

4. Who should decide for critically ill neonates and how? The grey zone in neonatal treatment decisions

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Editors' summary

This chapter distinguishes between essential features of the zone of parental discretion and the longstanding concept of a grey zone in neonatal treatment decision-making. The grey zone has traditionally described a gestational age range where the outcomes of medical treatment for newborn infants are uncertain, and therefore parents have discretion to choose between resuscitation or palliative care options. In contrast, the ZPD refers to a space where parents may make decisions for their child (not restricted to newborns) even if their decisions conflict with the decisions a clinician would make. A key difference between the two zones is that the boundaries of the grey zone are defined on the basis of published evidence about medical outcomes, whereas the boundaries of the ZPD are based on the broader but arguably vaguer notion of harm to the particular child. The grey zone has usually been defined in terms of gestational age. Wilkinson argues instead for a prognosis-based grey zone in neonatal treatment decision-making, which incorporates a range of prognostic factors rather than focusing solely on gestational age.

Links

See Chapter 1 for detailed articulation of the ZPD, to contrast with the grey zone.

See Chapter 7 for Kilham, Isaacs and Kerridge's discussion of other cases involving neonates.

This is the author manuscript of the chapter published in *When Doctors and Parents Disagree: Ethics, Paediatrics & the Zone of Parental Discretion* edited by Rosalind McDougall, Clare Delaney, and Lynn Gillam.

NLM Citation: Wilkinson D. Who should decide for critically ill neonates and how? The grey zone in neonatal treatment decisions. In: McDougall R, Delany C, Gillam L, editors. *When Doctors and Parents Disagree: Ethics, Paediatrics & the Zone of Parental Discretion [Select Chapters]*. Sydney (AU): The Federation Press; 2016 Jun 20. Chapter 4.

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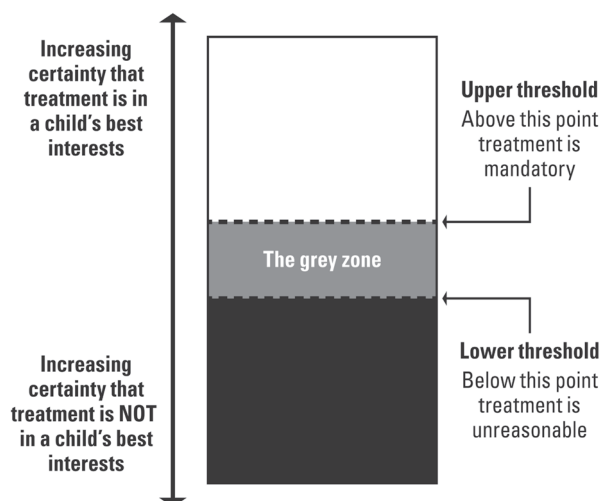


Figure 7. Conceptual framework for the grey zone in treatment decisions (modified and revised from Wilkinson, 2012).

Introduction

Case 6.

Mary presents in preterm labour at 23 to 24 weeks gestation (16 weeks prematurely). Infants born this early weigh as little as 500 grams, and have a high mortality rate. If resuscitation and intensive care are attempted, only half will survive to be discharged from hospital. The midwife has called the neonatal registrar to counsel Mary. What options should the registrar give to Mary? Should Mary and her partner's views be sought about treatment after birth, and should those views influence or determine management of the baby at delivery?

On further questioning it becomes apparent that the gestational age for Mary's fetus is certain at 24 weeks and 4 days (Mary conceived using in-vitro fertilisation). Recent ultrasounds have shown that the fetus is well grown (estimated fetal weight 750 grams), morphologically normal, and female. Mary received two doses of intramuscular betamethasone (to improve chances for the baby if delivered prematurely) 48 hours ago. However, in discussion with the registrar Mary reveals that she had a previous premature infant who survived with multiple disabilities. She does not want active resuscitation to be provided. Is resuscitation in the grey zone? Should Mary's wishes be respected?

By coincidence, in an adjacent room, Louise is also in premature labour at the same gestation. Louise's fetus is a boy with an expected weight of 550 grams (he has not grown well in the womb), and Louise has not yet received steroids. She also does not wish active resuscitation of her premature infant. Is resuscitation in the grey zone? Should Louise's wishes be respected?

