simply feel differently or perceive the situation differently when they are doing research with their own patients, where that research has a potential therapeutic aim. It is not only patients who are susceptible to a therapeutic fallacy in relation to research.

Another factor is the central role of the medical profession and its interests in shaping the contents of the Helsinki Declaration. The medical profession is only one of the many stakeholders in relation to biomedical research and share the stakeholder space with the potential research participants, everyone as potential beneficiaries of research results, and the state as protector of basic rights of citizens. Bioethics (or bioethicists) is not strictly speaking a stakeholder in its own right but may provide arguments that support or undermine the positions of the main stakeholders. But the revision processes for the Declaration has always been dominated by the profession. This is difficult to justify (Holm 2011), but is a fact that needs to be taken into account when considering the original

shape and development over time of the Declaration. For a long time the medical profession saw the distinction as important, because it marks out a clinical sphere of action where the doctor who is also a researcher can act legitimately with mixed motives pursuing at the same time the good of the patient and the good of research, without having to worry too much about separating these two goals. And, perhaps more importantly without having to make the distinction between the two roles as healer and as researcher clear to the patient-participant. The distinction was therefore pragmatically important, irrespective of its philosophical coherence.

A lasting legacy in Europe?

As we have seen above the Belmont Report and the whole body of work of the National Commission influenced the development of biomedical research ethics in Europe but mostly in fairly indirect ways. Is there a lasting legacy of the Report in Europe?

The legacy is somewhat difficult to disentangle from the legacy of Helsinki II but the main legacy is probably the identification of the person as (potential) research participant as the central focus of our research ethical deliberations and the rules and systems that follow from those deliberations. To reiterate, these ideas were 'in the air' in the 1960s and 1970s and had also been the basis for Beecher's and Papworth's exposés of unethical research (Beecher 1966, Pappworth 1967, Gaw 2012), but they were expressed with great clarity in the Report and were given a plausible and understandable justificatory underpinning by the elaboration of the three principles.

This focus on the interests and rights of the person as research participant is now being put under pressure, especially in relation to the secondary use of routinely collected health data for research and development in the learning health care system. It will be interesting to see how the legacy from the Belmont Report will play out in this new context, and whether the increasing interdependence of international research endeavours will lead to more convergence between the US and European approaches. The World Medical Association has tried to influence these developments through its 2016 'WMA Declaration of Taipei on Ethical Considerations regarding Health Databases and Biobanks' but this declaration is unlikely to get anything like the same impact as the Declaration of Helsinki because it enters an already crowded field. In both Europe and the USA legislation governing the sharing and use of health data has had a significant influence in this area since the mid-1990s (EU 1995, US Congress 1996), and the importance of data protection legislation in the regulation of all types research using personal data in Europe is likely to increase with the EU General Data Protection Regulation GDPR which came into force in 2018 (EU 2016). The GDPR is likely to increase the protection of data subjects in Europe when research data is initially collected by enforcing consent requirements. However, the control mechanisms in the GDPR do not contain anything like a REC or IRB, but are based on a requirement for institutions to have privacy notices explaining how they handle research data, and subsequent enforcement action by regulators if these are breached. The GDPR will thus not be a driver for convergence between Europe and the USA.

Acknowledgements

I acknowledge many interesting discussions over the years about the history and practice of research ethics with my PhD supervisor, Professor Povl Riis† (1925-2017), and with my good friend and former colleague Peter H. Rossel.

References

Beecher, H.K. 1966. “Ethics and clinical research”. *N Engl J Med* 274:1354-1360

Ceci, S.J., D. Peters, and J. Plotkin. 1985. "Human subjects review, personal values, and the regulation of social science research." *American Psychologist* 40: 994-1002.

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 (European Treaty Series No. 164)*

Edwards, S.J.L., S. Kirchin, and R. Huxtable. 2004. "Research ethics committees and paternalism." *Journal of Medical Ethics* 30: 88-91.

