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This material has been published in Beyond Autonomy: *Limits and alternatives to informed consent in research ethics and law* by Kirchhoffer, David G.; Richards, Bernadette

https://doi.org/10.1017/9781108649247.007

BEYOND AUTONOMY

Limits and Alternatives to Informed Consent in Research Ethics and Law

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CAMBRIDGE
UNIVERSITY PRESS

CAMBRIDGE
UNIVERSITY PRESS

University Printing House, Cambridge CB2 8BS, United Kingdom

One Liberty Plaza, 20th Floor, New York, NY 10006, USA

477 Williamstown Road, Port Melbourne, VIC 3207, Australia

314–321, 3rd Floor, Plot 3, Splendor Forum, Jasola District Centre,
New Delhi – 110025, India

79 Anson Road, #06–04/06, Singapore 079906

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www.cambridge.org
Information on this title: www.cambridge.org/9781108491907
DOI: 10.1017/9781108649247

First published 2019

Printed and bound in Great Britain by Clays Ltd, Elcograf S.p.A.

A catalogue record for this publication is available from the British Library.

Library of Congress Cataloging-in-Publication Data
Names: Kirchhoffer, David G., editor. | Richards, Bernadette, editor.
Title: Beyond autonomy : limits and alternatives to informed consent in research ethics and law / Edited by David G. Kirchhoffer, Australian Catholic University, Bernadette J. Richards, University of Adelaide.
Description: New York, NY : Cambridge University Press, 2019.
Identifiers: LCCN 2019014857| ISBN 9781108491907 (hardback) | ISBN 9781108741309 (pbk.)
Subjects: LCSH: Informed consent (Medical law) | Medicine–Research–Moral and ethical aspects. | Biology–Research–Moral and ethical aspects. | Bioethics.
Classification: LCC K3611.I5 B49 2019 | DDC 174.2/8–dc23
LC record available at https://lccn.loc.gov/2019014857

ISBN 978-1-108-49190-7 Hardback

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Beneficence in Research Ethics

DAVID G. KIRCHHOFFER, CHRISTI D. FAVOR AND CHRISTOPHER D. CORDNER

This chapter examines the explicit and implicit roles that the concept of beneficence plays in the guidelines that govern biomedical research involving humans. We suggest that the role beneficence is actually playing in the guidelines is more comprehensive than is commonly assumed. The broader conceptualisation of beneficence proposed here clarifies the relationship of beneficence to respect for autonomy. It does this by showing how respect for autonomy is at the service of beneficence rather than in tension with it.

Beauchamp and Childress make the following observation about an apparent tension between respect for autonomy and beneficence (which are two of their four principles):

> As a person's interests in autonomy increase and the benefits for that person decrease, the justification of paternalistic action [which Beauchamp and Childress ground in the principle of beneficence] becomes less cogent; conversely as the benefits for a person increase and that person's interests in autonomy decrease, the justification of paternalistic action becomes more plausible.[1]

Beauchamp and Childress are addressing paternalism in medical ethics more broadly, but if we take their description to apply to human research ethics, then, it seems to suggest that where autonomy is present it has a stronger role in morally justifying a particular research protocol involving humans, whereas, as this capacity for autonomy decreases, considerations of beneficence become more important. This can create the appearance of two distinct values or principles – beneficence and respect for autonomy – that seem to work in tension with one another, in a sort of inversely proportional relationship.

[1] T. L. Beauchamp and J. F. Childress, *Principles of Biomedical Ethics*, 7th ed. (New York: Oxford University Press, 2013).

The apparent tension can also be seen in a particular reading of the historical development of human research ethics guidelines. On this view, considerations of beneficence seem to fill the gaps where respect for autonomy is unable to do the 'heavy lifting' in morally justifying research. The 1947 Nuremberg Code, responding to Nazi abuse of people in the name of so-called research, strongly emphasises the need for voluntary informed consent. Over the years, however, we see a significant expansion of guidelines to deal with the many cases of where research might seem necessary and beneficial but for which the obtaining of informed consent is impossible due to absent (a person in a coma), limited (addicts or people with dementia) or compromised (prisoners, asylum seekers or other vulnerable populations) autonomy. These 'non-autonomy' guidelines appear to have more to do with beneficent concerns to protect the vulnerable, where the vulnerable are precisely those unable, due to lack of autonomy, to protect themselves.

At the same time, guidelines are developed to prevent research that has no benefit or is downright dangerous, even if informed consent is obtained. In such instances, it seems that considerations of beneficence override respect for autonomy.

In this reading of the development of research ethics guidelines, beneficence is used to restrict or justify research where autonomy is absent, diminished or compromised, and restrict research where respect for autonomy would yield no benefit or cause harm. Again, we are left with the impression of two discrete principles operating independently and in tension with one another.

There are two problems with reading the relationship between autonomy and beneficence as a tension between two discrete competing values that turns on the degree to which autonomy and benefits are present.

First, it gives the impression that there are two different justificatory paradigms operating in human research ethics: one founded on respect for autonomy that applies to research involving competent adults, and one founded on beneficence for research involving everyone else. A single coherent justificatory framework for all guidelines is preferable.

