

Review Article

Legal and ethical implications of defining an optimum means of achieving unconsciousness in assisted dying

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Summary

A decision by a society to sanction assisted dying in any form should logically go hand-in-hand with defining the acceptable method(s). Assisted dying is legal in several countries and we have reviewed the methods commonly used, contrasting these with an analysis of capital punishment in the USA. We expected that, since a common humane aim is to achieve unconsciousness at the point of death, which then occurs rapidly without pain or distress, there might be a single technique being used. However, the considerable heterogeneity in methods suggests that an optimum method of achieving unconsciousness remains undefined. In voluntary assisted dying (in some US states and European countries), the common method to induce unconsciousness appears to be self-administered barbiturate ingestion, with death resulting slowly from asphyxia due to cardiorespiratory depression. Physician-administered injections (a combination of general anaesthetic and neuromuscular blockade) are an option in Dutch guidelines. Hypoxic methods involving helium rebreathing have also been reported. The method of capital punishment (USA) resembles the Dutch injection technique, but specific drugs, doses and monitoring employed vary. However, for all these forms of assisted dying, there appears to be a relatively high incidence of vomiting (up to 10%), prolongation of death (up to 7 days), and re-awakening from coma (up to 4%), constituting failure of unconsciousness. This raises a concern that some deaths may be inhumane, and we have used lessons from the most recent studies of accidental awareness during anaesthesia to describe an optimal means that could better achieve unconsciousness. We found that the very act of defining an 'optimum' itself has important implications for ethics and the law.

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Introduction

In countries where it is legal, the methods used to assist dying (voluntary, physician-assisted suicide or euthanasia) are intended to be humane, where there is unconsciousness at the time of death so that the individual suffers no pain or distress. Although the ethical dilemmas are widely debated, the precise means to achieve unconsciousness are rarely a focus of discussion. Ethical questions include whether the principle of autonomy extends to the right to die, or whether a physician's commitments to support life override (or not) their duty of care if their patient asks to die [1–4]. The ethical debate can be extended to capital punishment (which is also an example of assisted, albeit involuntary, death) and whether a physician should avoid involvement even if, by doing so, the prisoner will die in pain or distress [5, 6]. Important as they are, these ethical questions are not pertinent to this article. We will not discuss palliative or end-of-life care, where excessive sedation or analgesia might hasten death [7], although this too is debated [8, 9], nor where artificial ventilation or cardiovascular support is withdrawn from a critically ill or minimally conscious patient. Instead, we dispassionately examine whether the methods used to induce unconsciousness at the point of death in assisted dying achieve their objective.

Broadly, the topic of assisted dying can be divided into four separate themes. One is the ethical, legal and consent framework in which the intervention takes place. Second is the means used to achieve unconsciousness. Third is the means used to induce death, which may involve drugs such as neuromuscular blocking drugs or potassium chloride to ensure that death is rapid. This third may be an integral part of the second component where, for example, a sedative or anaesthetic drug is the sole agent. Fourth is the process of confirming and registering death, collecting data and undertaking audits. Each of these themes warrants a separate discussion, but this article focuses on the second theme and only briefly touches on others where necessary. We consider what might constitute a theoretically optimum method of inducing unconsciousness, with reference to recent research in anaesthesia (accidental awareness) which has revealed previous shortcomings in clinical techniques. Because induced unconsciousness to facilitate dying is also used now as part of the sole method of capital punishment, still practised in the USA, we also selectively draw on literature evidence from these experiences. Finally, we consider the implications of defining such a method on ethics, medical practice and the law.

Description of currently used methods

Discussions regarding the ethics of assisted dying assume that an optimum method to achieve unconsciousness and subsequent death already exists, and all that is required is to sanction this in law. If only painful methods were available, it is unlikely the question '*Should assisted dying be legalised?*' would ever be asked. The Canadian Supreme Court has recently legalised physician-assisted suicide, but did not specify what means were to be used or to be regarded as legal [10, 11]. The subsequent dilemmas faced by anaesthetists as this law is implemented in Canada have been discussed elsewhere [12].

There are several reasons for the lack of discussion of actual methods. Publication ethics require patient consent, which is absent or coercive in capital punishment [13]. Data collected during legally sanctioned assisted suicide (including video recordings) are generally passed to police for review and storage in order to protect those involved from later prosecution, and access to such sub judice material is limited [3,4].

