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An ethical analysis of coverage with evidence development
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Abstract

Sometimes a government or other payer is called on to fund a new health technology even when the evidence leaves a lot of uncertainty. One way to manage this problem is for the payer to provisionally fund the technology and reduce uncertainty by developing evidence. This is referred to as coverage with evidence development (CED). When the payer funds the technology only for patients who participate in the evidence development, the coverage is known as only-in-research. This type of CED raises the sharpest questions of coercion and inducement. Is the patient coerced or induced into participating in the evidence development? If so, under what circumstances, if any, is this ethically justified? Building on work by Miller and Pearson, we argue that patients have a right to funding for a technology only when the payer can be confident that the technology provides reasonable value for money. This means that patients have no right to technologies under a CED arrangement, since technologies are candidates for CED precisely because serious questions remain about value for money. It is for this reason that CED induces rather than coerces. The separate question of whether the inducement is ethically justified remains. We argue that CED does pose risks to patients, and the worse these risks are, the more difficult it is to justify the inducement. Finally, we propose conditions under which the inducement could be ethically justified, as well as means of avoiding inducement altogether. All of this has major bearings on the types of CED that are ethically justified and the governance structures that need to be in place. To develop our argument, we draw on the Australian context, so our conclusions apply most directly to comparable contexts, where the payer is a government that provides universal coverage with a regard for cost effectiveness that is prominent and fairly clearly defined.

Highlights

CED is the policy instrument most commonly used to reduce decision uncertainty at the point of funding a new health technology. Several ethical analyses have questioned whether CED inherently coerces or induces patients to participate in evidence development. Miller and Pearson have argued that patients are induced but not coerced, since patients are enticed by possible health benefits but there is no threat of harm for not participating and patients are not entitled to unproven technologies.

But CED technologies are partially proven. And whether foregone treatment results merely in foregone benefits or, more worryingly, in harms depends on whether anyone has a duty to provide the treatment. No payer has a duty to fund a CED technology because its value for money is precisely in question. So CED involves inducement, not coercion, but for reasons different from those advanced by Miller and Pearson.

CED does pose risks to patients, and the worse these risks are, the more difficult it is to justify the inducement. For every CED arrangement, there is a question of what inducement, burdens and risks can be levelled at patients for the sake of reducing uncertainty. Making participation in the evidence development optional would avoid inducement but potentially weaken the evidence. Ethical review bodies should be called on to assess these matters case by case.

Introduction

Health technologies encompass a wide variety of medicines and medical services, devices, procedures and tests. Governments often subsidise the cost of health technologies to make health care affordable and accessible for people. Governments typically subsidise a health technology only when they are confident that the technology is safe, effective and cost effective, overall providing reasonable value for money given the broader socioeconomic context. (While much of our argumentation may also apply to other payers such as private health insurers, we focus on governments for the sake of simplicity. And for the sake of brevity, we sometimes use the word "treatment" to refer to the use of a health technology.)

Technologies assessed for funding typically give rise to varying degrees of decision uncertainty. The reasons for this uncertainty are numerous. Many technologies are submitted for a funding decision before the evidence base is mature. Industry may seek to maximise profits by gaining earlier market access, applying for government subsidy earlier in the development of a health technology, before all of the benefits and risks are confidently grasped. Patients and the community increasingly demand earlier access to new health technologies that look to have promise. Technologies are increasingly being developed for rare diseases, where evidence is particularly hard to develop due to low patient numbers. Decision uncertainty is also likely to increase with changes at the regulatory level that will allow more use of "real-world" evidence, which has some limitations compared to evidence developed experimentally [1].

The government's concern to spend funds wisely, combined with increasing uncertainty about the value for money on offer, has resulted in policy instruments being developed to reduce decision uncertainty. There is a grey literature that details the policy instruments

being used [2, 3], alongside a health policy literature that studies the various policy instruments [4, 5, 6, 7] and provides guidance on the principles underpinning their successful design, implementation and evaluation [8, 9]. Coverage with evidence development (CED) is the most common such policy instrument, accounting for 34% of the 437 arrangements captured in an international review spanning from 1993 to 2016 [6]. CED is distinct in being the only policy instrument capable of reducing underpinning uncertainty about the safety, effectiveness or cost effectiveness of a technology.