Second, beneficence still seems to be the more important principle. In practice, despite the strong emphasis in research ethics guidelines on respect for autonomy, respect for autonomy alone is neither sufficient nor always necessary to morally justify research involving human participants. Respect for autonomy is not sufficient because we do not allow so-called research that is dangerous and promises little benefit; and respect for autonomy is not always necessary because we do allow some

research where obtaining the voluntary consent of the research participant is impossible. By contrast, beneficence is both always necessary (since we do not allow dangerous research with little benefit, even if autonomy is respected) and sometimes sufficient (since we do allow research where autonomy is absent, limited or compromised if there is sufficient direct benefit to the participant, and sometimes even where there is no direct benefit but very low risk).

To counter this perception that there are two competing paradigms – autonomy versus beneficence – we propose a complex relationship between beneficence and autonomy. Indeed, we shall argue that appeals to beneficence, properly understood, can explain both why we are concerned about respecting autonomy and a number of guidelines that deal with those instances where autonomy is limited or compromised in some way.

While we recognise that beneficence has always been an important part of the justification for human research ethics guidelines, whether explicitly[2] or, more commonly, implicitly, we do not believe there has been a clear and shared understanding of the nature or breadth of the justificatory role beneficence plays in a whole range of guidelines, nor of its relationship to autonomy. Accordingly, we offer a new conceptualisation of beneficence that makes a substantially larger claim for the importance of this concept as an underlying value in human research ethics than is made by others.

To bring out these justificatory relationships, we first consider philosophical conceptualisations of beneficence. Then, we propose four different ways in which beneficence is at work in the guidelines governing human research. From each of these ways, we derive a number of duties that correspond to a pattern of requirements consistently found in a range of important human research guidelines today. In other words, a fundamental reliance on this broader conceptualisation of beneficence is already implicit in many important human research guidelines. In addition, this analysis makes clear how guidelines addressing different cases

[2] For example, National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, *The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research* (1979), Part B2; available at www.hhs.gov/ohrp/humansubjects/guidance/belmont.html; The National Health and Medical Research Council, the Australian Research Council and Universities Australia, *National Statement on Ethical Conduct in Human Research* (Canberra: Commonwealth of Australia, 2007, updated 2018), Section 1; available at https://nhmrc.gov.au/about-us/publications.

of human research are related for their justificatory force under a multi-faceted conceptualisation of beneficence.

Beneficence

According to William Frankena's classic articulation, the principle of beneficence consists of 'a prima facie obligation to do good and prevent harm'.[3] He considers the principle of beneficence to include four elements, all of which are 'principles of prima facie duty', though he tends towards favouring the first over the second and so on in order of priority:

1. One ought not to inflict evil or harm.
2. One ought to prevent evil or harm.
3. One ought to remove evil.
4. One ought to do or promote good.

Tom Beauchamp and James Childress, by contrast, divide this terrain into two principles: the principle of non-maleficence, which directs us to 'do no harm', and the principle of beneficence, which refers to a positive duty 'to confer benefits'.[4] They consider non-maleficence to include the first of Frankena's elements above, and beneficence to cover the latter three, on the grounds that each of the latter three involves a positive act, while the first expresses a more stringent duty not to unjustifiably harm *anyone*. Consequently, non-maleficence is a principle that must be followed impartially, i.e., one should not harm anyone, whereas beneficence need not be followed impartially, i.e., one can choose to whom one confers benefits – family, friends and so on.[5]

While we see the value of Beauchamp and Childress's distinction, we do not believe it needs to be made so sharply. Beauchamp and Childress's desire to separate *not* harming from preventing harm, minimising harm and doing good is useful because, like the inclusion of respect for autonomy in the *Nuremberg Code*, it can help to avoid failures of beneficence where beneficence might be *mistakenly* understood to be doing good for others by harming some. Nonetheless, we favour including non-maleficence into the conceptualisation of beneficence as Frankena does with his first element.

[3] W. K. Frankena, *Ethics*, 2nd ed. (Englewood Cliffs, NJ: Prentice-Hall, 1973), 47.
[4] Beauchamp and Childress, *Principles*, 151–3.
[5] Ibid., 204.

To illustrate this point, it is worth considering how Frankena points out that adding 'to or for anyone' to the four duties itemised above (for example, one ought not to inflict evil or harm *to or for anyone*) makes them universalistic. By contrast, Frankena states that adding 'to or for others' instead of 'to or for anyone' would make these duties altruistic. It is not wholly clear what Frankena means by altruistic, but we suppose he means that one could then make certain choices about whom one does not harm depending on who constitutes an *other*, for example, kin, compatriots and so forth.[6] If this is so, then there could also be a darker side to this 'altruistic' phrasing. If one can choose who the others are, then it would pave the way to a utilitarian reasoning that would allow the harming of some (those who are not part of your group) for the net benefit of others (those who are). It is conceivable that many of the Nazi doctors or those who ran the Tuskegee syphilis study thought their research worthwhile, or indeed good 'for others', and the harm to their subjects as at best a necessary evil or, more disturbingly, a desirable good.[7]

By separating 'do no harm' out from the principle of beneficence, Beauchamp and Childress's principle of non-maleficence makes the wrong of these kinds of experiments explicit, which is a good thing. Still, the universalistic rather than the altruistic version of Frankena's duties nonetheless makes it impossible to justify doing moral evil to someone (harm with no direct benefit or consent) regardless of how much good would result for others. So, Beauchamp and Childress's distinction is unnecessary because it is already included in Frankena's universalistic understanding.