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Mary's infant, Eva, is resuscitated and taken to intensive care. She is unstable over the first two days and has a pulmonary haemorrhage. On the third day she has a routine cranial ultrasound, which shows a large unilateral intraventricular haemorrhage (IVH) with an area of periventricular haemorrhagic infarction (grade 4 IVH). She is still mechanically ventilated, though reasonably stable. Mary is devastated at the thought of caring for another child with significant disability. Should the option of withdrawal of mechanical ventilation be discussed? If Mary and her partner request it, should treatment be withdrawn?

Since neonatal intensive care was first established in the early 1970s, there have been public and academic debates about decisions to treat or not treat newborn infants and about the role of parents in those decisions. In an article in the *New England Journal of Medicine* in 1973, in one of the first papers to openly discuss the practice of allowing some newborn infants to die, paediatricians Raymond Duff and AG Campbell, described an “agonising” choice and the “awesome finality” of such decisions (1973: 890). They argued that parents and health professionals should together bear the burden of decision-making. A decade later, in 1983, the United States President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioural Research published a highly influential 540-page report on decisions about life-sustaining treatment (President's Commission, 1983). It contained a chapter on newborn infants and set out an approach that relates closely to the zone of parental discretion (Table 4, *opposite*).

Clinicians and ethicists working on these issues in newborn intensive care have often referred to a “grey zone”, alluding to the uncertain nature of some cases (Brody, 1981: 278). While some situations are clear-cut and easily resolved, others are not black or white, but somewhere in between. The President's Commission report explicitly acknowledged that in such “ambiguous” cases, parental views about treatment should be decisive. The grey zone is therefore closely related to the ZPD (Figure 7, *opposite*).

In this chapter, I will explore the boundaries of parental discretion in decisions about life-sustaining treatment for newborn infants. I will start by comparing the concepts of the grey zone and the ZPD. I will then move on to critique one common version of the grey zone, based on the gestational age of infants at birth. I argue that while a gestational grey zone helps to ensure consistency of approach between clinicians, it focuses too narrowly on only one factor, while ignoring other variables that influence prognosis. I will propose instead a prognosis-based grey zone that can be applied both to resuscitation decisions at birth, and to later decisions about continuation or withdrawal of life-sustaining treatment.

Table 4. Treatment options and parental preferences (edited framework from President's Commission, 1983: 218).

Physician assessment of treatment	Parents prefer to accept treatment	Parents prefer to forego treatment
Clearly beneficial to the infant	Provide treatment	Provide treatment (seek legal or other review)
Ambiguous or uncertain benefit to the infant	Provide treatment	Withhold/withdraw treatment
Futile	Provide treatment unless provider declines to do so*	Withhold/withdraw treatment

Note: In the President's Commission report, the authors concluded that: "As long as this choice does not cause substantial suffering for the child, providers should accept it, although individual health care professionals who find it personally offensive to engage in futile treatment may arrange to withdraw from the case" (1983: 220). I have elsewhere argued that even if treatment will not cause a child to suffer, it may be unethical to provide it (where doing so will harm others) (Wilkinson & Savulescu, 2011).

The grey zone and the zone of parental discretion

Although the grey zone has similarities with the ZPD, they may not be identical. Gillam has argued that "[t]he ZPD is ... quite different from, and wider than, the 'grey zone' in neo-natal medicine" (Gillam, 2016: 5). To explore this it may be worthwhile setting out some definitions.

The grey zone: a set of clinical situations in which resuscitation and intensive care will be provided to newborn infants if parents so wish, or will be withheld/withdrawn (and palliative care provided) if parents choose.

The zone of parental discretion: "the ethically protected space where parents may legitimately make decisions for their children, even if the decisions are sub-optimal for those children" (Gillam, 2016: 2).

Given that the grey zone explicitly endorses parental decision-making around resuscitation, all cases that fall within the grey zone will also fall within the ZPD. But there are three reasons why parental discretion might apply outside the grey zone. First, one simple way in which the ZPD is wider than the grey zone is that the ZPD relates to decisions other than merely resuscitation/nonresuscitation, and to other populations than just newborn infants.¹ Second, as noted in Figure 7, the grey zone is often justified in terms of uncertainty. However, Gillam notes that "the ZPD is not just a zone of medical uncertainty" (Gillam, 2016: 5). She claims that parental discretion may be appropriate in situations where there is no medical uncertainty. One example in newborn intensive care might be resuscitation for a newborn with a severe chromosomal disorder or congenital

¹ Some apply the grey zone only to initiation of resuscitation at birth for extremely premature infants. In this chapter I will use the grey zone more broadly to apply to all resuscitation decision-making in newborn intensive care.