CED refers to when a payer funds a health technology temporarily so that evidence can be developed to verify claims of safety, effectiveness or cost effectiveness. This evidence is either currently being developed, typically in another jurisdiction, or it must be developed by the party making the claims (typically the seller) in collaboration with the payer. In collaborating, the payer and seller may share the costs of the evidence development. If claims about the technology are not borne out, then the payer will discontinue coverage or renew coverage at a reduced unit price. Conversely, if the claims are borne out, then the payer will introduce normal, less conditional coverage at the existing price.

Garrison et al. [9] follow others [10] in distinguishing between two types of CED.

1. Payers can provide coverage "only with research", paying for the technology for all patients who need it while evidence to satisfactorily reduce the payer's uncertainty is developed either with a select subset of patients or outside of the health system [9, p. 708].

2. Payers can provide coverage "only in research", paying for the technology only for patients who participate in the evidence development [9, p. 708].

In this article, we focus on only-in-research CED, because it raises the sharpest questions of coercion and inducement. The fledgling literature that examines ethical issues rightly focusses on whether coercion or inducement is an inherent problem for CED [11, 12, 13, 14, 15, 16].

There is a conceptual question whether CED constitutes "research", mere "evaluation" (or "audit" or "quality assurance"), or a hybrid of these. The distinction can be drawn as follows: while research primarily aims to produce widely applicable knowledge, evaluation primarily aims to inform improvements in local service delivery or system performance. Australia's Pharmaceutical Benefits Advisory Committee sidesteps the conceptual question, referring to its CED simply in terms of "data provision arrangements" [3]. In this article, we also sidestep the conceptual question, writing simply of "evidence development". We do this because any answer to the conceptual question would not fundamentally change our argument, insofar as the ethical requirements for research and evaluation run along the same lines. They are taken to do so in Australia and elsewhere [17, 18]. In general, the ethical requirements simply intensify as the evidence development becomes more ethically problematic, most obviously in terms of risks of harm.

To date, Miller and Pearson have produced the most sustained ethical analysis of CED [14]. They are right to conclude that CED arrangements merely induce rather than coerce patients into participating in evidence development, but not for the reasons they think. We will outline our argument here then present it in detail below. Miller and Pearson argue that

patients have no right to government funding for technologies that are questionably effective, therefore patients have no right to government funding for CED technologies, which are by definition questionably effective. But it is value for money that really matters, not just clinical effectiveness. This is highlighted by the fact that sometimes a technology is clearly effective but precisely how effective remains uncertain, so the government introduces a CED arrangement to better determine whether the technology is worth the costs [19]. Patients only have a right to government funding for technologies that a government can be confident provide reasonable value for money. It is for this reason that patients have no right to CED technologies and therefore are not coerced.

Miller and Pearson's US context is notable for the ambivalent role that cost effectiveness and value for money play. Our argument encompasses more than Miller and Pearson's by including the issue of value for money. As we argue below, Miller and Pearson are also insufficiently attentive to how inducement can be ethically problematic. We argue that CED does pose risks to patients, and the worse these risks are, the more difficult it is to justify the inducement that CED typically involves, with access to the technology being conditional on participation in the evidence development. We propose conditions under which the inducement could be ethically justified, as well as means of avoiding inducement altogether. These ethical issues are important to grasp because they bear on the types of CED that are ethically justified and, moreover, on the governance structures that ought to be in place to regulate and improve CED. To develop our argument, we draw on the Australian context, so our conclusions apply most directly to comparable contexts, where the payer is a government that provides universal coverage with a regard for cost effectiveness that is prominent and fairly clearly defined.

Governments typically select for CED arrangements technologies that, among other things, show promise in terms of improved safety or clinical effectiveness. The clinical use of these new technologies would typically be in a patient's best interests, by which we simply mean it would typically be best for a patient, all things considered. Meanwhile, only-in-research CED arrangements require a patient to participate in evidence development to access the technology. More precisely, a patient must participate in evidence development to access funding for the technology. The patient could decline to participate and pay for the technology themselves, but technologies are often so costly that access to them is only possible with government funding or some other source of support. All of this raises two questions. First, is the patient coerced or induced into participating in evidence development, given that typically the technology is in the patient's best interests and cannot be accessed otherwise? Second, if the patient is coerced or induced, under what circumstances, if any, is this ethically justified? We tackle these two questions in order.

Does CED coerce or induce patients to participate in evidence development?