Regarding the ordering, Beauchamp and Childress, true to their method of weighing principles, resist any ordering, arguing that sometimes significant benefit may outweigh minor risks or harms. For Frankena, however, the impartiality of the universalistic claim that we should not inflict harm to anyone is prior to and stronger than duties to actively remove harm or do good, with doing good being the least binding.

[6] This would be similar to Beauchamp and Childress's distinction between general beneficence, which would be akin to the universalistic conception, and specific beneficence, which could be what is meant by altruistic.

[7] S. Stein (trans.), 'Translation of document 1617-PS. Letter from Himmler to General Field Marshal Milch concerning transfer of Dr. Rascher to the Waffen-SS', in *Nazi Conspiracy and Aggression*, Vol. 4. (Washington, DC: US GPO, 1946), cited in R. S. Pozos, 'Nazi hypothermia research: should the data be used', in T. E. Beam (ed.), *Military Medical Ethics*, Vol. 2 (Washington, DC: Office of the Surgeon General, 2003), 439–61, 439.

Nonetheless, because the duties are prima facie, it is still possible to justify some minor risks or harms where there are clear benefits for the individual or community. The priority of not harming means that any harms so justified would need to be minimal or at least proportionate to the benefits for the individual exposed to them. Thus, we can still affirm with Beauchamp and Childress that a minor risk to some can be justified by significant benefits to most, for example in the case of vaccination programmes. A substantial harm to one, however, can never be justified simply on the basis of a net gain. For example, one cannot kill a criminal to use organs to save two innocent lives.[8]

Moreover, since beneficence has to do with realising the good, it seems reasonable to more closely associate non-maleficence with this realisation of the good. In other words, non-maleficence is more than just the absence of doing evil. Not harming is good for the one not harmed, just like actively preventing harm, removing harm or promoting good are good. Moreover, a person's (A) commitment to not harming another (B) also expresses A's concern for the good of B. Not harming is not just good for the one not harmed; A's beneficent concern for B, by recognising the importance of not harming B, is itself an additional good.

This position is strengthened when we extend beneficence beyond Frankena's duties of omission (not harming) and commission (promoting good, as well as taking active steps to prevent and reduce harms) to include motives. According to Garrett Cullity, beneficence in contemporary moral theory means 'appropriately furthering the welfare of others, from that motive'.[9]

Ezekiel Emmanuel, David Wendler and Christine Grady offer seven ethical requirements that they see as universally required for ethical research, together with underlying value justifications.[10] Of these seven ethical requirements, they make 'Non-maleficence and Beneficence' the underlying values for just one: the requirement of a favourable

[8] Beauchamp and Childress, *Principles*, 153.

[9] G. Cullity, 'Beneficence', in R. Ashcroft, A. Dawson, H. Draper, and J. McMillan (eds.), *Principles of Health Care Ethics*, 2nd ed. (Hoboken: Wiley & Sons, 2007), 19–26, 19.

[10] '(1) social or scientific value requires the research to contribute to new knowledge or health benefits, (2) scientific validity requires methodological rigor, (3) fair subject selection requires that scientific validity rather than vulnerability or privilege determine subject selection, (4) favorable risk-benefit ratio requires risk to be minimized, benefits to be enhanced, (5) independent review, (6) informed consent, and (7) respect for enrolled subjects.' E. J. Emmanuel, D. Wendler, and C. Grady, 'What makes clinical research ethical?' *Journal of the American Medical Association*, 283 (2000), 2701–11.

risk–benefit ratio. Yet, even with such an apparently limited explicit role for beneficence as an underlying value, they recognise that 'the overarching objective of clinical research is to develop generalizable knowledge to improve health and/or increase understanding of human biology'.[11]

Since it is not controversial to consider such improvements in health and our understanding of human biology to be good things, one could assert, following Cullity, that this 'overarching objective' is a *beneficent* one: it leads to actions that achieve good ends for human beings. But beneficence is also a *motivation* to pursue this overarching objective. The point we are making is a conceptual point about what beneficence *is*, and a moral argument about what justifies human research. If beneficence is a motive and justification for this overarching objective, then arguably beneficence plays a role not only in a more 'consequentialist-style' risk–benefit analysis, but also in all of the seven requirements Emmanuel et al. propose, including informed consent. Or, as Cullity puts it, 'Since the point of health care is to benefit the person to whom it is provided, all questions in health care ethics are in one way or another about beneficence: its scope, limits and proper expression.'[12]

Finally, Frankena argues, and we agree, that prima facie duties can be derived from beneficence: 'Wherever one can form a general statement about what affects the lives of people for better or for worse, there one has a valid principle of prima facie duty.'[13] Our claim is that most of the requirements found in contemporary human research ethics guidelines can be understood as duties derived, at least in part, from a multi-faceted conceptualisation of beneficence.