brain abnormality. In such situations, there may be little prognostic uncertainty, yet it would often be thought to be appropriate to involve parents in decision-making about life-sustaining treatment.² Finally, the grey zone and the ZPD may diverge if there is a difference between situations in which resuscitation is regarded as optional and actively discussed with parents and situations in which resuscitation is regarded as non-optional, but nevertheless parents' wishes may be followed. For example, in Table 4, the President's Commission suggests that in the black "futile" zone, physicians should accept parents' decisions and provide treatment unless this would cause substantial suffering for the child.³ The concept of the ZPD is specifically designed to address disagreement between doctors and parents. Within the grey zone as traditionally used in neonatal medicine, such disagreement should not arise, since there is professional agreement that parents' views are decisive.

One possible way that these concepts might come together is with the idea that there are multiple "grey zones" for decision-making rather than a single grey zone (Wilkinson, 2014). There are some ethically optional treatments that might be strongly encouraged or recommended, but that would not be mandatory. There are others that physicians might see as being unwise, or that they would counsel against, even if they would ultimately respect those choices. Within the grey zone (particularly at the margins) it may be appropriate for neonatologists to provide recommendations for or against resuscitation. I will focus below on the wider grey zone (where resuscitation is subject to parental discretion), rather than where resuscitation should be offered or recommended.

The gestational grey zone

In recent years, the grey zone concept has been particularly applied to decisions about resuscitation for extremely premature infants like Mary's (Singh, Fanaroff, Andrews et al, 2007; Seri & Evans, 2008). Successive publications and guidelines (Pignotti & Donzelli, 2008) have provided specific advice on when parental discretion about resuscitation is appropriate (Figure 8, *below*). The idea is that an infant's gestational age determines whether or not resuscitation falls within the grey zone.

According to guidelines published in Australia, the United Kingdom and a number of other countries, at 24 and a half weeks Mary's and Louise's infants fall within the grey zone, and consequently resuscitation is optional – depending on the parents' wishes. But is this an appropriate way of determining the boundaries of parental discretion? While gestational age-based guidelines are simple and straightforward for clinicians to apply, there have been a number of critics (Janvier, Barrington, Aziz et al, 2008; Meadow &

² These cases would fit within my proposed definition of the grey zone. The justification would be based on a different type of uncertainty. There is uncertainty about the future subjective experience of the child (the extent and nature of positive and negative experiences). There is also moral uncertainty about how to weigh the benefits against the burdens within the child's life, and how to factor in the interests of parents (Wilkinson, 2013).

³ See note to Table 4.

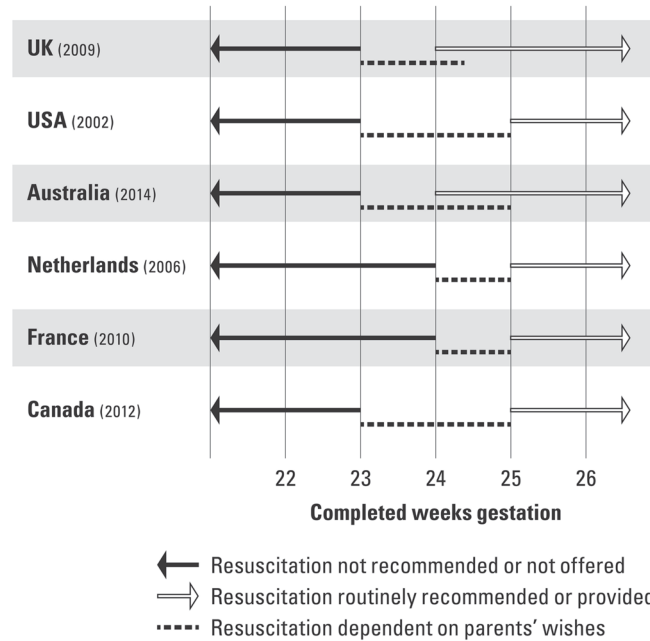


Figure 8. Resuscitation guidelines based on gestational age. MacDonald & American Academy of Pediatrics, Committee on Fetus and Newborn, 2002; Verloove-Vanhorick, 2006; Wilkinson, Ahluwalia, Cole et al, 2009; Moriette, Rameix, Azria et al, 2010; Jefferies & Kirpalani, 2012; Queensland Clinical Guidelines, 2014. Note that at least in some jurisdictions there is an overlap between gestational ages at which resuscitation is routinely recommended or provided, and where resuscitation will depend on parents' wishes. (This figure is a modified and revised version of a figure in Wilkinson, 2012.)