Does CED coerce or induce patients to participate in evidence development? Miller and Pearson suggest that this depends on whether patients have a right to the technology [14]. If patients do have a right to the technology, then they are coerced into participating in evidence development; patients must participate to avoid the harms of missing out. However, if patients do not have a right to the technology, then they are merely induced into participating; participation presents possible benefits.

Miller and Pearson emphasise that coercion involves a threat of harm. They define coercion by citing the Belmont Report, in which coercion occurs "when an overt threat of harm is intentionally presented by 1 person to another to obtain compliance" [14, p. 748]. On this definition, illness and its treatment may result in harms but in themselves illness and its treatment do not coerce since the harms are not intentionally threatened by someone to obtain compliance. Miller and Pearson also cite Wertheimer, whose conception of coercion they see as compatible with the conception that appears in the Belmont Report. Someone is coerced when there is: "(1) a threat of harm; (2) the threat violates the rights of the victim; and (3) the victim is made worse off than she otherwise would have been if she had not been forced to comply with the threat" [14, p. 748]. For the sake of argument, we do not challenge this conception.

Miller and Pearson do not define "inducement" but they use the word in the non-pejorative sense of someone simply being led on or persuaded to action by something attractive [20]. We use the word in the same sense but we are mindful of debates about whether inducement to participate in research constitutes undue inducement some of the time or even all of the time. Undue inducement occurs when "something is being offered that is alluring to the point that it clouds rational judgment" [21]. Undue inducement undermines the voluntariness, and therefore the validity, of consent [21]. We return to questions of undue inducement below.

Miller and Pearson see CED as merely inducing, not coercing: "in CED, an offer with strings attached, the "or else" is a legitimate condition attached to a benefit to which individuals are not otherwise entitled. It is not coercive" [14, p. 748]. Miller and Pearson argue that patients are not coerced because patients are not entitled to unproven technologies. They note that US Medicare patients have a legal right only to "reasonable and necessary" treatment [14, p.

748]. Miller and Pearson regard as reasonable and necessary only treatment that is good enough to definitively fund, not treatment that is merely good enough to fund for now under a CED arrangement. In this connection, they argue that

> CED is no different from … phase I through phase III clinical trials. In both cases, the lack of evidence sufficient to determine that a given treatment has a favorable risk-benefit ratio makes it appropriate to restrict covered access to research participation [14, p. 748].

But this reasoning is mistaken. When a CED arrangement is introduced, "a favourable risk-benefit ratio" is already suspected, perhaps even strongly suspected. In other words, uncertainty about the new technology's comparative safety and effectiveness is typically diminished enough that the technology can be regarded as probably being in the patient's best interests. This diminished equipoise actually makes the randomised controlled trial (RCT) highly questionable as a study design for only-in-research CED. Arguably, an RCT is only justified when there is sufficient equipoise, but CED is only justified when there is diminished equipoise.

CED is not merely research of an unproven and thereby unfunded technology. It is more so the partial (conditional) coverage of a partially proven technology. Several writers have made this observation when suggesting that CED arrangements may be coercive [12, 13]. CED is more like a phase IV clinical trial, namely post-market surveillance. Patients could be regarded as having a right to government funding for the technology, insofar as use of the technology is "necessary", in the sense of being in their best interests, and insofar as the

funding is “reasonable”. We return to funding being “reasonable” by discussing value for money. Before then, let us step through Miller and Pearson’s view a little more.

Let X be a health technology. Now suppose three things. First, without X, I will be worse off. Second, I have a right to X. Finally, to get X, I must participate in evidence development, which poses risks to me. Am I coerced to participate in the evidence development? To answer this question, let us return to Wertheimer’s three-part conception of coercion, which Miller and Pearson cite. First, am I threatened with harm? Yes. The harm I am threatened with is my being worse off by virtue of going without X. Second, does this threat violate my rights? Yes. I have a right not to be made worse off by virtue of going without X, since I have a right to X. Finally, am I worse off for being forced to comply? Yes, because participation in the evidence development poses risks to me. So supposing all this, I am coerced to participate in the evidence development. But Miller and Pearson contest the supposition that I have a right to X. This means that the first and second conditions of coercion no longer obtain, and therefore I am not coerced. Because I have no right to X, I am not threatened with harm, only lured by possible benefits. And because I have no right to X, my rights are not violated, even though I am made worse off by virtue of going without X. This is how Miller and Pearson see things.

