# Ethical Issues in the Use of Magnetic Resonance Imaging of the Brain in Newborn Infants with Hypoxic-Ischaemic Encephalopathy

Dr Dominic Wilkinson, Green Templeton College

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Thesis for the degree of Doctor of Philosophy

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# ABSTRACT

**Ethical Issues in the Use of Magnetic Resonance Imaging of the Brain in Newborn Infants with Hypoxic-Ischaemic Encephalopathy**

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Infants with hypoxic-ischaemic encephalopathy (birth asphyxia) have a high risk of death or disability. Those with poor prognosis are sometimes allowed to die after withdrawal of intensive care. In recent years, doctors have used new types of brain scan, magnetic resonance imaging (MRI), to predict the type and severity of impairment if the infant survives and to help with such decisions.

In this thesis, I analyse the issues arising from the use of MRI for prognostication and decision-making in newborn infants. I argue that previous prognostic research has been hampered by a failure to identify and focus on the most important practical question and that this contributes to uncertainty in practice. I outline recommendations for improving research.

I then look at existing guidelines about withdrawal of life-sustaining treatment. I identify several problems with these guidelines; they are vague and fail to provide practical guidance, they provide little or no genuine scope for parental involvement in decisions, and they give no weight to the interests of others. I argue that parental interests should be given some weight in decisions for newborn infants. I develop a new model of decision-making that, using the concept of a Restricted Life, attempts to set out clearly the boundaries of parental discretion in decision-making. I argue that where infants are predicted to have severe cognitive or very severe physical impairment parents should be permitted to request either withdrawal or continuation of treatment. I justify this model on the basis of overlapping interests, (prognostic, experiential and moral) uncertainty, asymmetrical harms, and the burden of care.

In the conclusion, I set out a guideline for the use of MRI in newborn infants with hypoxic-ischaemic encephalopathy. I suggest that this guideline would provide a more robust, coherent and practical basis for decision-making in newborn intensive care.

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## ABBREVIATIONS

ADC: Apparent Diffusion Coefficient (quantitative measure using diffusion weighted imaging)

aEEG: amplitude integrated Electroencephalogram – a form of continuous bedside monitoring of brain electrical activity.

CI: Confidence Interval

CP: Cerebral Palsy

CT: Computed Tomography

DDE: Doctrine of Double Effect

DWI: Diffusion Weighted Imaging

EEG: Electroencephalogram

GMFCS: Gross Motor Functional Classification System

HIE: Hypoxic-Ischaemic Encephalopathy

Lac/NAA: Ratio of Lactate: N-Acetyl Aspartate measured by magnetic resonance spectroscopy

LNWL: Life Not Worth Living

LST: Life-Sustaining Treatment

LWL: Life Worth Living

MCS: Minimally Conscious State

MR: Magnetic Resonance

MRI: Magnetic Resonance Imaging

MRS: Magnetic Resonance Spectroscopy

NAA: N-Acetyl Aspartate

PLIC: Posterior Limb of the Internal Capsule. (Area within basal ganglia corresponding to motor tracts.)

PVS: Persistent Vegetative State

QoL: Quality of Life

SFP: Self-Fulfilling Prophecy

# THESIS OUTLINE

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# PART 1: BACKGROUND

## *Introduction*

In this thesis, I analyse ethical issues arising from the use of a new form of neuroimaging, magnetic resonance imaging (MRI), to predict future impairment in a group of critically ill newborn infants.

My interest in these questions arose from working in newborn intensive care and from being involved in the care of infants and children with varying degrees of brain injury. During my paediatric training there was increasing use of MRI for imaging the newborn brain, and increasing emphasis on the results of such testing for decision-making. Over a period of 6 or 7 years MRI went from a test that was performed rarely, to one performed almost routinely in seriously ill term infants. It became apparent to me that such testing raised a number of difficult questions in practice, and that these questions had received little or no systematic attention.

The problem in practice is that existing guidelines for decisions on the basis of prognosis are hopelessly vague. Clinicians and parents do not know whether or not they should withdraw treatment, and whether or not they *can* withdraw treatment without risk of legal sanction. This leads to inconsistency – decisions vary between doctors and between units. It also tends to lead to conservatism, and to parents being denied the chance to have input into treatment decisions for their infant. I argue in this thesis that parents should have a greater say about whether or not treatment continues for their brain-damaged infant – within defined limits.

In the first part of this thesis (chapters 1-3), I set out the background to these issues and identify the principal normative questions that need to be addressed. In chapter one, I describe hypoxic-ischaemic encephalopathy and the use of different tests to predict outcome; I also outline the scientific evidence for the prognostic use of MRI. I next discuss treatment limitation decisions in infants with this illness (chapter 2), existing guidelines for decision-making and case law in the United Kingdom (UK). I argue that current guidelines are inadequate. In the third chapter, I provide a snapshot of the way that clinicians use prognostic tests in decision-making and the issues that arise in practice.

The second part of the thesis (chapters 4-9) comprises a philosophical analysis of the questions that emerge from part one, with the aim to develop a cohesive and coherent guideline for the prognostic use of MRI in newborn intensive care. There are specific issues related to MRI and HIE, but there are also general questions about prognostication and decision-making in newborn intensive care. In chapter four, I analyse the scientific research that forms the basis for testing, and the way in which it contributes to uncertainty in practice; I assess, in particular, the problem of self-fulfilling prophecies. I develop a series of recommendations for future research using MRI for prognosis. In chapter five, I address the timing of prognostic testing (a question emerging from interviews with

clinicians) and the potential window of opportunity for treatment withdrawal. Chapter six moves on to look at the results of testing, predicted impairment, and the best interests of the infant as interpreted by existing guidelines. I analyse the concept of 'intolerability' and the 'balance sheet' approach to assessing interests. I argue that even if prognostic uncertainty is set aside, this approach is unable to provide practical guidance in a large number of cases. In chapter seven, I assess one argument for permitting infants with moderate or mild degrees of impairment to be allowed to die – that there is a strong impersonal reason to *replace* impaired newborn infants. I suggest that this argument is implausible, and the principal reason to replace reflects the interests of parents. The following chapter (eight) develops an argument that parental interests should be given some weight in decisions though this would not justify replacement of mildly or moderately impaired infants. I contend that this is appropriate for infants where it would not be for older children because of the nature of their interests - their moral status lies in between that of fetuses and children. In the last chapter of this section, I describe an alternative account of the permissibility of treatment withdrawal that I call the Threshold View. I argue that this model is able to provide more specific and practical advice for decisions than the existing best-interests account. It gives scope for the views of parents within a range of cases, and explains how either treatment continuation or limitation may be permissible. It is able to set the boundaries for parental discretion either to continue or to limit treatment.

In the final part of the thesis, I draw together the recommendations from part 2 to set out a proposed guideline for magnetic resonance imaging in newborn infants with hypoxic-ischaemic encephalopathy. I set out the broader implications of such a guideline for newborns with other conditions, and for other groups of patients such as late-gestation fetuses. [1]

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[1] Sections of this thesis have been published, or will shortly appear in print in the following papers

Wilkinson, D. (2009) The self-fulfilling prophecy in intensive care. *Theor Med Bioeth*, 30, 401-10.

Wilkinson, D. (2009) The window of opportunity: decision theory and the timing of prognostic tests for newborn infants. *Bioethics*, 23, 503-14.

Wilkinson, D. (2010) Should we replace disabled newborn infants? *Journal of Moral Philosophy*, (forthcoming).

Wilkinson, D. (2010) 'We don't have a crystal ball': neonatologists' views on prognosis and decision-making in newborn infants with birth asphyxia. *Monash Bioethics Review*, (forthcoming).

# CHAPTER 1

## Prognosis and magnetic resonance imaging

### *1.1 Introduction*

Hypoxic-ischaemic encephalopathy (HIE) is a potentially devastating illness in newborn infants, for which treatment is largely supportive. It may be helpful to start with a representative hypothetical case to illustrate the nature of the questions that sometimes arise in the care of infants with HIE.

> A mother goes into labour with her first child. She is eagerly anticipating a healthy newborn, but late in labour complications develop. The fetal heartbeat tracing shows a dramatic slowing, and an emergency caesarean section is performed. The baby (Shaun) is born pale, floppy, and apparently lifeless. He is transferred to the resuscitaire in the corner of the operating suite where paediatricians quietly but urgently try to bring him back to life. He is intubated (has a breathing tube inserted into his airway) and receives cardiopulmonary resuscitation including administration of adrenaline. After a few anxious minutes his heartbeat is heard for the first time. Shaun is transferred to the neonatal intensive care unit where he is critically ill in the first days of life. He is comatose, dependent on life support, and has multi-organ failure involving his kidneys, heart, and liver. He has repeated seizures. Electrical tracings of brain activity are abnormal. It appears that Shaun's brain and other organs have been deprived of oxygen and blood supply during the birth process.
>
> After the first 48 hours Shaun's condition improves a little, and it appears that he will probably survive. But the doctors and Shaun's parents worry about the risk of him having permanent brain damage if he does survive. They wonder whether continuing to keep him alive is the right thing to do.
>
> Shaun's doctors decide to perform further tests of his brain to help predict the chance and severity of long-term impairment. They transfer him to a magnetic resonance scanner to obtain detailed pictures of his brain. His brain scan reveals abnormalities in deep parts of the brain responsible for controlling movement. But what do such results mean for Shaun's future? How good is the scientific evidence supporting the use of this type of new brain scan? How certain can doctors be of the nature and severity of problems for Shaun?[2]

In this chapter, I describe HIE and summarise briefly its cause, classification, and outcome. I outline the different methods of predicting outcome that have traditionally been available

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[2] Unless otherwise indicated the cases discussed in this thesis are hypothetical. They represent a realistic composite of cases that I have been involved with in neonatal and paediatric care.

to clinicians and distinguish between three different purposes of prognostication. I then describe magnetic resonance imaging (MRI) and related technologies, used in recent years to help with prognostication. Magnetic resonance imaging is claimed to be the most specific means of predicting outcome for newborn infants with HIE. I summarise the published evidence for the use of MRI to predict neurodevelopmental outcome in HIE.

The aim of this first chapter is to describe some of the medicine and science that will underpin ethical analysis in the second part of the thesis. It will set out the reasons why I focus in this thesis on one particular group of newborn infants, and on one type of testing.

## *1.2 Hypoxic-ischaemic encephalopathy*

Birth is one of the most dangerous points in human life (Save the Children 2006). Half of the 4 million global neonatal deaths occur on the first day after birth (Save the Children 2006). About 900,000 of these deaths are due to compromised blood and oxygen supply around the time of labour and delivery (Lawn et al. 2005a; Lawn et al. 2005b). Mortality rates in developed countries are much lower, but approximately 10% of newborn infants require some help with establishing breathing after birth and almost 1% need more extensive resuscitation after birth (Thornberg et al. 1995; American Heart Association and American Academy of Pediatrics 2006). Some of these infants subsequently manifest abnormal neurological symptoms and signs (encephalopathy) in the newborn period. In countries like Sweden, France, and Australia, 2-4 infants out of every 1000 live births have encephalopathy of moderate or severe degree (Thornberg et al. 1995; Badawi et al. 1998; Pierrat et al. 2005).

There are different terms that are used to refer to this illness (MacLennan 1999). The most generic is *neonatal encephalopathy*, which refers to abnormal neurological behaviour in the newborn period. *Hypoxic-Ischaemic Encephalopathy* (HIE) is used for neonatal encephalopathy occurring in the presence of presumptive evidence of perinatal hypoxia (lack of oxygen) and/or ischemia (reduced blood supply) (Box 1.1)(Volpe 2008, p. 401). This usually includes evidence of fetal distress in-utero as well as the need for resuscitation at birth. The older terms *birth asphyxia* and *perinatal asphyxia* have fallen out of favour (MacLennan 1999).

**Hypoxic Ischaemic Encephalopathy** (HIE): an illness marked by abnormal neurological behaviour in the newborn period combined with evidence suggestive of acute hypoxia/ischemia.

**Severe encephalopathy (Sarnat stage 3):** infants with HIE who are severely hypotonic (floppy), comatose, and have usually lost the drive to breath. They have at least an 85% chance of significant impairment if they survive.

**Moderate encephalopathy (Sarnat stage 2):** infants with HIE who have reduced tone and conscious state. They often have seizures. They have about a 30% chance of significant impairment if they survive.

**Mild encephalopathy (Sarnat stage 1):** infants with HIE who are usually hyper-alert with normal muscle tone. They do not have seizures. Virtually all such infants survive without impairment.

**Impairment:** reduction in physical, physiological or psychological capacities relative to species norm (Bickenbach et al. 1999; Buchanan et al. 2000, p. 285).

**Severe physical impairment:** physical impairment at a level of GMFCS 4 or 5 or equivalent (see p.5) ie wheelchair dependent (Wake et al. 2003).

**Severe cognitive impairment:** intelligence quotient ≤35, (more than 4 standard deviations from normal); individuals may have elemental language and self-care skills) see p.5.

**Moderate physical impairment:** physical impairment at the level of GMFCS 2 or 3, ie able to walk with aids, may require wheelchair in the community.

**Moderate cognitive impairment:** intelligence quotient 35-50, (individuals usually are socially interactive and able to carry out basic conversations).

*Box 1.1: Definitions.*[3]

I will focus in this thesis on term newborn infants with HIE. There are several reasons for this. The first is that HIE is associated with a high rate of mortality and morbidity. Approximately 15% of cases die in the neonatal unit, 10-15% develop cerebral palsy and up to 40% have other impairments including blindness, deafness, autism, or global developmental delay (Finer et al. 1981; Robertson and Finer 1985; Robertson et al. 1989;

[3] I use these definitions of severe physical and cognitive impairment since they correspond to standard and widely accepted disability classifications (Harris 2006; Himmelmann et al. 2006).

Marlow et al. 2005; Pierrat et al. 2005; Lindstrom et al. 2006; Volpe 2008, p. 441). Almost half of the more severely affected infants either die or have significant impairment (Jacobs et al. 2007; Volpe 2008, p. 441; Azzopardi et al. 2009b).

Secondly, HIE is a common reason for withdrawal of life-sustaining treatment in newborn intensive care. It is the commonest single cause of death in term newborn infants (The consultative council 2008; Verhagen et al. 2009), and the majority of such deaths follow decisions to limit or withdraw treatment (Wall and Partridge 1997; Pierrat et al. 2005; Verhagen et al. 2009). For a number of reasons that will become apparent in subsequent chapters, these decisions are often in practice particularly difficult and controversial (McHaffie and Fowlie 1996, p. 98).

Third, new forms of neuroimaging have been studied in HIE more than in any other defined condition in newborns. Thus it provides an ideal starting point for an analysis of the practical and ethical issues that arise from the use of such neuroimaging. I focus on HIE rather than the broader group of infants with *neonatal encephalopathy* because the majority of published studies have focussed on this group of infants. For the same reason I will also, almost exclusively, focus on infants who have reached at least 36 weeks of gestation (*term newborns*). However, as I will discuss in chapter 10, the issues that I identify in relation to neuroimaging in term infants with HIE also apply to other critically ill newborns.

### 1.2.1 Causes and classification

Although HIE is, by definition, accompanied by evidence of perinatal hypoxia-ischemia, not all HIE is *caused* by intrapartum hypoxia-ischemia (Volpe 2008, p. 400). Some infants have underlying metabolic, chromosomal or neuromuscular disorders that mimic the neurological syndrome (Cowan et al. 2003). Other infants have antenatal insults that present with compromise at birth (Volpe 2008, p. 400). Recent studies, however, indicate that the vast majority of infants with HIE have patterns of brain imaging in the neonatal period that are consistent with acute injury and hypoxia-ischemia (Cowan et al. 2003; Miller et al. 2005).

HIE is often classified clinically into categories of mild, moderate and severe (Fenichel 1983; Levene et al. 1985; Ambalavanan et al. 2006), and one of the most widely used classification systems is the Sarnat scale (Sarnat and Sarnat 1976). The severity of encephalopathy is prognostically extremely important (van de Riet et al. 1999; Volpe 2008, p. 441). In practice, however, it can be difficult to distinguish between moderate and severe categories, and the use of medications such as anticonvulsants or muscle relaxants can confound clinical assessment. In the thesis, when I refer to moderate or severe encephalopathy I have in mind classification along the lines of the Sarnat scale (Box 1.1).

Like the infant Shaun, many infants with moderate HIE and all infants with severe HIE require respiratory support with mechanical ventilation in the newborn period (Donn et al. 2002, p. 292). The majority have multi-organ dysfunction, including renal impairment with

anuria or oliguria, hypotension requiring cardiovascular support, hepatic involvement with deranged liver function tests or coagulopathy (Shah et al. 2004). More than half develop seizures in the first 12 hours (Volpe 2008, p. 402). The time course of illness varies, but there can be deterioration in neurological condition between 24 and 72 hours in severely affected infants related to delayed cell death (Volpe 2008, p. 403). After 72 hours, however, infants often start to improve (Volpe 2008, p. 403). Respiratory drive returns, though abnormalities of brain-stem function may persist with abnormal or absent gag reflex, sucking and swallowing. Infants who have recovered neurological function and are able to feed by the end of the first week are highly likely to have normal neurodevelopment (Sarnat and Sarnat 1976; Robertson and Finer 1985).

### 1.2.2 Outcome

Infants with HIE who survive the newborn period may have a variety of long term problems, including cognitive impairment, motor impairment, seizure disorders and sensory deficits. (In this thesis I use the term *impairment* to refer to reductions in physical, physiological or psychological capacities relative to the species norm (Box 1.1). I will generally avoid the contested terms disability and handicap (Rosenbaum and Stewart 2004; Shakespeare 2008).) The most specific form of impairment attributable to HIE is dyskinetic or athetoid cerebral palsy (CP) (Rennie et al. 2007), which manifests in abnormal tone and involuntary movements affecting all limbs. It may be functionally very disabling because of difficulty coordinating movements, although intellect may be normal (Rennie et al. 2007). A different form of cerebral palsy, spastic quadriplegic cerebral palsy, is seen in many infants who have had severe HIE. (The majority of children and adults with spastic quadriplegia, though, do not have a history of HIE (Badawi et al. 2005).) This is a motor disorder with increased tone and spasticity affecting all four limbs, and is often associated with severe global functional impairment.

The functional impact of cerebral palsy varies enormously (Himmelmann et al. 2006). In recent years a functional classification system has been developed, the Gross Motor Functional Classification System (GMFCS) (Palisano et al. 1997), that grades function from level 1 (walking without assistance) through level 3 (walking with assisted mobility devices) to level 5 (severely limited mobility) (Palisano et al. 1997; Himmelmann et al. 2006) (Box 1.1). Large outcome studies in HIE have not, to date, reported GMFCS scores. In one small study, of 9 surviving infants with HIE diagnosed with cerebral palsy at 2 years, 5 had spastic quadriplegic cerebral palsy. All were classified as GMFCS 5. Of the other infants 3 had dyskinetic cerebral palsy (GMFCS 2), and 1 had hemiplegic cerebral palsy (affecting movement on one side only, GMFCS 1) (van Schie et al. 2009).

Cognitive impairment resulting from HIE often coincides with spastic quadriplegic cerebral palsy. The degree of cognitive impairment in such children is often severe or profound. The mean intelligence quotient in a group of school age survivors of severe HIE

was 36 (Robertson et al. 1989; van Handel et al. 2007). As a brief aside at this point, severe cognitive impairment is usually used to refer to individuals with intelligence quotients (IQ) of 20-35, while profound impairment refers to individuals with testable IQ <20 (Harris 2006, pp. 54-55) (Box 1.1). The other standard categories of cognitive impairment are mild (IQ 50-55 to 70), and moderate (35 to 50-55) (Harris 2006). Individuals with severe impairment usually also have impairment of motor skills, difficulty in ambulation and limited communication ability. Most require close supervision and care throughout life. Those with profound impairment are only able to achieve even rudimentary self-care tasks with extensive training, and require total supervision and care (King et al. 2000; Harris 2006).

There can also be cognitive impairment in survivors without cerebral palsy (Marlow et al. 2005; Rennie et al. 2007). This seems to be generally mild, (for example an 11 point reduction in IQ in a cohort of children who had had moderate to severe encephalopathy) (Marlow et al. 2005; Rennie et al. 2007).

Sensory impairment in survivors of HIE is usually associated with other impairments. In one study, none of the children followed up at school age had significant visual impairment without physical or cognitive impairment, while 6 of 9 children with spastic quadriplegic cerebral palsy were cortically blind (Mercuri et al. 2004a). Similarly, isolated hearing impairment following HIE is uncommon (Rennie et al. 2007).

### 1.2.3 Quality of life following HIE

The above section outlines potential impairments for infants with HIE. But for subsequent chapters discussing treatment withdrawal it would be useful to know about the wellbeing or quality of life of such infants and children. There are to my knowledge, however, no studies that have systematically assessed the quality of life of surviving children with HIE.[4]

There is some evidence on the quality of life of children with cerebral palsy (from a range of causes, including HIE). Measures of functional status or health status are attempts to objectively quantify the impact of illness on individuals (Livingston et al. 2007). Unsurprisingly, physical health is markedly reduced in children with CP (Wake et al. 2003), more so in those with severe CP (Venkateswaran and Shevell 2008). But researchers have distinguished such objective measures from subjective reports of wellbeing. The largest published study (the SPARCLE study) reported subjective quality of life (QoL) in 500

[4] A search of medline (Pubmed) was performed using the terms "infant, newborn" AND (encephalopathy[All Fields] OR HIE[All Fields] OR ("asphyxia"[MeSH Terms] OR "asphyxia"[All Fields])) AND ("quality of life"[MeSH Terms] OR ("quality"[All Fields] AND "life"[All Fields]) OR "quality of life"[All Fields]). 37 studies were identified of which only one was directly relevant. One small study performed 30 years ago recorded the "quality of survival" in terms of psychological function in a group of infants who had required extensive resuscitation at birth (Thomson et al. 1977). It is not clear, however, how many of the infants were clinically encephalopathic. Two of the 31 children had severe physical and cognitive impairment, but their 'quality of life' was not reported.

children with cerebral palsy and found that children reported similar QoL to other children (Dickinson et al. 2007). This evidence has been drawn on to support the so-called 'disability paradox', and to challenge the assumption that cerebral palsy leads to lives that are impoverished and of poor quality (Rosenbaum 2008). Gary Albrecht and Patrick Devlieger described the disability paradox as the finding that many individuals with significant disabilities report high subjective quality of life (with similar levels to the general population), despite living what is judged by most external observers to be an undesirable existence (Albrecht and Devlieger 1999).

However, two thirds of the responses in the above study were from children with mild forms of motor impairment (GMFCS 1 or 2), while only 14% of respondents had severe motor impairment. Self-reports of QoL are not possible from children with severe cognitive impairment (Dammann and O'Shea 2007; Saigal and Tyson 2008). In a separate part of the same study, parents reported on their perception of the QoL of their children (Arnaud et al. 2008). While indices of QoL were not markedly different overall between children with CP and those without, there were differences in QoL for children with severe CP. Severe motor impairment was associated with reduced scores for physical wellbeing and autonomy while moderate or severe cognitive impairment was associated with reduction in the "social support" domain of QoL (Arnaud et al. 2008). Other studies have reported that children and adolescents with severe cerebral palsy are more likely to experience pain (Houlihan et al. 2004), and participate less in everyday activities (McManus et al. 2008).

One interesting result from the SPARCLE study was that the severity of cognitive impairment in children with cerebral palsy was inversely associated with certain aspects of parent-reported QoL - specifically in mood and self-perception domains (Arnaud et al. 2008). Children with severe impairment were *less* likely to have low scores in these areas of the QoL questionnaire. I will return to this in chapter 6.

### 1.2.4 Prognosis in HIE

Before talking about how prognosis is determined it is worthwhile clarifying the different reasons to do this.

#### *1.2.4.1 Reasons for prognostication*

There are three different purposes of prognostication for infants in HIE.

1. *Prognosis for neuroprotection.* One role is to identify infants who might benefit from neuroprotective therapies in the immediate postnatal period. It has recently emerged that cooling infants with HIE to about 34 degrees for 72 hours reduces the risk of death or significant impairment at 18 month follow-up (Gluckman et al. 2005; Shankaran et al. 2005; Jacobs et al. 2007; Azzopardi et al. 2009b). There is a need to determine within the first hours after birth whether infants are at risk of long-term complications, and consequently

whether to institute cooling or other neuroprotective treatment (Groenendaal and de Vries 2000).

2. *Prognosis for anticipation*. Secondly, prognostication may be used to identify infants with potentially abnormal neurodevelopment in order to inform parents and potentially provide targeted developmental interventions in early childhood (Majnemer 1998; Evans 2007).

3. *Prognosis for treatment limitation/continuation*. Thirdly, prognosis is used to inform decisions about the continuation or withdrawal of intensive care support.

These purposes differ in their importance. Neuroprotection with cooling is valuable. It has, however, only a modest effect on outcome (approximately 15% reduction in the risk of death or significant impairment) (Jacobs et al. 2007). Also, given that the treatment is low risk, it is sufficient to determine which infants have some risk of long-term impairment. There is no need to determine how high that risk is, nor the severity of impairment.

Prognosis for anticipation is also somewhat important. Parents are understandably anxious to know whether, and how significantly their child might be impaired. But to date, there is no evidence that providing this information to parents or providing early developmental intervention is better for either parents or child than waiting until impairment becomes apparent (Evans 2007).

On the other hand, prognostication for treatment limitation/continuation decisions makes a huge difference to outcome. It obviously has the potential to lead to the death of an infant or to survival. Mistakes in prognosis for treatment limitation decisions have very serious ramifications for the infant and for parents. This third purpose of prognosis is the most important, and the most important to get right.

#### *1.2.4.2 Means of prognostication*

There are a variety of clinical, electrophysiological and imaging tools that have been used to help clinicians determine the prognosis of infants with HIE (Shevell et al. 1999; Volpe 2008, pp. 438-48). The majority of these tools are able to predict the overall degree of impairment, but are not able to distinguish between different types of impairment.

The severity of encephalopathy is among the most useful and well-studied prognostic factor. Infants with the mildest form of encephalopathy have a uniformly good prognosis. Those with moderate encephalopathy have approximately 30% chance of death or significant impairment, while 85% or more of the most severe subset (Sarnat stage 3) die or are significantly impaired (Peliowski and Finer 1992; van de Riet et al. 1999; Dilenge et al. 2001; Pin et al. 2009).[5]

[5] I use the term *significant* impairment here to refer to levels of impairment that were judged by authors of research studies to be "severe". The definition of 'severe impairment' in these studies is different from that

Abnormalities of background electrical activity on electroencephalogram (EEG) are associated with poor outcome (Biagioni et al. 2001). In particular, burst-suppression patterns (with very low electrical activity interspersed with bursts of abnormal activation) are a very poor prognostic sign (Menache et al. 2002), as are patterns of 'extreme discontinuity' (Biagioni et al. 2001; Menache et al. 2002). Amplitude-integrated EEG (aEEG) is a form of EEG that can be reasonably easily applied at the bedside and monitored continuously in the neonatal intensive care unit (al Naqeeb et al. 1999; ter Horst et al. 2004). A recent meta-analysis has suggested that severe background changes on aEEG have 91% sensitivity and 88% specificity for predicting significant impairment or death (Spitzmiller et al. 2007). (In that meta-analysis, abnormal outcome included cerebral palsy (unspecified) or developmental quotient ≤85 (ie borderline or greater developmental impairment)).

Imaging of the brain also provides useful prognostic information. Changes in deep central areas of the brain (basal ganglia/thalamus) on ultrasound predict later motor impairment (Rutherford et al. 1994), though most scans do not identify such changes (Volpe 2008, p. 444). Patterns of increased cerebral blood flow and reduced vascular resistance using Doppler ultrasound have been found to be highly specific for adverse outcome in a small number of studies (Archer et al. 1986; Levene et al. 1989). Computed tomography (CT) has also been used to define the extent and site of brain injury. In recent years, it has largely been superseded by magnetic resonance imaging, which is more sensitive and specific and does not involve ionising radiation (Robertson et al. 2003; Volpe 2008, p. 443; Chau et al. 2009b).

## *1.3 MRI for prognosis in HIE*[6]

Nuclear magnetic resonance imaging (MRI) measures the 'relaxation' of protons in hydrogen atoms after they have been subject to intense local magnetic fields (Edelman and Warach 1993). As the protons return to their natural state they release energy, which is picked up by a radio receiver. So-called 'T1 relaxation times' reflect the recovery of longitudinal magnetisation, while T2 relaxation times reflect transverse magnetisation; these times are dependent in complex ways on the physical and chemical characteristics of tissues. Because variations in T1 and T2 values are considerably greater than differences in tissue density, magnetic resonance images provide far better soft tissue resolution than plain X-ray or CT images (Edelman and Warach 1993).

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used in this thesis. For example, in the meta-analysis by Pin and colleagues (2009), "severe impairment" included cerebral palsy of any type or cognitive impairment >2 standard deviations below the mean - ie IQ <70 or corresponding to mild or greater cognitive impairment on standard definitions; see section 1.2.2.

[6] MRI is also used for *diagnosis* in infants with encephalopathy (Filan et al. 2007). Supportive imaging patterns are included in some diagnostic criteria for HIE (MacLennan 1999). In this thesis I focus exclusively on the prognostic use of MRI.

Magnetic resonance (MR) technology has revolutionised imaging of the brain (Robertson and Wyatt 2004). Conventional MRI provides detailed structural images of the cerebrum, cerebellum and brain-stem. Its ability to detect injury in different areas of the brain is particularly important, and distinguishes it from earlier prognostic tools. Related techniques include Diffusion Weighted Imaging (DWI), which measures the translational movement of water molecules (Hunt et al. 2004) and Magnetic Resonance Spectroscopy (MRS), used to non-invasively assess the levels of different metabolites in tissue (da Silva et al. 2006). Other techniques include diffusion tensor imaging, functional MRI, and MR angiography (Robertson and Wyatt 2004; Rutherford et al. 2005; Chau et al. 2009a). What prognostic information do these different modalities yield?

### 1.3.1 Conventional MRI

Several distinct patterns have been observed in infants with HIE with conventional MRI. Some infants appear to have injury focussed on deep central areas of the brain (*basal ganglia* and *thalamus),* responsible, among other things, for coordinating movement. This sometimes includes a key region that motor pathways traverse on their way from the motor cortex to the spinal cord (the posterior limb of the internal capsule (PLIC)) (Rutherford et al. 2006). A second distinct pattern of injury involves principally the *white matter*, with extension to cortex in severe cases (Miller et al. 2005). (*White matter* refers to the part of the brain below the outer surface; it mainly contains myelinated nerve fibres travelling from the cortex to other parts of the brain or spinal cord, and appears macroscopically white.) Other infants have combinations of these patterns.

These patterns of injury are relevant prognostically (Table 1.1). Basal ganglia changes are associated with the development of severe cerebral palsy – particularly of the athetoid/dyskinetic form (Kuenzle et al. 1994; Rutherford et al. 1996; Barkovich et al. 1998; Mercuri et al. 2000; Biagioni et al. 2001; Barnett et al. 2002; Mercuri et al. 2004a; Jyoti et al. 2006; Ricci et al. 2006; El-Ayouty et al. 2007). A subset of infants with basal ganglia changes on MRI have abnormal signal intensity in the posterior limb of the internal capsule (PLIC), and it has been argued that this is the most specific MRI finding for severe impairment (Rutherford et al. 1998). In one relatively large study, all infants with bilaterally abnormal PLIC had an adverse outcome, while infants with normal PLIC (after the first few days of life) had a normal or mildly abnormal outcome (Rutherford et al. 1998). Other studies have been less conclusive (Boichot et al. 2006; Groenendaal et al. 2006; Rutherford et al. 2010).

On the whole basal ganglia injury appears to predict motor impairment, while coexistent white matter injury determines cognitive outcome (Cowan 2000; Rutherford et al. 2006). Thus, infants with isolated basal ganglia injury have been noted to develop moderate motor impairment with normal head growth and normal intellect (Biagioni et al. 2001). However, severe basal ganglia injury has been claimed to be associated uniformly with severe cognitive impairment (Rutherford et al. 2006).

| Pattern on conventional MRI | Usual Outcome |
|---|---|
| Normal scans, mild basal ganglia or mild-moderate white matter changes | Normal outcome (may include minor behavioural or learning problems) |
| Focal basal ganglia changes with bilateral signal abnormality in the PLIC | Moderate to severe motor problems (often dystonic/athetoid cerebral palsy), cognitive development may be normal |
| Severe white matter changes | Moderate to severe motor impairment, as well as moderate to severe cognitive impairment |
| Severe and diffuse basal ganglia changes | Severe motor impairment, severe cognitive impairment, microcephaly, often cortical blindness |

*Table 1.1: Patterns observed using conventional MRI and neurodevelopmental outcome.*

*(Rutherford et al. 1998; Biagioni et al. 2001; Mercuri and Barnett 2003; Mercuri et al. 2004a; Jyoti et al. 2006; El-Ayouty et al. 2007). This is not intended to represent an exhaustive list of all patterns on conventional MRI. Other patterns include cortical highlighting, or brain stem changes (Rutherford 2002, p. 101).*

White matter injury (without basal ganglia involvement) is less consistently associated with severe impairment (Miller et al. 2005). Severe white matter injury is associated with cognitive impairment, but the outcome for infants with mild or moderate white matter injury varies from normal to mildly abnormal (Mercuri et al. 2000; Mercuri et al. 2004a).

### 1.3.2 Spectroscopy

The earliest studies of magnetic resonance imaging for newborns with HIE used phosphorus MRS (Azzopardi et al. 1989). Very low values of phosphate energy metabolites were associated almost uniformly with death or significant impairment (Azzopardi et al. 1989; Martin et al. 1996). Recent studies have used the more widely available technique of proton MRS. High and persistently elevated brain levels of lactate (Hanrahan et al. 1999; Barkovich et al. 2001), and low levels of N-acetylaspartate (NAA) are seen in infants with severe HIE and associated with adverse outcome (Penrice et al. 1996; Robertson et al. 1999; Khong et al. 2004; Boichot et al. 2006; Shanmugalingam et al. 2006). Ratios of transmitters may provide an early and specific quantitative indicator of poor outcome (Shanmugalingam et al. 2006). On the other hand, MRS does not necessarily distinguish between different patterns of impairment. The method used for calculating the sensitivity and specificity of MRS in some studies may also exaggerate the apparent accuracy of the test (we will return to this in chapter 4).

### 1.3.3 Diffusion weighted imaging

Patterns of restricted diffusion on DWI of the brain are thought to reflect cytotoxic oedema (Rutherford et al. 2005) and may be able to define brain injury at an earlier stage

than conventional MRI or CT (Robertson and Wyatt 2004). It may be hard, however, to distinguish cytotoxic oedema from cell death on early scans (Brissaud et al. 2005). When compared to post-mortem histopathology DWI has been reported to overestimate the extent of injury (Roelants-van Rijn et al. 2001). Subjective appreciation of global changes in diffusion can also be difficult (Barkovich et al. 2001). For this reason quantitative measures, Apparent Diffusion Coefficients (ADC), have been calculated from diffusion images. Low ADC values in the PLIC were strongly associated with adverse outcome in one study (Hunt et al. 2004). Other authors have reported that reliable identification of this area can be difficult in the presence of oedema (L'Abee et al. 2005) and that false negative results can occur with early scans (Rutherford et al. 2004; L'Abee et al. 2005).

### 1.3.4 Timing of testing

The timing of testing influences the reliability of MRI results. Very early scans (especially those performed in the first 24 hours) appear to underestimate the extent of injury, potentially because delayed or secondary energy failure is yet to occur (Barkovich et al. 2001; L'Abee et al. 2005). In the first week of life brain swelling makes it difficult to identify changes in signal intensity on conventional imaging; the pattern and extent of brain injury are easier to detect in scans after 1 week (Kuenzle et al. 1994; Rutherford et al. 1995). This appears to be the most accurate time for predictions of the type and severity of neurodevelopmental consequences (Biagioni et al. 2001; Rutherford 2002, p. 127).

### 1.3.5 The strength of prognostic evidence for MRI

To summarise: prognostication in HIE takes place for a number of different reasons, but is particularly important when it is used to inform treatment limitation decisions. The major difference between MRI and other prognostic tests is the potential ability of MRI to predict the *nature of impairment* as well as the severity of future impairment. But how reliable is MRI or related technology at predicting outcome for infants with HIE? Which findings on MRI are the most useful?

The best published data to answer these questions comes from a recent systematic review. Thayyil and colleagues (2010) used Cochrane methodology for performing systematic reviews of diagnostic tests. They carefully reviewed studies that related MR findings in infants with HIE to neurodevelopmental outcome at 12 months or later. The authors included studies using conventional MRI as well as studies performing spectroscopy, diffusion weighted imaging (DWI), diffusion tensor imaging or fractional anisotropy. In order to determine the sensitivity and specificity of different biomarkers, outcome data was extracted from studies (favourable vs unfavourable) as well as the presence or absence of abnormality on testing.

Thayyil and colleagues identified 32 studies including a total of 860 newborn infants with HIE (Thayyil et al. 2010). They found that certain patterns of MRI were able to accurately identify infants who subsequently developed significant impairment. In particular, their

detailed analysis found MRS to be more specific and sensitive for predicting neurodevelopmental impairment than conventional imaging. Basal ganglia lactate/N-acetylaspartate peak:area ratio (Lac/NAA) was the most accurate prognostic marker in their review for predicting adverse outcome. Across all the studies included in the review Lac/NAA ratios were considerably more specific than conventional MRI (95% vs 51%), though slightly less sensitive for unfavourable outcome (82% vs 91%). In the small number of studies where both were reported and they could be compared directly, Lac/NAA again outperformed conventional MRI. The authors do not calculate positive predictive values, but this can be calculated assuming a standard prevalence of adverse outcome. For infants with severe encephalopathy (pre-test probability of significant impairment 0.85) 97% of those with abnormal Lac/NAA would have significant impairment (confidence interval 97-99.9%), while 88% (73%-97%) of infants with moderate encephalopathy would have significant impairment.

Contrary to suggestions from previous studies (Rutherford et al. 1998; Hunt et al. 2004), Thayyil found that the brain-water ADC and absence of myelin signal in the PLIC did not have adequate prognostic utility (PLIC sensitivity 71%, specificity 86%; ADC sensitivity 66%, specificity 64%) (Thayyil et al. 2010). They also noted one problem with assessing the prognostic accuracy of MRI: the potential for self-fulfilling prophecies.

## *1.4 Conclusions*

HIE is a major cause of mortality or severe impairment in newborn infants. In this chapter, I have described the natural history of this illness, and the techniques available for predicting outcome for affected infants. MRI and related technologies have emerged as potentially one of the most important and specific means of assessing prognosis for affected infants like Shaun, discussed at the start of this chapter. One novel feature of such imaging is its ability to predict the nature as well as the severity of future impairment. Certain patterns on MRI are able to accurately identify infants with a high risk of significant impairment, though no patterns are 100% specific. What issues arise from this review of the science of prognosis in HIE?

One of the features of prognostic testing that emerges from the above analysis is the effect of the timing of tests on their accuracy and on their relevance for treatment limitation decisions. This will also emerge as an important issue for clinicians in chapter 3. There may be a trade-off between prognostic accuracy and the possibility of treatment withdrawal. I will discuss this question and look at one approach to addressing it in chapter 5.

A second problem apparent in the above review of the literature is the potential for self-fulfilling prophecies in relation to prognostic tests. This was noted in passing by the authors of the systematic review discussed above. In chapter four, I will analyse in detail the epistemic and normative questions arising from self-fulfilling prophecies, and look at ways to reduce such problems in future research.

A third feature emerging from the above analysis is an ambiguity relating to reporting about outcomes. Studies use broad outcome categories encompassing a wide range of impairments and neurological abnormalities. They often use "severe disability" to refer to impairments that would be referred to as mild in standard classification of impairments (for example treatable epilepsy or an IQ of 68). I will return to the importance of this in chapter 4.

In the next chapter I will argue that existing guidelines are extremely vague when it comes to defining the severity of impairment that makes treatment withdrawal permissible. This may be a partial explanation for the vagueness of outcome classification in research. But determining an answer to this fundamental question (the severity of impairment warranting treatment withdrawal) is necessary before we can know what to do with MRI results for an infant like Shaun. This question will be the focus of chapters 6 to 8.

I have referred to treatment limitation decisions in the above analysis. But what are those decisions, how might prognosis from MRI relate to them, and what do existing guidelines have to say about them? That will be the focus of the next chapter.