Lantos, 2009; Janvier, Barrington, Aziz et al, 2014). One concern is that such guidelines can seem worryingly arbitrary. Does it make sense for decision-making to change at the stroke of midnight, when an infant moves from one week of gestation to the next? Although gestational age is clear-cut in Mary's case, in practice there can often be significant uncertainty about a fetus' exact gestation date, depending on how it has been estimated. Estimates based on ultrasound or date of the last menstrual period may err by one to two weeks, which could make the difference between treatment not being offered or being routine (Tyson, 1995). Furthermore, and importantly, such guidelines ignore a number of other prognostic factors that potentially have a major impact on an infant's chances of survival and of morbidity (Tyson, Parikh, Langer et al, 2008). In the case of Mary's infant, the fact that she is well grown, is a singleton (rather than part of a multiple pregnancy), has received steroids and is female combine to dramatically improve her chances.

It is possible to quantify the influence of these factors. The United States National Institute of Child Health and Development (NICHD) Neonatal Network has developed an online calculator using its very large database of the outcomes of preterm infants (Tyson, 2008). Based on this calculator, Mary's infant has an estimated 78 per cent chance of survival if resuscitation is attempted, and a 2 in 3 chance (if she survives) of having mild or no long-term impairment. In contrast, if Louise's son is born now and resuscitation is attempted he

would have only a 31 per cent chance of survival, and a 30 per cent chance (if he survives) of mild or no long-term impairment.

Perhaps more significantly, guidelines like the ones listed above have been criticised for being simplistic and reductive. In the words of Canadian neonatologist Annie Janvier, “ethics ain’t easy” (2008: 402). Janvier, writing with more than 30 neonatologists and ethicists, lambasted a 2012 Canadian Paediatric Society guideline, arguing that it represented an attempt to reduce complex ethical decisions to simple rules (Janvier, Barrington, Aziz et al, 2014). Interestingly, similar criticisms were levelled four decades earlier at a previous attempt to generate guidelines around non-treatment in newborn intensive care. In the 1970s, paediatricians and surgeons developed criteria for treatment/non-treatment of infants with spina bifida. For example, paediatric surgeon John Lorber proposed that surgery should not be performed for infants with one or more of four features (severe paraplegia, gross enlargement of the head, kyphosis, or other major congenital abnormalities) (1972: 854). However, others were critical of this approach. United States bioethicist Robert Veatch argued that these guidelines were guilty of the “technical criteria fallacy”: “In principle it is a mistake ... to assume that any set of technical criteria will be able to make a definitive separation between babies to be treated and those not to be treated” (1977: 15).

Veatch was highly critical of the apparent medicalisation of decisions that must, ultimately, be based on values. Articles like Lorber’s skated over the ethical justification for non-treatment decisions. They did not provide clear reasons why a particular set of criteria was chosen, why a particular probability of poor outcome was sufficient, or why a particular level of disability warranted non-treatment. Similarly, part of the criticism of gestational age guidelines has been that they fail to engage with the key ethical arguments that would justify such policies (or even to recognise that such ethical arguments are important) (Janvier, Barrington, Aziz et al, 2014: 22).

An individualised grey zone?

Gestational age-based guidelines, like those described above, recognise the importance of parental discretion about treatment (within a range of cases). However, they do appear too simplistic. As the examples above illustrate, infants with the same gestational age may have substantial differences in their prognosis. Instead of being guided by gestational age, some have proposed that decisions should be made on a case-by-case basis (Janvier, Barrington, Aziz et al, 2008; Batton & Committee on Fetus and Newborn, 2009). Janvier and colleagues have argued that decisions about resuscitation and life-support should be individualised, taking into account the nuances of individual infants and families, and incorporating all relevant prognostic factors (2008: 402).

The basic idea here is laudable. Thinking more broadly about the ZPD in paediatrics, it seems obviously correct that decision-making should be individualised, and should reflect the subtleties and unique features of each case. Yet there are a number of reasons for thinking that we need to do more than this. Moving away from gestational age will not

necessarily lead to more ethically robust decision-making. For example, one alternative to making decisions prior to delivery is to assess the infant after birth (Singh, Fanaroff, Andrews et al, 2007; Seri & Evans, 2008). This can involve assessment of the physical maturity, condition at delivery, response to resuscitation, and/or response to initial intensive care treatment. This individualised approach seems, on first glance, sensible. Yet, physicians' ability to assess gestational age soon after birth is not necessarily any more accurate than ultrasound (Donovan, Tyson, Ehrenkranz et al, 1999; Mercurio, 2005). Condition at birth is subjective and physician assessment of response to resuscitation is a poor predictor of mortality or neurodevelopmental abnormality (Manley, Dawson, Kamlin et al, 2010). Objective markers of illness severity in the intensive care unit are also poor predictors (Meadow, Lagatta, Andrews et al, 2008), albeit this can be improved by incorporating other prognostic variables (Lagatta, Andrews, Caldarelli et al, 2011).