European Union. 1995. *Directive 95/46/EC of the European Parliament and of the Council of 24 October 1995 on The Protection of Individuals with Regard to the Processing of Personal Data and of the Free Movement of Such Data.*

European Union. 2016. *Regulation of the European Parliament and of the Council on the protection of individuals with regard to the processing of personal data and on the free movement of such data (General Data Protection Regulation).*

US Congress. 1996. *Health Insurance Portability and Accountability Act of 1996 (HIPAA).*

European Union. 2001. *Directive 2001/20/ EC of the European parliament and of the council of 4 April 2002 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use.*

Faden, R., and T.L. Beauchamp. 1986. *A History and Theory of Informed Consent*. New York: Oxford University Press.

Foster, C.G, T,Marshall, and P. Moodie. 1995. "The annual reports of Local Research Ethics Committees." *Journal of Medical Ethics* 21: 214-219.

Gaw, A., 2012. Exposing unethical human research: the transatlantic correspondence of Beecher and Pappworth. *Annals of Internal Medicine*. 156: 150-155.

Gillon, R. 1986. *Philosophical Medical Ethics*. Chichester: John Wiley & Sons.

Haggerty, K.D. 2004. "Ethics creep: Governing social science research in the name of ethics." *Qualitative Sociology* 27: 391-414.

Harris, J. 2005. Scientific research is a moral duty. *Journal of medical ethics 31*: 242-248.

Hattix, L. 2018. "Expanding Notions of Self-Determination: International Customs of Informed Consent in Medical Experimentation Pre-1945." *Chi. J. Int'l L.* 19: 145-88.

Hedgecoe, A. 2017. "Scandals, ethics, and regulatory change in biomedical research". *Science, Technology, & Human Values 42*: 577-599.

van den Hoonaard, W.C. 2001. "Is Research-Ethics Review a Moral Panic?." *Canadian Review of Sociology/Revue canadienne de sociologie.* 38: 19-36.

van den Hoonaard, W.C., ed. 2002. *Walking the tightrope: Ethical Issues for Qualitative Researchers*. Toronto: University of Toronto Press.

Holm, S. 1992. "How many lay members can you have in your IRB?: An overview of the Danish system." *IRB: Ethics and Human Research* 14(6): 8-11.

Holm, S. 1995. "Not just autonomy--the principles of American biomedical ethics." *Journal of Medical Ethics* 21: 332-338.

Holm, S. 2011. "Who should decide the content of professional ethics?" *J Appl Ethics Philos* 3: 1-8.

Huth, E. 1981. "Style Matters: Manuscript requirements: the advance from Vancouver." *British Medical Journal* 282: 55-56.

Høyer, K, L. Dahlager, and N. Lynöe. 2005. "Conflicting notions of research ethics: The mutually challenging traditions of social scientists and medical researchers." *Social Science & Medicine* 61.8: 1741-1749.

International Committee of Medical Journal Editors. 1991. "Uniform requirements for manuscripts submitted to biomedical journals." *BMJ* 320: 338-341.

International Council on Harmonisation. 1996. "ICH Topic E 6 (R1) Guideline for Good Clinical Practice"

Jonsen, A.R. (1998). *The Birth of Bioethics*. New York: Oxford University Press.

Lahlum, E., and K. W. Ruyter. 2012. "The establishment of ethical committees for medical research." *Tidsskrift for den Norske Laegeforening: Tidsskrift for Praktisk Medicin*. 132: 1486-1489.