# CHAPTER 2

## Prognosis and withdrawal of life-sustaining treatment from newborn infants. Current guidelines and practice in the UK

### *2.1 Introduction*

In the previous chapter, I argued that it is the use of neuroimaging for informing decisions about life-sustaining treatment that is potentially the most important prognostic question. There are three types of decision that might lead to the death of a newborn infant with HIE. The first is to *withhold* treatment that could potentially save the life of the infant. For example a decision may be made not to perform cardio-pulmonary resuscitation if the infant has a cardiac arrest. The second is to *withdraw* treatments that are currently sustaining the life of the infant, and without which the infant may die. The prime example is when an infant is taken off the ventilator and their breathing tube is removed. The third type of decision is to take active steps to hasten the death of the infant, for example by giving them a large dose of opiates with the intent to suppress breathing. In this chapter, and in this thesis in general, I will focus almost exclusively on the first two types of decision. I refer to them generically as treatment limitation decisions and will not, for the most part, distinguish between them. I accept as valid the widely held assumption that decisions to withhold or to withdraw treatment are ethically and legally equivalent (Airedale NHS Trust v Bland 1993a, p. 866; American Academy of Pediatrics Committee on Fetus and Newborn 1995; Royal College of Paediatrics and Child Health 2004, p. 17; Nuffield Council on Bioethics 2006, p. 18). I will not discuss much the third type of decision - active euthanasia of newborn infants. This is firstly because in the majority of jurisdictions around the world neonatal euthanasia remains illegal. Even in those countries where it is legal it is performed extremely rarely, whereas treatment limitation decisions occur on a regular basis and precede the majority of deaths in newborn intensive care (Verhagen et al. 2009). But secondly, the issues raised for euthanasia in newborns by advances in neuroscience are essentially the same as those raised for treatment limitation decisions. Which patterns of neuroimaging would warrant such a decision?

There are, broadly speaking, two different reasons why treatment may be limited for a newborn infant. It may be believed that death is inevitable within a fairly short period and that further life-sustaining measures are therefore futile. Alternatively, there can be concern that although survival is possible for the infant they are likely to have significant impairment adversely affecting their future 'quality of life'. In practice, these two reasons

are not completely discrete. For infants who appear to be dying, the presence or absence of impairment often influences the judgement that further treatment is futile. Conversely, infants who have treatment withdrawn for what appear to be quality of life reasons often also have some chance, even if treatment were continued, of dying in the neonatal period or early infancy. I will focus, however, on the second type of reason. The relevance of brain imaging is almost exclusively its ability to predict future impairment if the infant survives. With rare exceptions it is less useful at identifying infants who are not able to survive.

In this chapter, I set out the context of treatment limitation decisions. I first review the legal and ethical guidelines that inform practice in the UK. I argue that current guidelines provide inadequate guidance for decisions. In the second part, I discuss some of the empirical literature on treatment limitation decisions in newborn intensive care.

I will focus in this analysis on three questions in particular.

1. How severe must future impairment be for treatment to be limited?
2. How certain must impairment be?
3. What role should parents play in decisions?

## *2.2 Current guidelines*

In this analysis, I draw mostly on guidelines and case law pertaining to the United Kingdom. This is largely for reasons of brevity and practicality, since a full discussion of law and guidelines from other countries would not be possible here. Guidelines in the UK are also more developed and explicit than those elsewhere in Europe, with the possible exception of the Netherlands (McHaffie et al. 1999). But the analysis has wider implications since the principles (and legal precedents) used in UK cases and guidelines are similar to those used elsewhere, or may be directly applicable to a number of other countries (eg Australia, New Zealand, Canada).

In only one or two recent cases has there been specific discussion of the results of neuroimaging (examples include An NHS Trust v MB (2006a, para 31) and Re OT (2009b, para 24)). None of the guidelines for clinicians explicitly discuss the use of neuroimaging. In what follows, I draw out the principles cited in guidelines and case law that could be applied to the interpretation of imaging results. I summarise the different guidelines and analyse these principles further in Chapter 6 (see p. 85).

### 2.2.1 Royal College

One of the most influential guidelines is that provided by The Royal College of Paediatrics and Child Health (RCPCH) (2004). The College's Ethics Advisory Committee published a revised framework for decisions about withdrawal or withholding life-sustaining treatment (LST) in 2004. This framework has been cited by the courts (An NHS Trust v D 2000a, para 77; K (A minor) 2006b, para 37-9; Re OT 2009b, pp. 29-30) and is used by clinicians

in practice (Street et al. 2000). It bases decisions fundamentally upon a best interests determination (RCPCH 2004, p. 12), but the guidelines delineate five settings where treatment limitation decisions could be appropriate.[7] Of these, the fourth, the "no-purpose situation" is most relevant to treatment withdrawal decisions on the basis of quality of life. The guidelines suggest that this situation is present when survival is possible but the degree of physical or mental impairment will be so great that it is "intolerable".

The framework links this justification for withdrawing or withholding treatment to the legal judgement in Re J (1991) (see below). It suggests two possible interpretations of intolerable: "that which cannot be borne" or "that which an individual should not be asked to bear", though seems to favour the latter (RCPCH 2004, p. 11). The guideline notes that:

> "…a quality of life which could be considered intolerable to an able-bodied person, would not necessarily be unacceptable to a child who has been born disabled." (ibid. p. 26)

Usefully, the guideline also provides some examples of what the committee believes this to refer to in practice: "when there is little or no prospect of meaningful interaction with others or the environment" (ibid. p. 24), and suggests that spastic quadriplegia with severe associated cognitive and sensory deficits may be one such condition (ibid. p. 25).

Since the RCPCH guidelines are reasonably specific about the type of impairment that would justify withdrawal of life-sustaining treatment, it might be thought straightforward to apply the guidelines to predictions of impairment for infants with HIE. Some difficulty in interpretation remains, however. It is not clear when interaction with the environment becomes 'meaningful'. For example, is the capacity to communicate what confers meaning, or would the recognition of faces or voices be sufficient? While it seems reasonably clear that severe cognitive impairment is a necessary component of intolerable disability as envisaged by the RCPCH committee there is no attempt to specify what this means in practical terms. Would it be permissible to withdraw life support if severe cognitive impairment were predicted in the absence of other major impairments?

There is also some difficulty in relation to uncertainty. The summary of the guidelines suggests that treatment limitation is permissible only when prognosis is certain.

> "where there is uncertainty about the degree of future impairment or disagreement, the child's life should always be safeguarded" (ibid. p. 11)

But this conflicts with statements later on in the document.

> "it is sufficient to have a *reasonable belief* that a particular outcome is *likely*…absolute certainty may be neither possible nor always necessary" (ibid. p. 27) [emphasis added]

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[7] The "Brain Dead Child", The "Permanent Vegetative State", The "No Chance" situation, The "No Purpose" situation, The "Unbearable" situation (RCPCH 2004).

> "Decisions to stop or withhold certain treatments will almost always be based on probabilities rather than certainties." (ibid. p. 29)

The RCPCH guidelines emphasise that decisions to withdraw treatment should be made with the consent of parents, but it does not make clear what role parents should have in deciding whether or not predicted impairment is intolerable, nor whether there are intolerable situations where parents may request that treatment is continued. In several places the guidelines state that the ultimate decision is the responsibility of the heath care team (ibid. p. 27).

### 2.2.2 General Medical Council

The General Medical Council (GMC) and the British Medical Association (BMA) have provided more generic guidelines about decisions relating to treatment withdrawal. GMC guidelines (GMC 2006) draw on case law, legislation and the European Convention on Human Rights (Tibballs 2007). They set out general principles for decision-making, emphasising the importance of best interests and a weighing up of benefits and burdens (GMC 2006, para 9-10). There is little specific guidance about whether or when impairment might be sufficient to justify withholding treatment, though the guidelines acknowledge that it may be appropriate to assess quality of life (GMC 2006, Appendix A. para 1). There is no specific discussion of uncertainty in prognosis. The guidelines do not discuss the role of parents in decisions beyond their legal responsibility to authorize or refuse treatments in accordance with the child's best interests.

### 2.2.3 British Medical Association

The British Medical Association last revised its guidance document in 2007 (BMA 2007). This guideline covers decision-making for both adults and children, and stipulates that the ethical principles covering infants should be the same (ibid. p. 102). According to this document quality of life considerations are unavoidable, and may legitimately be taken into account (ibid. p. 8). Specifically, criteria for assessing best interests in both infants and older individuals may include the capacity to develop awareness, to interact, and for self-directed action (ibid. p. 106). The guidelines discuss various legal cases, but do not provide examples of conditions that would justify withdrawal.

The BMA guidelines suggest that, in general, where there is uncertainty about treatment options parents should decide (ibid. p. 98). They also stipulate that "where there is reasonable uncertainty about the benefit of life-prolonging treatment, there should be a presumption in favour of initiating it" (ibid. p. 106). The guidelines note that parents may only make decisions in the best interests of the child. The relationship of uncertainty to best interests is not made clear.

### 2.2.4 American Academy of Pediatrics

Although American guidelines are less influential in countries such as the United Kingdom they are often referred to in the literature (Tibballs 2007; Ahluwalia et al. 2008). They are also of interest since they relate specifically to newborn infants. There are two policy statements from the American Academy of Pediatrics (AAP) that are relevant - a guideline from 1995 on forgoing life-sustaining treatment (AAP 1995), and a more recent guideline from 2007 on 'Non-initiation or withdrawal of intensive care for high risk newborns' (AAP 2007).

The earlier AAP guideline does not provide specific criteria for forgoing treatment. It specifies that for incompetent patients whose previous wishes are unknown (for example newborns), decisions should be guided by the best interests principle. It interprets best interests as involving a weighing up of the benefits and burdens of treatment; for life-sustaining treatment that specifically includes assessment of the benefits or burdens of ongoing life. Although the guideline refers to "irremediable disability" in the lists of burdens there is no attempt to spell out what this means in practice (AAP 1995, p. 533). It does not make clear the role of parents in decisions beyond a comment that for such serious questions decisions should usually conform to the family's wishes.

The later guideline also bases judgements on the best interests principle (AAP 2007, p. 401), and it, too, is vague about how this should be interpreted in practice. The title refers both to withholding or withdrawal of treatment, though the guideline itself appears mostly to relate to resuscitation decisions at birth, in particular for extremely premature newborns. The guideline refers in several places to "acceptable quality of life" (ibid. p. 401), though does not set out what this term means, nor to whom the quality of life should be acceptable. It sets out a grey zone of permissibility where parental wishes should determine the treatment approach:

> "cases…in which the prognosis is uncertain but likely to be very poor and survival may be associated with a diminished quality of life for the child" (ibid. p. 402)

The terms 'prognosis' and 'uncertain' here are ambiguous, and the statement might be taken to provide considerable scope for parental involvement in decisions where there is prognostic uncertainty. However, this statement refers in a footnote to the American Heart Association resuscitation guidelines from the preceding year which stipulate that parents' wishes about treatment should be determinative when "survival is borderline, the morbidity rate is relatively high, and the anticipated burden to the child is high" (American Heart Association and American Academy of Pediatrics 2006, p. e1035). This makes it clearer that parental discretion would be limited to situations with both a high chance of death and a high chance of poor quality of life. In the penultimate paragraph of the AAP guideline it expresses ambivalence about parents and their freedom to decide:

> "The important role of parents in decision-making must be respected. However… the physician must ensure that the chosen treatment, in his or her best medical judgement, is consistent with the best interests of the infant" (AAP 2007, p. 402)

### 2.2.5 The Nuffield Council on Bioethics

One of the most recent and relevant documents reviewing decision-making in newborn intensive care is the report by the Nuffield Council on Bioethics (Nuffield Council on Bioethics 2006). This report is not a professional guideline, but it has been extensively cited since publication (Costeloe 2007; Ahluwalia et al. 2008; Janvier et al. 2008b; Rennie and Leigh 2008; Wilkinson et al. 2009a), and may influence decision-making. It covers a range of decisions both before and after birth for extremely premature and term newborn infants. The report, as with other guidelines, emphasises the primacy of the best interests of the child in determining whether or not to provide treatment (Nuffield Council 2006, p. xvii). But, like the RCPCH guideline, it also draws on the concept of intolerability.

> "It would not be in the baby's best interests to insist on the imposition or continuance of treatment to prolong the life of the baby when doing so imposes an intolerable burden upon him or her" (ibid. p. 12)

What sort of impairment for an infant with HIE would impose an 'intolerable burden'? The report admits to some difficulty in defining this concept, noting that people may disagree both about what constitutes intolerability, and whether or not a particular infant's condition is intolerable. It suggests that providing burdensome treatment to a child predicted to have a life "bereft of those features that give meaning and purpose to human life" (ibid. p. 12 para 2.13) may impose an intolerable existence. These features are not elaborated, but in a separate part of the report the authors discuss the potential benefits of treatment to be included in a best interests determination: these include the capacity to establish relationships with others, the ability to experience pleasure, and independence from life support (ibid. p. 161 para 9.33).

The authors of the Nuffield report did not believe that the future was 'intolerable' for a premature infant with predicted moderate motor impairment (spastic diplegia), but uncertain cognitive impairment (ibid. p. 99-100). (It is not clear in that specific case whether the authors would have reached a different judgment if the infant had still been dependent on mechanical ventilation, nor how much of this judgement was related to uncertainty about prognosis). On the other hand the report judged that the future would be intolerable (and therefore that it was permissible to withdraw treatment) for a newborn predicted to have severe motor and cognitive impairment (ibid. p. 101).

The Nuffield report notes in several places the inherent uncertainty in prognosis for newborn infants. But, as with other guidelines, the report is ambiguous about the role of uncertainty in decision-making. For extremely preterm infants of 23 weeks gestation the uncertainty of the prognosis is cited as justifying giving parental wishes precedence in determining resuscitation (ibid. pp. 82, 151). This appears to contradict, however, other parts of the report that suggest that for it to be in the best interests of the infant to die a

"high degree of certainty" would be required that the infant will suffer intolerably (ibid. p. 16). One reason for this apparent contradiction is that the report distinguishes between what is *in* the best interests of the infant, and what *decisions may be made*. It differs from the above guidelines in that it explicitly embraces the idea that interests other than the child might be taken into consideration (ibid. pp. 16-17). While the best interests of the child are a "central" consideration in decisions about treatment, there is some scope to take into account the interests of parents. The implication is that these other interests would permit treatment limitation in the face of uncertainty. But though the report is explicit in setting out examples of how this could be applied to resuscitation decisions for extremely preterm infants it is less clear how this should be applied to withdrawal of treatment for infants with HIE. It also raises the question of whether this approach would be endorsed by the courts.

To conclude this section, existing guidelines are unclear about when impairment is severe enough that treatment may be withdrawn. Statements about uncertainty and the role of parents in decision-making are contradictory.

## *2.3 The Law*

How would the courts answer the questions I listed at the start of this chapter? [8] There is little statutory law relating to treatment withdrawal decisions. Legal judgements in the UK take into account the Children Act 1989 and the Human Rights Act 1998 though neither deal explicitly with decisions of this nature. The Children Act stipulates that the "child's welfare shall be the court's paramount consideration" (1989a, (s1 (1)). The Human Rights Act, in article 2, protects the right to life of infants, while Article 3 protects against inhuman or degrading treatment.

There is also relatively little case law relating to such decisions. Table 2.1 provides a summary of the most relevant cases (p 31). In what follows, I briefly outline the general features of those cases, and then discuss in more detail the courts' approach to these questions.

### 2.3.1 General features of case law relating to treatment withdrawal in the UK

Of the cases that have come before the courts only two (R v Arthur 1981a; Re B (a minor) 1981b) relate to decisions made in the newborn period (i.e. in the first month of life). This

[8] There are potential differences between different jurisdictions within the United Kingdom (ie between England and Wales, Scotland and Northern Ireland) (Nuffield Council on Bioethics 2006, p. 127). For the most part, however, these differences are not relevant to the decisions discussed here.

is perhaps understandable given the time-lag that is inherent in bringing cases before the courts. Cases where parents and doctors are in agreement about treatment decisions (to continue or to withdraw treatment) do not come before the courts. Where there is disagreement there is usually significant reluctance to resort to legal proceedings, and some time may pass before doctors or parents seek legal intervention. But there is no legal precedent for treating decisions in newborn infants differently from older infants and children so decisions in older infants may still be useful to review.

The majority of the cases that have come before the courts have related to *withholding* potentially life-saving treatment (Skene 2008, ch. 11). But the courts have also authorised withdrawal of life-saving treatment in a number of recent cases (Re C 1996; Re C 1998; K (A minor) 2006b; Re OT 2009b). Most cases arose when doctors wanted to limit or discontinue treatment but parents desired continued treatment. In several cases, the court was asked to adjudicate because the infant was in state care. There is only one case (Re B 1981b) in which parents sought limitation of treatment against the advice of doctors. There is also only one case in the UK in which there was an attempt to prosecute doctors or parents after decisions leading to the death of an infant (R v Arthur 1981a).

In almost all of the cases the courts ultimately endorsed the judgements of doctors, with the exception of one recent decision in which the court declined to authorise withdrawal of mechanical ventilation (An NHS Trust v MB 2006a). I will discuss that case further shortly.

All except three of the cases (Re C 1998; An NHS Trust v MB 2006a; Baby RB 2009a) involved infants with predicted cognitive impairment, and the majority had additional illnesses that were likely to lead to death within a fairly short period irrespective of decisions. Consequently in many cases decisions were based upon a judgement that further treatment was futile (for example Re OT (2009b), An NHS Trust v D (2000a), K (A Minor) (2006b)). In one or two cases, however, the courts explicitly made quality of life judgements. These were related to best interests in one of two ways: either using the concept of 'intolerability', or via a balance sheet of benefits and burdens.

### 2.3.2 Intolerability

The notion that impairment could be so severe that it would be permissible to withhold life-saving treatment was introduced in a case in 1981 (Re B 1981b). In that instance, the Court of Appeal authorised surgery for an infant with Down syndrome and duodenal atresia despite his parents refusing consent, on the grounds that the infant's life was not bound to be "demonstrably awful" or "intolerable" (Re B 1981b, p. 1424 para B, H). But one of the judges noted that

> "There may be cases, I know not, of severe proved damage where … the court might be driven to a different conclusion" (Re B 1981b, p. 1424C)

Several subsequent cases drew on this judgement as providing a guide to decision-making.

#### *2.3.2.1 Re C 1990*

C was a 4-month old infant who had been made a ward of court shortly after birth. She had severe congenital hydrocephalus, and, despite a shunt procedure in the newborn period, was predicted to develop "severe mental handicap, blindness, probable deafness and spastic cerebral palsy of all four limbs" (Re C 1990, p. 33). Doctors had applied for permission to manage her palliatively, and the court initially provided an order directing that this occur. Subsequently the Official Solicitor appealed the decision and the case went to the Court of Appeal.

The Court of Appeal endorsed the earlier judgement that palliative care was appropriate, though there was some equivocation about the grounds for the decision. Lord Donaldson in several places noted that C was dying. Lord Balcombe noted that the child was terminally ill based upon the opinion of the medical expert who stated: "I do not believe there is any treatment which will alter the ultimate prognosis, which is hopeless" (Re C 1990, p. 38). It is not clear, however, that this was actually the sense of hopelessness intended by the testifying doctor. The words immediately following 'hopeless' were "She has a massive handicap as a result of a permanent brain lesion". In other places the same doctor stated "The high standard of care makes it difficult to forecast how long she will live" (Re C 1990, p. 33).

The earlier judgement in Re C was more explicit about the decision being based upon impairment - specifically cognitive impairment, and linked this to the language used in the Court of Appeal judgements in Re B.

> "I adjudge that any quality to life has already been denied to this child because it cannot flow from a brain incapable of even limited intellectual function. In as much as one judges, as I do, intellectual function to be a hallmark of our humanity, her functioning on that level is negligible if it exists at all. Coupled with her total physical handicap, the quality of her life will be demonstrably awful and intolerable" (Re C 1990, p. 35C)

Another decision in the Court of Appeal the following year is often cited in support of 'intolerability'.

#### *2.3.2.2 Re J 1991*

J was an ex-premature infant with severe brain injury, and, like C, was predicted to develop spastic quadriplegia, blindness and deafness. In another parallel with that earlier case, J was a ward of the court (for reasons unrelated to the question at hand), and doctors sought approval to withhold ventilatory support in the event of a cardiorespiratory collapse. In this case, there was clear acknowledgement that J was not terminally ill, and that with treatment he may survive into late childhood or adolescence. The court rejected the Official Solicitor's argument that it was never justifiable to withhold life-saving treatment on the basis of a child's quality of life; it held that it could be in the best interests of a child to

withhold such treatment. In the summary of Re J, this decision was explicitly related to intolerability:

> "where, viewed from …[his position], his future life might be regarded as intolerable to him the court acting solely on his behalf might properly choose a course of action which did not prevent his death" (Re J 1991, p. 34 para C)

In Re B (1981), Down syndrome (which is usually associated with at most moderate cognitive impairment and mild physical impairment) was judged *not* to be intolerable. In contrast, in both of the above cases spastic quadriplegia and profound cognitive impairment combined with blindness and deafness were judged intolerable. But in another, more recent, case with very similar impairments there was disagreement about whether or not this level had been reached. Charlotte Wyatt was also an ex-premature infant with microcephaly, spastic quadriplegic cerebral palsy, and profound cognitive and sensory impairments. There was some equivocation about intolerability, since her day-to-day life was judged *not* to be intolerable (Portsmouth Hospitals NHS Trust v Wyatt 2005a, p. 4005E), though it would *become* intolerable if she were to be ventilator-dependent.

In fact, in Re J only one of three judges (Lord Justice Taylor) justified the decision on the grounds of intolerability (Re J 1991, p. 55F). Lord Donaldson and Lord Justice Balcombe explicitly rejected the idea that the phrases used in the initial Re B case should be applied as a test for determining treatment decision.

> "I do not think that we are bound to, or should, treat Templeman L.J.'s use of the words "demonstrably so awful" or Dunn L.J.'s use of the word "intolerable" as providing a quasi-statutory yardstick." (Re J 1991, p. 46F)

Several more recent cases have also rejected the 'intolerability' standard for treatment withdrawal ('Wyatt' 2004b; Re L 2005b; An NHS Trust v MB 2006a; K (A Minor) 2006b). Instead these cases have attempted to determine best interests through a weighing up of benefits and burdens for the child.

### 2.3.3 Balance sheet

In a case involving the proposed sterilisation of a 29 year-old man with Down syndrome, Lord Justice Thorpe suggested that in order to make an evaluation of best interests the first step was

> "…[to] draw up a balance sheet. The first entry should be of any factor or factors of actual benefit… Then on the other sheet the judge should write any counterbalancing dis-benefits to the applicant. … Obviously only if the account is in relatively significant credit will the judge conclude that the application is likely to advance the best interests of the claimant." (Re A 2000b)

This approach was a major part of the decision-making in the case of MB.

#### *2.3.3.1 An NHS trust v MB 2006*

MB was an eighteen-month old infant with a severe congenital neuromuscular disorder (type 1.1 spinal muscular atrophy). He had been in hospital since seven weeks of age, and ventilator dependent for 6 months. His condition led to progressive loss of muscle strength and tone, so that although he could initially cry audibly, smile and move his limbs, by the time of the court hearing he could only move his eyes. Although MB had profound motor impairment he was not believed to be cognitively impaired. MB's doctors believed that continuing mechanical ventilation was "cruel", and that it would be in his best interests to withdraw life-saving treatment and allow him to die. His parents, on the other hand, opposed the withdrawal of treatment.

Justice Holman asked the advocates on either side to draw up a list of the benefits and burdens of continuing or discontinuing mechanical ventilation, and included the list provided by the guardian in his judgement. He placed significant emphasis on the process of weighing up benefits and burdens, though noted huge difficulties in reliably appraising the benefits of treatment, deciding what weight to give to future burdens, and in arriving at an overall balance (An NHS Trust v MB 2006a, para 62). The judge ruled that continued mechanical ventilation (though not surgical tracheostomy) was in the best interests of MB. In reaching this decision the judge placed importance on the absence of cognitive and sensory impairment.

> "So far as I am aware, no court has yet been asked to approve that, against the will of the child's parents, life support may be withdrawn or discontinued,…[from] a conscious child with sensory awareness and assumed normal cognition and no reliable evidence of any significant brain damage." (ibid. para 11)
>
> "As he can hear and see, I accept the evidence of his parents that he is attentive to TV, DVDs, CDs, stories and speech; and as all these things may give pleasure to other children of 18 months, I must and do assume they give pleasure to him." (ibid. para 65)
>
> "[MB's] life does in my view include within it the benefits that I have tried to describe … Within those benefits, and central to them, is my view that on the available evidence I must proceed on the basis that M has age appropriate cognition, and does continue to have a relationship of value to him with his family, and does continue to gain other pleasures from touch, sight and sound." (ibid. para 101)

The significance of this case for treatment decisions lies in several factors. The judge's decision endorsed the idea of using a balance sheet of benefits and burdens to determine best interests, he supported MB's parents against the unanimous opinion of medical experts, and he placed significant emphasis on the presence of normal cognition and sensory abilities. But, given the substantial difficulties in the balancing process alluded to by Justice Holman, it is not clear how courts would respond to other situations. Would mild or moderate cognitive impairment sufficiently reduce the benefits of treatment to tip the balance in favour of treatment withdrawal? Would a single sensory impairment (for

example blindness) significantly affect the balance? I will return to these questions in Chapter 6.

### 2.3.4 Uncertainty

Lord Justice Taylor expressed the clearest statement of the court's view on certainty in prognosis. He rejected the contention of the Official Solicitor that treatment should continue because it was not "certain" that life was intolerable for J.

> "Certainty as to the future is beyond human judgment. The courts have not, even in the trial of capital offences, required certainty of proof. But, clearly, the court must be satisfied to a high degree of probability." (Re J 1991, p. 56A)

Similar sentiments were expressed in the Wyatt case, where the difficulties inherent in prognostication about survival were acknowledged ('Wyatt' 2004b). However, in that case the extent of brain damage was felt to be certain (ibid. para 2), and the most realistic chance of survival 5% or less (ibid. para 11). The court has not quantified what level of certainty would be required for prognosis, but it appears to require it to be very high.

### 2.3.5 The wishes of parents

What role has the court placed on the wishes or interests of parents? It might be thought that the court places little emphasis on parents' views since, in almost every case that has come before it, parents' wishes have been overruled. But this state of affairs is also likely to reflect two other factors. Firstly, it is only when doctors are convinced that continued treatment is against the child's interests that the courts become involved. The fact that the court goes against parents' wishes may reflect the exceptional nature of such cases. But secondly there is an additional legal principle that complicates rulings. As noted in the case of Re D (2000a, para 51) the courts have long held that a doctor cannot be forced to provide a treatment that he or she believes genuinely is not appropriate for the patient (see also (Re J 1993b, p. 27; Burke 2004a)).

In a number of cases the court has also appeared to explicitly reject the suggestion of the Nuffield report that interests other than the child might be taken into account.

> "it is settled law that the court's *prime and paramount* consideration must be the best interests of the child. This is easily said but not so easily applied. What it does involve is that the views of parents, although they should be heeded and weighed, cannot prevail over the court's view...of best interests." [emphasis added] (Re J 1991, p. 52H)

Similarly language echoing that of the Children Act appears in a number of other judgments, for example An NHS Trust v D (2000a, p. 48), and 'Wyatt' (2005a, p. 4022 para 87). Parents' views should be treated with respect, but the court will independently assess the interests of the child (Re Z 1997b, pp. 32-3). In the Re B case, the Court of Appeal ruled that the previous judge had been wrong to respect the wishes of the infant's parents;

the court's duty was to decide whether treatment was in the best interests of the child (Re B 1981b, p. 1424D).

In two recent cases, however, the courts have given somewhat more emphasis to the role of parents. In the case of MB, the court noted that parents have a particular role in assessing the interests of the child (I will return to this in Chapter 8, section 8.3.4). The court ultimately sided with the parents and ordered that life support continue. This was not because that was the wish of the parents, rather because the court believed that the doctors' assessment of the interests of the child was incorrect.

In an earlier case, the Court of Appeal supported parental refusal of likely life-saving treatment (a liver transplant) (Re T 1997a). The court in that case took into account the impact on parents of overriding their wishes given that they were likely to be the ongoing carers for the child, and considered that this would be detrimental to the interests of the child.

> "The welfare of this child depends on his mother" (ibid. p. 251G)

I will return to the potential interdependence of the interests of the child and parents in chapter 8. However, the jurisprudential basis of the judgement in Re T has been criticized (Mason et al. 2006, p. 571) and, given several unusual features of the case (Skene 2008, para 11.11), it is not clear whether it would be followed in future decisions.

To sum up, decisions in previous cases that have come before the courts have placed significant emphasis on the presence or absence of cognitive impairment, either because of its effect on whether such a life would be tolerable, or on the balance of benefits and burdens associated with treatment. The courts have not, however, indicated clearly the severity of impairment that would justify withdrawal or withholding of life-sustaining treatment. The courts have set a high threshold of certainty for treatment limitation decisions, and have placed little emphasis on parental wishes in such decisions.

## *2.4 Current practice*

How are these decisions actually made in practice?

There is relatively little data on the frequency and nature of treatment limitation decisions in newborns in the UK. Hazel McHaffie studied three neonatal units in Scotland in the 1980s; she found that 70% of deaths were preceded by discussion about treatment limitation (McHaffie and Fowlie 2001). In a London hospital similar decisions were documented in 39 infants (58% of deaths) over a four-year period (Roy et al. 2004). In neither of these studies is it clear how often such decisions were motivated by quality of life concerns, but studies from other countries suggest that they are not uncommon. In a retrospective review of all deaths in neonatal units in the Netherlands, quality of life was the primary motivation for treatment limitation in 42% of cases. Similarly, in a recent study

from a Swiss neonatal unit, quality of life was a significant influence in 53% of deaths (Berger and Hofer 2009). In two earlier studies from Australia and the United States, withdrawal of mechanical ventilation was motivated by quality of life concerns in 30-40% of cases (Singh et al. 2004; Wilkinson et al. 2006).

There is also little data specifically relating to decisions in infants with HIE. In one population study from France, 13 of 24 infants with HIE who died in the neonatal period had treatment withdrawn (Pierrat et al. 2005). In recent studies of cooling for infants with HIE, 60-70% of deaths followed treatment withdrawal (Shankaran et al. 2005; Azzopardi et al. 2009a). An Australian study compared end-of-life care in two epochs, (1985-7 and 1999-2001) (Wilkinson et al. 2006). There were 24 deaths in infants with HIE over both periods. In 5 infants death occurred without treatment limitation, while in 1 infant treatment was withdrawn on the grounds of futility. In 18 infants (75%) treatment was limited in the face of uncertain prognosis – they may have survived or may have died if treatment were continued; quality of life played a major role in such decisions (Campbell 1999; Wilkinson et al. 2006).[9]

What about the role of MRI? MRI has been used in newborn infants with HIE for over 20 years (McArdle et al. 1987). A guideline from the American Academy of Pediatrics in 2002 recommended that all encephalopathic term infants have MRI performed between days 2 and 8 (Ment et al. 2002). However, it is not clear how often this guideline is followed nor how MRI is used. In one recently published survey, a questionnaire was completed by 95 Australian or New Zealand neonatologists about their use of electrophysiological testing or imaging in a hypothetical infant with HIE (Filan et al. 2007). Almost 80% of surveyed neonatologists indicated that they would use MRI in that case. If considering withdrawal of life support 62% reported that they would attempt to organise an MRI prior to that decision.

Qualitative research provides more detailed information about how decisions to limit treatment are reached in newborn infants and how these are related to prognosis. A number of studies have looked at decision-making in newborn intensive care (for example (Anspach 1993; McHaffie and Fowlie 1996; McHaffie and Fowlie 2001; Brinchmann et al. 2002; Orfali 2004; Orfali and Gordon 2004; van Zuuren and van Manen 2006)). McHaffie found that almost 80% of doctors and nurses in Scottish neonatal units believed that there should be an option of limiting treatment in the face of severe impairment (McHaffie and Fowlie 1996, p. 94). Quality of life and the wishes of family (along with futility) were the most frequently cited criteria for determining when treatment should be withdrawn (McHaffie and Fowlie 1996, p. 101). But many of those that she interviewed described difficulty or discomfort in deciding what constitutes good quality of life and in articulating

[9] Unpublished data from these two studies.

the severity of impairment that would warrant consideration of withdrawal of treatment (McHaffie and Fowlie 1996, pp. 95, 97-8). Half distinguished between physical and cognitive impairments, almost all judging physical impairment preferable. Her interviewees found infants with HIE particularly difficult because of uncertainty about outcome (McHaffie and Fowlie 1996, p. 98).

McHaffie's research did not investigate the process of prognostication, but other studies suggest that doctors rely heavily on objective data from investigations in evaluating prognosis and establishing medical certainty (Anspach 1993, pp. 60-63; Orfali 2004). On the other hand there is also evidence from these studies of the potential subjectivity of prognosis. In a study of neonatal units in France and the United States Orfali and Gordon found that neonatologists systematically differed in their evaluation of prognosis in identical cases (Orfali 2004). In the French units, data that appear to reduce or erase uncertainty were valued and emphasised in justifying a decision to withdraw treatment. On the other hand, in the American unit clinical evidence that potentially contradicted the radiological evidence of brain injury was taken to preclude certainty and warrant continued treatment (Orfali 2004). Orfali argued that beliefs about whether or not treatment *should* be continued (including the value of survival with impairment and the impact of impairment on families and on society) influenced physicians' assessment of the *likelihood* of adverse outcomes for the infant (Orfali 2004, pp. 2018-9).

The role of parents in decision-making in newborn intensive care varies between countries (Cuttini et al. 2000; Orfali 2004) and has changed over time. Although neonatologists emphasise the importance of parents in decisions about life-sustaining treatment, in practice parental autonomy is constrained by a number of factors (McHaffie et al. 2001; Orfali 2004). Parents are reliant on medical staff for facts. They are only presented with the alternative of treatment withdrawal after doctors have made a prior judgement that this is "medically appropriate", and may be presented with strong recommendations or advice (McHaffie et al. 2001). Paradoxically, in one study, units ostensibly placing a strong emphasis on parental autonomy seriously limited parental choice by failing to offer parents the option of withdrawal of intensive care (Orfali 2004).

Renee Anspach, describing practice in two American neonatal units from the 1980s, referred to the decision-making process as one of "producing assent" to medical decisions (Anspach 1993, ch. 4). Doctors used a variety of techniques to persuade or coerce parents to agree with a decision to withdraw treatment, and consequently conflict with parents was rare (Anspach 1993, pp. 93-5). In a more recent study of decision-making in the US, parents were apparently given a much greater role in decisions; treatment was continued if parents disagreed with doctors (Orfali 2004; Orfali and Gordon 2004). On the other hand, in continental Europe, particularly in France, parental involvement in decisions may be very limited. In French neonatal and paediatric intensive care units, treatment withdrawal decisions are generally made by doctors alone (Orfali 2004; Carnevale and Bibeau 2007).

Medical and nursing staff in Scotland in the 1990s mostly favoured a joint approach to decision-making (McHaffie and Fowlie 2001).

## *2.5 Conclusions*

The above analysis of current guidelines influencing treatment limitation in the UK reveals little to help clinicians make decisions on the basis of neuroimaging and prognosis. Professional guidelines and legal decisions overlap in their approach, but both are vague about the severity of impairment that must be present for treatment limitation to be permissible. It is simply unclear from these sources whether or when treatment may be limited for infants with HIE.

The courts and published guidelines have used either 'intolerability' or a balance sheet test for assessing the best interests of infants. In chapter 6, I will critically analyse the application of such principles to predicted severe impairment and assess whether more specific guidelines could be generated using these principles.

Existing guidelines are also ambiguous about uncertainty and the role of parents in decisions. They appear to emphasise the importance of parents, but at the same time only permit treatment limitation if continued treatment would be intolerable or not in the best interests of the infant. These appear to conflict, however. If treatment would be intolerable how can parents request its continuation? If treatment would be in the best interests of the infant how could parents' wishes (for treatment limitation) be respected? Similarly, suggestions that parents' wishes may be decisive if prognosis is uncertain appear to conflict with the injunction that treatment only be withdrawn in the face of a very high degree of certainty. I will look at ways of reconciling these possibilities in chapter 9.

I have also reviewed the available empirical evidence on treatment limitation decisions in newborn intensive care. It is difficult to know how the existing guidelines influence practice. There is not much data on treatment limitation decisions in the UK. The largest study (McHaffie and Fowlie 1996) pre-dates most of the guidelines and legal cases that I have discussed. However, McHaffie's study emphasises the difficulty that doctors face in making decisions on the basis of quality of life, and the particular difficulties associated with prognostic uncertainty for infants with HIE. Are these issues still apparent for neonatologists, and how have advances in prognostic testing influenced practice and decision-making? Do they raise any new concerns? In the next chapter, I will provide a snapshot of current practice to shed some light on these questions.

*Table 2.1: Previous legal cases in the UK and decisions about withdrawal or withholding of life-sustaining treatment (LST)*

| Case | Medical condition | Age | Setting | Parents views (supported/ opposed doctors) | Type of decision (what was being sought?) | Ultimate decision | Concepts used in judgement |
|---|---|---|---|---|---|---|---|
| Re B (a minor) (wardship: medical treatment) [1981] 1 WLR 1421 | Down syndrome, duodenal atresia | newborn | Parents refusing consent for surgery, doctors seeking permission to operate | Opposed | Continuation (surgery) | Permission given for surgery | Referred to intolerability |
| R v Arthur (1981) 12 BMLR 1 | Down syndrome, uncomplicated | newborn | Review after death; given analgesia and water only. | Supported | Legality of treatment and palliative care | Prosecuted but acquitted | |
| Re C (a minor: wardship: medical treatment)(No.1) [1990] Fam 26 | Congenital hydro-cephalus, predicted severe mental handicap, blindness, probable deafness and spastic quadriplegic cerebral palsy; unclear duration of survival | 4 months | In care; doctors sought leave to manage palliatively. | In care | Withholding | Antibiotics, nasogastric and intravenous feeding withheld | Intolerability |
| Re J (a minor) (wardship: medical treatment) [1991] Fam 33 | Premature infant, blind, ?deaf, unlikely to be able to communicate or develop even limited intellectual abilities | 4 months | In care; doctors sought judgement on whether lawful to withhold ventilation if needed | In care | Withholding | Treatment withheld | Intolerability |

| Case | Medical condition | Age | Setting | Parents views (supported/ opposed doctors) | Type of decision (what was being sought?) | Ultimate decision | Concepts used in judgement |
|---|---|---|---|---|---|---|---|
| Re J (A Minor) (Child in Care: Medical Treatment) [1993] Fam 15 | Profoundly mentally and physically handicapped, microcephaly, cerebral palsy, cortical blindness, epilepsy (following head injury in infancy) | 17 months | Appeal - initially court granted injunction requiring doctors to resuscitate if C needed it | Opposed (in care) | Withholding | Treatment withheld | Importance of medical judgement; duty of doctors and hospitals to manage limited resources |
| Re C (A Baby) [1996] 2 F.L.R. 43 | Meningitis, severe brain damage, cortical blindness | 3 months | Doctors wanted to withdraw, | Supported | Withdrawal | Ventilation withdrawn | 'Hopeless'; Best interests |
| Re C (medical treatment) [1998] 1 FLR 384 | Spinal Muscular Atrophy type 1 | 16 months | Doctors sought authority to withdraw ventilation and not reinstitute if required; parents wanted infant to be reventilated if required | Opposed | Withdrawal/ withholding | Ventilation withdrawn | Judgement refers to "no chance" (RCPCH) and best interests of the child. |
| An NHS Trust v D [2000] 2 FLR 677 | Ex 31 week premature infant, severe lung disease, lissencephaly and Dandy Walker (severe developmental delay), heart failure, hepatic dysfunction, renal dysfunction | 19 months | Doctors wanted to withhold intensive care on the grounds that it was not in the child's best interests | Opposed | Withholding | Treatment withheld | Very poor prognosis, "no chance" (refers to RCPCH), terminal condition |

| Case | Medical condition | Age | Setting | Parents views (supported/ opposed doctors) | Type of decision (what was being sought?) | Ultimate decision | Concepts used in judgement |
|---|---|---|---|---|---|---|---|
| 'Wyatt' Portsmouth NHS Trust v Wyatt [2005] 1 F.L.R. 21<br>Portsmouth Hospitals NHS Trust v Wyatt [2005] 1 W.L.R. 3995 | Ex premature infant; blind, deaf, incapable of movement or response, chronic respiratory and kidney problems; | 1-3yrs | Doctors sought to withhold ventilation if needed, | Opposed | Withholding | Court initially sided with doctors - treatment could be withheld. Despite poor prognosis condition improved. At 2yrs earlier order rescinded. At 2.5 yrs - deteriorated - order reinstated. Treatment withheld, but condition improved | Best interests; rejected 'intolerability' - only one component of best interests, condition not 'intolerable', but ventilation not in best interests |
| Re L (A Child) (Medical Treatment: Benefit) [2005] 1 F.L.R. 491 | Trisomy 18, multiple heart defects, chronic respiratory failure, gastroesophageal reflux, severe developmental delay, epilepsy and hypertonia. | 9 months | Doctors sought permission not to ventilate if required. | Opposed | Withholding | Treatment withheld | Best Interests, risks of ventilation would outweigh the benefits, high risk of being permanently ventilator dependent if intubated - would be deprived of closeness with mother; life would not be worth living. |
| An NHS Trust v MB [2006] 2 F.L.R. 319 | Spinal muscular atrophy type 1, normal intellect | 18 months | Doctors sought authority to withdraw treatment, | Opposed | Withdrawal | Treatment continued | Best interests, weighing exercise |

| Case | Medical condition | Age | Setting | Parents views (supported/ opposed doctors) | Type of decision (what was being sought?) | Ultimate decision | Concepts used in judgement |
|---|---|---|---|---|---|---|---|
| K (A minor) [2006] 2 F.L.R. 883 | Severe congenital myotonic dystrophy, very poor long term neurological prognosis, predicted short survival, total dependecy if survives, dependent on intravenous nutrition | 5.5 months | Doctors and parents wanted to withdraw intravenous nutrition and manage palliatively, child in care of local authority - therefore came to court | In care | Withdrawal | Treatment withdrawn | Best interests, referred to RCPCH categories 3 and 4 (no chance and no-purpose), rejected intolerability |
| Re OT [2009] EWHC 633 (Fam) | Mitochondrial disorder, stroke, epilepsy, ventilator dependent | 9 months | Doctors wanted to withdraw ventilation, parents wanted it to continue | Opposed | Withdrawal | Ventilation withdrawn | Futility |
| Baby RB [2009] | Congenital myasthenic syndrome (completely paralysed, ventilator dependent), normal cognition | 13 months | Doctors wanted to withdraw. | Mother wanted to withdraw treatment. Father wanted treatment to continue | Withdrawal | Father withdrew opposition to ventilator withdrawal. No judgement – though decision by mother and doctors endorsed by judge. | Best interests, benefits and burdens |

# CHAPTER 3

## Prognosis and decision-making in practice

### *3.1 Introduction*

In the previous two chapters, I have described the science underpinning the use of MRI as a prognostic test, and existing guidelines relating to treatment limitation decisions and prognosis. But how is MRI used in practice, and what issues does its use raise for doctors and parents? There have been no previous studies looking at possible problems arising from technological developments in prognostication in newborn intensive care. My own experience of infants with HIE is that MRI is used frequently in centres where the technology is available. The results of imaging strongly influence parents and doctors in treatment decisions, perhaps more than any other single factor.