Next, a significant problem for the individualised approach is that it can fail to provide guidance for clinicians. The American Academy of Pediatrics produced a report in 2009 relating to counselling and resuscitation of extremely premature infants (Batton & Committee on Fetus and Newborn, 2009). Whereas previous guidelines from the same body had specified gestational age-based criteria for resuscitation, this new document (cognisant of the criticisms described above) avoided defining the grey zone in terms of gestational age. It strongly encouraged individualised decision-making. The guideline recommended that if "the physician's judgement is that a good outcome is reasonably likely, clinicians should initiate resuscitation" (Batton & Committee on Fetus and Newborn, 2009: 425). Yet the document provides no assistance for clinicians who might be wondering what counts as a "good outcome", or how likely is "reasonably likely". Imagine a clinician referring to the AAP document in order to help them counsel Mary, and to determine whether or not Mary's wish that her infant not be resuscitated should be respected. It is not clear that the guideline would help at all.

Related to the above concern, one risk of an individualised approach to decision-making is variability. In the absence of clear guidelines, management decisions may vary significantly depending on which clinician happens to be on duty (Kaempf, Tomlinson, Arduza et al, 2006). There is evidence that physician variables including personality type have an impact on decisions to limit life-sustaining treatment in intensive care (Wilkinson & Truog, 2013). This may be the cause of the wide variability between intensive care units in the prevalence of treatment withdrawal (Wunsch, Harrison, Harvey et al, 2005). One survey in the United Kingdom (prior to the publication of national gestational age-based guidelines) asked 100 consultants and trainees for their approach to resuscitation of extremely preterm infants (Duffy & Reynolds, 2011). At 23 weeks gestation, 63 per cent of those surveyed indicated that they would advise against resuscitation. In the presence of an explicit request from a mother to provide comfort care only, 55 per cent indicated that they would not resuscitate. However, 39 per cent answered that they *would* resuscitate if the infant was born in good condition, and 6 per cent of respondents indicated that they would resuscitate if the infant showed any signs of life (Duffy & Reynolds, 2011: 42).

A prognosis-based grey zone

An alternative approach to developing guidelines for resuscitation would be to articulate the ethical basis for the grey zone. For example, gestational age is relevant to decisions about resuscitation because of its influence on prognosis. But since it is prognosis that is doing the ethical work, perhaps we could develop instead criteria based on prognosis: parental discretion about resuscitation is warranted if there is an X per cent chance of mortality, and a Y per cent chance of disability?

While this may seem theoretically appealing, determining the values of X and Y can seem extremely challenging, if not impossible (Batton, 2010: 810).⁴ The chair of the American Academy writing group confessed that: “Despite long discussions, it became apparent that [committee] members could not agree on the precise morbidity and mortality thresholds for deciding when selective resuscitation is a reasonable option to offer parents” (Batton, 2010: 810). Here, the Scylla and Charybdis of guideline writing become apparent (McMillan, Hope, Wilkinson et al, 2013: 336). At one extreme, it is easy to reach consensus agreement on vague guidelines that are based on widely accepted normative principles. However, as noted above, such vague guidance is of limited practical value, and may lead to considerable variability in management. At the other extreme, highly specific and practically applicable guidelines can be very difficult to write (because of the challenge in reaching agreement), and may be guilty of the technical criteria fallacy (McMillan, Hope, Wilkinson et al, 2013: 336).

One approach to this challenge is the so-called PAGE framework (Wilkinson, 2012), incorporated into South Australian clinical guidelines for care of extremely preterm infants (South Australian Perinatal Practice Guidelines Workgroup & Wilkinson, 2013). PAGE stands for Prognosis for Average Gestation-Equivalent infant. Rather than trying to derive from first principles values for X and Y (the probability of death or disability that would mark out the boundaries of the grey zone), it builds on existing international consensus. There are four ethical principles and two empirical claims that underpin the PAGE framework.