One of the most important such duties, we propose, is the duty to respect autonomy where it is present. This duty can be derived in part from the duties of beneficence. Respect for autonomy means not harming a person's capacity to make informed choices. Respect for autonomy means protecting that capacity and removing obstacles to its exercise. And respect for autonomy means promoting the good insofar as we consider the exercise of reason and free choice to be good things in themselves and good for the flourishing of human beings.

[11] Ibid., 2701.
[12] Cullity, 'Beneficence', 19.
[13] Frankena, *Ethics,* 48.

The Four-Fold Role of Beneficence in Human Research Ethics

Following from the theoretical consideration of beneficence, we propose that there are four ways in which beneficence plays a fundamental role in the ethics of biomedical research involving human beings. Each of the four ways consists of a formal norm and a set of more concrete requirements of ethical human research (see Frankena's claim that duties can be derived from beneficence above). These four ways of conceiving of beneficence are interdependent such that it is not sufficient to consider only one aspect to be the fullness of the meaning of beneficence in the context of human research. Rather, these four ways need to be considered together as part of a holistic conceptualisation of beneficence. The value of this multi-faceted conceptualisation is that it provides a good way to explain why we do research, how the requirements to eliminate risk and show proportionate benefit operate, why we are concerned about respecting autonomy where this is possible, and why most guidelines will only allow direct benefit or low risk research in vulnerable cases. Once these facets of beneficence are taken together, it becomes clear how respect for autonomy and beneficence work hand in hand, rather than in tension.

In what follows, we describe these four ways of thinking about beneficence, and then look at how they are evident in existing research ethics guidelines as concrete requirements (derived duties). We examined a range of important guidelines to see how they make reference to beneficence, either implicitly or explicitly, and how these references may be related to any reference to respect for autonomy and informed consent. A remarkable level of consistency was revealed across the documents when the guidelines were viewed through the lens of the multi-faceted conceptualisation of beneficence proposed here. In this section, we use the Preamble to the Council of Europe's 2005 *Additional Protocol to the Convention on Human Rights and Biomedicine* – an additional protocol to the 1997 *Oviedo Convention*[14] focusing on biomedical research on humans – to structure our reflections on each of the four facets of beneficence. We also provide tables that demonstrate how this conceptualisation of beneficence appears in other key guidelines.

[14] Council of Europe, *The Oviedo Convention – 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* (1997), available at http://conventions.coe.int/Treaty/en/Treaties/Html/164.htm; Council of Europe, *Additional Protocol to the Convention on Human Rights and Biomedicine, Concerning Biomedical Research* (2005), available at http://conventions.coe.int/Treaty/en/Treaties/Html/195.htm.

In summary, we propose that most human research ethics guidelines can be framed in the following way, underpinned by the four-fold conceptualisation of beneficence elaborated below:

Beneficence$_1$: It is good to do biomedical research because progress in this field is good for human beings.

Beneficence$_2$: But, this progress requires research on some human beings, which could be harmful to them. To ensure that they are not treated merely as a means, first, risks and non-moral harms should be minimised, the knowledge should not be obtainable by another means, and methods should be sound.

Beneficence$_3$: Second, there must be a benefit proportional to the remaining risks and non-moral harms, and participants who are able to consent must do so with adequate information about these risks and benefits.

Beneficence$_4$: Finally, where some people are not fully able to consent, special protection should be given to ensure that there is either a direct proportionate benefit for the participant, or there is at least a proportionate benefit for those like him or her in some specific respect *and* there is very low risk for the participant. Furthermore, the consent of adequately informed guardians must be sought.

Now we look at each of these in more detail with specific reference to the Council of Europe's 2005 *Additional Protocol* to the *Oviedo Convention* and tables of references to each kind of beneficence in other key documents.

Beneficence$_1$ = Do Good

Here, beneficence serves as an overarching justification for the enterprise of human biomedical research itself (see the discussion of Emmanuel et al., the discussion of Frankena's universalistic clause and the motivational aspect of beneficence in the section on Beneficence).

This overarching beneficence is expressed in two ways in the *Additional Protocol's* Preamble. The first occurs when the Preamble reiterates the aim of the original *Oviedo Convention* to protect the dignity, identity, integrity and 'other rights and fundamental freedoms' of '*all* human beings' (italics our own).

This general concern for the good of all human beings includes a second element in the justification of the research enterprise itself. According to the Preamble, we want to, and should, engage in 'progress in medical and biological sciences' because it 'contributes to saving lives and improving quality of life'. Thus, in the context of biomedical research, from the formal norm of Beneficence$_1$ to do good, we derive

Table 6.1 *Evidence of Beneficence$_1$ in human research ethics guidelines*

Guidelines[a]	(i) Concern for the good of all human beings	(ii) Research is good for human beings
Nuremberg		Point 2
Helsinki	Para. 4, 7	Para. 6
Belmont	Part B, s. 1 and 2	Part B, s. 2
Common Rule		
CIOMS	Preamble, Guideline 1	Preamble, Guideline 1
Oviedo – Additional Protocol	Preamble; art. 1	Preamble
ICH–GCP	Intro. and 2.1 (follows Helsinki)	
National Statement	Preamble, Purpose	Preamble, Purpose