This chapter will build on my personal experience. In order to provide a broader basis for analysis of the ethical issues related to prognostication and magnetic resonance imaging in newborn infants, I performed an exploratory qualitative study, interviewing a small sample of neonatologists about their experience and views of prognostication in infants with HIE. The aim was to help identify normative questions to be analysed subsequently in the thesis and to ensure that the questions apparent from review of the literature (chapters 1 and 2), and from my own experience, mirrored those issues faced by other clinicians.

I summarise below the principal themes arising from those interviews. Clinicians raised particular issues relating to uncertainty around predictions, the timing of prognostication and decision-making and difficulty in predicting quality of life.

### *3.2 Interviews - Methods*

In-depth qualitative interviews were conducted with 10 consultant neonatologists over a 6 month-period in 2008. The research used a pragmatic approach (Ritchie and Lewis 2003) aiming to elicit a diversity of perspectives without necessarily achieving theoretical saturation.

Six tertiary neonatal units were identified (ie units providing intensive care including assisted ventilation), of which three had specific research experience in HIE (two of these had a research interest in neuroimaging). Three of the units were based in London, the other units were based in metropolitan centres in the south of England. Participants were

purposively selected to include both male and female consultants with a range of clinical and research experience. Informed consent was obtained.

A topic guide was developed to cover relevant issues for interviews (Box 3.1, Appendix A). Interviews were semi-structured using a series of open-ended questions and participants were encouraged to elaborate on their answers. At the conclusion of the interview participants were asked to comment on a case example (of an infant with severe HIE and an early MRI) (appendix A). The aim of the case was to bring together some of the different threads of discussion and relate them to a specific example. In the discussion below the themes emerging from the case are grouped with other discussion of those themes.

| |
|---|
| 1. Background and professional practice |
| 2. Prognosis for infants with HIE |
| 3. MRI for infants with HIE |
| 4. Decisions to withdraw or withhold life-sustaining treatment in HIE |
| 5. Role of parents in treatment-limitation decisions |
| 6. Case vignette |

*Box 3.1: Summarised Topic Guide for Interviews*

Interviews were recorded and transcribed verbatim. Transcripts were reviewed and coded on the basis of emergent themes (Ritchie and Lewis 2003). Analysis was iterative, returning to transcripts to ensure that coding reflected the content of interviews, and that relevant responses were identified and appropriately classified. The study was approved by an NHS Human Research Ethics Committee (Approval 08/S0709/10).

## *3.3 Interviews - Results*

Four male and six female neonatologists were interviewed, ranging in age from 37 to 61, and in consultant experience from 1 to 20 years. Four had long-standing research interests in prognostic tests in HIE.

In practice, prognostication in HIE was described as a question of putting together information from different sources. A number of neonatologists referred to this as akin to piecing together a "jigsaw puzzle", and noted that if some pieces of the puzzle did not fit with others it would lead to uncertainty and motivate clinicians to consider alternative diagnoses. Clinicians varied in the emphasis they placed on investigations. Some, particularly those from centres without research interests in HIE, relied heavily on history and clinical examination. (They noted, however, that their use of investigations such as imaging had increased over the last few years and anticipated that this may change further). Neonatologists from specialist centres placed more emphasis on the results of EEG and

MRI. One limitation of clinical and (to some degree) electrophysiological tools was the influence of anticonvulsants and sedatives. If infants had received large or repeated doses of sedatives (particularly benzodiazepines) the clinical and EEG assessment may be overly pessimistic. One consultant noted that the neurological examination was potentially subjective.

### 3.3.1 Uncertainty in prognosis

Neonatologists described a number of difficulties with prognostication. One difficulty related to unrealistic parental expectations. Parents wanted to know exactly what was going to happen to their infant, whereas clinicians were attempting to determine the range of possible outcomes for an infant.

> "I don't have a crystal ball" M50[10]

> "I don't think we can paint a black and white picture" F40

All of the participants talked about uncertainty in predictions. They identified a range of contributing factors to this uncertainty including limitations of the science, variability between families in their ability to cope, the impact of the family and environment on an infant's developmental outcome, and differences between patients. One noted that this was particularly a problem for infants:

> "Unlike the adult brain, when you see quite devastating stroke for example you know that A = B outcome. I don't think that you ... can always say A = B for outcome [in babies] because there are many different things happening" F50

A couple of neonatologists drew particularly on experiences where predictions of poor outcome had ultimately been proven wrong – leading them to be conscious of their own limitations.

> "I met a boy last week who had a massive [brain injury] and we withdrew on him. We had long, long discussions with the parents ... but this little boy was walking around our paediatric ward at 5 years of age ... he is at school, albeit with additional support, but is a lovely young man ... Actually we sent him to a hospice to die; he didn't die. He was 5 years old and had quite a good quality of life. That to me highlights how actually difficult it is for us to prognosticate" M50

> "I have had the situation more than once of somebody coming to visit and some child coming bounding down the corridor and they say to me "you know you told me that child should be taken off the ventilator" F60

[10] In this section quotes from consultants are followed by their sex and approximate age (rounded to the nearest decade). Words that have been omitted are indicated by '…' Additional words that have been added to clarify meaning (obtained from the context) are indicated by square brackets.

On the other hand, neonatologists also expressed a belief that a high degree of certainty was possible in some cases; some participants explicitly linked this to treatment withdrawal decisions and described graphically the outcome for such infants.

> "one child that I remember ... was completely hypotonic, was blind, who couldn't communicate, who literally just lay there, which was heart breaking I mean ... from my own perspective that is not a quality of life I would wish on anybody" F40

Some participants indicated that uncertainty would prevent withdrawal of life support.

> "we have a responsibility to have no reasonable doubt that the degree of disability is going to be so great that being able to participate in family life communicate and share in the things that are valuable in life is not going to be possible... if we really have doubt we will err on the side of life support" M60

On the other hand, other clinicians drew on uncertainty about prognosis and particularly quality of life (see section 3.3.5 below) to justify supporting parents who requested continuation of life-sustaining treatment.

### 3.3.2 The role of MRI in prognostication

What about MRI? All the neonatologists described using late MRI (performed after infants had recovered from acute severe illness) to help provide information to parents (prognosis for anticipation). One cited advantage of MRI was its ability to predict the type as well as the severity of impairment. Clinicians varied, however, in their use of MRI within the first few days of life. For some, this reflected limitations of the local MRI facilities and the difficulty in performing MRIs for ventilated infants. In one unit this was likely to require transfer of the infant to another hospital. Others expressed a lack of confidence in MRI findings during the acute period, preferring to wait until the second week of life before performing scans. On the other hand, a couple of clinicians from specialist centres placed a lot of emphasis on MRI in prognosis, and would be reluctant to make treatment decisions without that information.

> "I do find brain MRIs very helpful … it is something that personally I would rely on quite heavily … I would be reluctant to prognosticate very strongly without imaging to be honest" F40

One clinician specifically noted that early scans would be sought in order to aid treatment withdrawal decisions, although at that stage they are more difficult to interpret.

Participants were asked whether they had encountered ethical issues or concerns related to MRI, and few clinicians admitted to having concerns of this nature (many appeared perplexed when this question was asked). After reflecting on the question a couple of clinicians mentioned the potential use of MRI results by parents in subsequent litigation (relating to perinatal injury). Participants mentioned other practical concerns with MRI including the potential risk to infants from the high power magnet. Most indicated that they didn't think that there were any particular ethical issues arising from MRI.

### 3.3.3 The window of opportunity

When discussing the timing of prognostic testing and decision-making, a number of the neonatologists referred to a window of opportunity for withdrawal of treatment.

> "There is a "window of opportunity" to withdraw with dignity for the child and for the family and if you don't withdraw during that window of opportunity, the child then may start to respond, may then start to breathe, may come off the ventilator and may survive and is profoundly handicapped." M50

Clinicians who referred to the window, noted that it potentially applied in the first 2 to 4 days of life. Some suggested that this lent a degree of urgency to discussions with parents.

> "the longer one delays that decision to withdraw intensive care, the greater the possibility that the child might actually then survive" M60

But these clinicians also noted that this presented a problem for parents and doctors.

> "that is quite difficult to say to parents, really, that you have got a short time frame perhaps in which to make a very difficult decision" F60

The problem, noted by several, was that there was also a desire not to rush parents or push them into a particular decision; some parents needed time to come to terms with the severity of their infant's brain injury and a decision to withdraw treatment. Earlier prognostication could be more difficult or uncertain. Several clinicians described infants where decisions had been delayed leading to the infants surviving with severe impairment.

On the other hand, two clinicians who referred to the window of opportunity expressed a degree of ambivalence about it. They suggested that it was not a factor that influenced their own practice.

> "I am not sure I quite buy into that personally…The fact that the baby might survive doesn't mean to say that you have made the wrong decision" F40

### 3.3.4 Difficulty in defining or determining best interests

When discussing treatment withdrawal ethical concepts that were raised by clinicians were explored in more detail. Often participants used medical terms or descriptors such as the phrases "severe disability" or "severe brain damage", qualifying this in terms of particular types of physical impairment or cognitive impairment. Some explicitly mentioned the *best interests* of the infant.

> "And if we actually concluded...[that] this baby is going to be very, very severely disabled, unable to sit up, very likely to have severe learning problems, (there could be a little bit of leeway on that, because not everybody... with severe quadriplegia has got severe cognitive problems) and we are still ventilating,...this is the point where we think that actually it is not in the baby's best interest." M60

However, several expressed difficulty or discomfort in articulating what the best interests of the infant meant in practice.

> "that is very difficult to judge... I think it is dictated by the parents, it is dictated by the clinical circumstances and there is no hard and fast rule about how to approach [it]" M50

Another neonatologist also referred to the importance of the family in determining the best interests of the infant.

> "You can say that the best interest of the child is for them as an individual, irrespective of anybody else's views or wishes. They are an individual, they have legal rights, we should be doing what is right for them. But personally I put the child within the context of their family and what that particular family feels is right for them." F40

That respondent also related best interests to a judgement that life was "*unbearable*". She was, however, the only clinician to refer to this concept. None of the interviewees referred to the related concept of 'intolerability', nor did any of them refer to a weighing of the benefits and burdens of treatment. Two neonatologists referred to a life of severe impairment as being "worse than death" or being "better off dead". The first of these referred to 'futility' rather than best interests. The second observed that only a small number of individuals with severe impairment actually have lives as bad as this.

### 3.3.5 Difficulty in judging quality of life of child

Clinicians also expressed some discomfort with judgements about quality of life. A number of clinicians referred to individuals with severe disabilities who nevertheless had what they felt to be acceptable quality of life. Several mentioned that families differed both in their judgments about quality of life and in their ability to cope with a disabled infant. At the same time participants also felt that some infants with severe disabilities had very difficult lives.

> "For some children who are severely brain damaged it is what appears to be a miserable existence of being totally dependent for all their bodily functions." F50

> "I mean of course I know that ...some children [who are] wheelchair bound and all sorts of other things... say 'thank god somebody didn't take me off the ventilator' ...but I still think that ... if I think that there is likelihood that somebody is not going to be able to be independent, I think that it is important that the parents understand that" F60

The potential for 'independence' was referred to by several of the clinicians in discussion of the severity of impairment that might lead to treatment withdrawal. On further probing some referred to total dependence or very high levels of dependency as being significant.

A couple of the neonatologists referred specifically to the significance of intellectual impairment for decision-making. Severe cognitive impairment, particularly if combined with physical impairment, was seen to prevent participation in valuable activities, was worse than physical impairment alone, and was harder for parents to cope with.

> "[It is] quite well recognised that one can have severe motor disability and have considerable mental abilities and have a life. That isn't to minimise the huge

> problems from having quadriplegia and the suffering that is involved ... but if you do have microcephaly as well then that really does rule out participation in normal human communication and activities and family life and education and everything with a greater degree of certainty than being quadriplegic" M60

One respondent, however, articulated a view that a life with very severe physical impairment but preserved intellect may be extremely difficult and may also justify treatment withdrawal.

Some of the neonatologists with specialised experience of MRI referred to particular patterns on MRI that would support treatment withdrawal.

> "the imaging patterns that I would move towards suggesting withdrawal of care [include]... very global grey and white matter infarction so very, very severe injury to all areas including the cortex, ...[or] the very severe white matter and partial basal ganglia problems ... I think those two fall into the area of something I would feel might be able to offer withdrawal of care … I would feel less happy about withdrawal of care in an isolated focal basal ganglia lesion [or] ... severe white matter infarction," F50

A couple of interviewees referred to survival with very severe impairment as the worst outcome. One referred to the potential for error in prognosis but suggested that it was a worse error to keep a child alive with such a life. Several expressed concern for the impact of a very severely disabled child on families.

### 3.3.6 Infants with poor prognosis may not die after withdrawal of treatment

All of the respondents expressed the view that withdrawal of mechanical ventilation was appropriate in some cases of HIE even if long-term survival were possible with continued treatment. Nevertheless, several clinicians mentioned that they would warn parents when withdrawing assisted ventilation that they could not predict how long the infant would survive, and that, in fact, the infant may not die. Several also stressed that while sedation may be provided after extubation, the aim of such sedation was not to prevent the infant from breathing.

> "we are not sedating the children to an extent that they don't survive, we are sedating them if needed to keep them comfortable and seizure free" F60

One referred to an infant who had continued to breathe after mechanical ventilation was withdrawn, and whose parents had requested that the infant should not be provided with artificial feeding. The neonatologist had agreed to the parents' request despite initial misgivings. Two other clinicians mentioned the option of withholding artificial feeding as something that they were aware took place in some units, but that they did not personally support. Several doctors raised the possibility of adoption if parents felt unable to support a severely impaired, surviving infant.

### 3.3.7 Should parents have the final say in decisions?

When discussing such decisions with parents, clinicians presented them with options, or suggested that treatment withdrawal was an alternative for parents to consider. It was felt to be important to give parents choices and to respect their autonomy. Clinicians also suggested that parents differ:

> "Some parents will want their child to live at all costs, every family is different … I am just sharing my opinion with the parents" F50

However, several senior consultants expressed concern about placing the burden of decisions entirely on parents.

Respondents were unanimous that treatment would not be withdrawn if parents wanted to continue treatment.

> "We never withdraw life support against the parents' wishes" M60

Clinicians described attempting to avoid confrontation with parents, and expressed support (and sometimes admiration) for parents who did not want to withdraw life support. One clinician suggested that it would be unthinkable to go to the court in such a case because of the adverse publicity that it would attract.

> "but even if one felt that one was in an absolutely, ghastly, ghastly situation the last thing on earth I could hack ... [would be] being over the front of the [local newspaper] about taking a [religious] family to Court." F60

On the other hand, participants suggested that in their experience it was rare for parents to request withdrawal of treatment while doctors were uncertain of outcome. They described some examples of this type of disagreement with premature infants. But for infants with HIE it was suggested that this was less relevant, since less severely affected infants are likely to be breathing independently of the ventilator. Most suggested that treatment would not be withdrawn unless doctors were certain that infants would be severely impaired.

## *3.4 Conclusions*

For practising clinicians, prognostication and MRI raise questions about uncertainty, the timing of testing and judgements about impairment and future quality of life. This was an exploratory study, designed to help identify relevant questions for further analysis, and as such did not seek to achieve theoretical saturation. Nevertheless, at least across this group, the issues apparent to neonatologists were remarkably similar and there was not a great deal of new material in the last interviews.

One interesting finding was that on direct questioning clinicians generally did not identify specific concerns or ethical issues related to MRI. This may reflect cognisance that there are few issues that are unique to MRI (as opposed to other prognostic tests). Alternatively, it may be that this reflected a particular (limited) conception of what 'ethical problems' refers to. Wider discussion of the process of prognostication and decision-making

(including the use of MRI), revealed a number of areas where clinicians found it very difficult to know what was the right course of action and what they ought to do. These areas will be the focus for analysis in the second part of the thesis.

One broad theme described by clinicians was that of uncertainty. Uncertainty pervades prognostication for newborns; it provides a major challenge for those involved in making such decisions – both parents and medical professionals. Notwithstanding advances in prognostic technologies, uncertainty makes it difficult to know what lies in store for infants, and hard to communicate with parents who expect definitive answers. One question emerging from the interviews is how to respond to the uncertainty associated with test results in practical decisions. I will investigate one approach to managing uncertainty in chapter 5. In that chapter I will also address the question of the timing of testing and the potential *window of opportunity* for treatment withdrawal – referred to by a number of respondents. The difficulty in expeditiously arranging MRI noted by several neonatologists, risks exacerbating the window of opportunity problem.

The interviews also revealed some ambiguity about the significance of uncertainty for decisions, similar to that evident in professional guidelines. Uncertainty was sometimes taken to preclude treatment withdrawal, even if parents requested it; at other times uncertainty was taken to justify supporting parents who opted for continued treatment despite apparent poor prognosis. This highlights the need to clarify the relationship between uncertainty and decisions.

The other major question arising from MRI is which patterns of injury and which predictions of impairment warrant discussion of treatment withdrawal with parents. Some respondents referred to the 'best interests' of the infant, though a number found it very difficult to articulate how to determine this, or which patterns of impairment would make treatment withdrawal in the best interests of the infant. Similar difficulties were noted in Hazel McHaffie's study of Scottish neonatal units. In chapter 6 I will analyse the two main existing approaches to answering that question, and provide reasons why it is unsurprising that clinicians found this judgement difficult. They also found it difficult to reconcile treatment withdrawal decisions with the recognition that some individuals with very severe impairment appear to have lives that are worth living. I will look at this problem in some detail in chapter 9.

Some clinicians described particular patterns of imaging that might be sufficiently severe to permit treatment limitation. In chapter 9, I will work towards a definition and a justification of the patterns on MRI that would warrant allowing parents to choose treatment withdrawal.

# PART 2: ANALYSIS

## *Aims, methods*

In the first part of this thesis, I reviewed the scientific basis for the use of MRI in prognosis in HIE, existing guidelines relating to treatment limitation decisions, and the views of a small sample of clinicians. The aim of those chapters was to set out the background for ethical analysis and to identify the important ethical questions that will be the focus for the next six chapters.

The aim of this second part of the thesis will be to analyse the issues arising from the use of MRI for prognosis, and to develop a coherent guideline to help clinicians and parents. The key components of this analysis and that guideline include

1. The impact of prognostic research on treatment limitation decisions, and how that research could be improved
2. The timing of prognostic tests, and how caregivers might decide about such testing.
3. The severity of impairment for treatment limitation to be permissible.
4. The level of certainty about prognosis required for treatment limitation to be permissible.
5. The role of parents in decisions about withdrawal or continuation of treatment.

The principal method that I will use in the ensuing chapters is that of critical philosophical analysis. This will involve identification of questions, clarification of key concepts, and the development and criticism of arguments. I will set out how this analysis relates to existing literature, and its practical relevance for clinicians. I do not assume a particular philosophical framework or normative theory for this analysis, though I do assume that philosophical analysis has a useful and constructive role in determining what we ought to do. Even if there is not a single correct answer to these difficult questions, there are better answers, and worse answers, and philosophy may help us in determining which these are.

I will start by looking at one of the significant contributors to uncertainty for decision-making – existing prognostic research.

# CHAPTER 4

## Research and prognostic tests

### *4.1 Introduction*

In the first chapter, I reviewed the scientific evidence for the prognostic use of MRI in HIE by way of background for the thesis. In this chapter I return to the science of prognosis. Why discuss prognostic research when I am principally concerned with ethical issues? It might be thought that the issues relating to research are scientific rather than normative or philosophical. There are two reasons to do so. Firstly – such research contains normative *assumptions* – particularly about what is important to measure. Secondly, the way in which the research is carried out has normative *implications*. It contributes substantially to uncertainty in practice.

In the first part of the chapter, I extend the analysis of published evidence and identify a number of specific limitations of previous research in HIE. I re-analyse data from a published meta-analysis to assess the usefulness of MRI for predicting very adverse outcome in HIE. Existing evidence is hindered in its ability to assist decisions about withdrawal or continuation of life-sustaining treatment. I suggest that part of the problem with previous studies is a failure to be clear about the purpose of prognosis. This gives rise to the first recommendations from the thesis: the need for a different approach to research in prognosis in HIE.

In the second part of the chapter, I analyse in detail one generic problem with prognostic assessment in critically ill patients, the problem of self-fulfilling prophecies. I present a definition of self-fulfilling prophecies (SFPs). I then outline two types of problem. For populations such as infants with severe HIE, where a high proportion of deaths follow decisions to limit life-sustaining treatment, it can be extremely difficult to determine which came first – the high mortality in a particular group, or the prediction of high mortality. This is the epistemic challenge that the SFP creates. But there are also normative questions. Should doctors avoid the use of prognostic tests such as MRI if there is a risk of SFPs? Does a SFP lead doctors to act wrongly, or lead to patients being harmed? I argue that SFPs are inevitable if withdrawal of treatment occurs in the setting of uncertain prognosis, but that they do not necessarily make treatment withdrawal problematic.

I conclude the chapter by outlining a set of guidelines for improving prognostic research in HIE, and reducing the epistemic and normative problems arising from SFPs.

## *4.2 Limitations of existing prognostic evidence for treatment limitation in HIE*

In the systematic review discussed in chapter one, Thayyil and colleagues argue that abnormal Lac/NAA accurately identifies infants with the most severe brain injury, and may be useful for making "objective management decisions" (Thayyil et al. 2010). They do not explicitly discuss whether or not this includes decisions about the continuation or withdrawal of life-sustaining treatment. But this is arguably the most important management decision for infants with HIE. Do the results of the meta-analysis support the use of Lac/NAA to inform treatment withdrawal? Should the results of conventional MRI imaging *not* be used given their lower specificity?

One problem with using this evidence in treatment limitation decisions is that although the included studies in Thayyil's review have moderate to high quality on objective criteria (Thayyil et al. 2010), they have a number of important limitations.

### 4.2.1 Population

Firstly, studies of prognosis in HIE are mostly small (Shevell et al. 1999). The reviewed articles reported outcome for a median of 24 infants. Almost half the infants studied (in those that included Sarnat staging) were either stage 1 or 3, groups that are far less prognostically difficult than infants with moderate HIE (stage 2). Furthermore, the inclusion of significant numbers of very mildly, or very severely affected infants potentially distorts assessment of the usefulness of prognostic tests. For example, the inclusion of a large number of infants with mild encephalopathy increases the apparent specificity of tests (assuming that they are correctly identified).

In addition, many of the studies have potential selection bias, and few describe in any detail the population from which studied infants were drawn. This raises questions about representativeness of samples. In one study (that did actually report the source population), out of 259 patients meeting inclusion criteria, only 32 had imaging and completed follow-up (Barkovich et al. 1998).[11] Entry criteria for studies were reasonably consistent, but some studies included patients with seizures only, or with low Apgar scores but no encephalopathy (Barkovich et al. 1999; Brissaud et al. 2005; Meyer-Witte et al. 2008). Nine of the 32 studies in the meta-analysis included only *surviving* infants with HIE, making their results potentially less relevant to questions about withdrawal of intensive care (Peden et al. 1993; Kuenzle et al. 1994; Rutherford et al. 1996; Mercuri et al. 2000; Biagioni et al. 2001; Belet et al. 2004; Jyoti et al. 2006; El-Ayouty et al. 2007; van Schie et al. 2007).

[11] This study was not included in the systematic review since it did not report outcomes in a way that could be analysed with other studies. But another paper from the same centre (part of the same ongoing prospective study) was included in the review (Barkovich et al. 1999).

### 4.2.2 Timing

Secondly, studies included in the meta-analysis varied in the timing of magnetic resonance imaging. Some performed scans in the first days of life (Penrice et al. 1996; Shu et al. 1997; Brissaud et al. 2005; L'Abee et al. 2005; Cheong et al. 2006; Shanmugalingam et al. 2006), while others deferred imaging until after the first week (Rutherford et al. 1996; Gire et al. 2000; Mercuri et al. 2000; Biagioni et al. 2001; Jyoti et al. 2006; El-Ayouty et al. 2007). But, as I will discuss further in chapter 5, the timing of imaging may be crucial if it is to be used in treatment limitation decisions. In infants with moderate or severe encephalopathy in cooling trials, the majority of deaths relating to withdrawal of treatment occurred in the first 3 or 4 days of life (Gluckman et al. 2005; Shankaran et al. 2005). Delays in decision-making may mean that infants are no longer ventilator dependent, and consequently lead to the survival of infants with severe impairment, or to the potential need to contemplate withdrawal of artificial nutrition (Eicher et al. 2005). It is not clear how relevant scans performed in non-ventilated infants are to the majority of treatment limitation decisions.

### 4.2.3 Self-fulfilling prophecies

Third, many of the studies of prognosis in HIE include death as an adverse outcome. But if treatment withdrawal decisions are influenced by prognostic tests there is the potential for what are sometimes referred to as "self-fulfilling prophecies". This is a particular problem for assessing prognosis in conditions like HIE where a large proportion of deaths follow decisions to limit treatment. Nevertheless, in only one of the studies included in the systematic review was there discussion of the potential relationship between MRI and treatment withdrawal decisions. That study acknowledged that MRI results were available to clinicians making such decisions, and potentially influenced withdrawal (Hunt et al. 2004). Thayyil et al attempt to reduce the problem by considering outcomes of death or severe impairment together. This is only a partial solution since it depends upon the assumption that all infants who have treatment withdrawn would have survived with severe impairment. It also obscures for decision-makers a potentially relevant difference between death from multi-organ failure in the newborn period and survival with severe impairment. I discuss this problem in more detail in the second part of the chapter (section 4.3).

### 4.2.4 Outcome assessment

Fourth, and potentially most importantly, studies of MRI in newborn infants have largely used vague and non-standardised outcome assessments (Amiel-Tison et al. 2005). Only 12 of the 32 studies included in the review reported blinding of outcome assessment to MRI results. A particularly serious problem is that studies pooled a wide range of different outcomes together as abnormal (a problem noted for other prognostic markers in the first chapter) (Amiel-Tison et al. 2005). In many studies infants were classified as having unfavourable outcome if they had scores on developmental assessment more than 1 standard deviation below the mean (Hanrahan et al. 1999; Mercuri et al. 2000; Robertson et

al. 2001; Roelants-Van Rijn et al. 2001; Jyoti et al. 2006; Shanmugalingam et al. 2006). Other studies included infants with any neurological abnormality in this category (Robertson et al. 1999; Barnett et al. 2002; Zarifi et al. 2002; Khong et al. 2004; Leijser et al. 2007). Infants with mild developmental delay or treatable epilepsy are considered together with infants with spastic quadriplegic cerebral palsy. But this yields information that is of no relevance for treatment withdrawal decisions. Although there is no clear consensus about the exact severity of impairment that would justify allowing a newborn infant to die (Wilkinson 2006), almost all doctors and parents would consider it inappropriate to withdraw intensive care in an infant with mild physical impairment or developmental delay.

### 4.2.5 Quantitative or qualitative assessment?

Initial experience with MRI for infants with HIE assessed the presence of brain injury qualitatively, noting the distribution and apparent severity of signal abnormality in different areas of the brain (McArdle et al. 1987; Byrne et al. 1990; Kuenzle et al. 1994). But qualitative changes on MRI or DWI are potentially subjective (Thayyil et al. 2010), with difficulty distinguishing between degrees of signal abnormality, and difficulty detecting abnormalities when they are present symmetrically (Coskun et al. 2001). This has given rise to interest in developing more objective markers of brain injury.

In their meta-analysis Thayyil et al found quantitative markers on spectroscopy more useful than qualitative conventional imaging (Thayyil et al. 2010). Across all the studies included in the review Lac/NAA ratios were considerably more specific than conventional MRI (95% vs 51%), though slightly less sensitive for unfavourable outcome (82% vs 91%). In the small number of studies where both were reported and they could be compared directly Lac/NAA again outperformed conventional MRI.

But there are two problems with concluding from this that quantitative markers are better than qualitative ones for predicting adverse outcome in HIE. The first is that many of the studies of quantitative markers used cut-off points to categorise patients into low or high-risk groups. For example the median cut-off for Lac/NAA was 0.29. But in many studies (9 of 19 reporting quantitative markers) these cut-offs appeared to be determined post-hoc, selecting the cut-off that best distinguished between patients with and without abnormal outcome. This process inflates the sensitivity and specificity of the studied variable, and distorts meta-analysis including such studies (Altman 2001). Secondly, the meta-analysis categorised conventional imaging as abnormal if it included signal abnormalities in the basal ganglia, white matter, or cortex of any degree. But, as noted in chapter 1, the largest studies of conventional imaging found radically different outcome in infants with mild basal ganglia or white matter changes compared to those infants with severe or widespread signal abnormality (Rutherford et al. 1998; Barnett et al. 2002; Miller et al. 2005). It is unsurprising that the finding of any abnormality on conventional imaging is non-specific in infants with HIE.

### 4.2.6 Overcoming limitations: re-analysis of published data

I have argued above that existing research has focussed on the wrong groups of infants, and on the wrong outcome groups. But what difference does this actually make to assessment of the usefulness of MRI?

A number of the studies of conventional imaging provided individual patient data, so it is possible to calculate the relative usefulness of these severe patterns of injury for predicting severe impairment or death (Table B1, Appendix B). In the following analysis I have also included results from a large paper that was published synchronously with the Thayyil meta-analysis and was not included in their study. Table B2 (Appendix B) presents the relationship of severe injury to 'very adverse outcome' in studies where data extraction was possible. Patterns of moderate or severe basal ganglia injury or severe white matter injury had a sensitivity of 91% (CI 84-92%) and a specificity of 86% (82-89%) for identifying infants who either died or at 12 months appeared to have spastic quadriplegic or dystonic cerebral palsy or severe developmental delay (>3 standard deviations from the mean).[12] In the new paper by Rutherford et al (Rutherford et al. 2010), individual patient data was not available; nevertheless, the definition of severe impairment (GMFCS 3-5, cognitive impairment >2sd from mean) was sufficiently close to the one used above to include the results in this analysis. If this paper is excluded, the sensitivity of MRI is 91%, and specificity 89%.

We can refine this further by looking at the timing of imaging. Looking separately at studies that were performed in the first week of life (table B3) conventional MRI had a sensitivity of 88% (79-93%) and specificity of 88% (80-92%)[13]. This compares with a sensitivity of 92% (86-96%) and specificity of 85% (79-90%) for scans performed after the first week (Table B4).[14]

Although the numbers are small it is also possible to look at the prognostic efficacy of conventional MRI in the first week of life in infants with *moderate* encephalopathy (Table B5). In this subgroup, sensitivity of MRI was 79% (59-91%), and specificity 84% (68-93%). It is not possible from published data to extract the usefulness of quantitative markers such as Lac/NAA for predicting very adverse outcome as defined above, nor to look separately at its usefulness in infants with moderate encephalopathy.

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[12] (Confidence intervals here are calculated according to the efficient-score method corrected for continuity (Newcombe 1998).)

[13] If Rutherford 2009 is excluded (see above), sensitivity is 84%, and specificity 92%.

[14] If Rutherford 2009 is excluded, sensitivity is 94% and specificity 88%.

### 4.2.7 Overcoming limitations: future research

There are two important conclusions to be drawn from the above analysis of previously published studies. The first is that there is considerable uncertainty around predictions, particularly once the most appropriate questions are asked. The positive predictive value of the most specific patterns of conventional MRI changes in the first week of life is 79% for predicting very adverse outcome in infants with moderate encephalopathy. But there is a fairly wide confidence interval for this from 58% to 91%. Up to 1/3 or more of infants with such changes would not die or be very severe impaired if treatment were continued. No comparable figure for Lac/NAA ratios is available.

The other important conclusion from the above is that part of this uncertainty arises from the way that previous studies have been performed and reported. If we are to obtain relevant information to inform treatment decisions there is a need to change the way that prognostic studies in HIE are performed.

But why have scientists and clinicians failed to recognise and remedy the limitations in their research? One possibility is that they have simply failed to distinguish between the different purposes of prognosis and the need for different approaches. An alternative explanation is that these studies were deliberately designed to assist prognosis for anticipation rather than prognosis for treatment limitation/continuation. But if prognosis for treatment limitation is genuinely the more important prognostic question, this raises the question of why so much effort has been placed on prognosis for anticipation. An alternative and more speculative explanation is that clinicians involved in MRI research have been reluctant to openly discuss prognosis for treatment limitation because it is controversial. It is interesting to note that few studies even *mention* treatment limitation preceding death in infants with HIE. There was explicit acknowledgement of the role of treatment limitation decisions in death (and consequently of the potential for self-fulfilling prophecies) in only one (Hunt et al. 2004) of the 32 studies in the systematic review by Thayyil and colleagues. The majority of studies provided no information at all about the cause of death. A number use euphemisms, stating that death was due to "neurological problems" (Robertson et al. 2001; Leijser et al. 2007), or was a "direct consequence of their brain injury" (Rutherford et al. 1998; Hanrahan et al. 1999; Cheong et al. 2006; Shanmugalingam et al. 2006). It is possible that the deaths in these studies were not due to treatment limitation, however, if this were the case, it would seem to be an extremely important piece of information to provide.

A final possibility is that research has focussed on prognosis for anticipation because it is technically easier to do – for example, there is less need to be selective about patients and outcomes. In any case, regardless of the cause of this undue focus, there are strong reasons why future research *should* unambiguously focus on the important prognostic question.

How could future research reduce uncertainty about prognosis, and hence help treatment decisions? There is a need for larger prospective studies that assess a number of different prognostic factors in the first days of life, particularly focussing on infants with moderate to severe clinical encephalopathy. Prognostic studies should be registered (Rifai et al. 2008),

as is now standard for randomised trials. This would reduce the problem of publication bias in prognostic studies. Future meta-analysis would be strengthened by the use of individual patient data from primary studies (Riley et al. 2007).

Studies using continuous variables (such as quantitative biomarkers) should use cut-off points in a data-independent way (Altman 2001). The value of different prognostic factors should be identified by multiple regression analysis (Altman 2001). Follow-up should be performed using validated measures, blind to prognostic factors, identifying outcome groups in detail. Finally, when studies are reported they should conform to guidelines for observational cohort studies (Vandenbroucke et al. 2007).

## *4.3 Self-fulfilling prophecies*

> "The self-fulfilling prophecy is, in the beginning, a false definition of the situation evoking a new behaviour which makes the original false conception come 'true'. This specious validity of the self-fulfilling prophecy perpetuates a reign of error. For the prophet will cite the actual course of events as proof that he was right from the very beginning." (Merton 1968, p. 477)

In the first part of this chapter I identified one difficulty for assessing the evidence for neuroimaging as a prognostic tool in infants with HIE – that prognosis is influenced by self-fulfilling prophecies. This is a generic problem in prognostic research.

Sociologist Robert Merton famously introduced the idea of a self-fulfilling prophecy (SFP) in the 1950s. Merton was interested in the nature of enquiry in social sciences, and whether it is possible to get at the truth of the matter. Karl Popper, recalling the famous Greek myth, referred to the same idea as 'the Oedipus prophecy' (Popper 2002, p. 139). A paradigm example that Merton cites is of the groundless rumours of an imminent bank collapse that lead to a large number of people withdrawing their savings. This, in turn, leads to the actual collapse of the bank. The SFP raises the question of the overlap between prediction and predestination, echoed in mythology, literature and in science fiction.

In medicine the problem of the self-fulfilling prophecy has been raised in many different contexts. Predictions may affect the mental state and behaviour of patients. For example giving patients the news that they have a short time to live may cause them to become depressed, to stop taking medicines, and may contribute to their early demise. Awareness of this problem contributes to reluctance among doctors to prognosticate (Christakis 2001). In intensive care and newborn intensive care the SFP is particularly apparent in relation to decisions about withdrawal of life-support on the basis of predicted high mortality. The concern is that if life-support is withdrawn from patients who are predicted (if treatment were continued) to have a high risk of dying, this action then leads to a high mortality rate in that group of patients. This may occur whether or not the original prediction was correct. But since it is now true that the majority of patients with this condition die, subsequent similar patients are believed to have a high chance of dying and also have treatment withdrawn. For example, it has been argued that the SFP contributes

to mortality rates for extremely premature infants (McHaffie et al. 2001; Mercurio 2005), infants with trisomy 13 or 18 (Embleton et al. 1996; McGraw and Perlman 2008), as well as for adults with haemorrhagic stroke (Becker et al. 2001), hypoxic brain injury (Zandbergen et al. 1998), critical illness (Cook et al. 2003), or brain death (Truog and Robinson 2003).

### 4.3.1 Definition

> **Self-fulfilling Prophecy**: (SFP) A prediction (that a certain outcome is likely or inevitable) that has the potential to independently increase the probability of the outcome occurring.

There are a number of ways in which predictions can affect outcome. They may generate an outcome that would not otherwise have occurred. They may increase the chance of an outcome occurring that had some chance of occurring otherwise. Alternatively, in some circumstances they may lead, by virtue of the prediction, to an outcome not taking place (Christakis 1999, p. 136).

Merton had in mind the first of these possibilities. He defined the SFP as a "false prediction"; in his example Millingville bank would not have collapsed in the absence of the effect of rumours on consumer confidence (Merton 1968, p.476). Yet the situation in intensive care is more like the second possibility. In almost all situations there is some significant chance of the patient dying even if no attempts at prognosis were made, and treatment were continued. The SFP in treatment limitation decisions is more of a *self-reinforcing prophecy*. Yet a priori we cannot know whether a prediction is false (Miller 1961), is possibly true (and magnified by the effect of the prediction) or is actually true. In what follows I use SFP to refer generically to situations where there is the possibility of predictions increasing the chance of an outcome occurring.