- Ethical principles
 - Decisions about treatment should be based on the best available evidence about the prognosis for the infant
 - Decisions should reflect all relevant prognostic factors and should not be based on gestational age alone
 - Fetuses or infants with similar prognosis should be treated similarly
 - If the chance of mortality and serious morbidity for an infant is high (but not too high), parental discretion around provision of life-sustaining treatment is appropriate.

⁴ There are a number of reasons behind this difficulty. Different people will evaluate disability and death differently, as well as responding variably to risk and uncertainty.

- Empirical claims
 - There is international professional agreement that in general for premature infants born at around 23–24 weeks gestation parents' views about resuscitation should guide treatment
 - On average, infants born between 23–24 weeks gestation who receive resuscitation and intensive care have a chance of dying, or of profound impairment (if they survive) of more than 50 per cent but less than 90 per cent.

The PAGE framework is illustrated in Table 5 (*opposite*).

Applied to Mary's infant, this framework asks clinicians first to assess the fetus/infant's prognosis based on all available evidence and relevant factors. As noted above, a female, well-grown infant at this gestation, born after Mary had received steroid treatment, would have an estimated chance of death or profound impairment (if resuscitation is attempted) of approximately 33 per cent (Tyson, 2008). Her prognosis is better than the average 24-week infant. It is, in fact, closer to that of an average 25-week infant. Since it is usually felt by clinicians that 25-week gestation infants should receive resuscitation and intensive care, it seems that Mary's infant should be treated similarly. She falls into the white, uppermost category in Table 5.

Using the same approach, Louise's infant has an estimated 82 per cent chance of either dying, or of surviving with profound impairment (Tyson, 2008). Her infant's prognosis is equivalent to that of an average 23-week gestation infant. Accordingly, it appears that resuscitation should be seen as being optional, that is, within the prognosis-based grey zone (row 2 in Table 5).

There are several advantages of the prognosis-based grey zone (PAGE) framework. It is able to incorporate a range of different prognostic factors, rather than focusing solely on gestational age. It avoids the disconcerting and arbitrary nature of age-based guidelines, where a single day in gestation makes the difference between resuscitation or non-resuscitation. At the same time, the framework provides clearer, more easily applicable guidance than the individualised grey zone, and (hopefully) leads to less variability in decision-making. The PAGE framework is transparent about the ethical principles that underpin decision-making, and the ethical justification for a determination that in a specific case resuscitation is mandated, optional or unreasonable.

The PAGE framework is also flexible, since it could incorporate changes in outcome over time as well as differences in prognosis in different centres or countries. For example, one centre where I have worked has recently reviewed its own survival figures for extremely premature infants, as well as the rates of developmental problems in survivors. They have seen significant improvements in outcome over the past decade, and it appears from recent figures that the average chance of death or profound impairment for infants born at 24 weeks gestation is approximately 25 per cent (unpublished figures). Based on the principles articulated above, it appears that in that centre most infants born at 24 weeks gestation no longer fit within the prognosis-based grey zone.

The concept of the neonatal grey zone has been applied particularly to decisions about *withholding* life-sustaining treatment for extremely premature infants. The guidelines referred to in Figure 8 often refer to the possibility of later withdrawal of treatment if complications ensue. However, there is little or no explicit discussion in these guidelines about when this would be appropriate, and when parental discretion would be relevant.

The prognosis-based grey zone (PAGE) framework could be used to answer the above questions about Eva. We would need one additional ethical premise to extend the PAGE framework to treatment withdrawal:

- Other things being equal, it is permissible to withdraw a medical treatment that a patient is receiving if it would have been permissible to withhold the same treatment (not already provided) (Wilkinson & Savulescu, 2012: 32).

On this basis, the question that we then need to ask is whether following her IVH, Eva now has a prognosis that is equivalent to that of the average 23- or 24-week gestation infant at birth. In other words, does she have a greater than 50 per cent chance of either dying or of being profoundly impaired?

This empirical question is not straightforward to answer. One reason for this is that it is very difficult to determine the probabilities of different outcomes for individual infants. The more specific details that are available for an infant, the less likely it is that it will be possible to find published data on the outcome of similar infants. The second reason this is challenging is because of the way that outcome and prognosis are interconnected. If infants develop a complication that is thought to be associated with a very poor prognosis, this may lead doctors and parents to withdraw life-sustaining treatment. There will then be a high mortality in the condition, and it can be difficult to determine what the chance of death would have been if treatment had continued, or what long-term problems would have ensued (Wilkinson, 2009: 401).