[a] The documents abbreviated in the left-hand column are: *The Nuremberg Code* (1947); World Medical Association, *Declaration of Helsinki* (2013); National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, *The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research* (1979); US Department of Health and Human Services, *Federal Policy for the Protection of Human Subjects* (a.k.a. *The Common Rule*), Title 45, Code of Federal Regulations, Part 46, (2018); the Council for International Organizations of Medical Sciences (CIOMS), *International Ethical Guidelines for Health-Related Research Involving Humans* (2016); Council of Europe, *Additional Protocol to the Convention on Human Rights and Biomedicine, Concerning Biomedical Research* (a.k.a. *Additional Protocol to Oviedo*) (2005); International Council on Harmonisation of Technical Requirement for Pharmaceuticals for Human Use (ICH), *E6(R2) Good Clinical Practice* (GCP) (2016); National Health and Medical Research Council et al., *National Statement on Ethical Conduct in Human Research* (2007, updated 2018).

the duty to pursue progress in the medical and biological sciences for the benefit of all human beings. Table 6.1 shows references that can be interpreted as representing the two elements of Beneficence$_1$ in a selection of relevant documents.

Beneficence$_2$ = Avoid Harm

Beneficence$_2$ is about avoiding harm and minimising risk. Since good is the goal of research, it is desirable always to avoid or minimise

non-moral[15] evil. Frankena gives the example of choosing between 99 goods and no evils, versus a net gain of 100 goods though with a large number of evils.[16] Beneficence favours the former, unlike a purely utilitarian calculus, which favours the latter. This is important, because it prevents a too easy justification of research for the benefit of others at the expense of some, as in the cases of the Nazi doctors and the Tuskegee syphilis study; it prevents the ends justifying morally evil (as distinct from non-moral evil) means.

In the Preamble, this is more implicit than the other facets of beneficence. Having affirmed that progress in biomedical research is good, the Preamble identifies a problem: this progress or advancement 'necessitates research on human beings' (column (i) in Table 6.2a). In order to obtain the benefits of human research, humans will need to undergo *non-moral* evils, ranging from minor inconvenience, to discomfort, pain, the risk of side effects, or even possible death, which are obviously not desirable in themselves (column (ii) in Table 6.2a). Thus, the Preamble is expressing a beneficent concern for when it is morally licit to allow non-moral evils (risks or harms) for *some* human beings in order to achieve the good outcomes that research promises for *all* human beings. Two duties can be derived from the formal norm to avoid harm. The first concerns an absolute restriction on research that would use some human beings *merely* as means. The second concerns a series of guidelines to do with minimising risk and harms, as one condition of treating research participants as ends in themselves.

In the case of the first norm, the Preamble seems to concur that no benefits can justify *moral* evil, i.e., behaviour in which the means constitutes an intrinsically bad violation of certain basic human goods, most notably human dignity and rights: 'biomedical research that is contrary to human dignity and human rights should never be carried out'.

This is important, because, although Beneficence$_3$ (see below) appears to simply weigh risks and benefits in justifying research as ethically acceptable, the guidelines do highlight in accordance with Beneficence$_2$ that there are certain evils or disvalues that are always intolerable (even as

[15] We follow Frankena, *Ethics,* 62, in our use of the term *non-moral*. We use it to distinguish values and disvalues, such as pleasure and pain, that are not necessarily moral in their own right, but are nonetheless morally relevant in determining the moral goodness or badness, rightness or wrongness of a course of moral behaviour. In this specific context, this is similar to Beauchamp and Childress's use of *harms* as distinct from *wrongs* (*Principles*, 153).

[16] Frankena, *Ethics*, 46.

Table 6.2a *Evidence in human research ethics guidelines of the duty derived from Beneficence$_2$ not to use human beings only as means*

	(i) Human research necessary for medical progress	(ii) Human research involves risk to humans	(iii) Risk is permissible only if compatible with human rights and dignity	(iv) Interests/welfare of participant has precedence over sole interest of society
Nuremberg			Points 5, 10	
Helsinki	Para. 5, 6	Para. 6, 16	Para. 7–10	Para. 8
Belmont	Part B, s. 2	Part B, s. 2, esp. 2nd para.	Part C, s. 2, C.2.(i), to some extent also Part B, s. 3	Part C, Sec. 2 says 'carries special weight'
Common Rule				
CIOMS	Preamble, Guideline 1		Guideline 1 and Commentary	Guideline 1, Commentary to Guideline 4
Oviedo – Additional Protocol	Preamble		Preamble; art. 1; art. 9.2	Preamble; art. 3
ICH–GCP	Intro. & 2.1 (follows Helsinki)	2.1	3.1.1	2.3
National Statement		Preamble, 2.1	Purpose, s. 1, 5.2.5	s. 1, Intro. 'each human being has value in himself or herself'; 1.1 (d), 1.10

See Table 6.1 for explanation of document abbreviations used in first column.

so-called necessary evils) and that would make any research involving them morally wrong, regardless of the potential benefits. Since we have a beneficent concern for human beings derived from $Beneficence_1$, we also have a duty derived from $Beneficence_2$ not to undermine the very good that we claim we are working for, namely human beings.