### 4.3.2 Epistemic problem of the self-fulfilling prophecy

The problem that I alluded to in the earlier part of this chapter relating to the SFP (section 4.2.3) is the difficulty that it creates in getting to the facts about prognosis (Bernat 2009). Indeed, disentangling the prognosis for a group of patients from the effects of predictions can seem as intractable as the ancient conundrum of the chicken and the egg.

Predictions of *impairment* are not likely to be affected by SFPs in the same way as predictions of mortality. Treatment limitation usually leads to death and doesn't directly affect impairment. But there are three ways in which they could be affected. The first is that many studies of prognostic tests combine the outcomes of death or severe impairment, and physicians often use these combined statistics when talking to families. Second, if a very large proportion of patients with a condition die following treatment withdrawal there will be relatively few survivors to provide data on impairment. This makes data on the severity of impairment less reliable. Third, in a small number of cases treatment limitation may actually increase impairment. For example (as will be discussed further in the next chapter) some infants who have life-sustaining treatment withdrawn survive

because they are not in fact dependent on life support. However, they may have had a significant period of low oxygen levels or blood pressure after treatment withdrawal that could exacerbate future impairment.

One way to reduce the effect of the SFP for new tests that are being studied is to withhold the results of those tests from doctors in order to prevent them influencing decisions. But in practice this is often not done, as already noted for studies of MRI in HIE. Influential papers of cerebral blood flow velocity in HIE similarly failed to mention whether there was a potential relationship between test results and decisions (Archer et al. 1986; Levene et al. 1989; Ilves et al. 1998; Jongeling et al. 2002; Ilves et al. 2004). Only one out of 8 papers included in a systematic review of aEEG for prognosis in HIE discussed treatment limitation and the role of test results in decisions (Spitzmiller et al. 2007). (In that single study (Eken et al. 1995) it was clear that the test results *were* used in decision-making.) This is not confined to newborns with HIE. Clinicians were blinded to test results in only 6 out of 17 studies in a systematic review of prognostic tests for adults with anoxic coma (Zandbergen et al. 1998).

Factors that may explain the lack of blinding in many studies include a blurring of the boundaries between research and clinical care, the simultaneous use of tests for several purposes and ethical qualms about withholding or concealing results from patients and their families. This last is understandable given the emphasis that is placed in medical ethics upon truth telling and the provision of full information to patients. But when the prognostic value of a given test result is not known, there may be little benefit from informing patients or families of those results, and the provision of the information may make it difficult to gather accurate evidence about the test. For tests like MRI in HIE, where there is considerable data available on the prognostic usefulness of testing, (even if there also remains uncertainty about prognosis), it would be unethical to withhold the results of testing from doctors and families for the sake of future patients.

The first recommendation for reducing the SFP is to try to prevent test results influencing treatment decision. But even if test results are withheld from doctors and parents, the problem is not eliminated since treatment withdrawal decisions continue to be made on other grounds. It may be, for example, that a certain neuroimaging test pattern is strongly correlated with clinical features, such as the severity of encephalopathy, that are themselves highly influential in treatment withdrawal decisions. Yet we may have concern about the validity of those clinical features - after all that is one reason for studying the new prognostic test.

One way to obtain information about the validity of mortality predictions would be to deliberately avoid making any treatment limitation decisions in a cohort of patients, and to study their outcome (Becker et al. 2001; Rabinstein and Diringer 2007). It is usually recommended that treatment is standardised for patients in prognostic factor studies (Simon and Altman 1994). But this is not as easy as it might sound. If we have literally no

evidence about the risk of death in a group of patients, then it would be appropriate to continue life-sustaining treatment in all of them. It is far more common, however, that there is already some evidence that a high proportion of such patients die, and hence that withdrawal of treatment may be acceptable. Continuing life-sustaining treatment in order to determine the actual mortality rate risks prolonging the death of a number of patients, causing harm to them and to their family. Disregarding the wishes of patients and families in such a setting would be unethical (Becker et al. 2001). These features help explain why self-fulfilling prophecies are so hard to avoid in critically ill patients such as infants with HIE.

How else can the true validity of predictions be established? It may be possible to look at historical evidence of mortality in the first patients studied with a given illness, since SFP are least likely to have affected the management of such patients. For example, about 1/3 of infants with HIE died in a study from the early 1960s (Badawi et al. 2001). But if treatment has changed since that early experience (as it is likely to have), that evidence will not be relevant. It will also be irrelevant to the assessment of recently developed prognostic tools.

Another possibility would be to try to determine statistically the impact of different prognostic factors upon outcome. In one study, researchers looked at a number of variables in a multivariate analysis of outcome in adults with intracerebral haemorrhage (Becker et al. 2001). Although commonly cited poor prognostic factors (the Glasgow Coma Score and size of haemorrhage) were associated with death, when decisions to withdraw treatment were added in to the model no other factors remained statistically significant. The authors of the study claimed that this indicated a bias in decision-making, and that withdrawal of support was the most important determinant of outcome. But this conclusion is premature. All of the patients who had life-sustaining treatment withdrawn died. A combination of prognostic factors, as well as the wishes of patients and family (Rabinstein and Diringer 2007 are likely to have fed into treatment decisions. Consequently, variables other than the decision to withdraw are individually unlikely to have as clear an association with death. It does not seem particularly striking that decisions to withdraw dominated the model of factors that contributed to death. Alternatively, statistical models could use propensity scores to generate a matched cohort study that simulates a randomized trial {Chen, 2008 #984). This has been used to look at the effect on mortality of decisions to withhold life-sustaining treatment (Shepardson et al. 1999; Chen et al. 2008). But such models potentially ignore other prognostic factors that clinicians use in decision-making, especially those that are difficult to quantify. Treatment limitation decisions may be a marker for mortality, rather than a cause of mortality (Sulmasy 1999). There may also be other factors than mortality that influence decisions, including the probability of surviving with severe impairment. Such modelling may be useful but it is unlikely to provide a complete answer.

Finally, it may be possible to get an idea of the true mortality rate by looking at the outcome in patients predicted to have a poor outcome, but who nevertheless had intensive treatment provided. This might be a hospital or community that have a different philosophy about treatment withdrawal, or may be a group of patients whose family or surrogates refuse to permit treatment to be limited. For example, in a recent large study of outcome for extremely premature infants, researchers were able to distinguish the outcome for those infants who received mechanical ventilation (and hence were actively resuscitated) from those infants who died in the delivery room (Tyson et al. 2008). If all such patients die (or are severely impaired), we would then have good supporting evidence for the initial prediction. Conversely, a higher survival in this cohort may cause us to question the general assumption that prognosis is poor (Becker et al. 2001). There is a need for caution, however, in interpreting the outcome in the subgroup of patients who received intensive care or who had treatment continued. Firstly, they may not be representative of all patients who fit into a group predicted to have poor outcome. They may be younger, or fitter, from a different demographic or ethnic group. Any of those factors (or others less obvious) may impact both upon the doctors' decision to provide treatment or the family's willingness to withdraw life support, and on their chances of survival. In the study of premature infants, those infants who were ventilated were heavier, less premature, and needed less resuscitation at birth (Tyson et al. 2008). Secondly, the presence of the previous prediction of extremely poor outcome may influence other management decisions. For example doctors may agree to continue intensive care for a patient with apparently very poor prognosis but negotiate with the family for non-resuscitation in the event of a cardiac arrest. Finally, it may be hard to systematically study this group of patients. Where families have disagreed with doctors about prognosis and continuation of life-sustaining treatment, there may be ongoing anger or distrust of medical staff. They may be reluctant to participate in research, or they may seek ongoing care elsewhere and be hard to follow-up. Nevertheless, this is an extremely important cohort of patients to study since it may help in prognostication. The rate of favourable outcome in this group may help to estimate the maximum potential benefit of providing treatment (Tyson et al. 2008).

### 4.3.3 Normative problems of the self-fulfilling prophecy

The epistemic problems created by SFPs have obvious implications for research. But what about treatment limitation decisions? Does the SFP have any implications for decisions made on the basis of MRI findings in infants?

#### *4.3.3.1 Increase in mortality*

One concern about the SFP in relation to treatment decisions in intensive care is that it may lead to the death of patients who would otherwise survive. If predictions of high mortality lead to doctors or families foregoing life-sustaining treatment this may increase the mortality rate for that group of patients. SFPs may then lead to harm.

This will not always be the case. If the prognosis is accurate and treatment is withdrawn the mechanism of death will change, but not the outcome. Treatments are withheld rather than given, but patients succumb either way. But where death despite treatment is not certain treatment withdrawal decisions will *necessarily* increase mortality. Consider the following hypothetical example. A patient has severe multi-organ failure and a 1% chance of survival if intensive care is continued. However, survival is likely to require a prolonged period of invasive and potentially unpleasant treatment and hospitalisation. Some patients and families would choose to continue treatment in this setting, but many would not. Perhaps 10% of families would request continued treatment? One point worth noting is that it is inevitable that the mortality for this group of patients will increase. The chance of survival will fall to 0.1%.[15] But intuitively, a SFP in this setting is not inherently problematic. It is a necessary consequence of decision-making in the face of uncertainty.

It may also not necessarily be a problem if mortality is increased when patients would otherwise have survived with severe impairment. One of the reasons for treatment withdrawal is because of a judgement that survival in a state of severe impairment may be worse for the infant than dying in the newborn period. If this is the case it may actually be a good thing if SFPs lead to higher mortality rates. (I will return in subsequent chapters to the question of whether or when severe impairment in infants with HIE is actually worse than death.)

#### *4.3.3.2 Responsibility*

On the other hand, whether or not a SFP actually changes the outcome for patients, doctors who act on the basis of a SFP may feel responsible for the death of the patient. Nicholas Christakis, in his work "Death Foretold" looking at the attitudes of doctors towards prognostication, notes that doctors' fear of causing or hastening death leads them to attribute great significance to the possibility of self-fulfilling prophecies (Christakis 1999, p. 158). Christakis was talking about prognostication in general, but this might be even more important for prognostication that affects withdrawal of life-sustaining treatment.

But it is widely accepted that it is permissible for doctors to withdraw life-sustaining treatment. So it is not necessarily a problem for doctors to be causally implicated in death. And although the doctor may be responsible for the death of a patient who would not otherwise have died, they may nevertheless have acted in the most appropriate way. Philosophers sometimes distinguish between what we ought to try to do given what we know (the *evidence relative* sense of 'ought'), and what we ought to do if we had perfect knowledge of all of the facts (the *fact-relative* sense) (Persson 2008; Parfit April 2008, Chapter 6, pp. 120-135).

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[15] Assuming that all patients who have treatment withdrawn die, but only 1% of patients who have treatment continued survive.

When we make decisions we rarely if ever have access to all of the relevant facts. We cannot know for sure which action we ought to take in the fact-relative sense. But we still need to act. Doctors must make decisions (in collaboration with their patients) on the basis of the available evidence. So when a decision is made to withdraw life-support on the basis of evidence of an extremely high chance of dying, that can be the right thing to have done (in the evidence relative sense) even if in actual fact that particular patient would have survived. A SFP does not then lead doctors to do the wrong thing if they withdraw life-support on the basis of evidence of high mortality. They may be doing what they have most reason to do.

#### *4.3.3.3 Deception*

It is possible that the SFP may lead physicians to breach another duty – that of dealing honestly with patients and their families. SFPs may compromise honest communication with families by causing doctors to mislead families about the patient's chance of survival (Mercurio 2005).

For example parents anticipating the delivery of an extremely premature infant (say at 22 or 23 weeks gestation) may be told that all previous patients cared for at this gestation have died, or that the chance of survival in a published cohort of patients was very low or zero (Costeloe et al. 2000). However, the risk of death in both of these cited instances was likely influenced by treatment-limitation decisions, and doctors may be wittingly or unwittingly deceiving families (Mercurio 2005). Of course, it may be relevant to families to know that treatment is usually withdrawn in cases like this. But since the question is whether or not to continue life-support, what families need to know is the chance of survival for the patient *if all supportive measures are provided*. Doctors may not be able to provide this probability because of the epistemic problems outlined in section 4.3.2. Yet, sometimes at least, patients are misled into thinking that the answer they have been given is of this latter sort, when in fact it is the former.

#### *4.3.3.4 The effect of the SFP on uncertainty*

One reason for objecting to the SFP may be because of its effect on uncertainty and the threshold for treatment limitation. Some doctors and families are unwilling to allow a patient to die unless the outcome is poor "beyond reasonable doubt" (McIntosh 2002). Because of the epistemic problems outlined above, the presence of a SFP may create sufficient uncertainty about outcome that it is felt to be impermissible to withdraw treatment - ie it may create reasonable doubt.

Nevertheless, as discussed in chapter 2, some guidelines suggest that treatment withdrawal is still permissible in the face of uncertainty. The practical difficulty is that none specify what *degree* of uncertainty would preclude treatment withdrawal, so it is difficult to know how the additional uncertainty created by SFP should influence treatment decisions. This,

again, highlights the need for greater clarity about the role of uncertainty in the permissibility of treatment withdrawal.

The other issue about treatment decisions and infants with HIE is that the most important part of prognosis is probably not the high mortality in infants with severe established brain injury, but that those who survive have significant impairments. Even if there is uncertainty about the mortality rate (if treatment were continued), the rate of severe impairment is less influenced (as noted above).

One approach to dealing with uncertainty is to use decision theory (Savulescu 1994), (I will discuss that further in the next chapter in relation to the timing of prognostic tests). But a brief example will highlight one of the other problems that the SFP creates. The possible outcomes for an infant with severe HIE include death within a short period, a prolonged hospital and intensive care stay followed by death, survival to hospital discharge with severe impairment, or survival without severe impairment. These different outcomes are likely to be valued differently. But the problem with using decision theory is the need to know the separate probabilities of early death *or* late death *or* severe impairment if treatment is continued. The epistemic problems of the SFP may increase uncertainty about outcome; they also make it difficult to make rational decisions in the face of uncertainty.

## *4.4 Conclusions*

Prognostic research leads to uncertainty in decision-making for newborn infants with HIE.

Some of this uncertainty is avoidable. Analysis of previous studies of MRI for prognosis in HIE reveals specific problems that could be addressed. I have listed a set of recommendations for improving future research in this area in Box 4.1. The most important recommendation is that research needs to clarify the purpose of prognosis that it is attempting to address. Research should focus specifically on prognosis for treatment limitation.

1. Studies of prognosis in HIE need to be adequately powered and prospective
2. They should measure multiple different prognostic factors
3. They should focus on ventilated infants with moderate to severe encephalopathy in the first days of life
4. Cut-off points for continuous variables should be generated in a data-independent way
5. Follow-up should use validated, blinded outcome measures, present results in detail, and avoid overly inclusive outcome groups

*Box 4.1: Recommendations for improving prognostic research in HIE*

Some uncertainty, however, in prognostic research is *unavoidable*. Although SFPs might, in theory, arise in any treatment decision, they are a particular problem for decisions about life-sustaining treatment. In this setting randomised controlled trials are usually inappropriate and the potential outcomes involved (death, life, severe impairment) are enormously important to patients and their families.

The SFP presents a serious epistemic problem for assessing the genuine prognosis of patients who may or may not have treatment withdrawn. It makes it difficult to make rational decisions. Where the evidence of poor prognosis has been influenced by a SFP it can be extremely difficult to determine what the prognosis would be if all treatment were provided. Nevertheless, attempting to do so is one important way for doctors to justify their predictions, and their decisions to allow patients to die. I have suggested several ways to improve research into prognostic tests such as MRI in order to reduce the problem of SFPs (Box 4.2).

When it comes to treatment limitation decisions there are also a number of potential normative problems attributable to SFPs. SFPs may lead to an increase in the mortality for cohorts of patients predicted to have poor prognosis, they may lead doctors to feel causally responsible for the deaths of their patients, and they may compromise honest communication with patients and families about prognosis. If we are to avoid Merton's "reign of error" from self-fulfilling prophecies, it is essential to carefully collect and appraise evidence about prognosis. The other imperative is that doctors are honest with themselves and with patients and their families about uncertainty and the limits of knowledge.

1. Research into new prognostic tests should ensure, where possible, that test results are not used to influence treatment limitation decisions

2. Other prognostic factors should also be studied, and regression or propensity analysis used to determine the independent value of new tests for prognostication

3. Patients whose treatment is continued despite a poor prognosis should be followed-up, and reported separately

4. When talking to patients and families about prognosis doctors should distinguish between survival rates *if treatment is continued*, and survival rates in populations *where treatment is sometimes limited.*

*Box 4.2: Recommendations for reducing the normative and epistemic problems associated with SFP*

Do the limitations outlined above, or the problem of SFPs mean that MRI should not be used in decisions about withdrawal of life-sustaining treatment? Whether it is permissible to withdraw treatment depends crucially on how much uncertainty we can tolerate in such decisions. I have argued in chapter 2 that current guidelines provide no clear advice as to

how to deal with uncertainty. I will return in chapter 9 to the development of a novel guideline for decision-making, including the level of acceptable uncertainty in decisions.

We might also note that many of the above limitations in evidence about prognosis in HIE also apply to other tools often used in practice including aEEG, cranial ultrasound, even clinical assessment. We should not apply different standards of evidence to MRI than we do to other prognostic tools in HIE.

There may be ways to reduce uncertainty in the future, both by improving the tests used for predictions, and improving prognostic research. But what should clinicians and parents do in the meantime? In the next chapter I look at the use of decision theory as an approach to dealing with uncertainty in practice.

# CHAPTER 5

## Timing of prognostic tests

### *5.1 Introduction*

> "in a proportion of babies there is some urgency … on the one hand you don't want to push parents, you specifically say you don't want them to rush to a decision about anything, on the other hand they need to be aware that there probably is a much greater chance of the child to survive without the ventilator the longer you delay" M60

In chapter 3, I described an issue that a number of clinicians raised about the timing of prognostication and decisions about life-sustaining treatment (LST). As illustrated in the quote above, there can be conflicting values at stake. There may be a *window of opportunity* for withdrawal early on, but at the cost of greater uncertainty in prognosis. Similar dilemmas are often seen in adults or children with head injury or in extremely premature infants. Yet there has been little attention to this in previous literature, and no mention of it in guidelines for decision-making.

> ***Window of Opportunity***: the period of time during which patients with severe brain injury are dependent on life support, and consequently when withdrawal of LST is likely to lead to death.

There are different questions that we might ask about the window of opportunity.

1. Is it permissible to withdraw life support from patients who have severe brain injury, but who could survive to be unimpaired?
2. Should the window of opportunity influence treatment decisions?
3. How should caregivers[16] decide about the timing of testing given opposing and potentially incompossible values?

I return to the first of these questions in subsequent chapters; in chapter 9 I develop an account that sets out the role of uncertainty in treatment decisions. In this chapter, however, I will set that issue aside and focus on questions two and three. I first set out the features of HIE that relate to the timing of prognostic testing and the timing of withdrawal

[16] I refer in this chapter to 'parents', since they are often the most appropriate decision-makers. But the issues raised below could apply equally to other decision-makers (for example non-parent caregivers or doctors).

of LST. I argue that it *is* permissible to take into account the window of opportunity in decisions about the timing of prognostic questions. For the rest of the chapter I focus on the more practical third question, using the technique of decision theory to help caregivers decide when to perform an MRI. I use sensitivity analysis to assess how different features of the tests or different values would affect a decision to perform early or late prognostic testing; I draw some general conclusions from this model for decisions about the timing of testing in neonatal encephalopathy. Finally I consider possible solutions to the problem posed by the window of opportunity. This analysis leads to a set of recommendations relating to the timing of prognostication and imaging in HIE.

## *5.2 The window of opportunity*

I described in chapter 1 the various tools that can assist with prognosis in HIE, for example clinical examination, electrophysiological investigations or imaging of the brain. Most of these tools face the same problem – that early predictions are more fallible than late predictions. For example, in one study, neurological examination performed in the first four days of life had a false positive rate of 45%, but this fell to less than 1% when performed at the end of the third week (Mercuri et al. 1999). MRI also has greater predictive power if it is performed later. In the re-analysis of published data performed in the previous chapter MRI was more sensitive for detecting severe abnormalities after the first week of life, though specificity was unchanged (see p51). It is generally accepted that to obtain the most accurate prognosis it is best to delay prognostic testing (Shevell 2004).

On the other hand, as intimated by the clinician quoted at the start of this chapter, there are also reasons not to delay. Perinatal hypoxia-ischemia leads to multi-organ failure in the first couple of days of life, though in many cases there is improvement after 72 hours. These changes influence treatment withdrawal decisions. During the first couple of days after birth if mechanical ventilation is withdrawn the infant will die quickly in most instances. By contrast, if the decision is deferred by even a few days, infants have often resumed breathing and are more stable. At this stage, if a decision is made to withdraw treatment infants are unlikely to die quickly and may not die at all.

The use of MRI may compound the problem of the window of opportunity. As noted in chapter 3, obtaining an MRI can lead to delays in decision-making due to the difficulty in organising an available time in the scanner, arranging transport for the infant, and then waiting for the scan to be reported by someone with appropriate experience. A large proportion of neonatologists in an Australasian survey reported delays when requesting MRIs (Filan et al. 2007).

Where infants are no longer ventilator dependent, there is the possibility of withdrawal of other (less intensive) forms of treatment. The main option in practice is withdrawal of artificial nutrition. However, this option is highly contentious in newborn infants (Miraie 1988; Carter and Leuthner 2003; Levi 2003; Porta and Frader 2007). It is an alternative in infants with HIE because those most severely affected usually have impaired ability to

coordinate sucking and swallowing. They are dependent on the provision of artificial nutrition (usually by a nasogastric tube in the short to medium term) to survive. If artificial feeding is withdrawn infants usually die, but the dying process may be prolonged. It can take three weeks or longer for infants to die (Carter and Leuthner 2003). Although withdrawal of artificial nutrition is supported by some professional guidelines (Royal College of Paediatrics and Child Health 2004, p. 30; Diekema and Botkin 2009) many neonatal units do not support this practice. Some have argued that it is contrary to the interests of infants (Kuhse 1986).

There are, therefore, competing considerations in the timing of prognostic tests for infants with HIE. Certainty favours later testing. Early tests may miss infants who have in fact suffered severe brain injury (a *false negative* result) or they may falsely identify infants as having a poor prognosis who would not have been severely impaired had they survived (a *false positive* result). Parents also sometimes benefit from time to come to terms with prognosis. On the other hand, if decisions are delayed there is the risk that the infant will no longer be dependent on mechanical ventilation. The infant may then survive with severe impairment. While withdrawal of artificial nutrition is permitted in some centres, it has the potential to lead to a death that is prolonged and distressing for the infant, parent and carers.

## *5.3 Should the window of opportunity influence treatment decisions?*

There are good reasons to take into account the window of opportunity in decisions about prognostic tests and treatment. But although the window of opportunity issue has been referred to in passing by clinicians (Chiswick 1994) and researchers (McHaffie and Fowlie 1996, pp. 96, 105, 126) it is interesting that it does not feature in most descriptions of prognostication in HIE (eg (Shevell et al. 1999; Cowan 2000; Volpe 2008)). The Nuffield report on critical care decisions in newborns refers to the window, though not by name (Nuffield Council on Bioethics 2006, p. 94). Several of the neonatologists interviewed in chapter 3 referred to the dilemmas that the window raised in practice. But for some of the neonatologists the 'window of opportunity' was described with hesitation. Are there reasons to reject the window of opportunity?

It was not entirely clear from the responses of neonatologists what it was that led to discomfort, but one reason may be the term itself.[17] The phrase potentially connotes that the death of the infant is 'opportune', whereas for families (and for the infant) death represents a terrible misfortune. While it may be a greater misfortune in some instances if

[17] The term 'window of opportunity' is relatively recent. It was introduced into popular discourse during the 1980s, used initially in relation to the nuclear arms race (Oxford English Dictionary 1989b, http://dictionary.oed.com/cgi/entry/50285823/)

the infant survives, to raise or even just to contemplate this question might be thought of as insensitive.

A more significant reason that could underpin reluctance is that consideration of the window of opportunity potentially conflicts with the doctrine of double effect (DDE). The DDE is widely cited as providing boundaries for permissible actions in end-of-life decisions (BMA 2004, pp. 378-9, 391; Mason et al. 2006, pp. 634-5; Nuffield Council on Bioethics 2006, p. 20; Racine and Shevell 2009). One formulation of the doctrine is that it is impermissible to intend to hasten the death of the patient, but it is permissible to perform acts that *unintentionally (or as a side effect)* hasten that death (Mason et al. 2006, pp. 634-5; Levy 2008). Although none of the neonatologists interviewed referred to the doctrine by name, many implicitly referred to this principle when explaining the use of sedation after withdrawal of treatment. The problem is that if the timing of treatment withdrawal is influenced by whether or not the infant will die (when extubated) it may appear that death is either intended, or is, at least in part, one of the direct goals of extubation. One of the neonatologists who did not endorse the window of opportunity suggested that

> "in some respects the outcome is the outcome … you can decide [that] continu[ing] intensive care is not the right thing to do but you are not necessarily doing that so that the baby dies" F40

Is it possible to reformulate the window of opportunity so that it does not fall foul of the DDE? One possible approach might be to reframe the discussion in terms of the interests of the infant. It may be in the best interests of an infant to have treatment withdrawn earlier rather than later, if later withdrawal will lead to survival in a state of severe impairment or to a slow death following withdrawal of artificial nutrition. However, if it is believed to be in the best interests of the infant to die, and it is those interests that are the goal of treatment withdrawal, the DDE would still prohibit treatment withdrawal. The DDE usually requires that the doctor intends, or has as a goal, a *different* end. A doctor administering morphine to a patient may not do so in order to serve the best interests of the patient (where best interests are understood as involving the death of the patient). The doctor *may*, however, give morphine in order to provide pain relief (a different goal) even if this would also predictably lead to the death of the patient.

Alternatively, it may be thought that the reason to prognosticate early is to provide parents with an option that will not be available to them if discussions are delayed. A number of the neonatologists interviewed emphasised the importance of giving parents choices. But treatment withdrawal is still an option after infants have recovered – it is just that it will no longer lead to the death of the infant.

On the other hand, perhaps the doctrine itself should be rejected for treatment withdrawal decisions on the basis of predicted quality of life. A full discussion of the limitations of the doctrine of double effect is beyond the scope of this chapter (Glover 1990, pp. 86-91; Marquis 1991; Kamm 2007, pp. 21-3; Goldworth 2008). However, one reason to question

it is this: it is permissible to withdraw treatment though that will lead to the death of the infant. Indeed a necessary feature of withdrawal of life-saving treatment is that the death of the infant is judged to be preferable to continued treatment. It seems hypocritical to suggest that this cannot permissibly be one of the goals of action.

A different reason to eschew the window of opportunity for treatment withdrawal is avoidance of uncertainty. All of the neonatologists interviewed referred to the problem of uncertainty in prognostication. Observing infants over time to see if they manifest neurological recovery can reduce this uncertainty (Shevell et al. 1999). Consequently, American neurologist Michael Shevell has recommended that prognostication should be deferred until after the first week of life. He admits that "a strategy of waiting is unpopular from a personal and economic perspective" (Shevell et al. 1999).

But there is recognition that uncertainty is inevitable in decision-making for newborns (see chapter 2). The important question is not *whether* there is uncertainty, but rather whether there is *sufficient* uncertainty that treatment must continue. Attempting to reduce uncertainty may have costs – as highlighted by the above discussion, and whether that is worthwhile depends on how those costs are weighed against the benefits of avoiding uncertainty.

Finally, it may be argued that the window of opportunity is not a relevant consideration for treatment decisions because it is not permissible to withdraw treatment from infants who only need short periods of life support. There are two potential justifications for this. It might be believed that recovery of respiratory drive portends a good prognosis, or a sufficiently good prognosis that treatment withdrawal should not be countenanced. To my knowledge, however, there is no empirical evidence about the return of breathing and prognosis for infants with HIE. The experience of clinicians interviewed was that some infants maintain, or recover respiratory drive despite very severe patterns of brain injury. It was clearly the view of those clinicians that it would have been permissible to allow those infants to die if they had still been ventilator dependent. A second potential justification relates to the burdensomeness of treatment. If an infant will only require a short period of respiratory support, the burden of treatment is relatively minor. It is unpleasant for the infant to have a breathing tube in place, but sedation and analgesia is usually provided to reduce any discomfort. On some views, it is only permissible to withdraw or withhold treatment when the burdens *of treatment* outweigh the benefits, and this may not be the case for a short period of life support. But in the face of severe predicted impairment there are other treatments that may permissibly be withheld that are even less burdensome than a short period of respiratory support. For example, in such infants it is often felt to be acceptable (if the parents choose) to withhold treatment with antibiotics for a respiratory infection. Yet the discomfort and burden associated with a course of antibiotics is minimal. If it is permissible to withhold antibiotics for an infant it must be permissible to withdraw mechanical ventilation even where that would only be required for a short period.

None of the above arguments provide convincing reasons to reject out of hand the window of opportunity in decisions about treatment. If it is permissible to withdraw life support from a newborn infant on the basis of predicted quality of life, it is reasonable to take into account whether or not the infant will actually die following withdrawal of life support. This has particular implications for magnetic resonance imaging in HIE since in practice there is often a delay associated with obtaining an MRI for infants. It provides a strong case for improving access to MRI.

## *5.4 Decision theory*

I have argued that it is permissible to take into account the window of opportunity in decisions about the timing of testing and treatment limitation. But such decisions are extremely difficult. What should parents do when faced with this sort of choice? Is there a way of rationally appraising and reconciling these conflicting priorities?

One approach to decision-making under uncertainty is to use decision theory. Von Neumann-Morganstern utility theory remains the most widely used form (Sinclair and Torrance 1995). It allows complicated decisions to be broken into constituent parts (Cohen et al. 2000). The probabilities of different outcomes are combined with the values attached to those outcomes to determine which course of action will lead to the greatest expected utility. For example, if an action A is taken and there are two possible outcomes *a* and *b*.

Expected Utility (A) = Probability(a) x Value(a) + Probability(b) x Value(b)

Expected utility is also calculated for other possible choices; the alternative with the greatest expected utility should rationally be preferred.

Decision theory has been applied to many areas of medical decision-making (Lilford et al. 1998). There have been fewer studies applying decision theory to explicitly ethical problems (Cohen et al. 2000), nevertheless it may be valuable in understanding the interplay between different variables and in revealing underlying assumptions (Savulescu 1994). In one paper, a model of resuscitation decisions for a critically ill patient identified a number of important factors for such decisions including the chance of recovery to a good life, the estimated maximum quality of life and the length of life gained (Savulescu 1994).

In this section of the chapter I use decision theory to analyse the importance of different factors in decisions about the timing of prognostic testing in HIE. The aim is to see if decision theory can enrich our understanding of the problem. I first outline the characteristics of the decision-theoretic model, then look at the answers that it suggests for specific questions. In the final section of the chapter I return to the potential implications of decision theory for practice.

### 5.4.1 Characteristics of model

It will be helpful to start with a decision-tree (Fig 5.1). The left side of the figure reflects the initial decision, with the boxes on the right showing the possible outcomes. There is a

choice between performing no test, performing early testing or late testing. The outcomes include death, survival with severe impairment (*poor outcome*), or survival without severe impairment (*good outcome*). To calculate expected utility we need to know the probability of different outcomes (given each choice), and the values that parents assign to each outcome.

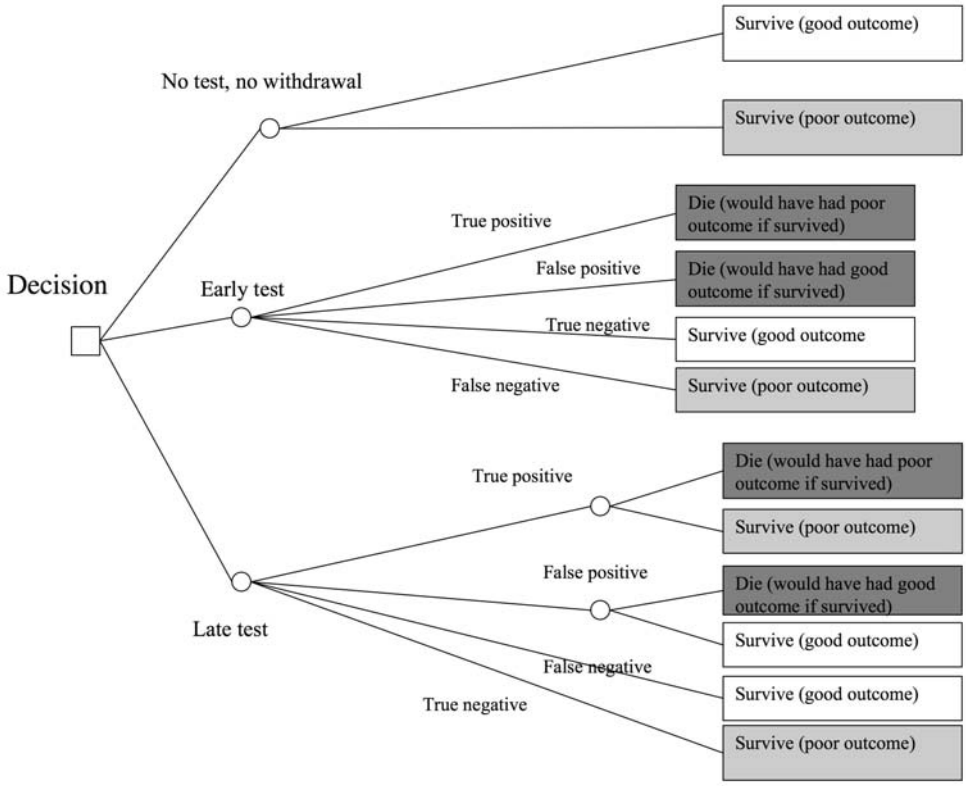


*Figure 5.1: Decision tree for early versus late prognostic test and decision-making*

*The square box on the left represents the decision. Circles represent chance nodes, and the rectangular boxes outcome states.*
*Some infants who die following withdrawal of life support would have survived with severe impairment if treatment had not been withdrawn. Others would have survived without severe impairment. Following a positive Late Test result, a proportion of infants who are predicted to be severely impaired survive, including some infants who are not, in fact, severely impaired.*

#### 5.4.1.1.1 Decisions

In the model I combine prognostic testing with decision-making. Although prognostic tests are sometimes performed without a view to discontinuation of LST I take it that this does not give rise to any particular difficulty in decision-making. I compare *Early prognostic testing and decision-making* (Early Testing) with *Late Prognostic testing and decision-making* (Late Testing). For the purposes of this analysis there is no need to specify exactly what is meant by 'early' and 'late' here. By way of illustration we could, for example, take Early Testing to refer to testing in the first two to three days of life, and Late Testing to refer to testing after one week.

I assume that the results of tests are used to inform decisions about the withdrawal of LST, and that if the test results reveal a poor prognosis LST is withdrawn. This is clearly a simplification since test results are not purely dichotomous, and neither is impairment. I also assume that in the absence of treatment withdrawal all infants survive. Some infants with HIE die of overwhelming organ failure in the first day or two of life despite maximal efforts to keep them alive (Volpe 2008, pp. 403-4). But of those infants who survive to two or three days of age, almost all can survive – if intensive care is provided.

| Variables | Starting value | Possible values |
|---|---|---|
| Pre-test probability of poor outcome | 0.8 | 0.2-0.95 |
| Early Testing - sensitivity | 0.8 | 0.3-0.9 |
| Early Testing - specificity | 0.8 | 0.6-0.9 |
| Late Testing - sensitivity | 0.9 | 0.8-0.95 |
| Late Testing - specificity | 0.9 | 0.8-0.95 |
| Survival with good outcome | 1 | |
| Survival with poor outcome | -0.5 | -0.05 to -1.0 |
| Death | 0 | |
| Disutility of late withdrawal | -0.05 | 0 to -0.5 |
| Proportion of infants surviving late withdrawal | 0.2 | 0.1-1 |

*Table 5.1: Starting assumptions for modelling of prognostic decision-making and plausible alternative values for these variables.*

Table 5.1 lists the assumptions used as a starting point for the model as well as plausible alternatives. I will shortly look at the effect of these variables on decisions. For example I start by assuming that there is a high pre-test probability of poor outcome (80%). This would be the case in an infant with severe encephalopathy. We will shortly see how decisions would be affected if the pre-test probability of poor outcome were as low as 20% or as high as 95%.

#### 5.4.1.1.2 Outcome values

The values that I use can be thought of as average values, representing a spectrum of outcomes. Some forms of economic modelling attempt to put specific values on quality of life and calculate quality-adjusted life years. For these purposes, however, we do not need the specific value of outcomes; to determine whether one course of action would be better than another we only need relative value (Froberg and Kane 1989).

By convention, life in full-health is assigned a value of one, and death a value of zero. Outcomes that are judged to be worse than death are given negative values. Some

approaches to outcome assessment specifically exclude the possibility of outcomes that are worse than death (Franic and Pathak 2003). But it is not uncommon for individuals for think death preferable to certain outcomes (for example dementia or coma or cancer recurrence) (Patrick et al. 1994; Franic and Pathak 2003). When parents or clinicians are considering withdrawal of life-sustaining treatment, this is based upon a belief that continued treatment would be worse than allowing the patient to die. We can only make sense of such decisions by assigning certain outcomes a negative value.

Note that there is a difference between the value that an individual would attach to their own existence (if able to do so), and the value that parents attach to their child surviving in such a condition. It might be the case that parents would choose to withdraw life support in the face of an impairment that (from the child's own perspective) would not be worse than death. I remain neutral here about the permissibility of withdrawal in such a case (we will return to this question specifically in chapter 9). Other parents would not assign a negative value to survival with severe impairment. They might assign it instead a reduced positive value. But for these parents it would not be rational to withdraw LST, and the problem of the timing of prognostic tests would not arise.

#### 5.4.1.1.3 Test characteristics

The probability of different outcomes is determined from the characteristics of the test and the pre-test probability (see Appendix C). The *sensitivity* of the test refers to the proportion of infants with poor outcome that are correctly identified. The test *specificity* is the proportion of infants with good outcome who are correctly identified. The sensitivity and specificity of a test depend not only on the properties of a test, but also on the cut-off point chosen for diagnosis. In this case it is the particular test result taken to predict severe impairment. Choosing a higher cut-off point results in lower sensitivity but higher specificity, and vice versa. We will start by assuming fairly accurate testing early but more accurate testing later (Table 5.1), similar to the figures obtained from the meta-analysis in chapter 4. In practice, Early Testing may have lower sensitivity than this but higher specificity. Again, we will subsequently see how this would affect decisions.

We can factor the particular features of Late Testing into the model by adding disutility to outcomes involving late withdrawal of LST and by factoring in survival after Late Testing. I have assigned a negative utility to deaths following late withdrawal. This accords with the general intuition that a death following early withdrawal of life support would be preferable to a death after late withdrawal. Although in some cases this might not be the case (for example if an infant were to remain ventilator dependent and die quickly following late withdrawal) this seems a reasonable assumption. As highlighted above, a proportion of infants who are predicted on the basis of Late Testing to be severely impaired will nevertheless survive.

Having set out the relevant characteristics of the model we can use it to examine the influence of different variables on decisions. I will divide this analysis into a series of focussed questions.

## 5.4.2 Applying decision theory to the problem

### *5.4.2.1 How does the severity of illness affect decisions?*

Infants with severe encephalopathy have a high *a priori* risk of poor outcome; those with moderate encephalopathy have a lower risk. We can perform a sensitivity analysis on the model of timing decisions to assess the effect of this variable on decisions. (The *sensitivity analysis* for the decision model should not be confused with the test sensitivity referred to earlier.) Figure 5.2 shows the results of this analysis, comparing Early Testing with Late Testing. When the pre-test probability of poor outcome is more than 0.6 (60%) the line corresponding to Early Testing is higher (ie has greater expected utility) than the line corresponding to Late Testing. It would be better to test *early* than to test later in infants with severe encephalopathy. Conversely, when the pre-test probability is between 0.2 and 0.6 (20 to 60%) the line corresponding to *Late Testing* is uppermost and has greater expected utility. This would be a better strategy for infants with moderate encephalopathy.