But now let us pressure Miller and Pearson’s view again. Only-in-research CED results in foregone treatment for patients who refuse to participate in the evidence development. (More precisely, it results in patients receiving the standard treatment rather than the new treatment.) If foregone treatment results merely in foregone benefits rather than in harms, then the CED arrangement merely induces, or tempts, namely with possible benefits; it does not coerce, since there is no “threat of harm” [14, p. 748]. This is how Miller and Pearson see things.

But the question of whether foregone treatment results merely in foregone benefits or, more worryingly, in harms itself hinges on whether patients have a right to the treatment. Put differently, it hinges on whether the government has a duty to fund the treatment. Our reasoning is as follows.

Suppose that the government declines to fund a technology that a patient needs. The patient cannot afford the technology and succumbs to disease. Does the government harm the patient? The answer to this question turns on whether the government has a duty to fund the technology or (the corollary) whether the patient has a right to access government funding for the technology. If the government has no duty to fund the technology, then we would say that the patient is harmed by the disease, not the government. The government, for its part, merely fails to benefit the patient. However, if the government does have a duty to fund the technology, then we would say that the government harms the patient. More precisely, the patient is harmed by the disease but also by the government in its dereliction of duty to stop the disease from harming the patient. In discussing what we would or could say here, we are trying to trace "grammatical" relations, in Wittgenstein's sense [22, 23, 24]. That is, we are trying to trace our customary ways of making sense and going on with things. In sum, does the government harm me or merely fail to benefit me by declining to fund a technology without which I am worse off? Things turn on the reasonable expectations or, more precisely, the duties that are in force [25]. Put another way, things turn on the norms that are alive in the context.

What does this mean for CED? Only-in-research CED results in foregone treatment for patients who refuse to participate in the evidence development. Whether foregone treatment results merely in foregone benefits or, more worryingly, in harms depends on the duties that

are in force. The idea can also be put as follows. Suppose that standard care would improve my health somewhat. The CED technology would probably improve my health even more. (That is partly what makes the technology a candidate for CED.) But I am denied the CED technology. So my health is improved but less than it could have been. I am worse off than I could have been. Have I been harmed? Or have I simply been denied a benefit? It depends on what I had a right to, that is, on the duties that others had to me. It then follows that whether CED coerces or merely induces also depends on the duties that are in force. We cannot retreat to the idea that only-in-research CED merely induces because foregone treatment results merely in foregone benefits rather than in harms. Instead, we must directly confront the underpinning question of whether the government has a duty to fund the technology. Only then can we establish whether an only-in-research CED arrangement coerces or merely induces.

Patients do not have a right to government funding for all technologies without which they would be worse off, because some technologies are so costly that either the government cannot afford to provide them to everyone or, more commonly, the resources required could be better expended in other ways (for example, on other health technologies). To reformulate the latter point, patients have no right to government funding for technologies that have too great an opportunity cost. This norm is alive in Australia and the UK, among other countries, where government funds are legitimately set aside for the express purpose of availing health technologies to the public. Funds are set aside with the implicit aim of maximising value for money across the population [26] or at least avoiding outrageous opportunity costs, which is to say achieving some reasonable level of value for money. The aim of avoiding outrageous opportunity costs is the less demanding and suffices for our argument. It equates to the government having a duty to fund only technologies that provide reasonable value for money.

Patients have a right to a technology only when a government can be confident that the technology will provide reasonable value for money, especially considering health benefits. We take for granted that the government's view of what constitutes reasonable value for money is itself reasonable in being responsive to the duties it owes to people. These duties include ensuring that basic respect and care are given to all and being responsive to the views of the public and patients when it comes to what is worth spending money on. Views on what is worth spending money on can differ without being unreasonable, which is one important reason why judgements of value for money can legitimately differ across jurisdictions.

If a government has good reason to believe that a technology provides reasonable value for money, then it has a duty to fund access to the technology. But suppose the government later discovers that the technology actually does not provide reasonable value for money, perhaps because the technology turns out to be unsafe and ineffective by the light of good evidence collected in the interim. Then in effect the government discovers that it now has a duty to remove funding from the technology, not that it never had a duty to fund the technology. Duties depend on epistemic conditions (what is known) at the time. The duty to disinvest from technologies that fail to provide reasonable value for money is a corollary of the duty to fund only technologies that provide reasonable value for money.