Not treating human beings merely as means, here, is more than simply about respecting autonomy. While it is true to say that we should respect autonomy as a duty derived from this concern to avoid harm, as discussed in the previous section, this concern nonetheless blocks certain kinds of research, such as that carried out by the Nazi doctors or in the Tuskegee syphilis study, even if the subjects were to consent. That their autonomy was not respected is clearly a wrong that violated the duty to avoid harm. But the manner in which they were treated, regardless of any capacity for autonomy, makes the experiments wrong.[17] They were treated merely as means to the ends of the researchers. No consideration was given to their humanity.

Table 6.2a shows references in various documents that support the idea that $Beneficence_2$ underpins a claim that human beings may never be used merely as a means.

The second concrete norm derived from $Beneficence_2$ is about expressing respect for human beings as ends through undertaking to minimise harms. In other words, it assumes that even if you are manifesting respect for human beings as ends, perhaps by including informed consent as in $Beneficence_3$, you are still obligated to minimise harms as a further requirement of respect for those human beings as ends. Recall Frankena's idea here that it seems to be better to get 99 'goods' with no harm than a net gain of 100 'goods' with lots of harm.

The Preamble expresses this by 'Stressing the paramount concern to be the protection of the human being participating in research'. This concern is more concretely worked out in research documents in requirements to eliminate any risk that is reasonably practical to remove, to demonstrate sound methodology, to demonstrate a study design that really is likely to produce new knowledge, and to demonstrate the necessity of using human participants. Sound methodology and study design both minimise risks. It is true that there is a dimension of potential benefit here too ($Beneficence_3$ below); however, we suggest that the consideration of benefits to actual people follows, procedurally

[17] K. Mellanby, 'Medical experiments on human beings in concentration camps in Nazi Germany', *British Medical Journal*, 1, 4490 (1947), 148–50.

speaking, assessment of the best methodology and study design in terms of minimising risk to possible subjects. Moreover, not only do sound design and methodology minimise risk, they also ensure people are not exposed to risk in the name of unhelpful, bad science that is merely promoting the interests of some scientists, institutions or corporations. This too is connected to not treating research subjects as mere means, as well as to ensuring a more positive risk–benefit ratio as per Beneficence$_3$. Also in this category are requirements that the research be carried out by qualified individuals, and reviewed by a Human Research Ethics Committee (HREC), Institutional Review Board (IRB) or equivalent in the event of anything more than low risk (see Table 6.2b).

If we start from Beneficence$_2$, then these guidelines can be seen to impose their demands independently of any operation of autonomy or consent from participants. We ensure that our research methods are sound, that the knowledge cannot be obtained any other way, and that risks are minimised *prior* to asking whether the participants even want to participate. This means that high-risk research, where these kinds of safeguards have not first been put in place, should not be carried out, even if informed consent could be obtained. Table 6.2b contains references to passages in key human research ethics documents that can be interpreted as expressing a similar concern to minimise harm.

Beneficence$_3$ = Proportionate Benefit

Beneficence$_3$ is a weighing of unavoidable remaining risks and benefits for the research participants and for the population as a whole. This weighing works with the requirement of consent in participants able to give it (see the discussion of Emmanuel et al. in the section on Beneficence). Total avoidance of any non-moral harm or risk is seldom possible. Unavoidable harms or risks should only be incurred where there are proportionate benefits. To illustrate, stopping the pain of a rotten tooth requires the non-moral harm of forcefully removing that tooth (but with anaesthetic in accordance with Beneficence$_2$).

At least part of the justification for the principle of respect for autonomy could come from its being a derivative duty of this kind of beneficence (noting that it can also be partly derived from Beneficence$_2$), since a very important way to ensure that risks are not disproportionate to benefit, as well as to ensure that a human being is treated as an end (see Beneficence$_2$), is to adequately inform a competent subject and then allow her to choose.

Table 6.2b *Requirements in human research guidelines derived from Beneficence$_2$ to minimise unavoidable harm*

	(i) Risk that is possible to avoid must be avoided	(ii) Scientific and research methods must be sound	(iii) Research must be impossible without humans, or must lead to information not otherwise attainable	(iv) Research must contribute to new knowledge or benefit	(v) Research must be carried out by qualified individuals	(vi) HREC must review all studies with greater than low risk
Nuremberg	Points 4,7	Point 3	Point 2	Points 2, 3	Point 8	
Helsinki	Para. 17, 18	Para.17, 21, 22		Para. 8, 17, 18	Para. 12	Para. 23
Belmont	Part B.2, and Part C.2 (ii)	Part C.2	Part C.2.(ii)			Final paragraph of Part A
Common Rule	S46.111 (a) (1)	S46.111 (a) (1) (i)		S46.111 (a) (2)		S46.103 (b) and (f)
CIOMS	Guideline 1	Guideline 1 and;	Commentary	Commentary to Guideline 1	Preamble, Guideline 1 and Commentary	Commentary to Guideline 1
Guideline 23 and			Commentary	Oviedo – Additional Protocol	Art. 21.1	Art. 7, 8
Art. 5	Art. 7	Art. 8, 21.2	Art. 7,9			
ICH–GCP	2.13; 3.1.1	2.5		2.1, 2.2	2.7, 2.8; 4.2.3; 4.3.1	2.6
National	Statement	1.7.(a); 2.1,	esp. 2.1.3.(d)	1.1.(a)-(c); 5.1.2. (a)		1.1-1.3, 5.2.5
5.1.2.b.i	5.1.6.a					

HREC: Human Research Ethics Committee.
See Table 6.1 for explanation of document abbreviations used in first column.