Nevertheless, there are some published studies on the outcome of preterm infants with severe unilateral IVH. Those studies suggest that 25 per cent or fewer of surviving extremely premature infants with periventricular haemorrhagic infarction (PVHI) have severe degrees of disability (Maitre, Marshall, Price et al, 2009; Roze, Koenraad, Van Braeckel et al, 2009; Davis, Hintz, Goldstein et al, 2014). Our own South Australian study looked at the outcome for a cohort of 145 newborn infants with severe brain injury (Brecht & Wilkinson, 2015). It included 38 infants with PVHI. Twenty-two (57 per cent) of these infants either died or had a severe degree of disability at follow-up at school age. Yet, further inspection of the data reveals that 18 of these 22 infants died, and all of the deaths followed decisions to limit treatment. In surviving infants, almost two-thirds had a normal functional status or only mild disability at follow-up.

It is difficult to say what Eva's outcome would be. However, it appears that her chance of dying (if treatment continues) or of very severe disability (if she survives) is less than 50 per cent. Accordingly, it seems that her prognosis remains equivalent to that of an average 25-week infant at birth. On the basis of the PAGE framework, it appears that treatment

limitation does not fall within the grey zone, and therefore that withdrawal of treatment is not permissible.

Table 5. A prognosis-based framework for decisions around resuscitation and intensive care for extremely premature infants (PAGE refers to “Prognosis for Average Gestation-Equivalent infant”).

Estimated chance of poor outcome* if intensive treatment is provided	PAGE	Treatment category	Obstetric management
≤50%	≥25 weeks	Usual (Life-sustaining treatment should usually be provided)	Maternal/fetus focused
50–90%	23–24 weeks gestation	Optional (Life-sustaining treatment should be guided by parents’ wishes)	Depends on parents’ wishes
≥90%	20–22 weeks gestation	Not reasonable (Life-sustaining treatment should not usually be provided)	Maternal-focused

* Note: “Poor outcome” refers to the probability of either death or profound disability (severe, non-ambulant cerebral palsy, or severe cognitive disability).

Challenges for prognosis-based guidelines

The PAGE framework is based on existing consensus about resuscitation decisions for extremely premature infants. It endorses an approach that is based on the ethical acceptability of withholding treatment from infants of 23–24 weeks gestation (or with equivalent prognosis). But perhaps the existing consensus is mistaken? It may be that the current attitudes to parental discretion around treatment for extremely premature infants are wrong, and accordingly that the thresholds in Table 5 are also incorrect. Are there any independent reasons for thinking that the probabilities in Table 5 are right?

There is some reason for thinking that a threshold of 50 per cent is potentially correct as the upper boundary of the grey zone, the upper threshold (Figure 7). If there is a less than 50:50 chance of an infant dying or being profoundly disabled, most times that treatment is provided the child will benefit from that treatment. On the “balance of probabilities”, it seems that treatment would be in the child’s best interests. Conversely, a decision to withhold life-sustaining treatment from a child who has a better than 50 per cent chance of surviving without profound disability, poses a significant risk of serious, imminent and preventable harm (Diekema, 2004). Arguably (and here others may reach a different conclusion because of the challenge of interpreting risks (Gillam, 2016)) the harm principle means that treatment must be provided, even if parents disagree.

What about the lower threshold – the chance of a sufficiently poor outcome that treatment should not be provided, even if desired? Again, we might think that this value seems approximately correct. If there is a >90 per cent chance of an infant either dying or

being profoundly disabled, for every 10 children treated, nine will receive treatment that is plausibly not in their best interests. Potentially nine children will be harmed for every one child who benefits from treatment. It accords with at least some interpretations of the legal proof standard (used in criminal prosecution) of “beyond reasonable doubt” (Franklin, 2007: 159).

Although this threshold has some intuitive plausibility, there are a couple of arguments that might be raised against it. First, we might wonder whether it is necessarily against the child’s interests to receive treatment if they subsequently die. From the point of view of the child it may be considered worthwhile to receive treatment even if there is only a very small chance of survival. After all, if they do not receive treatment there is a 100 per cent chance that they will die. In a related argument, Jim Stone has argued that a form of Pascal’s Wager can be applied to medical treatment in a persistent vegetative state: “you have everything to win and nothing to lose if you gamble on staying alive” (Stone, 2007: 84).⁵ Equally, some may challenge the suggestion that treatment would harm a child who survives with a very severe degree of impairment. That question is important, but I will have to set it aside here.⁶