The very uncertainty that underpins CED entails that the government cannot have a duty to fund the CED technology. The government has reason to believe that it will have a duty to fund the technology once evidence sufficiently speaks in favour of the technology, but the government does not have this duty yet. If a CED arrangement is justified in terms of epistemic need (the need for evidence to reduce uncertainty about the technology), then the

government has no duty to fund the technology, since serious questions must remain about value for money. All of this means that only-in-research CED involves inducement rather than coercion, just as Miller and Pearson argue, but for a different reason. Contrary to what Miller and Pearson argue, a CED technology can be in the best interests of the patient, especially when the CED is undertaken to reduce uncertainty about precisely how effective is the technology and therefore whether it provides reasonable value for money considering its cost. This sort of CED is undertaken in Australia [19], but cost features less explicitly in the US, where Miller and Pearson write. Nonetheless, it is conceivable that some CED in the US is undertaken to reduce uncertainty that ultimately pertains to value for money, even if a term like "value for money" is avoided in favour of determining whether definitive funding of a technology would be "reasonable" [14, p. 748].

If the patient is coerced or induced, under what circumstances, if any, is this ethically justified?

It is important to determine whether CED coerces or induces because coercion seems harder to justify ethically. This is perhaps because coercion is less respectful of people, or less respectful of people in their autonomy. But Australia also takes a dim view of inducing people to participate in research when participation presents possibilities of loss, especially in the form of discomfort or harm [27, ch. 2.1]. Australia's national research guidelines assert the following: "payment that is disproportionate to the time involved, or any other inducement that is likely to encourage participants to take risks, is ethically unacceptable" [27, 2.2.10]. The underlying idea seems to be that to induce someone to take risks relating to

research participation is typically to manipulate them or at least to distort their assessment of possible gains and losses. The concept of undue inducement is implied [21]. While there is considerable debate about inducement in research ethics, there is good reason to have moral concerns in view of the "structurally diminished voluntariness" and "routine powerlessness" observable among some research participants [28]. In short, inducement can be morally problematic, which is a point that Miller and Pearson neglect.

It is important to determine the possibilities of loss faced by participants in the evidence development of a CED arrangement. This is because the inducement that only-in-research CED involves is harder to justify as the possibilities of loss worsen.

Evidence development does face participants with possibilities of loss. It may impose additional burdens, such as blood tests or radiological examinations required purely for the purposes of evidence development and not treatment. More commonly, participants will simply face possibilities of loss in terms of their privacy and the confidentiality of their data, given that the data collection, storage and analysis involved in evidence development may be more extensive (and therefore riskier, even if very slightly) than it is with treatment alone. A participant also faces possibilities of loss insofar as gaining access to a beneficial technology only to have it withdrawn could reduce their welfare overall. For example, suppose that a participant gains health benefits from a technology but these are outweighed by the physical side-effects of withdrawal or by the psychological impact of losing access to the technology when it fails to perform well enough on average to warrant ongoing coverage from government.

On one reading, Australia's research guidelines suggest that all inducement to participate in research that poses risks to participants constitutes undue inducement [27, 2.2.10]. However, there is debate on this issue internationally. Some level of inducement to participate in evidence development could potentially be justified by the benefits of the evidence development, especially when the benefits stand to favour participants or disadvantaged groups. But the risks to participants probably need to be minor. To induce participants to take on serious risk is highly problematic ethically.

In Australia, Human Research Ethics Committees (HRECs) sometimes permit researchers to study people's data or tissue without requiring the researchers to obtain consent from those people. Committees do this when it seems justified in view of numerous considerations [27, ch. 2.3]. Committees consider the magnitude and probability of benefits attaching to the research. Committees consider the magnitude and probability of losses faced by research participants, especially risks of discomfort and harm. This includes the discomfort or harm that seeking consent may itself cause people. Committees consider the feasibility (including the cost) of seeking consent. Committees consider how people would be likely to react if they discovered that their data or tissue was studied without their consent in a specific way and for a specific purpose. How people would be likely to react also gives some indication of the severity of infringement to people's privacy and to the confidentiality of their data. Committees typically grant consent waivers for population-based studies that take care to link, de-identify, and then analyse data that is already routinely collected as part of clinical treatment, especially when the population is very large and gaining consent would be very burdensome, if not impossible. The Australian public is supportive of this [29]. In such cases, committees judge that the risks to research participants, which primarily relate to privacy and confidentiality, are minor compared to the potential wider benefits of the

research. This exact reasoning applies to some CED arrangements, such that the evidence development is justified, perhaps even in the absence of patient consent. But this reasoning does not apply to other CED arrangements. For example, the discomfort or harm of having blood taken from one purely for evidence development is probably greater than the discomfort or harm of having one's data de-identified and analysed. Ethical review by a HREC or analogous body is needed to determine whether the particulars of a CED arrangement justify evidence development in the absence of patient consent or, if consent is to be sought, the precise consent processes to be used.