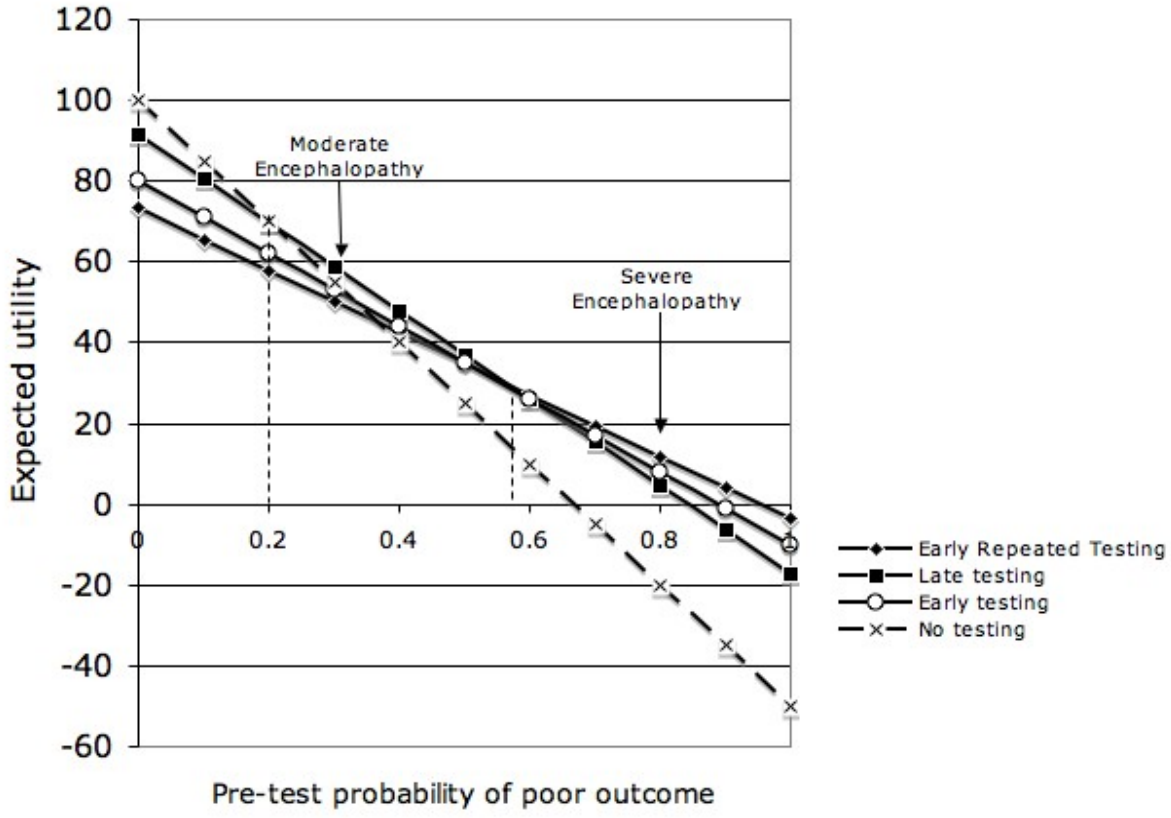


*Figure 5.2: One-way sensitivity analysis for the pre-test probability of poor outcome (see Appendix C for methods)*

*The vertical dotted lines indicate the intersection of different alternatives eg if the pre-test probability is >0.6 Early Repeated Testing has the greatest expected utility.*
*Expected Utility in this, and all subsequent figures, is multiplied by 100 for the sake of simplicity; this has no effect on comparisons.*

Apart from late or early testing there are two other strategies of testing we could consider. *No testing* would involve a strategy of performing no prognostic tests and continuing intensive care in all infants. *Early Repeated Testing* would involve performing early testing (with withdrawal of LST in those infants predicted to have severe impairment), then repeating tests at a later stage for surviving infants. This would have the advantage of detecting infants with poor outcome missed by early testing. Figure 5.2 also shows these additional strategies. Early repeated testing has the highest expected utility of any of the strategies when the pre-test probability of poor outcome is high. It is consistently superior to Early Testing alone, and in subsequent analyses I will focus on the comparison between Early Repeated Testing and Late Testing. If the pre-test probability of poor outcome is very low (less than 0.2 (20%)) the line for *No Testing* is highest; it becomes better not to perform any prognostic testing at all.

#### *5.4.2.2 How do parents' views about severe impairment affect decisions?*

Parents vary in their views about severe impairment. They may be more or less averse to their infant surviving in such a state. The starting assumption was that survival with severe impairment had a value of -0.5. This compares with a value of +1 for survival with good outcome. But conceptually it can be difficult to interpret or explain this sort of negative utility. How would parents decide what value to place on this? The traditional way of arriving at such a value uses the *standard gamble* (Froberg and Kane 1989). Parents would be asked about the chance of severe impairment at which they would consider withdrawing life-sustaining treatment. For example, imagine that there is a p chance of a good outcome, but a (1-p) chance of an infant surviving in a state of severe impairment. If we can determine the probability $p$ at which parents are indifferent between withdrawing and continuing treatment (given the chance of severe impairment) we can calculate the value of this outcome state (Froberg and Kane 1989). The value of the state is given by $-p/(1-p)$. A value of -0.5 for a state of severe impairment would correspond to $p$=0.33. In other words, if parents are willing to withdraw treatment when there is more than a 66% chance of severe impairment, it is equivalent to a value for this outcome of -0.5.

We can use the model to determine the effect of this variable on decisions and its interaction with the pre-test probability of poor outcome. Figure 5.3 shows a two-way sensitivity analysis. In this figure the line indicates those points where the two strategies have equal expected utility. The upper (shaded) region of the graph corresponds to those points where Early Repeated Testing has greater expected utility. The lower region corresponds to the points where Late Testing has greater utility.

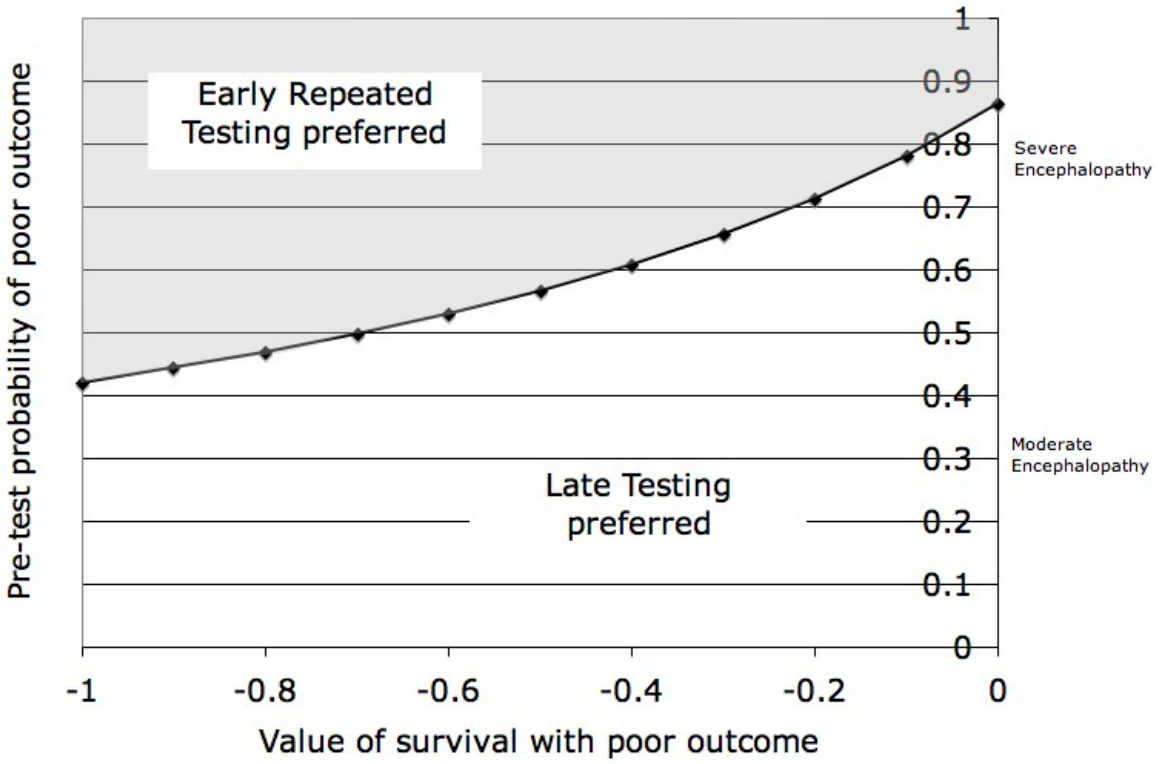


*Figure 5.3: Two-way sensitivity analysis for the effect of pre-test probability and the value of severe impairment (see Appendix C for methods)*

*The shaded region of the graph indicates the points when Early Repeated Testing is preferred.*

From the figure it is clear that for infants with moderate encephalopathy, Late Testing is almost always preferable. The line corresponding to the intersection of Early Repeated and Late Testing only falls below a pre-test probability of 30% if the value of severe impairment is <-1.8 (not shown). This would correspond to a value for *p* of 0.9 in the standard gamble, or parents being prepared to withdraw life support if the chance of a good outcome (ie survival without severe impairment) were more than 90%. Although it is possible that some parents would give a value this negative to survival with severe impairment I have limited analysis to values up to -1.0 (corresponding to *p* of 0.5). In practice it is hard to believe that clinicians would acquiesce to withdrawal of life support if the chance of severe impairment were less than 50%.

For infants with severe encephalopathy Early Repeated Testing is better as long as there is even a small negative value assigned to survival with severe impairment. In the figure, the line only rises above a pre-test probability of 0.8 when there is a value less than -0.1 for severe impairment. Along the lines of the reasoning outlined above this would correspond to withdrawal of life support being acceptable to parents if there were a 90% chance of severe impairment. One implication of this analysis, then, is that it may not be important for decisions to know *how* negatively parents view survival with severe impairment. It would be enough to know *whether* they view it negatively and would be prepared to withdraw life support in the face of probable severe impairment.

#### *5.4.2.3 How do test characteristics affect decisions?*

Do the characteristics of the prognostic test matter?. For example, we might be contemplating magnetic resonance imaging or electroencephalography. Early testing might be more specific but less sensitive, or vice versa. When the sensitivity of early testing falls it favours Late Testing because of the increased numbers of false negatives (infants with poor outcome missed by testing). Late Testing is also favoured if the specificity of the test is low, because of the increased false positive rate (infants with good outcome falsely predicted by the test to have poor outcome). But, from figure 5.4 it can be seen that the effect of this on decisions is relatively minimal. It influences decisions mostly where there is intermediate pre-test probability of poor outcome. Early testing has greater expected utility for infants with moderate encephalopathy (pre test probability 30%) only when both the sensitivity and specificity of early testing are very high (both more than 95%). For infants with *severe* encephalopathy, Early Repeated Testing ceases to be of greater utility if both sensitivity and specificity of early testing are relatively low (sensitivity and specificity less than 60%).

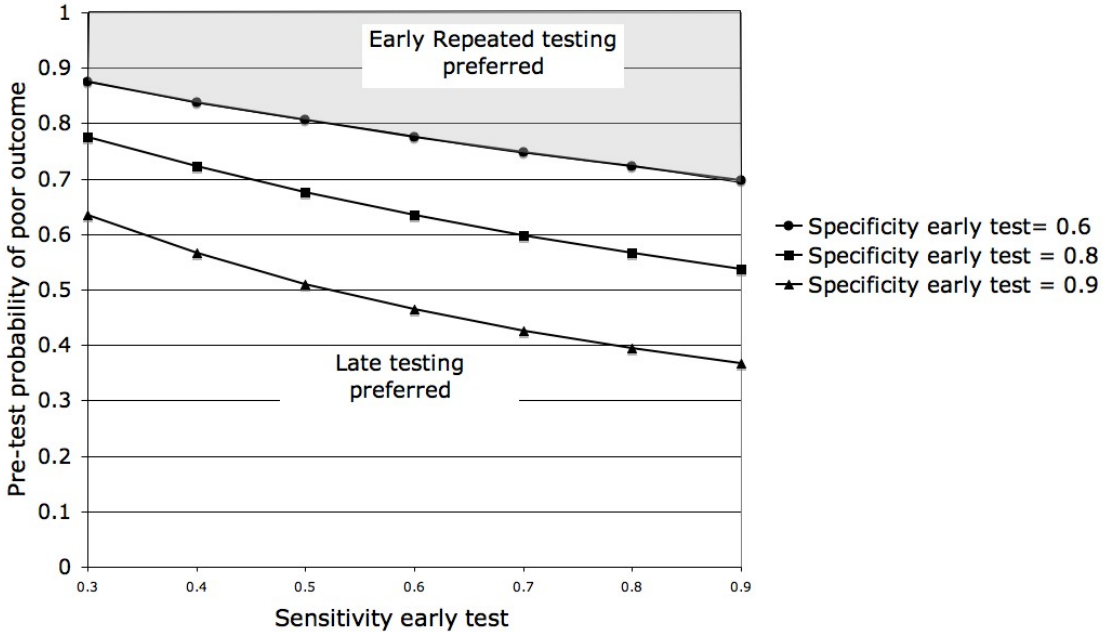


*Figure 5.4: Two-way sensitivity analysis for the effect of pre-test probability and early test sensitivity/specificity*

> *The lines represent testing with different specificity. The area on the graph above the curves represents the region where Early Repeated Testing is preferred. The area on the graph below the curves represents the points where Late Testing is preferred.*

#### *5.4.2.4 How do the negative features of late withdrawal influence decisions?*

Whether or not parents opt for Early Testing may be influenced by their attitude towards late withdrawal, for example their level of concern about withdrawing artificial feeding, or the possibility of missing the window of opportunity for treatment withdrawal. How is this reflected in the model? Figure 5.5 shows the interaction between the negative features of

late withdrawal and decisions. The curves represent testing for infants with different pre-test probability. The area below the curves indicates the points where Early Repeated Testing is preferred. For infants with severe encephalopathy Early Repeated testing is preferable to Late Testing unless late withdrawal is viewed neutrally (i.e. has no disvalue) *and* the chance of survival following Late Testing is close to zero. The curve for infants with moderate encephalopathy is not shown (pre test probability = 0.3), as Late Testing is always preferred – regardless of the disvalue of withdrawal, or the probability of survival after late prognosis.

When the pre-test probability of poor outcome is intermediate (0.5) the decision is more sensitive to these factors.

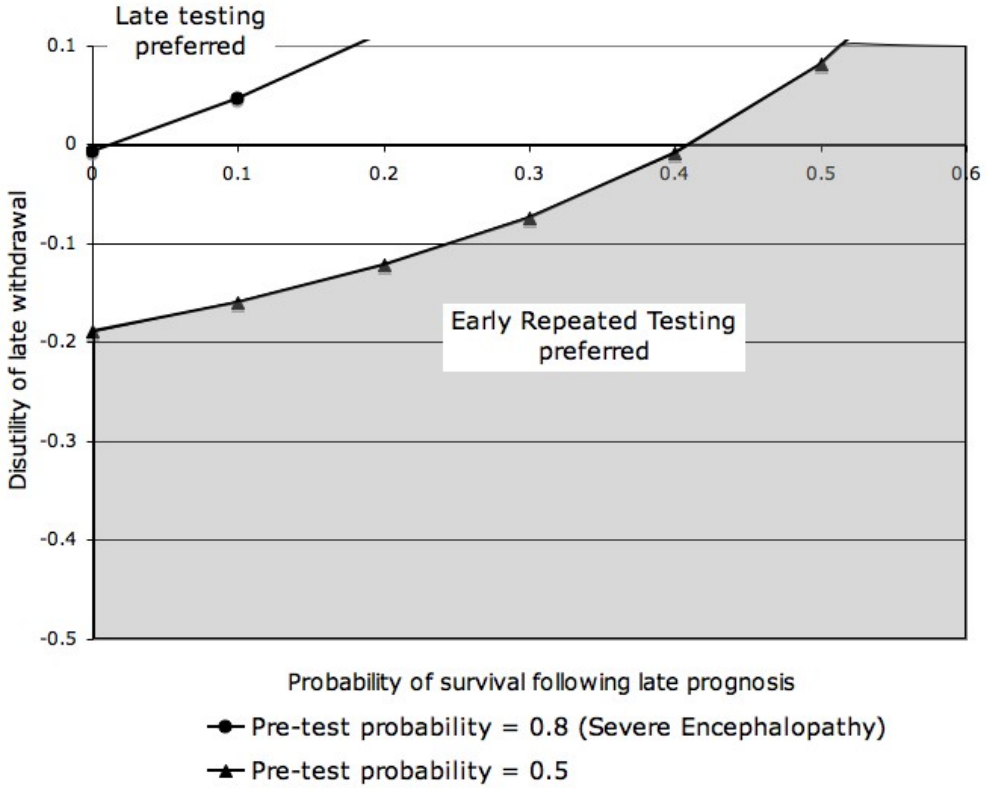


*Figure 5.5: Two-way sensitivity analysis for the effect of the disvalue of Late Testing/withdrawal, and probability of survival following late poor prognosis*

#### *5.4.2.5 Should decisions be delayed until tests are available?*

One clinical problem that arises in practice and was evident from interviews with clinicians relates to delays associated with prognostic testing. An infant may have a reasonably high pre-test probability of poor outcome based on their clinical condition. Performing additional prognostic tests (such as MRI) will improve the certainty of prediction, but because of the difficulty in arranging the test there will be a delay of at least one to two days before results are available. (A similar dilemma arises in practice with the use of phenobarbitone levels to ensure that the severity of encephalopathy is not related to very high anti-convulsant levels).

The options to consider are slightly different to those described above. The alternative is between withdrawal of treatment now, or Late Testing. Since withdrawal now will result in the death of all infants the expected value is 0. From figure 5.2 it can be seen that the line for Late Testing falls below zero when the pre-test probability is >0.85. If there is a greater than 85% chance of severe impairment it would be preferable to withdraw treatment now rather than wait for delayed prognostic testing.

### 5.4.3 Potential implications of decision theory

What conclusions can be drawn from the application of decision theory to the window of opportunity problem? What practical help can decision theory provide?

#### *5.4.3.1 Decision theory as a tool for specific cases*

One option would be to use decision theory to provide guidance to parents of infants. It would be possible to enter into the model features relevant to the infant (for example the estimated pre-test risk of poor outcome), as well as the values that his parents attribute to different outcomes. It has been suggested that the use of models for decision-making in the critically ill could enhance autonomy and help individuals make informed choices (Savulescu 1994; Cohen et al. 2000).

Parents may be reluctant to use a mathematical model for a decision of this nature. Decisions about the withdrawal of life support from a newborn infant are among the most difficult choices that parents ever have to make. They involve deep-seated and strongly held values. On the other hand, it is precisely the importance of such decisions and the difficulty in resolving the conflict between values that motivates the use of decision theory. Although decision theory is explicitly normative, (it is a theory about how decisions *ought* to be made) the aim would not be to *prescribe* a particular course of action for parents. Instead it would aim to help them think through the alternatives, and the reasons in favour of Early or Late Testing.

A more serious problem for decision theory in practice is the issue of metauncertainty (Savulescu 1994). Discussion thus far has largely been confined to first order uncertainty – i.e. uncertainty about which outcome will come about. But we may also be unsure of the likelihood of different outcomes (there could be a 60-90% chance of severe impairment for example). There may be doubt about the severity of different outcomes. Severe impairment might include permanent unconsciousness, or spastic quadriplegia with moderate intellectual impairment. Parents may also be deeply ambivalent about the value to place on those outcomes. These difficulties potentially make it extremely difficult to apply a decision-theoretic model.

Nevertheless, more sophisticated models could be developed to incorporate a spectrum of outcomes. Tools could help parents assign value to different outcomes. Improvements in prognostic tests may yield more specific predictions. In the meantime, empirical research is

needed to assess the acceptability of decision theoretic models for parents and clinicians. The process of applying decision theory may (even granted the uncertainties listed above) help parents to clarify values and options.

#### *5.4.3.2 Generation of guidelines for decision-making*

Another possibility is that the results of analysis could be used to generate guidelines or heuristics for decision-making. Within the bounds of the assumptions outlined above, the following conclusions could be drawn.

1. A strategy of Early Repeated Testing is preferable to Early Testing alone
2. The pre-test probability of poor outcome is important for decisions. If the pre-test probability of severe impairment is low prognostic testing and decision-making should be deferred. If the pre-test probability is high Early Testing would be preferable.
3. It is more important to know whether severe impairment is viewed negatively (ie whether withdrawal of LST would be contemplated if severe impairment were predicted) than to know the exact value assigned to this outcome.
4. Test characteristics do not change decisions unless the test is very accurate (high sensitivity and specificity favours Early Testing), or very inaccurate (low sensitivity and specificity favours Late Testing).
5. If Late Testing is associated with a risk of survival with severe impairment, or if late withdrawal is viewed negatively (i.e. has additional disutility) Early Testing is favoured.
6. If testing is going to lead to a significant delay in decision-making withdrawal of treatment without further testing should be considered.

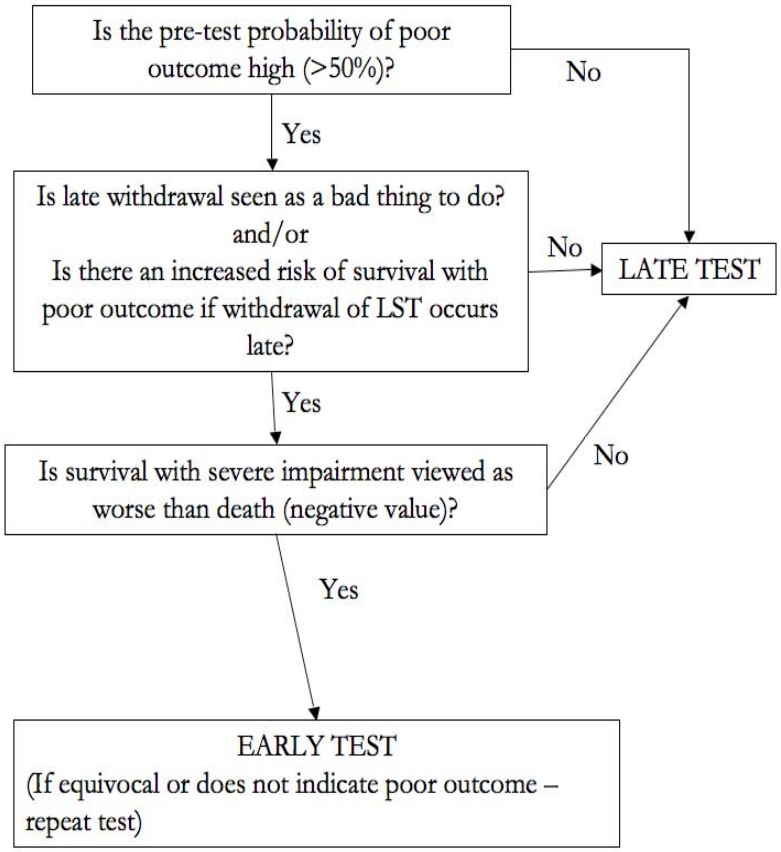


*Figure 5.6: Guideline for the timing of prognostic tests and decision-making*

As an example of the way that decision theory could be applied to the practical problem, these conclusions are combined in the form of a guideline in Figure 5.6 above. This guideline does not require knowledge of the exact probabilities of outcomes nor the specific values attributed to different outcomes. It provides a simple framework for decisions about prognostication in the face of the window of opportunity.

#### *5.4.3.3 The costs of uncertainty*

Decision theory makes uncertainty explicit (Lilford et al. 1998), and to that extent is able to highlight the consequences of imperfect knowledge. For example, in the model outlined above Early Repeated Testing had greater expected utility than Late Testing for infants with a high pre-test probability (0.8) of poor outcome. For every 100 infants with severe encephalopathy undergoing Early Repeated Testing there would be 5 false positives and 5 false negatives. The number of these is small, but it is still striking that for each infant who survives with severe impairment one infant dies who would have otherwise survived unimpaired.[18] On the other hand, a strategy of Late Testing was preferable for infants with

[18] Assuming that treatment is withdrawn in all infants with a test indicating poor prognosis.

moderate encephalopathy. For these infants Late Testing would yield 6 false positives and 8 false negatives per 100 infants. Although the specific numbers are only meaningful within the assumptions I have outlined, they highlight the costs of uncertainty. One implication of the window of opportunity is that some infants will survive with severe impairment, while others will die who would not have been impaired.

## *5.5 Solutions to the window of opportunity problem*

Decision theory provides one way of attempting to resolve the competing considerations posed by the window of opportunity problem. But an alternative approach would be to attempt to change the factors that give rise to the problem in the first place.

One obvious way to reduce the problem would be to improve prognostic tests. Advances in imaging or other technologies may allow early, accurate detection of severe brain injury and predict infants who will be severely impaired with high degrees of certainty. (In the next chapter I will look specifically at the implications of such a development for decisions). This would remove one important reason to delay testing and decision-making. It provides a strong incentive for further research. Nevertheless, the problem wouldn't be completely resolved, since families may still take some time to come to terms with prognosis and decide about withdrawal of LST. In any case, at present no such test exists.

A second possible solution would be to address the features of late withdrawal of LST that motivate Early Testing. The problem arises because most infants are no longer dependent upon mechanical ventilatory support. In a recent paper Thomas Cochrane discusses the window of opportunity in adult patients with stroke, and argues that there is no need for decisions to withdraw LST to be rushed since there is always the option of later withdrawal of oral or artificial nutrition (Cochrane 2009). But withdrawal of nutrition – particularly in children, is sufficiently contentious that it may motivate decision-makers to consider early prognostic testing and withdrawal of treatment even at the cost of uncertainty (Kon 2009). (It is also unclear whether Cochrane's autonomy-based argument for a right to refuse any intervention, including oral hydration and nutrition, can be extended to those who have never been competent.)

The prospect of withdrawal of nasogastric-tube feeding raises concerns about infants suffering during the dying process, concerns for the wellbeing of parents, and disquiet amongst medical and nursing staff about whether this form of end-of-life care is ethical or legal. Most of these factors are amenable to change.

The concerns about the infants themselves and families could be alleviated by the implementation of a concerted and coordinated palliative care model (Catlin and Carter 2002). A dedicated team of caregivers could look after the infant and support the parents – either in hospital, or, preferably, in the community. A team of this sort that regularly looked after dying infants would be able to assess and manage distress or discomfort experienced by the infant, and reduce the risk of suffering during the dying process.

If professional guidelines clearly supported withdrawal of artificial nutrition from newborn infants with severe brain injury this would provide reassurance to staff. Although some current guidelines refer to the ethical acceptability of withdrawal of artificial nutrition in certain circumstances in children (notably in persistent vegetative state) (Royal College of Paediatrics and Child Health 2004; Diekema and Botkin 2009), others suggest that it may be permissible only in exceptional circumstances (Nuffield Council on Bioethics 2006, pp. 98-99). There may also need to be legal clarification, since in the UK the court has suggested that withdrawal of artificial feeding requires High Court approval (Mason et al. 2006, p. 586; British Medical Association. 2007, p. 97), and the legality of withdrawal of artificial nutrition from patients not in a permanent vegetative state is unclear.

The other factor that drives Early Testing is the knowledge that some infants with poor outcome survive if prognostic testing occurs late. Is this amenable to change? If withdrawal of artificial nutrition is acceptable this may reduce the risk of survival with severe impairment. One option that has been proposed to manage uncertainty in treatment limitation decisions would be to defer decision-making until the outcome were clear, and then to offer euthanasia if the patient rationally wished to die, or would rationally choose death if he were competent (Savulescu 1994). Euthanasia in newborn infants is even more controversial than in competent adults (Costeloe 2007). It has been legally permitted only in the Netherlands, where a set of guidelines for its practice have been published and endorsed. The Groningen Protocol stipulates that "hopeless and unbearable suffering" that cannot be alleviated must be present (Verhagen and Sauer 2005). It is not clear that infants with HIE and predicted severe impairment would fall into this category, and the only cases in which the protocol has been applied to date have been infants with severe spina bifida and hydrocephalus (Verhagen and Sauer 2005). Nevertheless in the Netherlands at least, one response to the window of opportunity would be to defer decision-making until greater certainty could be achieved, and then resort to euthanasia if a poor outcome were predicted.

## *5.6 Conclusion*

The generic features of the window of opportunity are early critical illness with uncertain prognosis and later physiological recovery coinciding with more certain predictions of future impairment. Similar situations are seen in many forms of acute brain injury. In this chapter I have outlined the way in which this problem affects decision-making for infants with HIE and its relevance for the use of MRI. This was a significant problem noted by clinicians interviewed in chapter 3, and is ignored by current guidelines. I have argued above that it is permissible for caregivers to take into account the window of opportunity when making decisions about the timing of prognostic tests, but that this raises difficulties in balancing different priorities. One implication of this is that centres where ventilated infants with HIE are managed should have access to urgent MRI, with the capacity to perform scans and have them reported within a short (say <24 hour) time frame.

Decision theory provides one way to help caregivers manage the conflicting priorities and values at stake, and I have outlined a decision-theoretic model for this type of decision. It could be applied to individual patients, though the problem of meta-uncertainty makes it challenging to know what to put into the model. Alternatively, decision theory could be used to generate guidelines like the above flow-chart (Figure 5.6) or the recommendations in Box 5.1.

Neonatal intensive care units that care for ventilated infants with HIE need to have the ability to organise and obtain reports for MRI urgently (within 24 hours)

For infants with severe encephalopathy early prognostic testing should be seriously considered because of the high pre-test probability of severe impairment if the infant survives.

If testing is equivocal or reassuring parents should consider repeating it subsequently.

If the pre-test probability of severe impairment is high and testing is going to be delayed parents should be given the option of withdrawing intensive care without further tests.

Clear guidelines should be developed relating to withdrawal of artificial nutrition in infants with predicted impairment

If artificial nutrition is withdrawn parents and infants should be supported as part of a coordinated palliative care program

*Box 5.1: Recommendations relating to the timing of MRI and treatment withdrawal decisions*

The analysis in this chapter also suggests that detailed knowledge of all variables is not necessary. Within a plausible range, the value assigned to different outcomes and the test characteristics do not greatly influence which strategy has the highest expected utility.

The other benefit of decision theory is that it highlights the costs of uncertainty. This may prompt further research into improving prognostic tests. But it may also prompt us to reconsider our current attitudes towards the palliative care of newborn infants predicted to be severely impaired. It is the lack of palliative options for such patients that creates the problem of the window of opportunity.

I have focused, in this chapter, on *how* caregivers might decide about the timing of prognostic tests such as MRI. I have assumed that if severe impairment is predicted and parents are in agreement that treatment is withdrawn. But is it permissible to withdraw life-sustaining treatment in this setting? How severe does the impairment need to be? And how certain must we be of this outcome for withdrawal to be an option? These fundamental questions will form the basis for the next four chapters.

# CHAPTER 6

## Best interests and predicted impairment

### *6.1 Introduction*

> "our MRI definition for such an outcome might be clear severe basal ganglia abnormalities and almost always in conjunction with cortical abnormalities as well so that usually translates into major physical handicaps together with major mental, cognitive deficiency. And I think we are unanimous in our view that that prognosis is terrible" M60

Some of the neonatologists that I interviewed in chapter 3 suggested that in the setting of severe basal ganglia injury it would be appropriate to offer parents the option of withdrawal of LST. As discussed in chapter 2, current legal and ethical guidelines draw heavily on the best interests of the infant for determining the permissibility of treatment withdrawal. But is it in the best interests of an infant with severe basal ganglia injury to die? Would such a decision be consistent with the law and with existing ethical guidelines?

There are two immediate problems with determining the answer to this question. The first, as noted in chapter 2, is that previous cases and official guidelines do not clearly set out the severity of impairment that would make it in the child's best interests to die (Table 6.1). Secondly, the problem of prognostic uncertainty complicates decisions considerably. It has perhaps allowed the courts and those drafting guidelines to avoid answering the difficult question of when life is sufficiently impoverished or challenging that it is not worth living.

In the previous chapter I discussed the use of decision-theory as a way to approach a practical question arising from the uncertainty associated with predictions. In this chapter and the next I propose to set aside the problem of prognostic uncertainty. I do this for several reasons. Firstly, some guidelines suggest that it is only where prognosis is certain that treatment may be withdrawn (Royal College of Paediatrics and Child Health 2004, p. 11). There are reasons to doubt whether complete certainty is ever possible. But, as noted by several of the neonatologists that I interviewed, a fairly high degree of certainty about prognosis is possible for at least some infants. We should be able to answer the question of when treatment may be withdrawn for this subgroup of infants. Secondly, it is possible that further advances in imaging technology and science may diminish the problem of uncertainty. One of the important tasks of medical ethics is to anticipate future developments in technology, the impact that they may have on medical practice, and the potential ethical issues that they may generate. It will be useful to know what decisions may

be made if and when this improved prognosis is available. But thirdly, and more importantly, it is only possible to develop an approach to decision-making in the face of uncertainty if we know how to make decisions in the face of *certain* prognosis. This does not necessarily mean that there need be a single accepted or correct response to certain prognosis. There may be, indeed there are likely to be, competing answers to this question. We then have to determine an appropriate response to moral uncertainty (Lockhart 2000). But we need to understand which impairments, if certain to occur, would be sufficiently severe to justify treatment withdrawal and which would not. I will return to the problem of decision-making in the face of uncertainty in chapter nine.

In this chapter, I analyse two different approaches currently used in guidelines and by the courts to determine best interests and decide about treatment limitation. I draw on a thought experiment - a hypothetical form of neuroimaging able to predict with a very high degree of accuracy future impairments in newborn infants, a machine that I will call the Carmentis Machine. I argue that both 'Intolerability' and the 'Balance Sheet' face substantial epistemic and conceptual problems in responding to predictions from the machine. Even when prognosis is certain it is unclear when treatment may be withdrawn. I argue that the indeterminacy of these tests gives rise to significant practical problems for decision-making. An alternative approach to determining the permissibility of treatment limitation is needed. In the final part of the chapter, I discuss the possible implications for the law, and for practice, of developments in prognostic tests such as the hypothetical Carmentis machine.

| Guideline | Severity of impairment warranting treatment withdrawal | Uncertainty and treatment withdrawal | Parents and treatment withdrawal |
|---|---|---|---|
| RCPCH | "intolerable"<br>Little or no prospect of meaningful interaction. | Treatment should be continued where there is uncertainty.<br>It is sufficient to have a reasonable belief that a certain outcome is likely. | Ultimate decision is responsibility of healthcare team. |
| GMC | Weighing of benefits and burdens. | ? | Parents are legally responsible for treatment decisions in the child's best interests. |
| BMA | Best interests: may include capacity to interact, to develop awareness, and for self-directed action. | Parents should decide if there is uncertainty.<br>Treatment should be initiated if uncertain. | Parents should decide where there is uncertainty.<br>Parents may only make decisions in best interests of child. |
| AAP | "irremediable disability"<br>High chance of death and a high chance of unacceptably poor quality of life. | Treatment may be withdrawn if prognosis uncertain but likely to be poor. | Parental wishes should determine treatment in the grey zone.<br>Chosen treatment must be consistent with the best interests of the infant. |
| Nuffield report | "intolerable burden"<br>Bereft of those features that give meaning and purpose.<br>"extreme" levels of suffering or impairment. | Where prognosis is uncertain parental wishes may be given weight. | Parental interests may be considered, though they have less weight than the interests of the child. |

*Table 6.1: Summary of guidelines relating to treatment withdrawal (see chapter 2 for details)*

## *6.2 Thought experiment: The Carmentis Machine*

To help clarify the question of when it is in the best interests of a severely impaired newborn infant to die it may be useful to consider the following thought experiment:

> It is 2025. Newborn intensive care has come a long way since its earliest attempts to keep critically ill infants alive in the late 1960s and early 1970s. No longer is it a place of intense noise, artificial light and feverish activity. Acoustic and luminescent shielding and thermal cocoons provide an environment that allows newborns undisturbed rest for large portions of the day maximising growth and neurodevelopmental potential. Sophisticated liquid ventilators provide gas exchange for infants unable to breathe independently without tearing and destroying fragile developing lung sacs. Infants' clothing includes built in continuous monitoring of their physiological state with automatic dynamic adjustments to the environment and organ support.
>
> But despite improvements in the capacity to mitigate and prevent the complications of serious illness some newborn infants still have irreversible brain injury. In the centre of modern units is a new machine that provides highly detailed images of the structure and functional connections of the newborn brain. Within a couple of days of life, or following major changes in condition, all infants in the neonatal unit undergo neuroprognosis. Like the goddess Carmentis in ancient Rome the machine is consulted for a vision of the future for a newborn.[19] The Carmentis machine provides detailed and highly accurate predictions of the future cognitive capacity of infants (including sub-scores for capacities such as language, abstract reasoning, creative thinking, emotiveness), sensory deficits and motor abilities. These predictions form the basis for decisions about the continuation or withdrawal of intensive care.

In order to make the thought experiment plausible and useful, it will be worthwhile setting out the limits of our hypothetical machine. The Carmentis machine provides accurate predictions of future capacities. But it isn't going to be able to determine whether or not other co-incident illnesses will occur that could affect the future of an infant (for example the infant might develop meningitis, or might suffer head injury after a fall). Nor is it going to be able to predict whether or not future treatments (currently unavailable) will alter capacities or abilities. Furthermore the machine is not going to be able to determine the future mental states of an individual – it will not predict whether that individual will or would have pleasurable or painful experiences, or will or would want to continue to live.

---

[19] In ancient Rome, Carmentis was revered as a goddess of pregnancy and childbirth. It is said that newborn infants were brought to the temple of Carmentis, where the priestess would sing the child's future after drinking from a spring. (Grimal 1990; Roy 2005, p. 264). While the killing of deformed infants, and the abandonment of unwanted infants are thought to have been commonplace in ancient Rome (Harris 1994), such practices were not usually related to prophecies. There is, though, an intriguing story that an evil prophecy led the father of the emperor Augustus to consider destroying him shortly after his birth (Harris 1994, p. 14 n.121).

Although I am attributing to it semi-magical powers of prediction, it isn't going to be able to quantify interests, benefits, burdens, or tolerability.

It will be helpful to have some specific cases to discuss. These cases include conditions other than just HIE.

> **Case 1**: Baby Amelia was unexpectedly delivered in very poor condition following a planned home birth. She received resuscitation from the ambulance officers when they arrived at 15 minutes of age, but had early evidence of hypoxic brain damage with severe encephalopathy and refractory seizures. Neuroprotective treatments were commenced on arrival in intensive care. Nevertheless, the machine predicts that she will have profound motor impairment with severe spastic quadriplegic cerebral palsy and mild intellectual impairment (IQ 68). Expressive language will be limited by the degree of physical impairment but communication will be possible.
>
> **Case 2**: Baby Angelos was noted before birth to have polyhydramnios (excess amniotic fluid) and to be growth restricted. After delivery he was noted to have multiple dysmorphic features, contractures and a paucity of movements. He is diagnosed with a severe congenital myopathy (a disorder of muscles). The Carmentis machine predicts that he will remain dependent on the mechanical ventilator and will require home ventilation if he survives. He will be moderately intellectually impaired with an IQ of 45. He will have severe muscle weakness and limited voluntary movements. He will develop progressive scoliosis and restrictive lung disease without major surgery in mid childhood.
>
> **Case 3**: Baby Phillip was born prematurely. He was resuscitated and initially stabilised using partial liquid ventilation. On day 3 of life the Carmentis machine reveals evidence of widespread white matter injury, and evolving changes in the periventricular area. The machine predicts that he will be severely cognitively impaired with a predicted IQ of 30, and have mild motor impairment with spastic diplegic cerebral palsy. He will have moderately difficult to control epilepsy. He will have up to 10 words of expressive language.
>
> **Case 4**: Baby Chloe developed abnormal movements in the first days after birth. She is found to have an inherited form of bilateral fronto-parietal polymicrogyria (a congenital abnormality of brain development) (Piao et al. 2005). The machine predicts profound intellectual impairment (IQ unmeasurable but <20). She is not predicted to have major motor impairment.

These cases obviously do not encompass all possible combinations of impairments. The aim is that they represent a spectrum of realistic cases involving fairly substantial cognitive or motor deficits.

| | |
|---|---|
| Case 1: Baby Amelia | Mild cognitive impairment (IQ 68), severe physical impairment |
| Case 2: Baby Angelos | Moderate cognitive impairment (IQ 45), profound physical impairment, ventilator dependent |
| Case 3: Baby Phillip | Severe cognitive impairment (IQ 30), mild-moderate physical impairment |
| Case 4: Baby Chloe | Profound cognitive impairment, minimal physical impairment |

*Table 6.2: Case summaries with details of physical and cognitive deficits.*

Although it represents an oversimplification of the issues figure 6.1 illustrates the above cases in relation to previous legal cases and decisions (see chapter 2, and Table 2.1 page 31 for details of these previous cases).