Nevertheless, since 1987, the Royal Dutch Medical and Pharmaceutical Societies (KNMG/KNMP) have jointly published guidance for assisted dying, specifying two different methods [14]. In 'passive participation', a physician prescribes a high-dose barbiturate to be taken later orally (or administered via a nasogastric tube) by the patient them self, such that death occurs slowly as a result of cardiorespiratory collapse and asphyxia. In 'active participation' (also termed 'euthanasia' within the guidelines) a physician administers a high dose of intravenous (i.v.) anaesthetic, followed by a neuromuscular blocking drug. Euthanasia is also recommended when passive participation fails to cause death within 2 h (i.e. this being an explicit recognition that the first method can fail). The most recent data indicate that, in the Netherlands, 58% of all deaths now involve an end-of-life decision; ~18% involve physician-prescribed continuous deep sedation and ~5% involve physician-assisted suicide or euthanasia [15]. The Dutch active participation method resembles (except for the use of potassium) what is now de facto the only method used in the USA for capital punishment [16]. We decided to draw on evidence from capital punishment, not because we erroneously conflate the ethics with those involved in voluntary assisted dying, but because the method used is designed to be 'humane' and bears technical similarities to a method used in voluntary assisted dying. Also, US court cases are revealing of judicial attitudes to the technical aspects, including drugs, dosage and monitoring. A separate critique of capital punishment is

outside the scope of this article, but we refer to such evidence where appropriate in order to inform our argument. Based on the Chapman method (named after the Oklahoma medical examiner who first described it in 1977 after consulting Stanley Deutsch, Chief of Anaesthesia at Oklahoma University), a high-dose i.v. drug (originally sodium thiopental) induces unconsciousness, followed by a long-acting neuromuscular blocking drug (originally pancuronium) in order to cause respiratory paralysis and also to abolish distressing muscular spasms that might occur following administration of the third drug, potassium chloride, which induces rapid, fatal ventricular fibrillation [17]. Various propofol or midazolam (as anaesthetics/sedatives), tubocurarine, succinylcholine, vecuronium or rocuronium (as neuromuscular blocking drugs) have been employed, albeit with mixed results (see also Supporting Information, Data S1) [17].

The problem of ensuring unconsciousness: in science and as tested in law

In all of these techniques (the two Dutch methods and the Chapman protocol), there remains the scientific problem of knowing whether or not the patient is unconscious at the time of death. Prisoners have been reported to be clearly awake and in distress during some executions, which has led to reviews of the technique [16–19]. This has been the case especially where midazolam has been used to induce unconsciousness (see also Supporting Information, Data S1). It is experience from US capital punishment that sheds light on this issue. From death row, Baze and Bowling petitioned the US Supreme Court to consider that there should be a requirement for a physician to confirm unconsciousness after the barbiturate, and before neuromuscular blocking drugs and potassium were administered [20]. Otherwise, they argued, they might be awake but paralysed at the point of death, making the method a 'cruel or inhumane punishment' in violation of the US Constitution's Eighth Amendment. This situation has clear parallels with the problem of 'accidental awareness during general anaesthesia' (AAGA), where the patient awakens unnoticed and paralysed during surgery, which is known to be a potent cause of distress [21, 22]. However the Court rejected their arguments, concluding that the anaesthetic doses used reliably achieved unconsciousness without any need to check that this was the case. We now know that the Court was wrong. Accepted anaesthetic practice, known before, but cemented by, the recommendations of the 5th National Audit Project (NAP5) [21, 22], is indeed to confirm unconsciousness before

administering neuromuscular blocking drugs, as indicated clinically by lack of movement to command or response to a painful stimulus. This need for clinical confirmation is also emphasised in the Dutch guidelines [14]. It is a common dilemma faced by anaesthetists: how do we know if an apparently anaesthetised but paralysed person is actually unconscious? Justice Ginsburg's dissenting minority opinion in the Baze ruling appreciated the correct science: *"The inmate may receive enough sodium thiopental to mask the most obvious signs of consciousness, without receiving a dose sufficient to achieve a surgical plane of anesthesia. . . [This] creates [the] risk of inflicting severe and unnecessary pain."* [20]. In effect, Ginsburg was referring to what also happens during AAGA.