An alternative challenge to the PAGE framework might point to the difference between the thresholds used to define the grey zone for extremely premature infants, and those apparently used to define the ZPD in older children with critical illness (Lantos, 2012). Janvier asked clinicians in a series of surveys whether they would respect a parental request not to resuscitate and provide intensive care for a 24-week infant (with a stipulated 50 per cent mortality rate and 50 per cent risk of disability in survivors), or a two-month old child with meningitis (with identical statistical prognosis) (Janvier, Leblanc & Barrington, 2008a; Janvier, Leblanc & Barrington, 2008b; Lavalent, Spelk, Andrews et al, 2011). While 80 per cent of United States physicians were prepared to forego resuscitation for the 24-week infant (indicating that they believed this to be within the grey zone), only 25 per cent would do so for the older infant with identical prognosis (Lavalent, Spelke, Andrews et al, 2011: e1221). Several authors have argued that this difference in approach represents discrimination against extremely premature infants.

However, establishing that there is a difference in the thresholds for parental discretion for newborn infants compared with older infants or children does not mean that the newborn thresholds are wrong. For example, it could be that those used in older children are wrong, and that paediatric intensivists should give parents more discretion in decision-making. (Other chapters in this book examine in more detail the scope of parental discretion in paediatrics.) Or it may be that there are relevant differences between a newborn infant and an older child needing paediatric intensive care that would warrant a different approach. For example, one difference might be in the burden of

⁵ Pascal’s Wager refers to a famous piece of writing about religious belief by 17th century French philosopher Blaise Pascal.

⁶ I have discussed those questions in some detail in *Death or Disability* (Wilkinson, 2013).

treatment involved. While the prognosis-based grey zone (PAGE) framework focuses on the *outcome* of treatment, one important consideration in determining whether or not it is permissible to withhold treatment is how burdensome it would be for the child (and for the family). Extremely premature infants typically face weeks and months of intensive care, with multiple, frequent painful procedures (Carbajal, Rousset, Danan et al, 2008). In comparison, children admitted to paediatric intensive care units (PICU) with meningitis typically have a short stay. In one study, children with meningitis who were comatose on admission to PICU (the sickest group of children) had a median length of stay in intensive care of three days (75 per cent were in PICU for six days or less) (Odetola & Bratton, 2005: 92). I have argued elsewhere that there are also important differences in the nature of a newborn's interests, and that this should yield greater parental discretion in decision-making for newborn infants compared with children (Wilkinson, 2013: 298).

Shedding light on the grey zone

In this chapter I have analysed some approaches to the zone of parental discretion in newborn intensive care, focusing on decision-making for extremely premature infants. I have described one model for developing prognosis-based guidelines for the boundaries of the grey zone, using existing professional consensus. I have argued that such a model, even if imperfect, has significant advantages over available, currently used alternatives.

Although the guidelines that I have proposed here have some intuitive plausibility, it is an open question whether the upper and lower thresholds are the right ones to use in newborn intensive care. How could we answer that question? Is there an independent way of determining or verifying the chance of a poor outcome that would justify parental discretion about treatment?

One factor, which I have not been able to cover here, is the role of limited resources. Resources are relevant to the grey zone in two ways. Limited public healthcare resources provide a justification for declining to provide treatment that has a low chance of benefit, or a low magnitude of benefit (in other words, the lower threshold for treatment). It could potentially be in an infant's interests to provide treatment even if there is only a minuscule chance of survival. However, in a finite, resource-limited public health system, providing treatment to that infant potentially means that other patients (with a much higher chance of benefit) are thereby denied treatment. Resources are also relevant to the upper threshold. Finite social care resources provide a limit to the ability of society to take over the long-term care of a child. If a child's treatment is considered to be in the 'white zone', but parents are adamant that they do not wish it to be provided, the only available option may be foster care or adoption. If that is a readily available, well-funded alternative, it may be an option even in the face of substantial illness or impairment or uncertainty about the benefits of treatment. Where that is not a readily available option, it seems that parents are likely to be given much more discretion about treatment.

Resources then, are important. They could provide us with a way to shed further light on the boundaries of the grey zone. Yet, consideration of finite resources and their

application to intensive care or to social care is controversial and ethically complex. There is much more work to be done in determining how these should factor into decision-making in newborn intensive care. It will have to be the subject of another day.

Acknowledgments

DW was supported for this work by a grant from the Wellcome Trust WT106587/Z/14/Z.

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