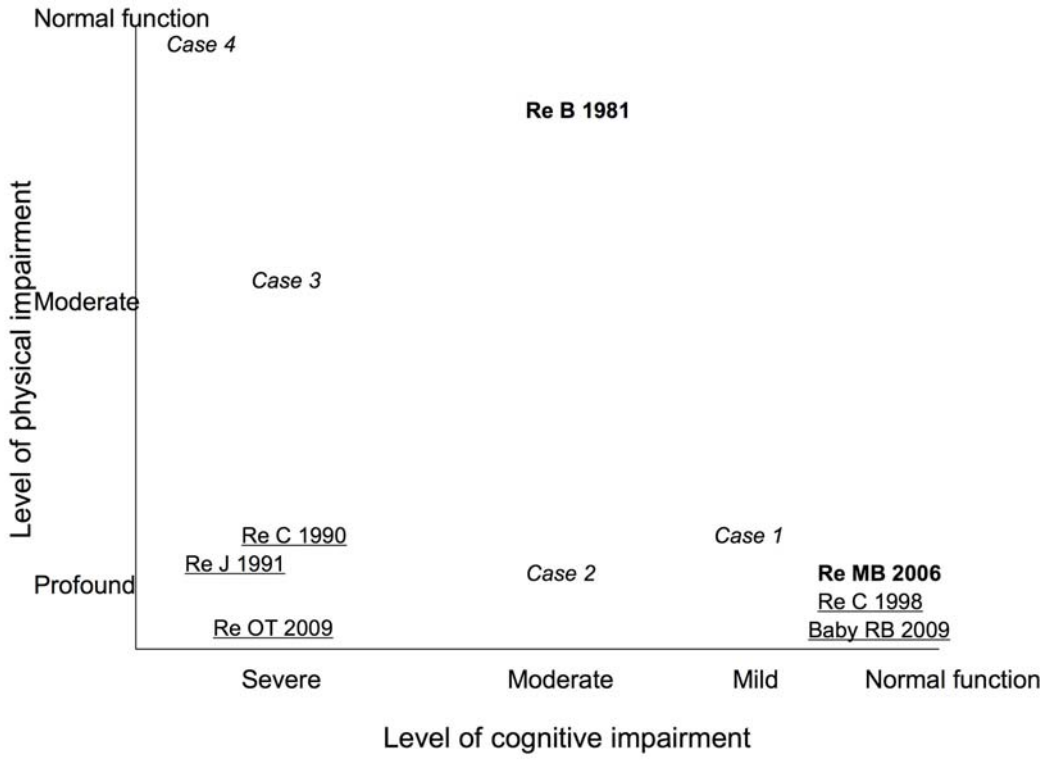


*Figure 6.1: Physical and cognitive impairment and treatment decisions. Where should the line be drawn?*

*(Cases in bold are those where treatment was continued following court review. Those that are underlined had treatment withdrawn or withheld following court review. Cases in italics are the hypothetical cases described above.)*

## *6.3 Application of best interests tests to the Carmentis Machine*

There are two different approaches to determining the best interests of infants in relation to treatment withdrawal. Some guidelines and cases draw on the concept of 'intolerability'; the key question is to determine whether future life would be *intolerable*, if so it would be in the best interests of the child to withdraw life-sustaining treatment. Others emphasise a balancing of benefits and burdens: life-sustaining treatment is not in the best interests of the child and may be withdrawn if the burdens outweigh the benefits. In this section, I will apply a philosophical analysis to the two different approaches, and assess how predictions of certain impairment such as those derived from the Carmentis machine, could or should be interpreted using these two tests. Interestingly, none of the guidelines or legal decisions refer to the idea of a 'Life Worth Living' (LWL), a concept that is used by philosophers and ethicists. I will discuss this latter concept in more detail in chapters 7 and 9, but briefly, as I understand them, the difference between the 'intolerability' and the 'balance sheet'

approaches is that the former emphasises the subjective sense of a LWL, while the latter is closer to the objective sense of a LWL (see p142).

### 6.3.1 Intolerability

The concept of intolerability is not defined in legal or ethical guidelines. Indeed, the Nuffield report and Royal College guidelines go so far as to suggest that it *cannot* be defined.

> "In proposing 'intolerability' as a threshold to justify decisions not to insist on life-prolonging treatments, the Working Party acknowledges the fallibility of language and the uncertainty of interpretation of evidence. Reasonable people may disagree … about what constitutes 'intolerability'" (Nuffield Council on Bioethics 2006, p. 13)

> "A severe/intolerable disability is indefinable" (Royal College of Paediatrics and Child Health 2004, p. 25)

But there seem to be a number of common elements in discussions that draw on the concept, and it may be possible to set out a definition. The Oxford English Dictionary defines intolerable as something:

> "that cannot be tolerated, borne or put up with; unendurable, unbearable, insupportable, insufferable. a. physically. b. mentally or morally. c. in loose sense, as a strong intensive: Excessive, extreme, exceedingly great (cf. awful)." (1989b, http://dictionary. oed.com/cgi/entry/50119957)

From this starting point the following components can be elaborated:

First, there is the *subjective* nature of the judgement. It requires the perspective of the individual. Thus, Lord Justice Taylor in Re J wrote:

> "I consider the correct approach is for the court to judge the quality of life the child would have to endure if given the treatment and decide whether in all the circumstances such a life would be so afflicted as to be intolerable to that child. I say "to that child" because the test should not be whether the life would be intolerable to the decider. The test must be whether the child in question, if capable of exercising sound judgment, would consider the life tolerable." (1991, p. 55F)

This description of intolerability has some similarity with the use of substituted judgement in decision-making for incompetent patients (Buchanan and Brock 1989, p. 10; Tibballs 2007). For previously competent adults, one way of approaching medical decisions is to determine (if possible) the decision that the patient would have made if they were competent now. This is most straightforward if the patient has previously made a written advance directive, but in other cases family and friends provide evidence of the preferences of the patient.

The second component of intolerability is the sense that it involves a *particularly negative* state of existence. Lord Justice Taylor referred to "extreme" circumstances and the "cruelty" of life (Re J 1991, p. 55). The judge in re B referred to a life "full of pain and suffering" (1981b, p. 1424C). Similarly the Nuffield report refers to "extreme suffering or

impairment" (Nuffield Council on Bioethics 2006, p. 13). This relates to part c of the dictionary definition given above.

A third conceptual element relates to the process of toleration. To tolerate something is usually understood to involve putting up with the negative features of a situation. It requires *awareness* of those negative features, (it makes no sense to tolerate something of which we are unaware or that causes no discomfort or annoyance) and, often, a *conscious weighing up* of those negatives against some other goal, or benefit. For example, we might tolerate a toothache because we wish to continue our day's work, or because we hope that it will improve with time without the need to go to a dentist. The severity of pain that can be tolerated will depend in part on what else we need to do; even a severe toothache might be tolerated if there were an urgent work deadline or personal commitment. Conversely a toothache that is intolerable disrupts our daily activity and prevents us from working or participating in planned activities. (This element of weighing negatives against positives is similar to that involved in the Balance Sheet approach, see below.)

These three elements might be combined as individually necessary and jointly sufficient conditions for intolerability (Box 6.1).

| An *intolerable* condition is one that |
| --- |
| 1. From the perspective of the individual patient P |
| 2. involves extreme suffering or adversity and |
| 3. is more than they are able or willing to endure |

*Box 6.1: Intolerability (1) – three conditions. LST may be withdrawn if a patient's condition is intolerable.*

The last condition suggests that there may be degrees of intolerability. Some conditions may be *literally intolerable*, in the sense that there is no benefit that could persuade the individual to bear the condition. (Perhaps some forms of physical torture are literally intolerable in this sense). Other conditions are *relatively intolerable*, they are sufficiently bad that the individual would not choose to endure them, but may physically or psychologically be able to tolerate them if necessary or if sufficiently motivated to do so.

Although the above definition is plausible there are problems in its application, as we will see shortly, and other versions are possible. The Royal College guideline suggests that the first condition above is optional.

> "Intolerable may mean "that which cannot be borne" or "that which people should not be asked to bear"." (Royal College of Paediatrics and Child Health 2004, p. 25)

This guideline also seems to imply a modified version of the third condition.

> "It is possible to envisage a level of disability that doctors believe to be intolerable, i.e. no reasonable person would want to live with it, and yet an individual sufferer may attach value to their existence." (ibid. p. 26)

This version of intolerability explicitly adopts the perspective of an impartial third party (ie not the patient), and introduces an additional normative dimension in suggesting that the patient *should not be asked* to endure it. It appears to place more emphasis on the second criterion listed above. So the concept would be

| |
|---|
| An *intolerable* condition is one that |
| 1. From the perspective of a reasonable third party (T) |
| 2. involves such extreme suffering or hardship that |
| 3. They would not be willing to endure it themselves |

*Box 6.2: Intolerability (2)*

It is not clear why Intolerability (2) is actually referred to as 'intolerable', since the guideline admits that individual patients may be able and willing to tolerate such conditions, and presumably T could or would be in a similar position if they actually experienced the condition. One possibility is that this is a probability judgement: conditions that are Intolerable (2) are probably or potentially Intolerable (1) (ie to P). A second possibility is that it is a hypothetical judgement (T believes that they (T) would not be able to tolerate it), though the truth of this is in doubt, or may be unknowable. A third possibility is that it is intolerable for T that P is in this condition (Box 6.3).

| |
|---|
| An *intolerable* condition is one that |
| 1. From the perspective of a reasonable third party (T) |
| 2. involves such extreme suffering or hardship that |
| 3. They are not able or willing for P to endure it |

*Box 6.3: Intolerability (3)*

There are significant epistemic problems for the first 2 versions of Intolerability. As noted above, Intolerability (1) invokes a form of substituted judgement. Substituted judgement for patients who have never been competent (for example infants) is problematic, since they have not been in a position to express preferences about treatment. It necessarily involves an attempt to imagine what the judgement of the individual would be.

Consider case 3, Baby Phillip, with severe cognitive impairment and moderate physical impairment. There are different ways of arriving at a substituted judgement for an infant (Archard 2008). The first is to imagine that Phillip now were able to weigh up his condition and able to tell us whether his future life is tolerable to him. But since we have no knowledge of the opinions and preferences of infants, let alone infants with significant future impairments it is difficult, if not impossible to know what judgement Phillip would make. The second possibility is to imagine Phillip grown to maturity (with impairment),

and to substitute his future retrospective judgement ie. what he would have preferred to have happened, and whether he judges his life to have been intolerable. This possibility is somewhat more appealing since we have the evidence of adults with impairment and their views about the quality of their lives. But the views of such individuals may not be representative of the future anticipated for Phillip. For example we have no way of knowing what the views of severely cognitively impaired adults would be about their treatment in the newborn period. They also represent only the views of those who have survived. Infants and children who died prior to reaching adulthood would be unrepresented. The third alternative, is to imagine Phillip as a competent adult reflecting on treatments that may or may not be provided for him in infancy. This alternative is like the hypothetical form of Intolerability (2). It is also problematic, however, since it is potentially subject to bias (Boddington and Podpadec 1999), and requires the judger to imagine lacking (and never having had) capacities that are essential to their identity and to their judgement (Wilkinson 2006). Intolerability (3) avoids the difficulties of substituted judgement since it asks only whether a third party is able or willing to tolerate for an infant/child/adult (Phillip) to be in such a state.

When we try to apply the concept of intolerability in practice other problems emerge. Which predictions of the Carmentis machine are intolerable? Many of those who have invoked the concept of intolerability have cited conditions involving severe physical suffering. But they have also referred particularly to conditions involving severe or profound cognitive impairment. For example Lord Justice Taylor described

> "a child … so damaged as to have negligible use of its faculties and the only way of preserving its life was by the continuous administration of extremely painful treatment … or …sedated continuously as to have no conscious life at all" (Re J 1991, p. 55c)

The judge also listed as first amongst the factors justifying withholding treatment in the specific case of J that "…the severe lack of capacity of the child in all his faculties which even without any further complication would make his existence barely sentient…" (Ibid. p. 56B) Justice Ward in the case of baby C referred to "intellectual function as the hallmark of our humanity" (Re C 1990, p. 35C). The RCPCH guideline argued that the lack of the capacity for meaningful communication would make life intolerable (Royal College of Paediatrics and Child Health 2004, p. 24), and the Nuffield report refers to lives lacking those features that give life meaning and purpose as an intolerable existence "even in the absence of great pain or distress" (Nuffield Council on Bioethics 2006, p. 12 para 2.13).

But one potential problem for these accounts is the Tolerability Paradox (Figure 6.2)(Wilkinson 2006).

> ***Tolerability Paradox*:** Intuitively, the more severe a child's future impairment, the harder it will be for them to bear, and the more likely that their condition will be intolerable. There are some reasons, however, to think that beyond a certain point more severe degrees of cognitive impairment may make life *more* tolerable.

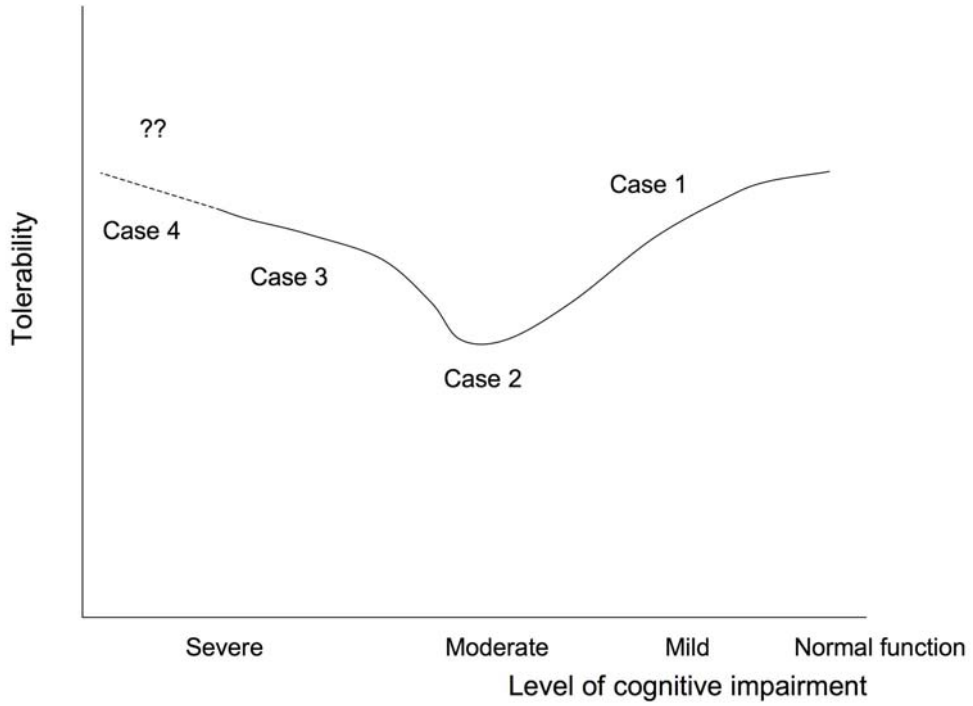


*Figure 6.2: Tolerability and cognitive impairment*

There is a sense in which it may be *better* for an individual to be severely cognitively impaired than to be mildly impaired or cognitively normal. Why should this be the case? The first reason is that the experience of cognitive limitation may be inversely related to its severity. Individuals with mild intellectual impairment may be aware of their limitations and frustrated by their disability. They may be sensitive to the looks and attitudes of others, and be conscious of being treated differently. They may be distressed by difficulty in communicating and achieving their desires. There is some evidence that clinical depression is more common in those with cognitive impairment (McBrien 2003). But more severe cognitive disability may be *less* likely to cause this sort of distress. For example, in a large study of quality of life in children with cerebral palsy (the SPARCLE study, see chapter 1), those with an IQ <50 were *less* likely to have low ratings for mood, emotions and self-perception than children with mild cognitive impairment or normal IQ (Arnaud et al. 2008). Recall the case of MB mentioned earlier, the 18 month-old infant completely paralysed and dependent on a mechanical ventilator. The judgement in that case was not based on intolerability, but placed great emphasis on the lack of brain damage in his case. However, his experience of life could be significantly worse if he were cognitively normal and aware of his surroundings than if he were impaired and (to some degree) unaware (Nuffield Council on Bioethics 2006, p. 139). Life may be more tolerable for Case 3, Phillip, than for case 1, Amelia, despite much more severe cognitive impairment in the former case. A similar problem arises with the question of consciousness and individuals in a persistent vegetative state. It may be worse for them to have some degree of awareness than to be completely unconscious (Wilkinson et al. 2009b).

Secondly, very severe forms of cognitive impairment may be incompatible with the second condition of all three versions of Intolerability described above. Lord Justice Taylor described as an example of an intolerable life one where a child is continuously sedated and permanently unconscious. Yet in fact, such a life appears a paradigm example of a life that is able to be tolerated since it involves no negative experiences whatsoever. Similarly, since it would seem incoherent to describe anencephaly (a condition where there is absence of the cerebrum) as involving any suffering or hardship for the patient, it would not be Intolerable (1 or 2).

What is more, at severe or profound degrees of cognitive impairment, the 3rd element of intolerability may lose traction. As highlighted above, to tolerate implies a sense of trade-off, of enduring some experiences for the sake of others. It requires a minimum level of personal identity and psychological continuity. But at very severe levels of cognitive impairment, such as that experienced by Baby Chloe (case 4) the individual may not only be unable to judge and communicate whether their life is tolerable, the concept of tolerance itself may not apply.

In summary, the problem with interpreting 'intolerability' in relation to certain predictions of impairment such as those provided by the Carmentis machine, is that there are substantial epistemic problems in determining tolerability (1 or 2) of conditions for infants – even where there is certainty about prognosis. Moreover it is difficult to take into account the apparent importance of severe cognitive impairment within a conventional analysis of intolerability.

The third person version of intolerability (Intolerability (3)) does not necessarily have the same problems. A parent (or doctor) might find it intolerable for a child to be on life support in a persistent vegetative state for example, though that state involves little or no actual negative experiences and the perspective of the child themselves may be unknowable. Nevertheless, this version of intolerability is vulnerable to other objections. The tolerance of a third party may depend on what they have been exposed to, or are accustomed to, or equally on their views about impairment. In the past it was judged by many reasonable parents to be intolerable for a child to have Down syndrome, whereas now it is cited as a paradigmatically *tolerable* condition. Can tolerability be contingent on societal attitudes? Secondly, it risks circularity in its specification of a 'reasonable' third party. If, for example, members of one society found all impairments, no matter how severe, tolerable (3), we might wish to question whether or not this was the judgement of reasonable people. But on what grounds is reasonableness to be judged? It cannot be on the basis of the tolerability of mild impairments without begging the question. Finally, if tolerability is related so fundamentally to the tolerance of a third party, why think that this is a test for the best interests of the *patient*? Lord Justice Taylor appeared to exclude Intolerability (3) in his comments on Re J, when he noted that "the test should not be whether the life would be intolerable to the decider" (1991, p. 55F). There may be reasons to take into account the wishes and views of parents (I will return to this in chapter 8), but

we should distinguish that question from the question of whether life with certain severe impairment is in the best interests of the child.

### 6.3.2 Balance sheet

As described in chapter 2, the recent case of MB was decided on the basis of a weighing up of the benefits and burdens of different treatment alternatives (see page 25) rather than on the basis of Intolerability. The Balance Sheet approach described by Lord Justice Thorpe in Re A (2000b) includes both the *process* of determining best interests, as well as a threshold for decision-making (Box 6.4).

1. Surrogate decision-makers are instructed to document the separate benefits and disbenefits of treatment.

2. If the benefits of treatment outweigh the burdens it is in the best interests of the patient to provide it.

3. If the burdens of treatment outweigh the benefits it is not in the best interests of the patient to provide it.

*Box 6.4: Balance Sheet approach to determining best interests. LST may be withdrawn if the burdens of treatment outweigh the benefits.*

This definition does not specify how much the burdens need to outweigh benefits for it to be in the best interests of the patient to withdraw life-sustaining treatment. It might be thought that as in the probability threshold for civil legal cases (balance of probabilities), that a small excess of negatives over positives would be sufficient to sway the judgement. But, as noted by Charles Foster in a criticism of the Balance Sheet approach (Foster 2005), Lord Justice Thorpe appeared to require a higher standard in his initial description in Re A.

> "Obviously, only if the account is *in relatively significant credit* will the judge conclude that the application is likely to advance the best interests of the claimant." (2000b, p. 560) (emphasis added)

The Balance Sheet has been favoured over intolerability in recent court judgements, and there are several potential reasons for this. One reason is that it appears to be more instructive. The concept of intolerability, as elaborated above, does not provide any guide for how to determine whether a condition is intolerable. (And, as noted, there are formidable epistemic difficulties in doing so).

Secondly, some have suggested that Intolerability expresses a *conclusion* about best interests rather than a test for best interests (An NHS Trust v MB 2006a, para 17). Although I have tried to set out the conceptual elements of intolerability in the above analysis there is a risk that its definition becomes a form of concealed tautology (Parfit April 2008, p. 65). In particular the third condition (being 'able or willing to endure') in each of the definitions provided could be vulnerable to this, and there is a risk that the definition becomes

equivalent to the open tautology "an intolerable condition is one that is intolerable" and consequently trivial.

A third reason that intolerability has been recently downplayed is that it relies on a form of substituted judgement (at least in forms 1 and 2 above). In the UK, the courts tend to place less emphasis on substituted judgement than US courts (British Medical Association. 2007, p. 13); they prefer an 'objective best interests' test, with the patient's wishes comprising only one component of their best interests (British Medical Association. 2007, p. 13). For example in W Healthcare NHS Trust v H (2004c) the court held that a decision about treatment for an incompetent patient about the reinsertion of a feeding tube should be based on their best interests, rather than what they would have chosen if capable. It was accepted that the patient would not have wanted the feeding tube reinserted, nevertheless the judge held that it was in the patient's best interests to do so. The Balance Sheet determination of best interests appears, at least at first glance, more objective than intolerability.

Is this approach to determining best interests able to provide an answer to the question of whether treatment should be provided in the face of certain impairment, such as that predicted by the Carmentis machine? I will consider the role of different impairments separately.

#### *6.3.2.1 Physical impairment*

Physical impairment or illness may lead to burdens for the child, particularly where those impairments are associated with significant pain or suffering. For example, a congenital abnormality that will predictably require multiple surgical procedures would impose a definite burden. Case 2, baby Angelos, will likely require major spinal surgery for progressive scoliosis in mid-childhood, and will have ongoing burdens relating to his ventilator dependence. These burdens will appear on the negative side of the balance sheet when weighing up life saving treatment. But one problem for the Balance Sheet approach is that even if future impairment is known with certainty, the degree of pain or suffering associated with that impairment may not be predictable. For example, one child might have a relatively uncomplicated course and short hospital stay, while another child might develop a post-operative infection, require repeat surgery and have a long hospital admission. Children also vary in their tolerance of pain, making it difficult to know how adversely affected they would be. It might be possible to assess the average burden of a given impairment, but some uncertainty will remain.

Other impairments may cause limitations in activity without leading to physical suffering - for example muscle weakness or paralysis. They wouldn't necessarily lead to burdens for the child, (though they could if the child were frustrated, depressed or anxious as a result of the impairments) but might be included instead as relative reductions on the benefits side of the balance sheet. For example, life may provide less benefit to baby Phillip with spastic diplegia (Case 3), if he is unable to walk or run and is confined to a wheelchair.

Another problem, however, with weighing future physical impairments is that the degree that the individual is disabled by their impairment is contingent upon the society in which they live and the support that is provided to them. This is one component of the social model of disability (Silvers 2003). If there is little provision for wheelchairs in society an individual may be very limited in their ability to take part in social activities. On the other hand, if society provides a high level of support (for example free or subsidized wheelchairs, adaptation of buildings and public transport) the limitation attributable to their impairment may be much less. So an attempt to include physical impairment in a weighted balance of benefits and burdens will need to take into account both the current level of support provided by society, and the anticipated future level of support.

The final point to note about weighing up the benefits and burdens of physical impairment is that some individuals appear able to realise high levels of personal achievement and wellbeing despite overwhelming physical impairments. For example writers Christy Brown and Christopher Nolan with severe cerebral palsy, or the physicist Stephen Hawking with amyotrophic lateral sclerosis are often cited (Doyal and Durbin 1998; Wyatt 2005). Perhaps the life of Baby Amelia (Case 1) will be like this? The balance sheet approach does not rely on the subjective judgements of individuals with impairment, but the evidence of individuals like these could be used to substantiate the potential balance of benefits and burdens. In the Wyatt case, Hedley J noted that intolerability might provide an evidentiary role of this sort.

> "the concept of "intolerable to that child" should not be seen as a gloss on, much less a supplementary test to, best interests. It is a valuable guide in the search for best interests in this kind of case." (2004b, para 24)

The testimony of Christy Brown and others therefore might be used to question whether physical impairment alone would tip the balance in favour of withdrawal of life support.

#### *6.3.2.2 Other impairments*

How should other impairments be taken into account in the balance sheet? Sensory impairment might be thought to affect the balance in a similar way to some physical impairments. Blindness or deafness could reduce the benefits of life but would not necessarily lead to burdens for the individual. Again, this would be contingent on the amount of support provided to the child/adult, but it would not necessarily preclude a life that was of net benefit.

But what about cognitive impairment? The examples cited of individuals who had overcome severe physical impairment all had normal cognitive capacity. (Indeed they had greater than normal cognitive capacities.) In the previous section, I outlined the Tolerability Paradox, and suggested that cognitive impairment would not necessarily increase the burdens experienced by the future child or adult (indeed it may reduce them). But the other possibility is that cognitive impairment may reduce the benefits of life for the child

(Wilkinson 2006). By preventing the individual from accessing a number of the intrinsic goods of life, (for example deep personal relationships, the development and attainment of personal goals) cognitive impairment, especially if severe, may make it easier for burdens to outweigh benefits. This is reflected in the judgements in re MB (2006) and re K (2006). While in the former case the presence of normal cognition was felt to outweigh the burdens of extreme physical impairment, in the latter case the absence of the benefits afforded by normal intelligence tipped the balance in the other direction.

> "In this case K …has a developmental age of only 3 months. She has no accumulation of experiences and cognition comparable with that of MB. She is not, and with her short expectation of life is never likely to be, in a position to derive pleasure from DVDs or CDs and the only indication of real feelings of pleasure in her limited developmental state is enjoyment of a bath." (K (A Minor) 2006b, para 57)

I noted earlier that there is a balancing element to Intolerability. So it is possible that a reduction in the benefits of life may lead to a convergence of Intolerability and Balance Sheet approaches. Perhaps even minor negatives would become Intolerable if the benefit provided by interaction, communication etc is absent? However, the second necessary condition in the concept of Intolerability, the presence of extreme suffering or hardship, makes it less likely that such conditions would be judged Intolerable (1, 2 or 3). Minor discomfort could not be Intolerable in this sense, even for a child bereft of positive conscious experiences. The Balance Sheet approach may be thus better able than Intolerability to explain why it would be in the best interests of a severely or profoundly cognitively impaired child to withdraw LST.

On the other hand, the Balance Sheet also has inherent epistemic problems. While it is clear that future physical and cognitive impairment may affect the balance of benefits and burdens for treatment it is far more difficult to know to what degree, and whether the balance has been tipped in favour of discontinuing LST. Even if we knew with certainty the degree and nature of future impairments for a child there is no straightforward way of deciding how much weight to give to different benefits or burdens, how they should be aggregated or combined, and how they should be weighed against each other. In the case of the paralysed infant Angelos (case 2) how does the benefit of watching DVDs, or the comfort of familiar voices weigh against the potential distress of being unable to move (Judt 2010), the pain of suctioning breathing tubes, the sense of suffocation when secretions build up or breathing tubes become transiently blocked? What is more, there is no obvious way of arbitrating whether a particular evidential threshold has been reached. It is not clear what the 'significant credit' level, mentioned above, would correspond to in practice. The Balance Sheet approach is sometimes referred to as an 'objective' best interests test (An NHS trust v MB 2006a, para 16) because it involves a weighing up of different interests and does not rely on the preference or choice of the individual. But the above analysis suggests that there is no truly objective way of determining the balance.

There are problems with both of the tests that have been proposed for determining best interests in infants and deciding about withdrawal of LST. Although uncertainty about prognosis is a major problem for decisions, when such uncertainty is removed, as in the thought experiment of the Carmentis Machine, the underlying conceptual problems are brought into sharp relief. Determining whether future life is intolerable, or whether the benefits outweigh the burdens is not only difficult to answer, for infants with significant cognitive impairment it is fundamentally unanswerable. And yet, ironically, it is for infants with such impairment that there is the greatest consensus that treatment may be withdrawn. One of the reasons why guidelines and the courts have failed to provide specific guidance in this area may be that the tests that they have recommended for the task are simply inadequate. But does it matter that guidelines are vague and non-prescriptive? In the next section of this chapter I will outline some reasons why more specific guidelines are needed.

## *6.4 Problems with vagueness*

> "that is very difficult to judge... I think it is dictated by the parents, it is dictated by the clinical circumstances and there is no hard and fast rule about how to approach [it]" M50

The first problem with the vagueness of guidelines for prognosis and treatment decisions is that it has the potential to lead to inconsistency in management. Some patients will have LST continued, while other patients (with identical conditions) will not (Ravenscroft and Bell 2000; Poulton et al. 2005). This is not to suggest that management need be identical in all cases. For example the wishes of parents may influence decisions (and I will argue that this should be the case in chapter 8). But, it is troubling that treatment withdrawal may be contemplated and offered to parents in some units, while in other units there would be no discussion of this alternative and treatment would be continued regardless of parental views.

There is relatively little literature comparing end-of-life practice between different neonatal units, nevertheless, there appears to be considerable variation in decision-making. Renee Anspach, in her study of several large tertiary centres in the United States, found significant differences in their approach to treatment limitation decisions (Anspach 1993). In a study of neonatal units in France and the United States, Orfali and colleagues found that neonatologists systematically differed in their evaluation of prognosis in identical cases (Orfali 2004, p. 2015) In a large European survey of doctors working in neonatal intensive care there was variability in self-reported experience of withdrawal of LST between countries, but also within countries (Cuttini et al. 2000). For example, a quarter of UK neonatologists reported that they had never decided to limit treatment on the basis of poor neurological prognosis (Cuttini et al. 2000). In addition, physicians who reported that religion was important in their lives were less likely to report treatment limitation. But the location of the patient, and the preferences or religious beliefs of the treating physician are

not morally relevant factors that ought to determine whether or not treatment is withdrawn.

Secondly, the lack of clarity may lead to conflict between medical staff, or between medical staff and parents (McHaffie and Fowlie 1996, pp. 59-61). Individuals may differ about whether or not treatment withdrawal is permissible (ibid. pp. 154-78). Inconsistency in management is cited by junior medical staff and nursing staff as a significant cause of distress and moral discomfort (ibid. pp. 135-6).

This contributes to the third problem, namely that vagueness leads to potential legal vulnerability (Endicott 2001; De Crespigny and Savulescu 2004). Although very few cases reach the courts, doctors worry about the possibility that they are breaking the law when they withdraw life support (Nuffield Council on Bioethics 2006, p. 46). While in previous cases the courts have tended to support doctors (Skene 2008, ch. 11), the possibility of being prosecuted frightens doctors and nurses (Alpers 1998). There is also the possibility of legal action being brought for personal or political reasons. In 1991, after a local Right to Life organization lodged a report with the police, the coroner in the Australian state of Victoria investigated the death of a newborn infant with spina bifida (Kuhse 1992). The coroner exonerated medical staff and was highly critical of the involvement of the Right-to-Life group in initiating the enquiry (Kuhse 1992).

The fourth problem is that legal uncertainty may contribute to over-treatment of infants (Guillemin and Holmstrom 1986). There is an asymmetry in legal vulnerability, such that treatment withdrawal but not treatment continuation may render doctors liable to prosecution. Although the chance of prosecution for withdrawal of treatment is small, there is virtually no chance of legal action if treatment is continued inappropriately. In a related context, there is some evidence that concerns about possible legal liability contribute to physician reluctance to prescribe analgesia and to inadequate pain management in dying adults (Alpers 1998).

The above problems with vague guidelines should motivate us to try to develop clearer guidelines for treatment decisions on the basis of prognosis in newborn intensive care. Much of this thesis is devoted to that task, and I will propose a set of guidelines in chapters 9 and 10. However, it is worthwhile considering the potential reasons *not* to develop such guidelines, and to retain significant vagueness when it comes to treatment guidelines.

One reason to embrace ambiguity is that debates over life and death decisions in newborn infants are highly contentious. Public debate about treatment guidelines would be likely to be divisive, and, as with abortion debates, it is likely that those at opposing ends of the debate would hold irreconcilable viewpoints. It may not be realistically possible to achieve a consensus about more specific treatment guidelines.

Secondly, there is the danger that greater clarity about prognosis and treatment withdrawal decisions would come at significant cost. For example, there is the risk that the law or guidelines would become clearer, but also much more conservative, as occurred in the

United States with the Baby Doe rules (Arras 1984), prohibiting treatment limitation except in extreme circumstances. Such a change would deny parents a say in a large number of decisions where they are presently able to decide about treatment. It would risk prolonging suffering for a significant number of infants who are harmed by continued treatment.

Thirdly, there is the risk that guidelines that were more precise would be inflexible, unwieldy and impractical. They might leave no room for taking into account the relevant subtle differences between individual cases.

Finally, it might be argued that the law or guidelines are *necessarily* vague, since they rely on generally evaluative or normative considerations (Endicott 2001).

However, while complete precision in guidelines may be neither desirable nor achievable, and borderline cases will always cause difficulties, it may be possible to develop guidelines that are substantially *less* vague than those currently available. Similarly, although such guidelines might be controversial, it is not necessarily the case that they would be unachievable, nor that they would become more restrictive. In chapter 9 I will set out a proposed model that would not radically change current practice in newborn intensive care, but that would, I argue, provide more consistent, practical and coherent guidance for decisions.

## *6.5 Implications of technological development in prognosis*

In the preceding section I have set out how the legal principles reflected in current guidelines and case law might be applied to certain predictions of impairment, such as those provided by the Carmentis machine. I have argued that current guidelines are inadequate. In this final section I will briefly outline what the significance of developments in prognostic accuracy themselves might be for legal judgements and treatment withdrawal decisions in practice. Although I focus on the hypothetical Carmentis machine, less dramatic improvements in prognosis will potentially have similar implications.

### 6.5.1 Highlight conceptual and moral uncertainty

Advances in prognostication akin to the Carmentis machine will reduce or eliminate scientific uncertainty about the degree of future impairment. But the question of whether or not it is in the best interests of the newborn to be kept alive will remain highly problematic. One of the impacts of the machine may be to highlight other forms of uncertainty that play into such decisions. This includes what we might call *conceptual* uncertainty about how the terms 'intolerability' or 'best interests' should be interpreted. But it will also highlight the ineluctable value judgements in such decisions. There is another type of uncertainty, *moral* uncertainty, about how to value different benefits and burdens of life, and about when impairment is sufficiently severe that life support may be limited. The development of MRI for newborns, even though it is far from a perfect prognostic tool, has already highlighted these uncertainties.

### 6.5.2 Force explicit criteria for withdrawal of life support

The small number of cases previously considered by the courts make it hard to link concepts such as 'intolerability' to specific clinical situations. In addition, uncertainty about the prognosis in some cases makes it hard to extrapolate from one case to another. But if the Carmentis Machine is able to provide detailed and accurate predictions of impairment the relationship between specific conditions and normative judgements will be necessarily more explicit. The courts will be forced to say whether, and why, particular levels of impairment are not in the best interests of the child. Professional guidelines would need to deal in far more specific terms with the outputs of the machine and relate those to decisions. This may mean that the development of the technology itself will contribute to the development of more specific guidance about treatment withdrawal.

### 6.5.3 May decrease or increase withdrawal of life support

In practice the development of highly accurate and specific predictions of future impairment may reduce the number of cases where withdrawal of life support takes place. Firstly, this may be because infants who would previously have been allowed to die because of a risk of a profound impairment are now saved (where the machine predicts that in fact impairment will not be so bad). This would relate particularly to those decisions that are currently made without court oversight, and uncertainty about future impairment is sometimes taken to justify parental discretion about decisions. Secondly, it is possible that some parents at least will be less willing to withdraw if they can be given specific information about the nature of impairments that an infant will suffer. Knowing exactly how impaired a child will be may help them to come to terms with disability, as well as to seek advice from parents of similarly impaired children. And third, there may be a type of expressivist concern (Edwards 2004) about withdrawal where there is sure knowledge of the degree of impairment. If there are living children and adults with the same impairments, allowing parents/doctors to withdraw may seem to express a judgement about the value of those specific lives. Although this same concern applies to decisions made currently, it is the greater prognostic certainty that may make the expressivist objection more forceful. This type of concern may make courts reluctant to judge such lives as being intolerable, or may give doctors or parents qualms about choosing to withdraw treatment.

But specific predictions may also *increase* withdrawal of life support. It will identify infants with very severe impairment who would previously have had life support continued. For example infants with moderate HIE have a 30% chance of severe impairment, as noted in chapter 1. It is generally believed not to be permissible to withdraw life support in the face of such a low chance of severe impairment. But the machine will identify which of these infants will be impaired and may lead to withdrawal in such infants. Finally it is possible that predictions from the machine may lead to a shift in attitude amongst parents about impairment and treatment continuation. The availability of neuroprognosis may make

parents reluctant to continue treatment in the presence of predicted impairment. It might conceivably lead to parents being criticised if they decide to continue treatment.

### 6.5.4 May raise the question of two normative thresholds for withdrawal

If it is permissible to withdraw life support from an infant is it obligatory? Some professional guidelines have discussed the idea of a 'grey zone' of prognosis, where prognosis is uncertain and the views of parents may determine whether or not treatment is withdrawn (American Academy of Pediatrics Committee on Fetus and Newborn 2007). On the other hand legal decisions have specifically discounted the idea that parental wishes could affect the interests of the child and so make a difference to whether or not treatment should be withdrawn. One way in which the Carmentis machine may influence the framework within which treatment decisions are made is if it leads to the evolution of two different legal judgements: a level of future impairment so severe that continued life support would represent an assault on the child, and a level of impairment such that parents may request life support be continued even though doctors disagree. I will explore this possibility further in chapter 9.

### 6.5.5 May highlight question of resource allocation

Finally, and perhaps more speculatively, if infants are predicted with a high degree of certainty to have severe impairment (but not necessarily severe enough for treatment withdrawal to be obligatory) it may raise questions of relative priority for scarce resources, for example intensive care beds, cardiac surgery or transplantable organs. Currently, uncertainty about the degree of impairment provides one reason not to prioritise on this basis, but it may be that the Carmentis Machine will put pressure on doctors and medical administrators to include future impairment in decisions about who should receive life-saving treatment.

## *6.6 Conclusions*

At the start of this chapter I asked whether withdrawal of life-sustaining treatment on the basis of severe basal ganglia injury was in the best interests of the infant, and consistent with current ethical and legal guidelines. At the end of the chapter I have no definite answer to give. It is probably consistent with the clinical guidelines from the Royal College of Paediatrics and other medical organizations. But it is difficult to know whether the courts, if asked to decide, would support treatment withdrawal. On the other hand, it is very *unlikely*, in the UK at least, that a doctor would be prosecuted for withdrawing life support in this setting if parents had consented to this.