The US Supreme Court was again petitioned on a potential violation of the Eighth Amendment in the use of midazolam, described as a 'cruel' induction agent [23] (see also online Supporting Information, Data S1 as to why midazolam is considered at all for use in executions). By majority opinion, based largely on its interpretation of conflicting expert testimony, the Court sanctioned execution using midazolam. Indeed, the Court went further and placed the onus on the petitioners themselves (not the authorities) to offer a better alternative: *"...the Eighth Amendment requires a prisoner to plead and prove a known and available alternative...the fact that a low dose of midazolam is not the best drug for maintaining unconsciousness during surgery says little about whether a 500 mg dose is constitutionally adequate for purposes of conducting an execution."* As dissenting Judge Sotomayor observed, this was akin to asking prisoners to justify and plan the means of their own execution [23]. Sotomayor recognised (and cited) the emerging consensus that not all anaesthetic agents are equivalent in their ability to induce unconsciousness. Each general anaesthetic acts on its specific range of target molecular receptors [24–27]. These proteins, encoded by alleles, exhibit polymorphisms across individuals such that different individuals are variably susceptible (or resistant) to different agents [25, 27]. For example, sodium thiopental was associated with a higher incidence of AAGA in the NAP5 study [21] and, unlike other agents, midazolam does not produce isoelectric EEG patterns, even in high-dose [28–30].

To summarise, the literature concerning US capital punishment indicates that although similar agents are used as during clinical anaesthesia, conduct in their administration falls well short of being able to satisfy the requirement of achieving unconsciousness at the point of death. Expressed another way, the lesson from these unfortunate experiences is that any optimum method used

to achieve unconsciousness in voluntary assisted dying must be tangibly different from, and superior to, all the methods currently used in capital punishment.

Common methods used in voluntary assisted dying

Data from the Dutch protocols, and other similar methods used elsewhere, suggest that after oral drug sedative ingestion, patients usually lose consciousness within 5 min. However, death takes considerably longer. Although cardiopulmonary collapse occurs within 90 min in two-thirds of cases, in a third of cases death can take up to 30 h [31–33]. Other complications include difficulty in swallowing the prescribed dose (in up to 9%) and vomiting thereafter (in up to 10%), both of which prevent suitable dosing, and re-emergence from coma (in up to 2%). Each of these potentially constitutes a failure to achieve unconsciousness, with its own psychological consequences, and it would seem important explicitly to acknowledge this in suitable consent processes. Complications are still reported: difficulties with intravenous access which preclude proceeding (3%); prolonged time to death (up to 7 days from drug administration in up to 4%); and failure to induce coma (with patients re-awakening, even sitting up, in up to 1.3%), and are more common in those who are not frail [31–33].

It is striking, that the incidence of 'failure of unconsciousness' is approximately 190 times higher when it is intended that the patient is unconscious at the time of death [31–33], as when it is intended they later awaken and recover after surgery (when accidental awareness is approximately 1:19,000) [21, 22].

Recent lessons from anaesthesia: AAGA and l'exception Française

Although it has always seemed intuitive that unconsciousness at the point of death should be necessary for assisted dying to be humane, the concept is now enshrined in (French) law. Since 2016, terminally ill patients have a legal right to unconsciousness (continuous deep sedation) until the point of death [34]. Termed the 'French exception' ('l'exception Française'; to emphasise the country's distinct legal/cultural values compared with those of others), the important implications of this law are currently being debated [35]. At the very least, the law brings into clear focus the similarities of the aims of clinical anaesthesia with those of managing consciousness during assisted dying. Ensuring a right to unconsciousness as required by this law rests on the same principles as reducing the risk of AAGA.

There are three pertinent lessons from studies of AAGA: (1) the anaesthetic state can be difficult to monitor, especially in the presence of neuromuscular blockade; (2) certain drugs are more frequently associated with AAGA than others; (3) anaesthetic delivery must be uninterrupted in order to avoid AAGA [21, 22].

Brain activity monitoring has been an attractive option and several processed EEG monitors (e.g. the bispectral index, BIS) have been designed to help ensure unconsciousness. They produce a dimensionless number from 0 (isoelectric) to 100, and a recommended target range for clinical anaesthesia is 40–60 [36]. Values < 40 may indicate deeper anaesthesia than is required for surgery, putatively correlated with poorer clinical outcomes [37] but several AAGA cases are still reported at values < 40 [21, 22]. Agent specificity is again relevant: agents such as ketamine or nitrous oxide can produce paradoxical EEG activation despite the patient being suitably anaesthetised [38, 39]. Although EEG monitoring is not yet routinely used to guide unconsciousness for voluntary assisted dying, it was used at Willie Brown Jr's execution, after the US State Appeals Court granted that this would allow the determination of unconsciousness [40]. Yet, the BIS target that was employed was just < 60 [41], a value known to be associated with several cases of AAGA [21, 22]. Again, it was a dissenting opinion (Judge M Blaine Michael) that properly reflected the science: "...use of the BIS monitor will not adequately ensure that Brown will remain unconscious..." [41]. In a very different way EEG monitoring could, and therefore should, be used to monitor assisted dying in an optimum technique, but only if titrated at or near to the very low burst suppression or 'isoelectric point' of 0, which represents de facto cessation of cerebral cortical activity [42–45].