The Preamble affirms the aim of the *Oviedo Convention* to guarantee respect for people's integrity and fundamental freedoms. These must include freedom of choice. So, one ought to be able to choose to undergo certain foreseeable risks or even harms for research purposes.

This choice, to be in accordance with Beneficence$_3$, must still entail some proportionate potential benefit, i.e., the potential benefit must be in proportion to the risk undertaken. This benefit may be either for the individual research subject or for others, possibly those afflicted with the same condition, belonging to the same group or even for humanity in general, in accordance with the Preamble's Beneficence$_1$ concern for 'saving lives and improving quality of life'. So, where autonomy is present, all parties, including participants, researchers and ethics committees, have to agree the benefit is proportional to the risks.

Note that this benefit, in the case of Beneficence$_3$, need not be for the individual research participant. Here, respect for autonomy is important, though not a value that necessarily trumps all others. Suppose, for example, you are a legally competent person, have a terminal disease and are asked to participate in research that will cause discomfort and pain, and there is no guarantee of direct physical benefit for you. The research could benefit many other people suffering from the same condition. Since there is a potential benefit for others, Beneficence$_3$ may still permit this research *provided you consent*.

By requiring consent where possible, Beneficence$_3$ not only protects and promotes dignity, freedom and so on, but also provides the possibility of allowing the research participant to participate in the value of beneficence, i.e., to choose to do good things. She can embrace the beneficent goals of the research as her own. This is one of the few ways to explain why a person might choose to participate in research where there is no direct physical benefit (for example, Phase 1 clinical trials), assuming there are no other pressures such as compromised autonomy due to power relationships.

Table 6.3 shows the requirements associated with this third facet of beneficence and their specific locations in the various documents.

Beneficence$_4$ = Special Protection for the Vulnerable

Beneficence$_4$ involves special protection for vulnerable individuals or groups and can be seen clearly in the Preamble's affirmation that 'particular protection shall be given to human beings who may be vulnerable in the context of research'. This can be seen as a combination and extension of Beneficence$_1$ and Beneficence$_2$ in cases where Beneficence$_3$'s

Table 6.3 *Requirements in human research guidelines derived from Beneficence$_3$ to ensure proportionate benefits*

	(i) Benefits and risks should be weighed such that benefits outweigh or justify unavoidable risks	(ii) Voluntary informed consent must be obtained, AND	(iii) EITHER there is a proportionate expected benefit for the subject	(iv) OR there is a proportionate expected benefit to others
Nuremberg	Point 6	Point 1, 9	Implied in Points 6, 10	Implied in Point 6
Helsinki	Para. 16, 17, 18	Para. 25, 26, 27, 31	Para. 16, 17, 18	Para. 16, 17, 18
Belmont	Part C, s. 2	Part C, s. 1	Part C, s. 2	Part C, s. 2
Common Rule	S46.111 (a) (2)	S46.111 (a) (4) and S46.116	S46.111 (a) (2)	S46.111 (a) (2)
CIOMS	Guideline 4 and Commentary	Guideline 9	Guideline 4	Guideline 4
Oviedo – Additional Protocol	Art. 6	Art. 13, 14	Art. 6.1	Art. 6.2
ICH–GCP	2.1, 2.2	2.9, 4.8.1–11	2.2	2.2
National Statement	2.1.2	2.2	2.1.3, 2.1.5	2.1.3, 2.1.5

See Table 6.1 for explanation of document abbreviations used in first column.

concern for autonomy is inadequate to avoid harm and ensure good. The categories of research participants who require stronger protection include: (a) those with *diminished* autonomy such as children, participants with mental illness and those with a temporary incapacity, for example, unconsciousness; (b) those with *compromised* autonomy, such as asylum seekers, prisoners and those in hierarchical contexts such as students or employees; and (c) when an HREC has granted a Waiver of Consent, or where consent would undermine the specific research question at issue.

In all these cases, the diminished or compromised capacity to consent necessitates protecting the participants involved. The overarching concern for beneficence (Beneficence$_1$) recognises that we can still often (and should aim to) benefit people in these categories by learning from research that includes them as participants (Beneficence$_3$'s proportionate benefit aspect). Yet, beneficence also involves protecting people from harm and unjust exploitation (Beneficence$_2$). When we cannot rely on the informed judgment and consent of participants as part of this protection from harm, more stringent protections, tolerating less in the way of risk or harm, are required. What made the Nazi abuses wrong was not simply that they did not respect autonomy; they exploited people with compromised autonomy (effectively prisoners threatened with death for non-compliance). It would have been morally wrong even if the victims had apparently consented.