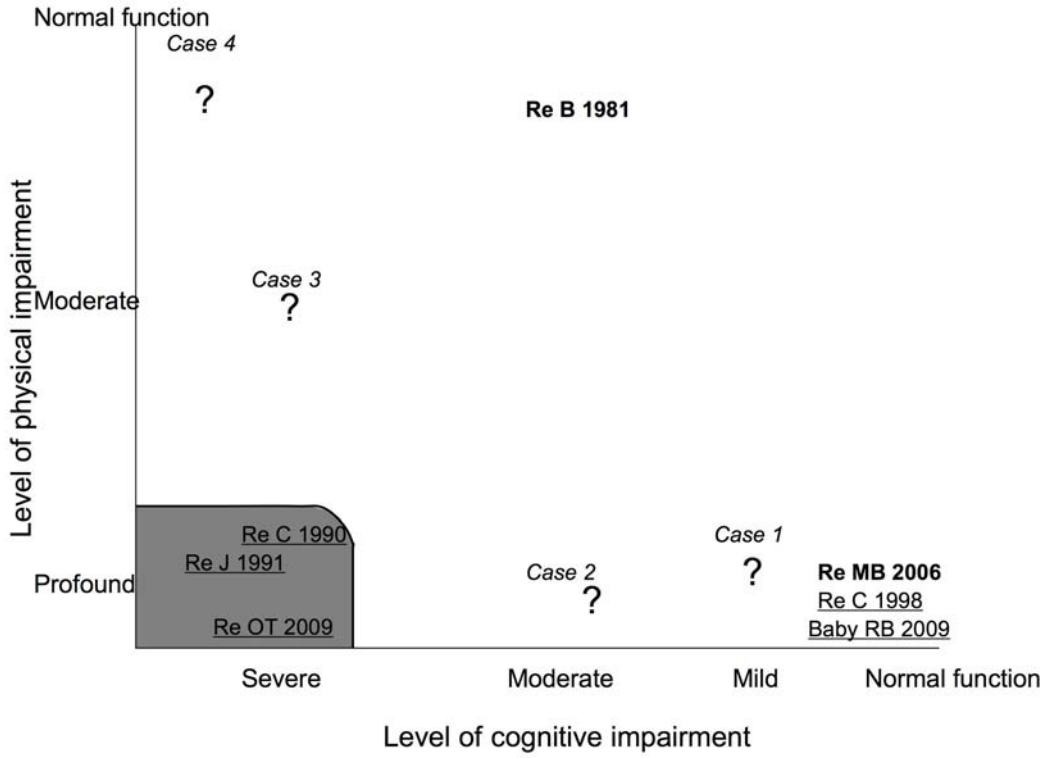


*Figure 6.3: Physical and cognitive impairment and treatment decisions. Drawing the line based on past cases and guidelines*

> *The shaded area indicates the cases where case law and guidelines appear to consistently indicate that treatment is not in the best interests of the infant (though earlier parts of the chapter highlight the conceptual and epistemic problems with even this judgement). It is unclear based on these guidelines and cases whether treatment limitation would be permissible for any of cases 1-4.*

Part of the difficulty in answering this question is that, as highlighted in chapter 4, there is some uncertainty about the neurodevelopmental outcome of such infants. Although it is unlikely that a perfect prognostic machine will ever be developed, technology continues to improve the ability of doctors to predict future impairment. Even if it is not possible to predict outcome for all infants, for at least some infants it will be possible with a high degree of certainty to predict that they will be impaired, the degree of their likely impairment, and the range of outcomes that are conceivable. However, I have argued in this chapter that even where prognosis is certain there are substantial difficulties in deciding whether it is in the best interests of an infant to withdraw or continue treatment. It is very difficult to know across a range of cases, including the infants Amelia, Angelos, Phillip and Chloe, whether or not life is going to be Intolerable, or whether, using the Balance Sheet approach, burdens outweigh benefits. (This difficulty may be one reason why none of the clinicians interviewed referred to either intolerability or the Balance Sheet). The only condition in which guidelines and case law appear to clearly indicate that treatment would not be in the best interests of the child is where there is certain severe physical *and* cognitve impairment (Fig 6.3)

The foregoing analysis highlights the practical limitations of current legal and ethical guidelines. It also highlights the nature of uncertainty that is at the heart of the problem.

Even where there is no prognostic uncertainty, there remains uncertainty about which ethical concept, test or principle should be applied, and how to evaluate the benefits and burdens of severe impairment. It is understandable that guidelines and case law provide only vague guidance for decisions, but I have suggested that this causes significant problems in practice. The other problem with these guidelines, as noted in chapter 2, is that they potentially yield little or no role for parents in decisions.

Current guidelines are inadequate. It is possible that over time developments in prognosis may lead to improved guidelines, simply through the judicial review of cases with particular prognosis. But this is likely to be slow, ad hoc, and dependent on the cases that end up in the courts. It also raises the question of whether the courts are the appropriate place to develop policy and guidelines for practice in this area. The role of the law in the development of policy is beyond the scope of this thesis, but there is good reason to think that perhaps the courts are not the best place. In the ensuing parts of this thesis I will investigate other alternatives for policy.

What alternative principles might be used to develop more specific guidelines for prognostication and treatment withdrawal in infants with HIE? In the next chapter I will examine the philosophical arguments that have been proposed to permit the withdrawal of LST from infants with mild or moderate impairment. Are newborn infants replaceable?

# CHAPTER 7

## Impairment and Replacement

### *7.1 Introduction*

> **Case**: Christine is born following a caesarean section. She is noted to have seizures in the newborn period and is treated with anticonvulsants. She was suspected of having HIE, but MRI performed on day 3 of life reveals a large left sided cerebral infarction (stroke) involving the cerebral hemisphere, basal ganglia and internal capsule. Christine's doctors tell her parents that she is highly likely to have movement problems affecting her right side (a right hemiplegia) of moderate severity (Mercuri et al. 2004b). Her cognitive function is likely to be normal (Ricci et al. 2008).

In the previous chapter I argued that existing guidelines based on the best interests of the infant are inadequate for determining whether or not it is permissible to withdraw life support from a newborn infant with predicted impairment. They are unable to provide practical guidance to doctors or parents even when the considerable problem of prognostic uncertainty is set aside. Nevertheless, the epistemic and conceptual difficulties in using the best interests of the infant to decide about life sustaining treatment do not in themselves provide a decisive reason to reject the best interests principle. It may be difficult to know whether or not it is in the best interests of an infant with severe impairment to die. But it is clear that, if we are to be guided by their best interests, treatment should not be withdrawn from infants who are predicted to have mild or moderate impairment such as the infant Christine described above. Yet there are some philosophers who have argued that parents and doctors *should* be free to allow such newborn infants to die. Are there reasons to reject the best interests of the infant and have a considerably more permissive approach to newborn treatment decisions?

One reason that has been proposed for allowing mildly impaired newborn infants to die is that if the infant dies her parents could conceive another child who would be likely to have a better life. This possibility is sometimes referred to as "replacement". Some philosophers, notably Peter Singer and Richard Hare, have claimed that replacement is highly relevant to decisions about newborn infants (Kuhse and Singer 1985, pp. 155-61; Singer 1993, pp. 185-91; Hare 2006). In this chapter I will assess, and ultimately reject, this claim.

In newborn intensive care replacement is not often raised. None of the clinicians interviewed in chapter 3 referred to it. If doctors discuss it at all it is often criticised as abstract, irrational or irrelevant (Kuhse and Singer 1985, p. 156). Yet some parents do

appear to consider the replacement child, for example Peggy Stinson in her book about a very premature infant in intensive care: "I keep thinking about the other baby – the one who won't be born" (cited in Kuhse and Singer 1985, p. 155). In other settings it would be perfectly reasonable for parents to think about the effects of their decisions on future (as yet unconceived) children. Is there a reason why parents *should* replace? What is the nature of this reason, and how should it impact on treatment limitation decisions?

There are two distinct arguments for replacement. The negative case is that newborn infants lack moral status, and therefore it may be permissible to kill them in the same way that it is permissible to kill fetuses or destroy embryos. The positive case is that there is a prima facie moral obligation to bring into existence a child with the greatest chance or level of wellbeing. Most counterarguments to replacement focus on the negative case and the question of moral status. In this chapter I address the positive case and the apparent benefit of replacement. I draw on an argument suggested by Jeff McMahan that undermines the positive case for replacement.

I will start by briefly summarising the case for replacement as well as the standard objections. I outline and then extend McMahan's argument. The *impersonal* reasons to replace are weak and easily outweighed. I assess and reject several potential responses to this argument. I then assess an alternative justification for replacement – in *individual-affecting* terms. I conclude that the strongest reason to replace may be the interests of parents, but that the moral force of this reason is different from the standard justification of replacement. The central question (to be pursued in chapter 8) is about the weight that we should give to the interests of parents in decisions.

## *7.2 Definitions/assumptions*

Before going any further I will set out certain definitions and assumptions. This chapter touches on a number of difficult issues relating to identity and future individuals that I do not have the space to fully explicate or defend.

I take *Replacement* to refer to the following:

> **Replacement**: a decision to kill or allow to die an existing individual in order to cause a different individual to exist, when that second individual *would not otherwise exist* (Singer 1993, p. 185; McMahan 2002, p. 351).

I contrast this with *Substitution:*

> **Substitution**: a decision to cause one individual to exist rather than another individual (who does not already exist).

and Causing an Individual to Exist:

> **Causing an Individual to Exist**: a decision to bring one individual into existence where there is no individual who thereby dies, or whose coming into existence is thereby prevented.[20]

I refer to a life worth living

> **Life worth living (LWL)***:* a life that contains or will contain overall more intrinsically good experiences than intrinsically bad ones (Broome 2004, pp. 66-68).

This is equivalent to a condition where the benefits outweigh the burdens using a Balance Sheet approach (chapter 6). A subjective measure of whether a life is worth living is whether the individual whose life it is, prefers for his own sake to continue to live rather than die. In chapter 9 I will expand further on the concept of a LWL.

The type of case that I will focus on in particular in this chapter, is one where a newborn is predicted to have a life worth living and a *moderate* degree of impairment. For example, we might consider an infant with HIE and moderate white matter injury (see table 1.1 p11), or Christine with predicted hemiplegia (see above). Peter Singer refers to haemophilia or Down syndrome as relevant examples (Kuhse and Singer 1985, p. 158; Singer 1993, pp. 185-6). I will not discuss infants with predicted severe impairment in this chapter. For such infants, as noted in the previous chapter, it is hard to know whether their future lives will be of net benefit, and consequently whether, for their own sake, we should let them die.

I assume in this chapter that in the *absence* of replacement (for example if the parents cannot have another child) we do not have decisive reasons to allow the child to die. If decisive reasons already exist then there is no need to invoke replacement. One distinctive feature of the argument for replacement is that it may justify the killing, or the allowing to die of infants who will have lives worth living (Singer 1993, p. 185; McMahan 2002, p. 345)).

I am also going to assume that such impairments are associated with reduced wellbeing. This last assumption may be disputed. I am not claiming that individuals with moderate impairment cannot have lives with high levels of wellbeing. (In the previous chapter I referred to several famous individuals who have appeared able to achieve high levels of achievement and wellbeing despite very severe physical impairments). I think that it is fair to assume, however, that such impairments relevantly and significantly affect wellbeing and the capacity for human flourishing (Harris 2000a; Glover 2006, pp. 8-26).

I will refer to *individual-affecting* and *impersonal* reasons (Parfit 1982, p. 149; Parfit 1984, pp. 386-7, 393-5; Parfit April 2008, Chapter 1, p. 42). (In order to avoid confusion with the

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[20] Although I will sometimes use the term 'conception' as shorthand for the act of bringing an individual into existence I do not intend to be committed to the view that our lives begin at conception.

moral sense of personhood, I will follow Jeff McMahan in using the term 'individual-affecting' in the place of Parfit's 'person-affecting' (McMahan 2009a).) We have individual-affecting reasons to do something, when a course of action will affect existing or future individuals for better or for worse. We may also have reasons related to wellbeing where individuals are not made either better or worse. They arise from the 'non-identity problem' (Parfit 1984, p. 359). For example, we might face a choice between bringing a child with a high level of wellbeing into existence, and bringing into existence a *different* child with a miserable life. The wellbeing-related reason to choose one child over the other is non-individual-affecting or *impersonal*. (For an example that may clarify this distinction see the next section).

Finally, the arguments against the impersonal reason to replace assume transitivity of value (Broome 2004, pp. 21, 50-63). In other words, if situation A is better than B, and B is better than C, it follows that A is better than C. As will become clear, I believe that transitivity is inherent in the nature of impersonal value. When the justification for replacement is framed in other ways, this assumption breaks down.

## *7.3 Replacement*

### 7.3.1 The case for replacement

Replacement of newborn infants is often justified by analogy with Substitution (Singer 1993, pp. 186, 189). In a typical example a mother has a medical condition such that if she conceives a child now the child will have a moderate impairment, whereas if she waits six months to conceive her child will not be impaired (Parfit 2006, p. 111). (The nature of the medical problem is not specified, but, for example, it might be that she is currently required to take a course of teratogenic medication such as methotrexate, but it is anticipated that she will be able to be weaned off it in the coming months). Many people believe that it would be wrong for the mother in this case not to wait. Yet such thoughts cannot be based upon the interests of the child that she conceives, nor on a conventional (comparative) notion of harm. The child she would conceive now is different from the child she would conceive in 6 months time. The child conceived now who turns out to be impaired cannot complain about her mother's decision not to wait, since she would not otherwise exist. Singer and Parfit argue that we can make sense of our intuitive response that the mother should wait through the notion of impersonal reasons. (Some people, for example Rebecca Bennett (2008), have different intuitions about this sort of case and believe that because of the non-identity problem the mother does *not* do the wrong thing by conceiving now. For further discussion of an alternative individual-affecting understanding of such cases see section 7.5.)

Although this case is an example of *Substitution* rather than Replacement it highlights the potential relevance and intuitive appeal of impersonal considerations in parental decision-making. Similar considerations might be in mind when parents undertake prenatal testing.

In many countries only a minority of parents choose to continue a pregnancy after a diagnosis of Down syndrome (Boyd et al. 2008). A variety of factors could lead parents to reach this decision. But one reason to terminate the pregnancy would be in order to conceive a different child whose level of wellbeing is likely to be higher.

Singer's argument for replacement is not simply based on the analogy with Substitution. He explicitly bases it upon a maximizing form of utilitarianism that aims to increase the total amount of wellbeing in the world, either by increasing the number of individuals with happy lives, or increasing the wellbeing of those already in existence (Singer 1993, pp. 103, 184-6). Such a view explains why Singer believes it would be wrong for a mother to fail to delay conception in the case described above. More formally, it seems that Singer's argument for replacement of newborn infants could be abstracted as follows (Box 7.1).

| |
|---|
| 1. There is greater wellbeing in the life of the next possible child than in the current child |
| 2. The next child will only exist if the current child dies |
| 3. We should maximise wellbeing |
| 4. Therefore we should kill the current child or allow her to die in order that the next possible child will live |

*Box 7.1: The argument for Replacement*

As we will see, there are other possible justifications for Replacement, but the most commonly cited reason is impersonal.

### 7.3.2 Standard arguments against replacement

There are a number of arguments that have been proposed against replacement. As already highlighted, the usual target is the negative case. If infants like Christine have moral status such that they may not be *killed*, this would undermine Singer's argument for infanticide on the basis of the acceptability of substitution or prenatal testing and abortion (Uniacke and McCloskey 1992; Uniacke 1997; Morrow 2000). I return to the question of moral status in chapter 8. But in this chapter I am focusing on cases that involve allowing infants to die. It is widely accepted that in certain circumstances it is permissible to withdraw LST from newborn infants. The argument from moral status would have to make a further claim in order to prevent replacement from being a reason in favour of letting infants die.

Other arguments against replacement include *reductio ad absurdum* arguments (Calef 1992; Uniacke 1997; Morrow 2000; Louhiala 2003, pp. 99-100). For example, some have asked why, if newborn infants are replaceable, older infants or children are not replaceable. HLA Hart suggested that utilitarians who accept replacement for newborns must be committed to the replaceability of adults (cited in Singer 1993, pp. 127-8).

I do not propose to write further about these objections to replacement. I wish to look at a different type of objection - one that goes to the heart of the positive case for replacement.

## *7.4 The impersonal reason to replace*

### 7.4.1 The Insubstantial-Reason argument against replacement

Jeff McMahan in *The Ethics of Killing* analyses in detail Singer's argument for replacement (McMahan 2002, pp. 345-362). He disagrees with Singer on the moral status of the newborn, and argues that if the negative case were sound it would have unacceptable implications (ibid. p. 357). But McMahan also believes that the positive case is problematic. The reasons that Singer gives to have a child with more wellbeing are impersonal. Yet, if we have an impersonal moral reason to maximise the overall amount of wellbeing, it would seem to imply that there is a moral reason to cause an individual to exist. Assuming that an individual will have a life worth living, it would be good to bring that individual into existence. This is a striking suggestion. It conflicts with many people's intuitions about conception. Generally people do not think that there is a moral reason to conceive a child, nor that someone does wrong by using contraception (Narveson 1976, pp. 72-73; Broome 2004, pp. 143-5).

The idea that total versions of utilitarianism may have counterintuitive implications for the morality of conception is not new (Hursthouse 1987, pp. 143-4; Glover 1990, pp. 69-70; Singer 1993, pp. 103-5). Compromise utilitarian positions might argue that there *is* a moral reason to cause an individual to exist, but that it is weak and easily overridden, and hence has less major implications for the morality of conception decisions (Rachels 1998, p. 94). McMahan argues, however, that accepting such a compromise has implications for the argument for replacement. The minor reasons that would potentially justify not having a child (for example personal preference for number of children, the need to buy a larger car, a desire to travel) would be enough to justify replacement. McMahan believes that this is untenable.

McMahan's line of reasoning can be turned around to answer a different question – that of the strength of the impersonal reason to replace. The impersonal reasons to replace and to cause an individual to exist are related. But the impersonal value of replacement in cases where the current child is predicted to have a life worth living has to be *less* than that of conceiving a child. Why should this be the case? We believe that there will be greater wellbeing in the life of the next child than in the current child. Yet this difference in wellbeing - the net gain in wellbeing - is less than the increase in wellbeing that would be likely to result from a decision to cause an individual to exist (where the alternative is not to have a child, see Figure 7.1). Consequently there is a weaker reason to replace an impaired newborn infant than to conceive. If we accept that there is only a weak reason to cause an individual to exist, the reason to replace is slender indeed. Call this the Insubstantial Reason argument against replacement (Box 7.2).

1. The positive case for replacement is based on impersonal reasons

2. There is a weak impersonal reason to cause an individual to exist

3. The increase in wellbeing with replacement, is less than the increase if an individual is caused to exist

4. There is less impersonal reason to replace than to bring a child into existence

5. There is an even weaker reason to replace (than to bring a child into existence)

*Box 7.2: The Insubstantial-Reason argument against replacement*

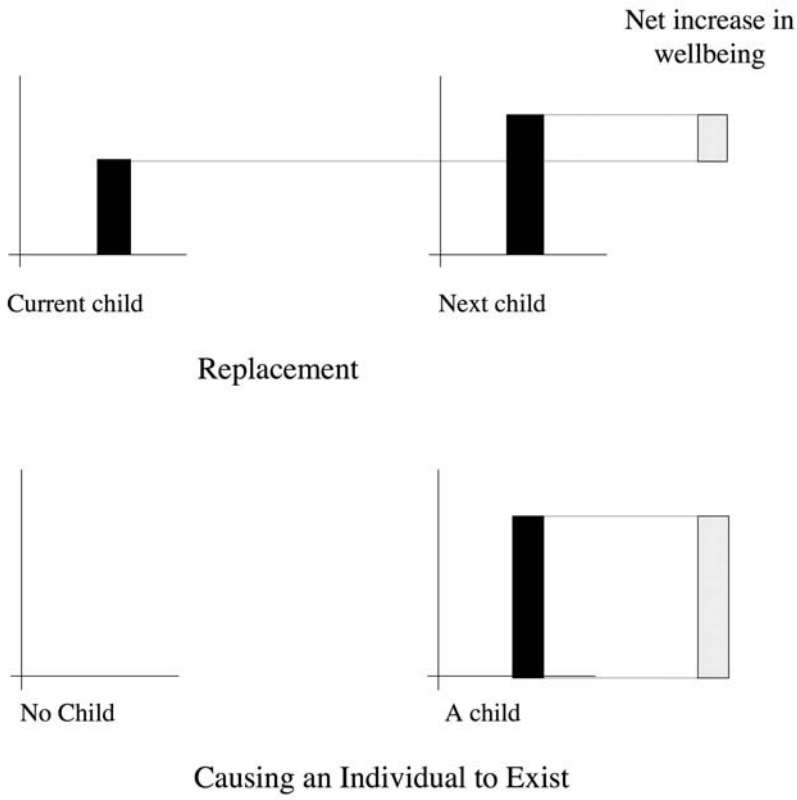


*Figure 7.1: The impersonal reason to replace*

> *The height of the black rectangles represents the amount of wellbeing in different individuals' lives. The grey rectangles represent the difference in wellbeing between the current child and a future possible child, or between having no child, and bringing a child into existence.*

To put this into perspective: couples often decide not to have a child (or another child) for a range of often fairly minor reasons (for example, the size of the family in which they were raised, costs). If we believe that these sorts of consideration can justify not bringing a child into existence, then similar considerations would outweigh the impersonal reason to replace an infant such as Christine.

As an aside it is worth noting one consequence of this argument against replacement. Replacement and Substitution decisions overlap in their dependence on impersonal

reasons. One implication of the Insubstantial-Reason argument is that it may also undermine Substitution. Julian Savulescu has argued that there is an obligation on parents to bring to birth, of possible children they could have, the one with the greatest expected wellbeing – the so-called principle of procreative beneficence (Savulescu 2001). On the basis of the preceding arguments, however, there is less reason to *substitute* than there is to conceive a child. The types of reasons that would justify a couple choosing to limit family size or not to have children would also justify a decision to conceive a child with less than the best possible wellbeing. The mother taking teratogenic medication might be able to justify, merely on the basis of personal preference, a decision to conceive a child with moderate impairment rather than waiting and having a subsequent normal child.

### 7.4.2 Potential responses to the Insubstantial-Reason argument

#### *7.4.2.1 A strong moral reason to conceive*

There are a number of possible responses to the Insubstantial-Reason argument. Someone who wished to defend replacement may dispute the third premise in the above argument. They may disagree with the general intuition and suggest that there *is* a strong moral reason to bring a child into the world. If that were the case there would also be a strong moral reason to replace (albeit less strong than the reason to conceive).

Although this is a possible response to the argument, it has some fairly unattractive implications for the morality of population policy, contraception and abortion. One implication is that we may all be obliged to have as many children as we possibly can. It may be wrong for mothers to have an abortion, unless they plan to subsequently become pregnant again (Calef 1992). Many of our decisions about having children would be indefensible. I think that few would be willing to accept these implications.

This objection might be seen as a variation on a frequent criticism of certain moral theories (particularly utilitarianism) that they are too demanding (Williams 1973). It might be argued that there are many moral obligations that conflict with personal projects or commonsense morality, and that this conflict does not in itself render implausible the idea of a strong moral reason to conceive. Nevertheless, the relationship between conception and replacement means that there is *more* impersonal reason to conceive additional children, than there is to replace. There is greater impersonal reason to advocate increased reproduction, and oppose contraception and abortion, than there is to advocate replacement of impaired newborn infants. This, I suspect, few will be keen to embrace.

#### *7.4.2.2 A costs model of bringing individuals into existence*

Alternatively, it could be argued that although bringing someone into existence is in principle a very good thing to do (there is a strong *prima facie* reason to conceive*)* - there are other factors to consider. In an overpopulated world with finite resources, this means that, all-things-considered, there is not a strong moral reason to conceive (Kuhse and Singer

1985, p. 134; Glover 1990, p. 70; Singer 1993, p. 155; Rachels 1998, p. 94). There are a number of costs that are incurred when a child is brought into existence; these include the effects on the interests of parents or other siblings. They might also include the resource and environmental costs of adding to the population. It may be that there are multiple individual-affecting factors that combine to weigh against the impersonal value of bringing someone into existence. But the Insubstantial-Reason argument would still apply; if the all-things-considered moral reason to conceive is not strong, there is an even weaker all-things-considered reason to replace. This is represented graphically in figure 7.2 (and demonstrated formally in Appendix D).

An objection to this argument might be that the costs are not equal in the two cases. There may be greater costs to Christine's family and to society if she lives than would be occasioned by a child with average wellbeing. But unless those costs outweigh the impersonal value of bringing Christine into existence, there will still be greater reasons to conceive than to replace. (In the figure $V_1$ will still be less than $V_2$). In general we do not think that the costs of looking after a child with moderate cerebral palsy or haemophilia, for example, outweigh the value of that child's life. On the other hand, if the costs of keeping the current child alive *do* outweigh the impersonal value there would already be a decisive reason to let that infant die. There would be no need to justify the decision by invoking the wellbeing in another possible child.

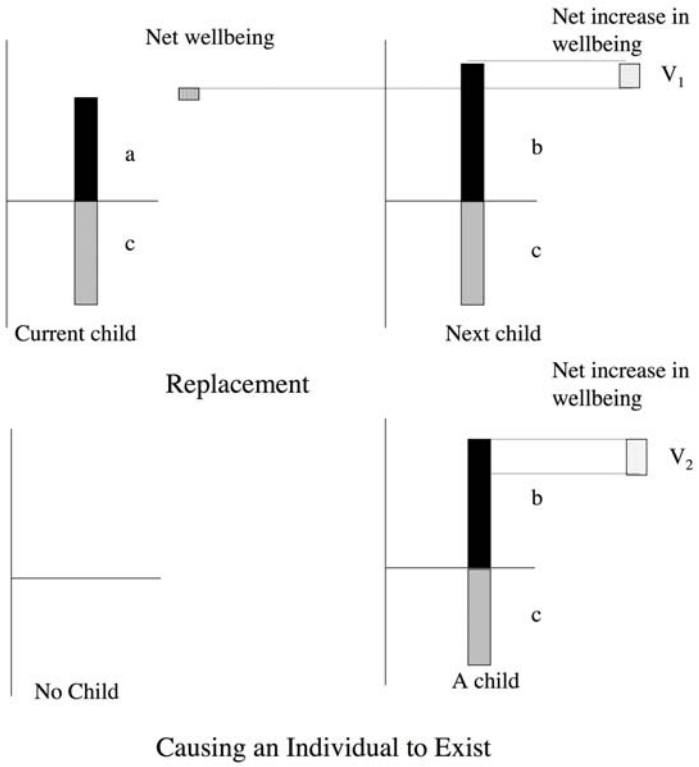


*Figure 7.2: The impersonal reason to replace (costs model)*

*The wellbeing of the current child is represented by 'a', the wellbeing of the next child by 'b', and the costs of bringing a child into the world by 'c'. $V_1$ is the net value of replacement, $V_2$ the net value of Causing an Individual to Exist. From the figure it is clear that $V_1 < V_2$. (I assume that the next child has a life with an average level of wellbeing. We cannot know for sure how good their life will be, but it seems safe to assume that it will be average for the population, or average for the children that a given set of parents could conceive.)*

Some philosophers have argued that coming into existence is always a harm (Benatar 2006, pp. 18-57). Alternatively it might be argued that the costs of bringing even a healthy child into the world outweigh the impersonal value of their existence. If such views were true, then it *would* be better to replace than to conceive a child with average wellbeing (since there would be a net increase in wellbeing with replacement). However, it would be better again not to have any children, or to let the current child die without having another child. There would be more reason to do so to replace them. Thus this view does not provide a compelling argument for replacement in newborn intensive care decisions.

#### *7.4.2.3 Critical level utilitarianism*

An alternative way to reconcile the obligation to conceive with common intuitions is to appeal to a *critical level* for determining whether or not it is good to bring an individual into existence. This is the view that some have adopted (Kavka 1982; Parfit 1984, p. 412; Blackorby et al. 1997; Broome 2004). Would this rescue the argument for replacement?

John Broome, for example, suggests that it is only impersonally good to bring someone into the world if they will have more than a certain minimum level of wellbeing (Broome 2004, pp. 140-9). He thinks that this level (the 'neutral level for existence') is above the level of a life worth continuing (Broome 2004, pp. 255, 259).

The impersonal reason to bring someone into existence on this model is proportional to the difference between the amount of wellbeing in their life and the critical level. Since there may not be a great difference between the level of wellbeing in an average life and the neutral level, there is not a strong reason to conceive. (Singer suggests a view that is similar to a critical level model in his account of the modified moral ledger (Singer 1993, p. 129).)

Although Critical Level Utilitarianism fits with the intuition that there is not a strong obligation to bring individuals into existence it also has some counterintuitive features. Many versions suggest that it is impersonally bad to bring individuals into existence who will have lives of net benefit, lives that are worth living. And it potentially leads to absurd conclusions when applied to large populations (Parfit 1982, p. 415). In any case, this model yields an answer that is identical to the costs model. If the current child has a life that is predicted to be above the critical level, there is a stronger reason to conceive than to replace (see Appendix D).

#### *7.4.2.4 Average utilitarianism*

Yet another way of preserving a form of the common intuition about conception, while still accepting an impersonal reason to substitute or replace could be to adopt a version of

average utilitarianism. On this view, it is not the total amount of wellbeing that matters, but the average level of wellbeing of those in the population. From an impersonal point of view there would be no moral reason to bring a child into existence who would be at or below the average, since this would not lead to greater average utility.

It should be noted, however, that replacement on this view provides no impersonal reason to replace when the person added would be of average wellbeing or lower. In fact, on plausible versions of average utilitarianism that include the wellbeing of all individuals who ever exist, even if the replacement child were predicted to have greater than average wellbeing, replacement would lower average utility. It is sometimes claimed that average utilitarianism would instruct us to kill individuals with less than average wellbeing. If this were the case there would be a decisive reason to allow any impaired newborn to die (replacement would be unnecessary to justify this). But several authors have argued that average views should take into account the wellbeing not just of survivors, but also of all individuals who ever live (McMahan 1981, p. 113). On this view killing an individual lowers average wellbeing since their lifetime wellbeing is lower than it would otherwise have been. Unless a replacement child is predicted to have more than twice the lifetime wellbeing of the current child, replacement would lower average utility. There would be an impersonal reason *not* to replace. On the other hand, average views *would* seem to justify Substitution.

#### *7.4.2.5 Separating replacement and conception*

Following McMahan, I have related the reason to replace to the reason to conceive. I have assumed that the relationship is transitive. Conceiving an impaired child (I) is better (in impersonal terms) than having no child (0), and conceiving a healthy child (H) better than conceiving an impaired child.

H>I>0

Some people would question this. It might be thought that the question of *which* child is conceived could be separated from the question of *whether* to conceive (McMahan 2002, p. 355). Some may believe that it would be better for a healthy child to exist rather than a child like Christine, but deny that this entails a moral obligation to bring children into the world. How would this be justified?

One reason to separate these judgements is on the basis of another distinction drawn by Derek Parfit. In Substitution cases the same number of individuals exist in either option (they are what Parfit refers to as 'Same Number Cases'), while Causing an Individual to Exist involves adding an extra individual (it is a 'Different Number Case'). Different Number Cases raise perplexing questions for population policy that are hard to resolve (Parfit 1984, pp. 381-441). It might be thought that we should use different rules for deciding Same Number and Different Number Cases. Since impersonal reasons yield highly counterintuitive conclusions in Different Number cases perhaps we should only take account of them in Same Number cases?

But there are problems with this line of argument. Replacement is also a Different Number case, so impersonal reasons would potentially not apply to it either. Although the same number of individuals exist after replacement as before, the total number of individuals who ever exist is different.[21] In any case it seems *ad hoc* to apply impersonal considerations in one type of case but not the other. It is in the nature of impersonal reasons that the number of individuals affected does not affect the value of an outcome (McMahan 2002, p. 356). If it is morally important to increase overall wellbeing when that will not benefit any existing or future individual, it does not seem relevant whether that increase occurs by causing an additional individual to exist.

An alternative way of undermining the relationship between conception decisions and replacement or substitution would be to reframe these decisions as permissible or obligatory actions. Comparative permissibility or obligation may not be transitive (Parfit 1982, p. 130). So, for example, an advocate of replacement might argue that it is obligatory to choose to bring into existence a child with average wellbeing rather than a child with below-average wellbeing (Substitution). But they may also hold that is not obligatory to bring a child into existence with average wellbeing rather than have no child at all. However, if they did, it would be necessary to explain *why* it is obligatory to increase wellbeing in one case but not in the other. I have outlined three possible ways in which this could be done (the costs, critical level or average models), but in each case they yield at best a weak reason to replace.

## *7.5 The individual-affecting benefit of replacement*

If the justification of replacement is impersonal, I have argued that it must be related to decisions about conception. Once this relationship is clear, the reason to replace becomes weak and easily outweighed. Although Singer does not raise the possibility, could the reasons in favour of replacement be *individual-affecting* rather than impersonal?

There are two ways in which replacement could be construed as providing a benefit to individuals. Firstly it might be thought that the benefit is to the replacement child. The idea of someone benefiting from being brought into existence is controversial, though it is generally accepted that individuals can be harmed by being brought into existence if they have a life that is not worth living. Derek Parfit, for example, argues that individuals can be benefited from their conception (Parfit 1984, p. 487-490). In this case the idea would be that both the current child and the replacement child benefit from their life - but since there is greater wellbeing in the life of the next child, that child will benefit *more*. Richard Hare seemed to have something like this in mind when he wrote of the next child having a

[21] I am grateful to Jeff McMahan for this point.

greater interest in coming into existence than the current child by virtue of the better life in store (Hare 2006, pp. 331-332).

There are two things to say about this. Firstly, we should note that replacement on this basis would not be consistent with the 'Individual-affecting view' as originally described (Parfit 1984, p. 370), and as many would think of it. There is no existing or future individual who is *worse* off if the current child exists. The replacement child fails to receive a greater benefit if they are not brought into existence – but they are not harmed. (This benefit would, however, be consistent with a modified view described by Parfit as a 'wide total person-affecting principle' (Parfit 1984, p. 396)) Secondly, it seems that if the benefit to the child of their future life *is* a relevant moral consideration in decisions about replacement or substitution, the same sort of benefit would apply to conception decisions. This reason would apply to both types of decisions, and, once again, there would be a stronger reason to conceive a child than to replace.

The second way that replacement could be construed as providing benefit to persons would be for *other* people who exist or who will exist, for example Christine's parents, other siblings, and other members of society. (We could call this an *indirect* individual-affecting reason, since it does not relate to the individual whose existence will be affected by our decision.) We might think that parents' lives, and those of their other children will go better if they have a healthy child rather than one with impairment. And it may be better for others in society who are spared the financial burdens of looking after Christine.

If replacement is justified in this way, indirectly, then the link between replacement decisions and conception breaks down. Although it may be clearly better for parents to have a healthy child rather than a child with impairment, it would not necessarily be better for them to have a healthy child than none at all. When parents conceive a healthy child, we may be unsure whether the effect of this on others will be positive or negative. The lives of parents may go better if they have a child, or they may go worse. Siblings may benefit from companionship, or they may suffer from competition. Others in society may benefit from the contributions of that child in the future, or may have to bear the costs of supporting them (if they are sick, or unemployed for example). On this argument, the benefit of replacement is not related to the benefit of bringing a child into existence.

It is worth noting three points about this type of justification for replacement.

Firstly, the way that utilitarians typically refer to replacement is to suggest that it provides a separate, or additional reason to allow an infant to die. Thus Hare writes

> "…[T]here is the interest of the mother…[t]he other members of the family have a similar interest…[t]hen there are the interests which belong to those outside the family…and lastly there is another interest which is commonly ignored in these discussions, and which is so important that it often, I think, ought to tip the balance…that of the next child in the queue" (Hare 2006, p. 330)

But if the benefit of replacement is understood as actually reflecting the interests of parents, family and society, then in one sense replacement disappears as a separate factor in decisions about letting a newborn infant die. Doctors and parents already think about the interests of the child (however those are construed), the interests of the family, and the interests of others. Replacement is not an *additional* reason, though it may explain how the interests of others would be affected by the death of the infant.

Secondly, we need to recall that, in the absence of replacement, the effect of the current child on the interests of the parents or others (remember that we are thinking about a child with a moderate impairment) was *not* enough to justify letting the child die. So it seems that the *costs* to parents, siblings or to society of caring for a disabled child cannot be the motivator for replacement. Instead it is the relative *increase* in parental wellbeing if the next child is conceived. The reason to replace is not that other people's lives will go particularly badly if the current child lives – rather that they will be better off if the next child is conceived instead.

In addition, there is a widely accepted argument that the costs or benefits to *society* of a child's existence are not factors that should be considered when treatment limitation is being considered (Nuffield Council on Bioethics 2006, pp. 21, 45). This is not to say that potential costs should have no role in decisions about newborn intensive care. Such costs might be relevantly considered by policy-makers (and I have elsewhere discussed the relevance of replacement for these (Wilkinson 2010)). However, the costs of future treatment (or by extension the benefits to society) are not thought to be factors that should have any role in decisions about life-sustaining treatment in *individual* patients in intensive care. So the relevant reason for replacement comes down to the benefit to parents and siblings of having a different child instead of the current newborn.

Thirdly, we might ask whether this prudential benefit provides a sufficient justification for letting a newborn infant die. Some might think that improvements in parents' lives are not the sort of consideration that should be taken into account in such decisions. The question of the potential conflict between moral and prudential reasons is a long-standing and difficult one. Henry Sidgwick regarded it as "the profoundest problem in ethics" (Sidgwick 1999, p. 386, n17). Yet it is enough, perhaps, to note that this type of reason is a different sort of justification than the one traditionally given. Whether it provides a *decisive* reason to let a newborn infant die will depend upon the reasons that we have not to let them die, and how the interests of parents and family should be weighed against these reasons.

## *7.6 Conclusions*

To return to the question that we started with: does replacement justify the withdrawal of LST from newborn infants with mild or moderate impairment?

In this chapter I have set out the Insubstantial-Reason argument against replacement: if replacement is justified in impersonal terms, then the reasons to replace a newborn infant

are weaker than the reasons to bring a child into existence. If we accept that there is a strong moral reason to conceive, there would remain a strong justification for replacement, but this has unpalatable implications. On the other hand if we believe that there is not a strong moral reason to conceive, then there is an even weaker impersonal reason to replace.

Alternatively if the benefit of replacement were understood in individual-affecting terms, the reason to replace would be the increase in wellbeing in other individual's lives (principally parents and other siblings) if a healthy rather than an impaired child lives.

On both of these accounts there may be reasons to replace, even if they are not strong moral reasons, and advocates of replacement may still argue that all-things-considered the newborn infant Christine should be killed or allowed to die. Then we would be led back to the reasons *not* to let the infant die, and the question that I have not addressed in this chapter - that of the moral status of the newborn. If newborns have moral status such that they may be permissibly allowed to die only if there are strong non-prudential reasons to do so, then replacement would not appear justified. On the other hand, if the newborn has *no* moral status, then it does not matter that the justification for replacement is weak - it could still justify letting the newborn die, or killing them.

One interesting point to note is that if the newborn has no moral status, then in fact replacement is redundant. There is no need for another child to be conceived in order to justify letting them die. In that case, why talk about replacement at all? One reason for Singer's argument may be that both doctors and parents have strong nurturing and protective feelings towards newborn infants. Singer argues that our instinctive protective feelings should be set aside; they are understandable from an evolutionary point of view, but irrelevant (Singer 1993, p. 170). But the preferences of parents for the treatment of their newborn, and the grief that will ensue if the newborn dies *are* relevant considerations in a utilitarian account of such decisions. Parents have a strong desire that their children's lives be saved if possible. If we are able to save a newborn infant's life we need a good reason to convince parents that we should instead let her die. If doctors believe that a child's future life will be so full of pain and illness that it would not be worth living, many parents (though not all) will reluctantly agree to withdrawal of life support. If there were a strong impersonal moral reason to replace, it might convince some parents to let their newborn die. But the strongest reason to replace is a prudential one. It would be a question of telling parents that their lives would go better if they let this child die, and had another child instead. I personally suspect that few parents would find this persuasive, though this empirical question could be answered by further research.

The key question then, comes down to the role of parental interests in newborn treatment decisions. I have argued that there is not a strong impersonal reason to replace, and I believe that few parents are likely to be moved by an argument for replacement on the basis of their own interests. It remains possible however, that some parents may feel

strongly that their lives would go better if they had a different child without impairment. Should parents be *permitted* this choice, and allowed to let their newborn infant die? How much weight should be given to the interests of parents? What role should parents have in decisions? These questions will be the focus for the next two chapters.

# CHAPTER 8

## Parental interests and the impaired newborn

### *8.1 Introduction*

> "You can say that the best interest of the child is for them as an individual, irrespective of anybody else's views or wishes. They are an individual, they have legal rights, we should be doing what is right for them. But personally I put the child within the context of their family and what that particular family feels is right for them." F40

In the previous chapter I argued that 'replacement' is best justified, *if* it is justified, in terms of the interests of parents. Whether it is permissible to allow a moderately impaired infant to die, depends crucially on how those parental interests are weighed against the interest of the infant in continuing to live. In this chapter I address that question specifically. Should the interests of parents be taken into account when they conflict with the interests of the infant? In particular, should they be given more weight than they would for an older child?