An important cause of AAGA identified in NAP5 was the use of a bolus administration of anaesthetic with subsequent gap in timing before maintenance anaesthesia [21]. Similarly, in the context of capital punishment, Lubarsky's group has noted, using blood sample data from executed prisoners, that sodium thiopental levels at the point of death after a bolus injection were unlikely to be compatible with loss of consciousness [18, 46]. This problem can be overcome by a continuous infusion, and drugs can be readily administered via infusion pumps set to maximum levels (e.g. > 1000 ml.min⁻¹; or several pumps could even be used simultaneously). In turn, however, anaesthetic infusions, when combined with neuromuscular blockade, require EEG monitoring because plasma concentrations cannot be directly measured [47].

The isolated forearm technique (IFT) is a means to ensure that a patient paralysed with a neuromuscular

blocking drug is unconscious. Described elsewhere [48], the construct allows the patient to signal their awareness by movement using their single, non-paralysed forearm. Publicly available videos of this are dramatic (see: <https://www.youtube.com/watch?v=ZEAYsEbkJrw>, accessed 02/11/2018). The phenomenon is easily reproducible by any anaesthetist, anywhere and the usual finding is that, while few if any patients move spontaneously, up to a third of patients respond to verbal commands, even when receiving suitable anaesthetic concentrations [49]. The underlying reasons for this are discussed elsewhere, but this response to command can be eliminated by increased anaesthetic dosing [50, 51]. The method could be incorporated into protocols for assisted dying, if it were felt desirable to ensure the patient had not changed their mind even after initial induction of anaesthesia, as well as to confirm loss of unconsciousness.

Defining an optimal method of assisted dying

Recent lessons from anaesthesia lead us to conclude that, if we wish better to ensure unconsciousness at the point of death (e.g. meet the requirements of the 'French exception'), then this can be achieved using: (1) continuous drug infusions at very high concentrations; (2) concomitant EEG-based brain function monitoring, targeted to the very low, burst suppression or isoelectric values; and (3) clinical confirmation of unconsciousness by lack of response to command or to painful/arousing stimuli (and this last could include an IFT). Alternative methods that do not include these elements entail a higher, possibly unacceptable, risk of remaining conscious and so, by definition, are suboptimal.

Only after unconsciousness is achieved in this way should other interventions be used to ensure death is not prolonged. Whether this last step should include neuromuscular blockade (to stop breathing and prevent distressing muscular spasms) and/or potassium chloride (to ensure death is rapid via ventricular fibrillation), or insulin overdosage, etc, is for separate discussion. Table 1 illustrates how the means to induce and confirm unconsciousness should, in any protocol, be distinct from the means to induce or confirm death. It is important to note that although lessons from AAGA have been used to develop Table 1, and although similar drugs are used, these principles do not set any standards for clinical anaesthesia. The aim of anaesthesia for surgery is to administer the minimum possible concentration that preserves physiological function and recovery while making the intervention psychologically acceptable (even perhaps

where this rarely entails some 'dysanaesthetic' awareness of events [51]). The aim in assisted dying is to minimise the risk of being aware, regardless of any cost to physiological stability.

Implications and conclusions

Notwithstanding the details, the very act of defining any optimal method of achieving unconsciousness in assisted dying itself has several important implications.

First, the technical requirements (i.e. administration of an anaesthetic drug via an infusion pump, interpreting EEG monitoring, etc.) clearly require the involvement of trained practitioners, and hence currently the role of physicians, specifically anaesthetists, becomes necessary. If ever assisted dying was sanctioned in law, the relevant anaesthetic societies would need to develop guidance for the conditions under which their members could, or should, take part, as well as be involved in refining the methods and techniques to be used. This precedent has already been set by the Dutch experience [11]. Canadian colleagues are facing this reality post-hoc, without having first been involved in framing the law [10–12].

Second, any method of inducing unconsciousness that is defined as 'optimum' should logically be adopted for both assisted dying and capital punishment. This is not to regard the two as morally equivalent, or to imply that approving of one automatically requires support for the

Table 1 A theoretical protocol for assisted dying, organised into four components. It is only the steps of the second component that are discussed in this article as being an optimum means of achieving unconsciousness.