We argued above that the government has no duty to fund a CED technology. But from this it does not follow that the government can attach whatever conditions it wishes to attach to funding for CED technologies. The question becomes which conditions are ethically acceptable. Perhaps the government is justified in linking and analysing the patient's medical records but not in requiring additional blood tests or radiological examinations. For every CED arrangement, there is a question of what burdens and risks are acceptable to attach to funding for the benefit of reducing uncertainty, especially remembering that patients are induced with possible health benefits to take on these burdens and risks. Would it be ethically permissible to burden participants a lot only to reduce uncertainty a little? Again, there is a need for ethical review here, by HRECs and analogous bodies. And they should probably apply the principle of the least restrictive alternative, requiring that uncertainty be satisfactorily reduced with the least possible inducement, burden and risk. The government has good reason to reduce uncertainty by a particular amount, and the ethically acceptable levels of inducement, burden and risk follow partly from that.

The government could avoid inducing people by designing a CED arrangement such that involvement in the evidence development is untethered from gaining funding for the technology. Participation in the evidence development could be optional in the sense that declining to participate would not entail foregoing funded treatment. The arrangement would then resemble only-with-research CED, with the subset of studied patients being volunteers [9]. Voluntary participation could also ease a potential ethical problem pertaining to only-with-research CED. It could eliminate the potential injustice of only a subset of patients bearing the burdens of evidence development when all patients benefit in the form of gaining funded access to the CED technology.

Respect for people in their autonomy suggests that a CED arrangement should feature a consent process whereby it is reasonably easy for a person to act in line with their wishes. The precise consent process to be used should be reviewed for its ethical acceptability case by case. For example, confusing and manipulative recruitment materials would undermine the informed and voluntary nature of participants' consent, invalidating it.

Miller and Pearson rightly observe that making participation in the evidence development optional could result in "delaying or even precluding development of the needed evidence" [14, p. 749]. It could weaken the evidence by introducing self-selection bias, for instance. But this problem is not specific to CED. It would need to be carefully considered for each CED arrangement, just as HRECs regularly consider whether a consent waiver is justified in any particular research project.

When the possible losses attaching to participation in the evidence development are minor, it may well be ethically permissible for the government to fund the CED technology only for

patients who agree to participate in the evidence development. This would be a case of justified inducement to participate in evidence development. However, when the possible losses attaching to participation in the evidence development are more than minor, the government probably ought to fund the technology even for patients who decline to participate in the evidence development. This would be to avoid unjustified inducement. More importantly, these matters need to be carefully assessed on a case-by-case basis under an appropriate governance structure, and existing HRECs and analogous bodies are well positioned to do this work.

Do patients perhaps have a duty to participate in the evidence development? And does any such duty perhaps function to reduce or justify the inducement involved? These questions extend beyond the scope of this article, but they should feature in future research that expands the ongoing debate about whether people have a duty to participate in research [30, 31, 32, 33, 34, 35].

Conclusion

We have argued that patients have a right to government funding only for technologies that the government can be confident provide reasonable value for money. This is at least the case in situations where a government has legitimately set aside funds for the express purpose of availing health technologies to the public and there is an accepted aim of achieving reasonable value for money. Patients have no right to funding for a CED technology because a technology is only ever a candidate for CED by providing questionable value for money given what is known at the time. For this reason, CED that results in foregone treatment for

patients declining to participate in the evidence development does not coerce but merely induces patients to participate in evidence development. In many cases, the losses faced by participants will be limited to minor risks regarding privacy and confidentiality. The benefits of the evidence development may well justify these and the inducement involved. But inducement will rarely be justified when CED arrangements involve greater risks to participants. In such cases, patients should be given the option to participate in the evidence development without having to forego funded treatment should they decline to participate. Importantly, these matters should be assessed for each CED arrangement through appropriate research ethics review.

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