When autonomy is diminished or compromised, guidelines usually only permit research participants to be exposed to risk if (a) the study cannot be carried out in a non-vulnerable group, (b) consent is sought and gained from a legal representative where possible, (c) assent is gained where possible, and dissent is respected where expressed, (d) consent is sought if the participant's situation changes, *and* (e) *either* there is proportionate expected direct physical benefit to the participant, *or* (f) there is proportionate benefit to others like the participant and *only* if the harm and risk to the participant are minimal.

Without the additional protection afforded by informed consent, Beneficence$_4$ permits no more than minimal risk in vulnerable populations *unless* those risks are in the service of proportionate benefit to the participants themselves (Beneficence$_3$), and do not undermine their integrity, dignity and so on as human beings (Beneficence$_2$), or, in some documents, if an HREC has considered the matter and approved a minor increase over minimal risks.

The requirements associated with beneficence for vulnerable groups are delineated in Table 6.4.

Table 6.4 *Conditions and requirements in human research guidelines derived from Beneficence$_4$ to provide special protection for the vulnerable*

	(i) It must be impossible to conduct the study in a non-vulnerable group	(ii) Consent must be obtained from a legal representa-tive where possible, AND	(iii) Participant must be informed, assent obtained if possible, participant's dissent respected, AND	(iv) Consent sought if subject's circumstances change to make consent possible, AND	**(v) EITHER There is a propor-tionate expected benefit to the partici-pant,** OR	(vi) There is proportionate expected benefit to others in the group represented by the participant, AND in that case, only if the risk is minimal (or an HREC approves a minor increase above minimal)
Nuremberg	Not applicable to Nuremberg; Point 1 requires all research subjects have legal capacity to consent and full exercise of their free power of choice					
Helsinki	Para. 20, 28, 30	Para. 28, 30	Para. 29	Para. 30	Para. 14, 20, 28	Para. 14, 28, 20
Belmont	Part C, s. 2, considera-tion (iv); Part C, s. 1 with respect to 'waiver of consent'	Part C, s. 1	Part C, s.n 1, 'to the degree they are capable'		See B.1, B.2 and C.2	Part B.2 considers this for children, but does not strictly adopt this, Part C.1 does so for 'waiver of consent' cases

Common Rule	S46.116 (c) (2); S46.116 (d) (3)	S46.116, S46.408	S46.404–408	246.117 (c)–(f)	S46.405 (a) and (b)	S46.116 (d) (1); S46.406–407
CIOMS	Guidelines 15–17	Guidelines 15–17	Guidelines 15–17	Guidelines 15–17	Guidelines 15–17	Guidelines 15–17
Oviedo – Additional Protocol	Art. 15.1.ii and art. 19.2.i; art 20.i	Art. 15.1.iv	Art. 15.1.iii; 15.1.v and 19.2.iii	Art. 19.3	Art. 15.1.i	Art. 15.2.i & 15.2.ii; art. 17; art. 19.2.iv, art. 20.ii and iii
ICH–GCP	4.8.14(a)	4.8.5	4.8.12	4.8.15	2.2	4.8.14, esp 4.8.14 (b) & 4.8.14 (c)
National Statement	2.3.1.a; 4.2.4 (at least with children)	2.2.12; 4.2.7, 4.5.5	2.3.2.c; 4.2.7; 4.2.14; 4.5.11	2.3.1.e; 2.3.2.b; 4.5.6; 4.5.9	2.2.12; 2.3.1.b; 4.2.13; 4.5.4; 4.4.1 (c) (i)	2.2.12 (wording is 'must not be contrary to best interest'); 2.3.1.c; 2.3.2.a; 2.3.10.a 4.4.1 (c) (ii) (but see also 4.5.3)

See Table 6.1 for explanation of document abbreviations used in first column.

Conclusion

Respect for autonomy plays an important role in biomedical research involving humans. We do not dispute that. Nor do we deny that the concept of beneficence already plays a role in biomedical research involving humans.

We have demonstrated, however, that a broader conceptualisation of beneficence, understood in a complex, multi-faceted way, reveals its justificatory role in a broad range of guidelines, which may previously have appeared unrelated. Furthermore, this way of understanding beneficence in the guidelines also clarifies and strengthens the relationship between beneficence and autonomy, often previously thought simply to be separate values in tension. Remaining consistent with Frankena's theoretical framework for the concept of beneficence, we have identified four ways in which beneficence seems to contribute to grounding a range of specific requirements, including the principle of respect for autonomy. We have also demonstrated a large degree of consistency in these patterns of beneficence-derived requirements in research guidelines.

That said, we do not claim that beneficence solves all of the issues associated with how to conduct morally good research. There are still difficult questions, such as what constitutes proportionate benefit, which beneficence cannot answer. Moreover, it is likely that beneficence, even in this complex, multi-faceted understanding, is itself related to other values that work with it to justify the kinds of ethical requirements we have been discussing. For example, though respect for autonomy could be justified by an appeal to beneficence, it is equally reasonable to ask what value justifies the appeal to beneficence, that is, what justifies the requirement to do good to others? It would seem that one way to answer this might be to say something like 'the value we ascribe to human beings'.

That said, respect for human beings is arguably simply empty without beneficence, while beneficence either has no motive power or is itself hollow in the absence of such respect. This possible interrelationship of respect and beneficence warrants further investigation.

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