Component 1: Steps required to obtain informed consent and fulfil other legal requirements*

Component 2: Steps required to induce and confirm unconsciousness:

Intravenous supramaximal dose by continuous infusion of anaesthetic agent

Monitoring to end-point of burst suppression or isoelectric EEG

Unconsciousness confirmed by lack of response to verbal command (or IFT) and to arousing stimulus (e.g. jaw thrust or supramaximal peripheral nerve stimulation)

Component 3: Steps required to induce rapid death**

Component 4: Steps required to confirm death†

EEG, electroencephalogram; IFT, isolated forearm technique.

*Not discussed.

**Not discussed but should take place only after achieving the second step, and could include potassium chloride injection or neuromuscular blockade.

†Not discussed but would require definition by timing, and certification by a medical practitioner, and might also include appropriate ongoing audit and data collection.

other. Rather, it is simply to acknowledge the hard logic that there seems no a priori reason to deny one group an optimum that is offered to the other, in those jurisdictions that already sanction both. It is possible, however, that despite public and constitutional protestations that executions should be 'humane', there may in fact be an element of suffering intended as punishment. Nevertheless, if logic did apply then the relevant medical societies would need to develop guidance for conditions under which their members could, or should, assist in executions, if at all. If, as is the case in the USA, medical societies prohibit their members from taking part as being against fundamental ethical principles of medical practice [52, 53], then this automatically makes any alternative method of inducing unconsciousness for execution suboptimal and therefore potentially unconstitutional. Expressed differently, the act of defining an optimum means to achieve unconsciousness for assisted dying empowers medical societies to challenge the very legality of capital punishment.

To some readers, what we now define as the optimum method (Table 1) may appear overly 'medicalised' (i.e. use of infusion pumps and brain monitors; involvement of physicians). Society or individuals might prefer to retain a choice for alternative methods, even if these are suboptimal and carry a greater risk of consciousness at the point of death [54]. If so, then legal frameworks and consent processes should explicitly acknowledge this choice. The Dutch protocols would seem to have incorporated this balance in their 'passive' vs. 'active' participation methods.

Although the principles we outline in Table 1 will certainly better ensure unconsciousness at the point of death than alternative methods, there are many details that we have not expanded upon, which we anticipate will become a focus for debate. One is the agent(s) to be used; propofol is perhaps most amenable to i.v. infusion, but adjuncts such as opioids may be justified. Another is the infusion type (e.g. closed loop systems or target controlled infusions; the latter being not yet approved in the US) [55]. A third question is, if the patient moves or is judged 'light' when checked for adequate depth of anaesthesia (or responds to an IFT command if this is used), should the appropriate action be to deepen anaesthesia while giving positive verbal reassurance? Or to terminate the process and recommence later after re-awakening, in case the movement is a sign of distress in the last moments of life?

In summary, any decision by a society to sanction assisted dying should logically go hand-in-hand with resolutions to mandate the acceptable method(s). Otherwise, there is a risk that vulnerable citizens may be

killed by suboptimal, or even cruel, means. In some countries, individuals have resorted to hypoxic methods ('debreather' hoods, involving helium rebreathing) [56, 57] where death is accompanied by noisy, obstructed breathing and which have considerable shortcomings (see also online Supporting Information, Data S2) [57]. These considerations also apply to other non-injection methods of capital punishment (see also online Supporting Information, Data S1) [58]. When compared with clinical anaesthesia, the complication and failure rates of assisted dying by these other methods seem extraordinarily high.

Defining an optimum method for inducing unconsciousness in assisted dying now places certain responsibilities on the public, legislators and physician groups. For the public, this includes accepting that all interventions can fail. All choices involve risk and that includes exercising the choice to die, or to be unconscious at the point of death. The public should also be comfortable in allowing professionals it normally expects to help preserve life, now to be required also to assist in death – or to create alternative professionals for this latter task. For legislators, this responsibility entails clarifying both the legal/ethical framework and the technical means of killing, including setting the minimum qualifications for those involved in assisting. The US Supreme Court has previously articulated, but notably failed to help deliver on, this legislative responsibility (our parentheses to encapsulate the wider principle): *"Because capital punishment [or assisted dying] is constitutional, there must be a constitutional means of carrying it out."* [23]. For physicians, this responsibility means freely and dispassionately advising legislators and the public on the science underpinning methods to reduce pain and suffering at death, regardless of its context, without as individuals being or feeling compelled to assist in any given case.

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The views and recommendations expressed in this article are the authors' and not the Publishers or the Association of

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Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Data S1. Comments on drugs used in executions and non-drug methods in the USA.

Data S2. Comment on asphyxia methods of voluntary assisted dying.