Levine, R.J. 1979a "The Boundaries Between Biomedical or Behavioral Research and the Accepted and Routine Practice of Medicine". In: *The Belmont Report – Appendix 1*. Available at https://videocast.nih.gov/pdf/ohrp_appendix_belmont_report_vol_1.pdf

Levine, R.J. 1979b "The Role of Assessment of Risk Benefit Criteria in the Determination of the Appropriateness of Research Involving Human Subjects." In: *The Belmont Report – Appendix 1*. Available at https://videocast.nih.gov/pdf/ohrp_appendix_belmont_report_vol_1.pdf

Levine, R.J. 1979c.”The Nature and Definition of Informed Consent in Various Research Settings.” In: *The Belmont Report – Appendix 1*. Available at https://videocast.nih.gov/pdf/ohrp_appendix_belmont_report_vol_1.pdf

Levine, R.J. 1979d. “Appropriate Guidelines for the Selection of Human Subjects for Participation in Biomedical and Behavioral Research.” In: *The Belmont Report – Appendix 1*. Available at https://videocast.nih.gov/pdf/ohrp_appendix_belmont_report_vol_1.pdf

Levine, R.J. 1979. "Clarifying the concepts of research ethics." *Hastings Center Report* 9(3): 21-26.

Levine, R. J. 1999. "The need to revise the Declaration of Helsinki." *The New England Journal of Medicine* 341: 531-534.

The National Commission for the Protection of Human Subjects of Biomedical and Behavioural Research. 1978. *Report and Recommendations – Institutional Review Boards*. Washington DC: DHEW.

Neuberger, J.1992. *Ethics and Health Care: The Role of Research Ethics Committees in the United Kingdom (Research Report).* London: King’s Fund.

Nuffield Council on Bioethics. 2015. *Children and clinical research: ethical issues*. London: Nuffield Council on Bioethics.

Pappworth, M.H. 1967. *Human guinea pigs: Experimentation on man*. London: Routledge.

Ploug, T. and Holm, S. 2017. Informed consent and registry-based research-the case of the Danish circumcision registry. *BMC medical ethics 18*: 53.

Porsdam Mann, S., Savulescu, J. and Sahakian, B.J. 2016. Facilitating the ethical use of health data for the benefit of society: electronic health records, consent and the duty of easy rescue. *Philosophical Transactions of the Royal Society A: Mathematical, Physical and Engineering Sciences*, *374*(2083): 20160130.

Riis, P. 1977. "Letter from... Denmark. Planning of scientific-ethical committees." *British Medical Journal* 2.6080 (1977): 173-174.

Riis, P. 1983. "Experiences with committees and councils for research ethics in Scandinavia." *Progress in Clinical and Biological Research* 128: 123-129.

Riis, P. 2003."Thirty years of bioethics: the Helsinki Declaration 1964-2003." *New Review of Bioethics* 1: 15-25.

Rothman, D.J. 1991. *Strangers at the Bedside: A History of How Law and Bioethics Transformed Medical Decision Making*. New York: Basic Books.

Rossel, P. 1979. *Medicinsk Etik*. København: GEC Gads Forlag.

Rossel, P. 2017. *Brystkræftprojektet – Forskning Uden Informeret Samtykke.* København: FADL’s Forlag.

Sass, H-M. 1983. "Reichsrundschreiben 1931: pre-Nuremberg German regulations concerning new therapy and human experimentation." *The Journal of Medicine and Philosophy* 8: 99-112.

Schrag, Z.M. 2010. *Ethical imperialism: Institutional review boards and the social sciences, 1965–2009*. Baltimore: JHU Press.

Seiler, L.H., and J.M. Murtha. 1980. "Federal Regulation of Social Research Using" Human Subjects:" A Critical Assessment." *The American Sociologist*: 146-157.

Solbakk, J.H. 2010. "National Ethics Advisory Bodies and Committees in Norway: history, lessons learnt, and common challenges ahead." In: *National Bioethics Committees in Action*. Paris: UNESCO. p. 56-64.

Wiley. 2014. *Wiley's Best Practice Guidelines on Publishing Ethics - Research Ethics in Journal Articles*. https://authorservices.wiley.com/ethics-guidelines/research-ethics-in-journal-article.html . Accessed 26 June 2019.

Woodward, B. 1999. "Challenges to human subject protections in US medical research." *JAMA* 282: 1947-1952.