In most countries there is a legal presumption that parents have a right to make decisions on behalf of their children (Dare 2009). Parental decisions are usually respected, even if they do not promote the best interests of the child, unless they appear to risk a substantial harm to the child (Diekema 2004). This presumption may have some basis in historical ideas of the child as the property of their parents (Fost 1981; Kipnis and Williamson 1984; Downie and Randall 1997). Contemporary writers have defended it on the basis of the value of parenting and the importance of preserving intimate family relationships (Schoeman 1985; Downie and Randall 1997). However it is justified, parents are given discretion for a wide range of decisions, including decisions about housing, education and basic health care. For example, it would often unquestionably be in the best interests of the child if parents were to purchase private education or private health insurance for the child. But parents are permitted to take into account the impact on themselves and on other family members of such decisions and to elect not to provide these significant benefits. More controversially, parents are usually permitted to make medical decisions that potentially impose some risk on their children, for example electing not to have routine childhood immunisations (Dawson 2005). But when it comes to decisions about life-sustaining treatment there is far less weight given to the views and interests of parents (Paris and Schreiber 1996). As noted in chapter 2, existing guidelines suggest that for

children and incompetent adults, the best interests of the patient are paramount. The interests of parents and family members are not considered at all.

On the other hand, various authors have defended the idea that the interests of family should be given some weight in treatment decisions in newborns.

> "The Working Party is clear that parents have interests and that it is reasonable for these interests to be given some weight in any relevant deliberations about critical care decisions for a child who is, or who will become, severely ill." (Nuffield Council on Bioethics 2006, p. 17)

> "In the best neonatal intensive care units today, clinicians and parents, … work collaboratively in an effort to promote and protect the infant's interests while taking reasonable account of the parents' wishes and interests." (Fost 1999)

Furthermore, as noted by the quote at the start of the chapter, it seems that in practice clinicians *do* think about the interests of parents (see also McHaffie (1996, pp. 67, 73, 87)). But why should this be the case for infants and not older children or adults?

I start by setting out a brief definition of interests. I then highlight the potential overlap between the interests of the child and parents. These interests are not completely discrete; parents' interests may be relevant partly through their effect on the interests of the child. Next, I argue that in some situations the interests of parents outweigh those of the infant. I outline the nature of the interests at stake. Parents vary in the strength of the interest that they may have in the infant not surviving. This is likely, however, to be related to the severity of the child's impairment. I suggest that an infant's interest in continued existence also varies. It is proportional to the amount of wellbeing in their future, yet at the same time, their interest is less than that of older children or adults. I argue that in the face of severe predicted impairment parental interests may outweigh the interests of the infant. In the concluding section I discuss two objections to this claim. Taking parental interests into account would not lead to treatment withdrawal from infants with minor impairments; the possibility of adoption provides a limit to the role of parental interests in decisions about LST. Secondly, this view does not have unacceptable implications for termination of pregnancy decisions.

This chapter touches on difficult and contentious questions relating to value theory and the moral status of newborn infants. I do not aim here to develop or defend a full account of newborn moral status. My aim is more limited, to render plausible the idea that the interests of parents should be given *some* weight in decisions about LST for newborns, at least in some cases. The conclusions, about the relevance of parental interests, and the difference between infants and older children will form key parts of the framework for decisions that I will develop in chapter 9.

## *8.2 Definitions/assumptions*

Before going any further it will useful to be clear about what I mean by interests.

> **Interest**: P has an interest in X if they stand to gain or lose by the nature or condition of X (Feinberg 1984, pp. 33-4)

Put even more simply, we have an interest in something when we can be benefited or harmed by it. Crucially then, what counts as being in an individual's interest depends on what we understand as benefiting them. It is intimately related to theories of axiology or prudential value (DeGrazia 1995; Veatch 1995). There are various axiological theories, and these are often divided into those that place emphasis on the presence/absence of pleasure and pain (mental-state theories), on preference or desire satisfaction (preference-based theories), or on the presence or absence of objectively valuable components of flourishing (objective list theories) (Parfit 1984, pp. 493-502; Griffin 1986, pp. 7-74; DeGrazia 1995). Detailed discussion of these theories is beyond the scope of this thesis. Much of the following discussion will be relevant whichever view is held (though potentially in different ways, as I will highlight). Nevertheless, I should perhaps state that the view that I hold (and take to be most plausible) is a hybrid containing both subjective and objective elements such that positive experience and preference satisfaction are sufficient, but not sole conditions for prudential value (Parfit 1984, pp. 501-2; Brock 1993, p. 98).

In this chapter I talk largely about parents. The other group potentially negatively influenced by the child's survival are existing siblings in the care of the parents. For simplicity I will not discuss siblings separately, but the principles are likely to be similar.

I discuss the potential interest of the child in withdrawal of life support. This raises the question of whether it is coherent to think that an individual can be benefited or harmed by death since if they die they will cease to exist. I assume in what follows that an individual *can* be benefited or harmed by their death. (For a thorough discussion and defence of this claim see McMahan (1988).)

Finally, I will focus in this chapter on the *interests* of parents. An alternative way of justifying parental discretion in treatment decisions would be on the basis of parents' *right* to make such decisions. In the next chapter I briefly discuss the arguments in favour of parental discretion on the basis of the rights or duties of parents and the concept of supererogation.

## *8.3 The argument from overlapping interests*

How are the interests of parents and the interests of the infant related? The first thing to note is that although these interests may conflict they will often coincide. The most common situation in intensive care is that of an infant whose life will be worth living, and whose parents have a strong interest in the infant's survival. In such cases, obviously, there is no conflict and no difficulty (A, Table 8.1). Nor is there any problem when both the interests of the infant and the interests of parents lie in withdrawal of life support (D). These interests may also come apart, however, either when the infant has an interest in continued life, but the parents have an interest in withdrawal of the infant's life support (B)

(case PM), or when the opposite is true (C) (Case IM). In this chapter I will focus on type B conflicts, albeit the principles are similar for type C conflicts.

| | |
|---|---|
| **A – Life/life agreement**<br>Infant – interest in continuing life<br>Parents – interest in infant continuing to live | **B – Life/Death conflict**<br>Infant – interest in continuing life<br>Parents – interest in life support withdrawal |
| **C – Death/Life conflict**<br>Infant – interest in life support withdrawal<br>Parents – interest in infant continuing to live | **D – Death/Death agreement**<br>Infant - interest in life support withdrawal<br>Parents – interest in life support withdrawal |

*Table 8.1: The relationship between interests of parents and the interests of the infant*

> **Case of PM (Type B conflict):** PM had severe HIE in the newborn period. Her parents were informed that she was likely to be severely intellectually and physically disabled if she survived, as well as blind and deaf. Together with doctors, her parents reached a decision to withdraw mechanical ventilation. PM continued to breathe off the ventilator, and doctors raised with parents the possibility of withdrawing artificial feeding. Her parents consented to this, but shortly afterwards the hospital ethics committee ruled that feeding and other necessary treatments should be continued.
>
> At 16 months of age PM's parents brought a lawsuit against the hospital claiming that the ethics committee unlawfully interfered with their decision, and seeking support for PM's ongoing medical care. At that age she appeared to have very severe motor impairment (she could not roll or lift her head). The severity of any cognitive impairment was not clear from media reports. (Canadian television 2010; Canadian television company 2010; The Current 2010)
>
> **Case of IM (Type C conflict):** IM also had severe HIE in the newborn period. The case reached media attention after his parents sought a court injunction to prevent doctors from withdrawing mechanical ventilation. At that point he was 3 months old, and had required mechanical ventilation since birth. He was believed to have sustained very severe brain injury. The doctors believed that he had no chance of recovering "meaningful function". His parents were determined that his life, even if impaired, was worth fighting for.
>
> The courts granted the parents a chance to obtain a second medical opinion. His parents subsequently agreed to withdrawal of life support after this doctor confirmed IM's prognosis. (Bailey and Amann 2010; Castagna 2010; Priest 2010).

In both of the above cases there is a potential conflict between the desires (and interests) of parents and the interests of the child. In the case of PM it appeared that her interest may have lain in continued treatment, though her parents desired that life sustaining treatment be withheld. (Interestingly, at 16 months of age her parents appeared to believe that her life, despite significant impairment, was worth living). In the case of IM, the doctors believed that withdrawal of LST was in his best interests, while his parents desired that treatment continue.

The above classification assumes that it is possible to separate the interests of parents and the interests of the child. There are also, however, a number of ways in which the interests of infants and of parents intertwine (Duff 1981; Diekema and Fost 2010).

### 8.3.1 Determinative

Firstly, the interests of parents may, in some cases, influence or *determine* whether or not the infant has an interest in continuing life. For example, some parents of very severely impaired infants and children devote enormous amounts of time, energy and financial resources into the care of those children (see for example Wyn (2007)). They are able to enrich the lives of such children and help them experience benefits despite enormous challenges. Though it might be anticipated that for a child with such severe impairment LST would not be in their best interests, the strength of their parents' interest in the child surviving makes the difference for the child between a life that is worth living, and one that is not.

Conversely, some parents with limited financial and personal resources, perhaps with other existing children, may be unable to devote sufficient attention to a child with severe impairment. They do not neglect the child, but nor are they able to care for them optimally. The benefits of life for that child may be outweighed by burdens, though in other environments they would have had a LWL.

### 8.3.2 Evaluative

Secondly, there is the possibility that the values of parents will influence how we *evaluate* the interests of an infant. I referred above to different theories of prudential value, and the lack of consensus about which theory should be adopted. Given such disagreement it is difficult to know how to weigh up different values or preferences. We cannot be guided by the infant's own values, but nor is there a value neutral perspective that can yield an answer. One option would be to adopt the parents' values (or at least to give them greater weight in deliberation). We might do this because it respects the point of view of parents (and avoids privileging the perspective of the doctor). But we might also do so because the values that the child will or would adopt (if they survive) are likely to be influenced by those of their parents. They will not *necessarily* share the values of their parents, but this is at least somewhat more likely than not. Consider, for example, the infant Amelia described in Chapter 6 p87) with very severe predicted physical impairment and mild cognitive impairment. If her parents have a strong attitude of optimism, and a determination to overcome physical adversity we might anticipate that this will influence whether or not Amelia has a LWL (see point 8.3.1 above). But it also seems plausible that this will influence her attitude towards her own condition, and make it more likely that she, too, will have this sort of outlook. It would potentially influence her future judgement about whether her condition is tolerable.

### 8.3.3 Interdependent

Third, in many families at least, there is a sense in which the interests of child and parent are interdependent. The parent has an interest in promoting the child's interests, and the child has an interest in promoting those of their parents. An infant may, therefore, have an

interest in a decision that is consistent with their parents' wishes. There are two ways of justifying this. We might point to the future desires of the child. It is reasonable to think that a child will have, or would have (if capable of forming it) a desire that their loved ones are happy. Alternatively, if a rational preference or objective value theory is adopted, the child could have such an interest now even if they are never capable of actually desiring it.

Imagine, for example, that we believe that IM had a life in which the burdens just outweigh the benefits, yet are aware that his parents had a strong desire (and interest) in his continued life. IM's interest in his parents' wellbeing (however that is conceived) might have tipped the balance for him in favour of continued life. It is difficult to know how strong the interdependent interests of a child are, and whether they could outweigh the harm of ongoing existence. But in another context, we could imagine a patient with a sufficiently severe and debilitating illness that they are led to contemplate ending their life. Yet they determine not to do so for the sake of a partner or other family member who would be devastated if they died.

### 8.3.4 Epistemic

Finally, there is a sense in which parents are in an epistemically privileged position to *assess* the interests of the child (Diekema 2004). This perhaps makes most sense for older children, where parents are usually going to be in the best position to know the child's preferences, desires, dislikes and ability to tolerate physical suffering. But it could have some relevance to infants. In the case of MB (discussed in chapter 2, p25), the judge placed significant emphasis on the evidence of parents about the experience of the paralysed infant, and the degree that MB was aware of, and able to appreciate, his environment (An NHS Trust v MB 2006a, para 16). The parents had spent large periods of time at his bedside and had done so since birth. As a result they were perhaps in a better position than medical or nursing staff who would have cared for multiple different patients over the same period. There is also the possibility that parents are better able to anticipate the future environment for the child and their own ability to care for him or her. On the other hand, the parents' lens may be distorted by their need to maintain hope (Day 2009), or by their consideration of their own wellbeing and interests (Dare 2009), and consequently their assessment may be inaccurate.

The above four factors make it hard to separate out the interests of parents and the interests of the infant. In practice, when there is conflict, even if it *appears* that the interests of parents and the interests of the infant are opposed, it is almost always claimed by parents that they are representing the interests of the child. Thus, for example, parents who wish to continue treatment against the advice of doctors usually claim that it is in their child's interest to continue to live (see for example IM above). Parents who wish to discontinue treatment despite the belief of doctors that it should be provided usually claim that such treatment is not in their child's interest eg (Kopelman and Kopelman 2007). The

second and fourth reasons listed above provide some reason to give extra credence to the assessment or value judgement that parents have made. The first and third factors may serve to bring the infant's interests closer to the parents' and resolve the conflict.

The relevance of these intersecting interests for the question posed at the start of the chapter is that it is reasonable to give some weight to parental interests in part because they may *influence* the interests of the infant. They are relevant to an assessment of whether, for the sake of the infant, treatment should continue. There are also some reasons why the argument from overlapping interests is stronger for infants than for older children. The determinative and evaluative components of this argument may be more relevant to infants because their own values are yet to develop, and because they are likely to have a longer period of dependency on the care of parents. On the other hand, the interdependent/epistemic reasons for overlapping interests do not appear any stronger in infants than older children.

Some authors have argued against parental discretion in decisions about children and newborns. They point out that parents may *not* be in the best position to assess the child's future interests (Fost 1981; Dare 2009). They may be mistaken about the effect of impairment on the child's life and on their own ability to care for the child (Fost 1981). Their own conflicting interests (to be discussed shortly) mean that they cannot be impartial judges of the child's best interest (Fost 1981; Fost 1986). These reservations are valuable, and should be taken into account. Sometimes parental interests will not overlap with the child's in the ways that I have described. But these arguments do not mean that parental interests can *never* or should never influence our assessment of the interests of the child. At least in some situations, as argued above, I believe that they can and should.

One possibility that I am not able to fully explore here is that the above factors provide *asymmetrical* support for parental interests. They may provide greater support for parental views in type C conflicts (where parents interests are in favour of continuing treatment) than for type B conflicts (where parents have an interest in withdrawing treatment). For example, if parents are unable to devote the time and energy to make an infant's life worth living, the infant could be cared for by a different set of parents. It is also unclear whether to take into account the degree that a child would share the values of her parents, or would have an interest in the wellbeing of her family – if the only way to respect those values or interests is for the infant to die.

The force of the argument from overlapping interests relates largely to cases where infants have lives that are close to the level of a LWL. It would not justify giving weight to parental views where an infant clearly had a LWL or where it was clearly contrary to the infant's best interests to continue treatment.

## *8.4 The argument from the weight of interests*

Having noted that the interests of parents and child are not completely discrete, I will temporarily set that aside to consider whether, if there is a genuine conflict between interests, weight should be given to those of parents. I will assess separately the strength of the interests at stake in type B conflicts.

### 8.4.1 The interests of parents

There are two potential ways in which the infant may affect the interests of parents. There are the parents' desires or preferences about the infant and her treatment. Then there is the effect of the infant's survival or non-survival on parents' other interests including their personal relationships, finances, career, recreational and life plans.

Parents' lives are not necessarily worse if an infant survives with severe impairment. Some parents eloquently describe the ways in which their personal life, and those of other members of their family are enriched by the experience of caring for an impaired child (for example see (Wyn 2007)). On the other hand, other parents describe substantial negative consequences of the illness or impairment of their child (see for example (Brinchmann 1999; Hollander 2008)). There are well-documented potential costs for families. Having a child with a serious illness or impairment increases the incidence of parents divorcing or living apart, (by 10-20 percentage points) (Corman and Kaestner 1992; Reichman et al. 2004) and is associated with higher rates of psychological and physical ill health (Thyen et al. 1999; Raina et al. 2005; Murphy et al. 2007; Harrison 2008; Reichman et al. 2008). Primary caregivers are at significant risk of clinical depression and abnormally low subjective quality of life (Cummins 2001; Olsson and Hwang 2001). (Half of mothers of children with intellectual disability or autism had elevated depression scores in one study (Olsson and Hwang 2001)). Care needs of children with severe impairments do not diminish with age, and mothers are frequently unable to work outside the home with negative effects on family income (Thyen et al. 1999; Curran et al. 2001). In one study, out-of-pocket expenses for severely impaired children consumed more than 10% of family income (Leonard et al. 1992). In another more recent study, ¾ of mothers were unable to return to paid employment because of the needs of their impaired children (Curran et al. 2001). The financial demands of caring for a child with impairment are estimated to be more than three times the cost of bringing up a non-impaired child (Curran et al. 2001).

The relationship between the desires of parents and their interests may be complex. For example parents' lives may predictably go worse overall if they have to care for a surviving child, and yet parents may have a very strong desire that the child does survive. It may often be the case that parents have interests both in the survival of the infant *and* in withdrawal of LST. It is not clear how such competing interests should be weighed against each other.

Given all this variation it is somewhat difficult to generalise about the strength of the interest that parents have in withdrawal of life support. But two points appear reasonably

plausible. Some parents will have a strong interest in LST not being continued for their newborn infant. Secondly, the strength of this interest is likely to be proportional to the severity of the child's impairment. This is because the greater the severity of impairment, the greater the demand that a child's care is likely to place on caregivers. (This is a necessary corollary of the way in which severity of impairment is related to function and functional independence see Chapter 1 p5). Higher caregiving demands in turn, are associated with lower physical and psychological wellbeing in caregivers and greater financial cost to families (Leonard et al. 1992; Raina et al. 2005). Furthermore, the greater the severity of impairment, the less the benefit of life for the child, and the less strong the parents' desire for the child's survival may be.

### 8.4.2 The interests of the infant

In my description of type B conflicts I have specified that the infant has an interest in continued life. But what is the nature and the strength of this interest? It is generally thought that an individual's interest in continuing to live is one of the strongest interests that they hold. At least for adults and children it is usually believed that the lesser interests of others cannot outweigh their interest in continued life. No weight is usually given to the interests of other family members in decisions about life sustaining treatment in paediatric intensive care or adult intensive care (Janvier et al. 2007). If the interest of the newborn in their future life were of this nature it would seem to preclude any weighing of parents' interests against those of the infant. I will consider (and reject) two opposing suggestions.

#### *8.4.2.1 No interest?*

Peter Singer has controversially argued that infants have *no* interest in continued existence (Singer 1993, pp. 97-8). Singer's argument is based on three claims. Firstly, he holds a preference-satisfaction view of the good, on which basis it is necessary for individuals to have a desire for something for it to be in their interest (ibid. p. 13, 94). Secondly, he claims that infants lack self-consciousness, and consequently lack an interest in continued existence (ibid. p. 169). Thirdly, he makes a claim about personal identity: that infants are not identical with the adult they subsequently develop into (ibid. p. 97-8).

In making his third claim, Singer writes "I am not the infant from whom I developed" (ibid. p. 97), and "When I think of myself as the person I now am, I realize that I did not come into existence until some time after my birth" (Kuhse and Singer 1985, p. 133). The implication is that the toddler or young child who develops self-conscious is a different individual from that toddler at a slightly younger age. (Singer is vague about the onset of morally relevant self-consciousness, but suggests that it may occur as late as 2 or 3 years of age (Singer 1993, p. 171)). This claim is highly counterintuitive, but it also risks non-coherence (McMahan 2002, p. 349; Kaposy 2007, pp. 309-312). As pointed out by Jeff McMahan, self-consciousness is typically thought to require higher order awareness of ongoing conscious experience. But if identity only begins when that individual develops the

higher order awareness, then the lower order conscious experience that they are starting to appreciate must belong to a different individual (McMahan 2002, p. 350). There are also reasons to think that there is *some* psychological continuity between the newborn and later fully self-conscious individual. Although few children or adults have any memory of early infancy (Hayne 2004), there are psychological ripples of unremembered events. For example, six-month old infants who had been circumcised in the newborn period had a stronger pain response to routine vaccination at 6 months of age; this was attenuated by providing local anaesthesia for the procedure (Taddio et al. 1995). Two year-old children have been demonstrated to retain non-verbal memories from events or training at 6 months of age (Hartshorn 2003; Bornstein et al. 2004).

There are also reasons to cast doubt upon Singer's second claim, that infants lack self-consciousness. Newborn infants distinguish tape-recordings of their own cry from that of other infants (Martin and Clark 1982); in one study they stopped crying on hearing their own voice, while they continued to cry on hearing a recording of another infant. In other studies infants, as early as an hour after birth, have been shown to imitate adult facial gestures (Meltzoff and Moore 1977; Meltzoff and Moore 1983). Imitating behaviour appears to be non-reflexive, involves memory, and improves over time (Meltzoff and Moore 1994). These experiments, and others, suggest that infants have a degree of proprioceptive (ie non-visual) awareness of their own face (Gallagher 1996). They appear to have a form of primitive, non-conceptual self-consciousness (Bermudez 2001; Lagercrantz and Changeux 2009).

Still, even if newborn infants have some degree of self-consciousness, they do not appear to possess a desire or preference for continued life. If Singer's first claim were true they would still potentially lack an interest in living; they would not be harmed by their death, nor would they benefit from life-saving treatment in the newborn period. There is, however, a coherent and plausible sense in which a newborn who has a life worth living is benefited by having their life saved in infancy. If we compare two scenarios, A1, where a newborn dies shortly after birth, and A2, where they live to adulthood (and have a LWL), it is clear that there is greater wellbeing in A2 than in A1. If the newborn shares identity with their older self, they would benefit from experiencing the wellbeing in A2, and correspondingly they have an interest in not dying in the newborn period (McMahan 2002, p. 352). (In terms of the concepts used in the previous chapter there is an individual-affecting reason to save the life of the newborn). This interest in future wellbeing would be consistent with mental-state theories of wellbeing, and is likely to be consistent with most objective-list theories. It would also be consistent with some versions of desire-based theories, those that admit informed desires or rational desires (Boonin 2002, p. 84).

The above arguments provide reasons to reject Singer's claim; infants do have an interest in continuing to live as long as that future life would contain more intrinsically positive than negative experiences (ie they would have a LWL) (Kaposy 2007). But how strong is that

interest? The most widely held view is that newborn infants have a strong and overriding interest in continued life, equivalent to that of older children and adults (Kaposy 2007).

#### *8.4.2.2 Strong and overriding interest?*

Most people, I suspect, have instinctively strong protective feelings towards newborn infants. Enormous efforts are made to save the lives of infants who are critically ill after birth. Parents and family members are usually devastated by the death of a newborn. It is believed to be a tragedy when this occurs – both for the parents and for the infant.

In the previous section I argued that death is a harm to such infants because it deprives them of future wellbeing. But given that a newborn is typically deprived of significantly more years of wellbeing than a child or an adult, this loss appears *greater* for a newborn than for the child or adult who dies. This conflicts, however, with other widely held intuitions.

A simple case may illustrate the point:

> A 6 year-old child with a severe cardiomyopathy is awaiting a heart transplant. She has had multiple admissions to hospital, and is becoming more unwell each time. It is feared that if she has to wait much longer she will either become ineligible to receive a transplant (because she will be too unwell), or will die. At the same hospital, a newborn infant is born with a rare congenital form of the same illness. He is critically ill and is put on a heart bypass machine. If he does not receive an urgent heart transplant he too will die.
>
> A heart becomes available that would suit either the older child or the infant. With transplantation the child and infant would have equal chances of surviving to early adulthood at least. Who should receive the transplant organ? (Whoever does not receive the heart is likely to die.)

The usual response to this dilemma is to refuse to choose between the children. But if forced to make a choice like this, the vast majority of respondents choose the 6 year-old (Ross 2007). In a more systematic survey, when doctors and non-doctors were asked to make hypothetical resuscitation decisions for a series of children and adults of varying ages, greater priority was consistently given to resuscitating an older child than to resuscitate a newborn, even when the older child's prognosis was poorer (Janvier et al. 2008a; Janvier et al. 2008b).

Even if such intuitions are widespread, it does not follow from this that newborns *should* be treated differently than other children. Our intuitions may be unjustified or unreliable. The authors of that survey suggested that there is a bias against newborns, and premature infants in particular, and that such attitudes might have anthropological and evolutionary roots in the high neonatal mortality rates present throughout most of human history (Janvier et al. 2007; Janvier et al. 2008a). Others have suggested that the difference lies in the older child's lived experience, and the potentially greater grief for her parents (Ross 2007).

#### *8.4.2.3 A reduced interest*

However, one plausible way of explaining this intuition is that death is a greater harm for the 6 year-old than for the newborn. Death is bad for us because it deprives us of future wellbeing. The better and longer our life would have been, the greater the harm it is to us to die. But death is also bad for us because it cuts short our desires, plans and hopes for that future and severs the relationships that we have developed with those around us. The more of these that we have developed, the greater our psychological connection with that future and the greater the harm it is for us to die. In *The Ethics of Killing* Jeff McMahan argues that the combination of these two elements helps to explain many of our intuitions about death (McMahan 2002). Thus, it is worse for a 20 year-old to die than a 40 year-old (because the 20 year-old would be deprived of more life). But it is also worse for a 6 year-old to die than a newborn or a fetus, because of the older child's greater awareness of herself, and psychological links with her future. The interest of a newborn in his future is less than that of an older child, while greater than that of a fetus.

The above argument does not establish just how strong the interest of a newborn is in their future. The difference between newborns and children might be sufficiently small that it only makes a difference in exceptional treatment dilemmas like the one described above. Alternatively, it might mean that treatment decisions for newborns are completely different from those in older children. I do not propose to settle that question here (though the next section provides a separate argument against the latter possibility). It raises difficult questions about the relationship between different elements of interests, the weighing of different types of interests, and whether there can be degrees of moral status (DeGrazia 2008), questions that are beyond the scope of this thesis. Nevertheless, the argument above provides support for the idea that decisions in newborns are not identical to decisions in older children.

The other point to note is that infants will vary in the strength of their interest depending on the amount of wellbeing in their future life. In chapter 6 I described some of the challenges in determining the interests of an impaired infant. But while it is difficult to know when the burdens outweigh benefits in an infant's life, it was clear from that analysis that impairment can affect the interests of the infant. Severe physical impairment is likely to increase the intrinsically negative features of future life for the infant. Severe cognitive impairment reduces the benefits of life. Both may thus reduce the strength of the newborn's interest in their future. Infants who are predicted to have such impairments have a relatively weak interest in their future life.

To sum up, I have argued that a newborn has an interest in their future, but that it is not as strong as it would be if they were older. We should give greater weight to the interests of parents in deliberations than we would for decisions about LST in older children. For infants with predicted severe impairment, their interest in continuing life support is relatively weak, while the parents' interest in not keeping the infant alive may be strong.

### 8.4.3 Objections

There are two potential objections to this conclusion.

#### *8.4.3.1 Unlimited treatment withdrawal*

The first objection is that allowing parents' interests to be taken into account in such decisions would amount to parents being given free rein in decisions about life-sustaining treatment. It would potentially lead to withdrawal of LST from infants with only mild degrees of impairment, or on the basis of relatively trivial reasons.

There are several reasons, however, why this would not follow. The first is simply that the overwhelming majority of parents have a strong desire that their infants live – even if they will be impaired. In my experience, and in the experience of the neonatologists interviewed in chapter three, it is very rare for parents to want to withdraw LST in situations when doctors believe that survival without severe impairment is probable. It is not likely that allowing parental interests to be considered would lead to withdrawal of LST from a large number of mildly impaired infants. But secondly, and more significantly, the relative balance of interests is potentially quite different for an infant with mild or moderate impairment (Figure 8.1). As noted above, the strength of parents' potential interest in withdrawal of treatment is likely to be proportional to the severity of impairment. The impact on parents' lives is likely to be much less for an infant with mild or moderate impairment than for a more severely affected infant. What is more, for infants with mild or moderate impairments the strength of their own interest in future life may not be substantially less than unimpaired infants.

The other reason that the above arguments would not lead to withdrawal of life-sustaining treatment from mildly impaired infants is that for such infants there is the alternative of adoption or foster care. For infants who will have a LWL, adoption would respect the interests of parents to a similar degree as allowing the infant to die. (It would not be identical, since parents may feel guilty about giving the child up for adoption or worry about their ongoing care). But adoption would also be consistent with the infant's interest in future wellbeing. In terms of the interests at stake (and, impersonally, on the basis of arguments discussed in the previous chapter) it would be better to adopt the infant than to allow them to die.

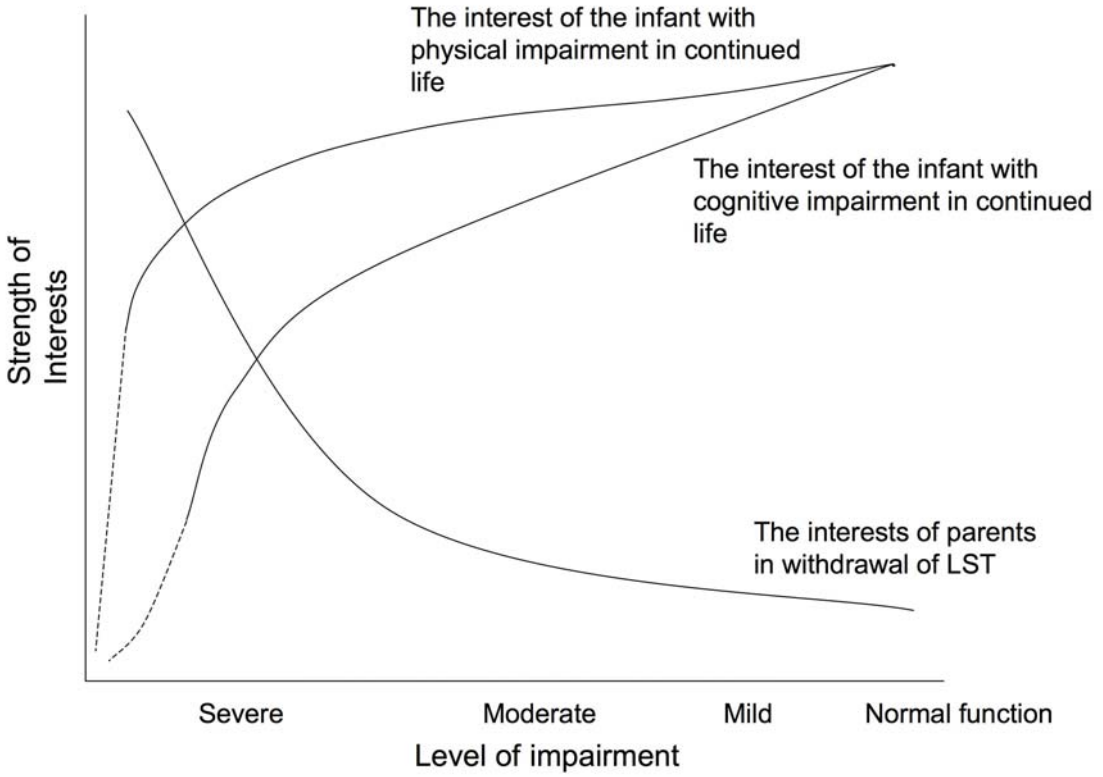


*Figure 8.1: The conflicting interests at stake in Type B conflicts*

On the other hand, adoption would not as easily resolve the conflict in interests for infants with predicted severe impairment. Permanent adoptive parents or foster placements are significantly harder to find for children with severe impairment than for unimpaired or less impaired children (Bain 1998; Local Government Association 2001). The impact on adoptive families is also likely to be just as great as that noted above for birth families. Children who are unable to be placed and end up in institutional care, or those who have a succession of temporary foster placements may experience additional emotional trauma. There is a risk that as a consequence such children are harmed by ongoing life. (I will return to the significance of this risk for decisions in the next chapter). Finally, the supportive care of such children is very expensive, for example costing in excess of 50,000 Australian dollars per year to support a high needs individual in a small group home (Bain 1998).

#### *8.4.3.2 Unacceptable implications for termination of pregnancy decisions*

A parallel (though quite different) objection to the arguments above is that they would potentially have serious implications for pre-natal decision-making. If a newborn infant has a relatively strong interest in their future because of the wellbeing that they have at stake if they die, then correspondingly so would a fetus. It is difficult to know how much wellbeing a fetus experiences in utero, but they would potentially have somewhat *greater* future wellbeing than a term newborn. I argued that a term newborn infant has a primitive degree

of self-conscious and some psychological connections with their future. But so too might a near-term fetus in utero. If parents' interests are to be given only limited weight in newborn decision-making, then perhaps this should also apply to decisions about termination of pregnancy. This might have major implications for the morality of abortion.

There are three responses to this objection, however. Firstly, there are relevant differences between the fetus and newborn that would potentially warrant different treatment. There is an explosive phase of synaptic development in late gestation and especially in the period immediately following birth as the newborn responds to their environment (Bourgeois 2001). The infant rapidly adapts to her changing environment and starts to develop reciprocal relationships with those around her. Furthermore, some have argued that the primitive self-consciousness evident in newborns cannot be present in utero because of the lack of interaction that is required to manifest phenomena such as the imitative features described above (Bermudez 1996). Consequently there may be a significant difference in moral status between the near-term fetus and the ex-utero newborn, even though they are neurophysiologically similar. Although Bermudez's argument about near-term fetuses may be challenged (Gallagher 1996), there is no doubt that there are substantial differences in neurodevelopment between *early* fetuses and newborn infants. Prior to 20 weeks gestation there are no cortical synapses in the fetus and no apparent capacity for consciousness (McMahan 2002, p. 267). This would justify the significant difference in treatment between first trimester fetuses and newborn infants that is present in most societies.

Secondly, there are differences in the interests at stake when the fetus is in utero, compared to the ex-utero newborn. As famously argued by Judith Jarvis Thomson, even if the fetus has an interest in their future (or a right to life) as strong as that of an adult, there may be reasons to permit a mother to have an abortion (Thomson 1971). It is beyond the scope of this chapter to outline Thomson's argument in detail or the many responses to it. Nevertheless, the adoption alternative discussed in the previous section makes the situation for a newborn significantly different. We might require parents who do not wish to care for an infant with moderate or mild impairment to give the child up for adoption. This would not problematically conflict with the rights of parents in the way that prohibiting abortion would.

Thirdly, although I have not yet set out what the implications of my arguments would be for decision-making in newborn intensive care, the view that I will set out in the next chapter defends a process for newborns that is not radically different from that currently applied to late-term fetuses, at least in some jurisdictions.[22] In the United Kingdom, for

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[22] Abortion is permitted in the third trimester in the setting of severe abnormalities or disorders in Albania, Belgium, Bulgaria, Cyprus, Czech Republic, France, Germany, Iceland, Israel, Italy, Luxembourg, Macedonia (FYR), the Netherlands, Norway, Russia, Slovak Republic, Switzerland, Turkey, United Kingdom (International Planned Parenthood Federation 2008).

example, abortion is permitted in the later stages of pregnancy only if there is substantial risk of serious handicap, or if there is a grave risk to the life or health of the mother (Nuffield Council on Bioethics 2006, p. 55). The above arguments might have implications for abortion in jurisdictions that are more restrictive about third trimester abortion.

## *8.5 Conclusions*

In this chapter I have argued that some weight should be given to the interests of parents in newborn treatment decisions. One reason for doing so is that in such cases the interests of parents and the interests of the child overlap in ways that make it hard to separate them. Although it may appear that their interests are conflicting they may in fact coincide. We should give some weight in our deliberation to the parents' *assessment* of what would be best for the child. What is more, parents' interests may *influence* the interests of the child, and cause the two to converge. The argument from overlapping interests is somewhat stronger for infants, but would also potentially apply to older children.

The second reason to give some weight to the interests of parents in decisions for newborns is because a newborn's interest in their future wellbeing is relatively reduced by their developmental immaturity. This means that, compared to older children, it is more easily outweighed by other considerations. It is difficult to know how to balance different competing interests. I have argued, however, that it is most likely that the interests of parents would outweigh those of the infant where a newborn is predicted to have severe impairment. The infant has a relatively weak interest in future wellbeing because of their immaturity and because of the reduced wellbeing in their future. In contrast the impact on parents and siblings may be substantial. They potentially have a strong interest in LST not continuing.

At the same time, the possibility of adoption provides a limit to the freedom of parents to opt for withdrawal of treatment in the face of lesser degrees of impairment. It means that replacement of newborn infants with mild or moderate impairment would not be permitted.

Taking parents' interests into account does not mean that they are given precedence, nor that they will be decisive. Where their decisions would pose a "significant risk of substantial harm" (Diekema 2004), they may be overruled. It means, however, that as in other decisions, parents are acknowledged to have a key role in important decisions about their children. But what are the implications of this argument for treatment decisions in newborn intensive care? How might it be put into practice? What would the implications be for cases like those of IM and PM discussed at the start of the chapter? That is where we will turn next.

# CHAPTER 9

## The Threshold view: a new model for decision-making

### *9.1 Introduction*

In the previous chapter I argued that there are several reasons to give parents a role in decision-making about newborn infants. As noted in chapter 2, however, existing guidelines offer conflicting advice about the role of parents. On the one hand there is general support for parents' role in decisions. On the other hand, guidelines state that decisions may only be made in the best interests of the child. There is support for the idea that parents should make decisions about treatment where there is uncertainty, but in other places guidelines suggest that treatment may only be withdrawn in the face of a very high degree of certainty about prognosis. Similar problems were apparent from interviewing clinicians in chapter 3.

The difficulty in reconciling apparently contradictory judgements is also evident in the following pair of cases.

> **Case:** Henry is a term infant with severe HIE. At 72 hours of age Henry remains dependent on a breathing machine, but his condition has stabilised. It appears likely that he will survive if intensive care is continued. Henry undergoes magnetic resonance imaging of his brain. The MRI reveals abnormal signal in the basal ganglia, and absence of the normal signal in the internal capsule. His parents are told that based on his clinical condition and brain scan appearances Henry has a very high likelihood of developing severe spastic quadriplegic cerebral palsy with at least moderate cognitive impairment.[23] *Is it permissible to withdraw life support?*

> **Case:** Michael is aged 7. He has severe spastic quadriplegic cerebral palsy, microcephaly and epilepsy. He is cortically blind, and has severe intellectual impairment. Michael attends a school for children with special needs. He appears to recognise the voices of his parents and teachers - he responds with a smile. He also smiles and sometimes laughs in response to familiar music. Most of the time he does not appear to be in pain or discomfort. But he is not able to communicate verbally, nor with the aid of communication tools. He is not able to sit unsupported. He has a specially fitted wheelchair, but does not have any control over it. He is fed via a gastrostomy. He was in the newborn intensive care unit for a month after birth with severe HIE, and has had several hospital admissions since that time with either

[23] See chapter 1 p10

> prolonged seizures or chest infections. Michael's capacity for interaction is unlikely to change over time. His life expectancy is hard to predict. If he has a severe chest infection or difficult to control seizures he may die during childhood, but it is conceivable that he will survive into adult life, perhaps for several decades yet. *Would it have been permissible to withdraw life support from Michael in the newborn period?*

For infants like Henry, parents are often presented with the option of withdrawing life-sustaining treatment. Several of the clinicians interviewed in chapter 3 specifically suggested that it would be appropriate to withdraw treatment in the face of MRI results such as this. The apparent basis for this decision is that it would be in Henry's best interests to do so. But there are at least two problems for this view. The first is that it is by no means clear that Henry *would* necessarily have a life so bad that it would have been better for him to have died in infancy. On the basis of the analysis in chapter 4 (and given the combination of severe encephalopathy and suggestive changes on imaging in the first week) the chance of him avoiding a 'very adverse outcome' is small but not zero. It is probably less than 5%.[24] But if he does have severe impairment it is quite conceivable that he will have a life like that of Michael. And it is not clear that the lives of children like Michael are so dreadful that it would be better for them to die than to continue to live. The parents of such children often do not believe this is the case. There are, to my knowledge, no surveys of such parents, but the narrative accounts of parents with severely impaired children confirm this impression. See for example (Yorgason 2003; 'The Ashley Treatment' 2007; Sheffield 2007; Wyn 2007; Cogan and Whardall 2008; Nugent et al. 2008). If such children require short-term treatment for life-threatening illnesses it is usually provided.

The second problem is that faced with a prognosis such as that described for Henry some parents request that life-support be *continued*, and doctors usually support their request (see (Whitelaw 1986; McHaffie and Fowlie 1996, pp. 205-15; van der Heide et al. 1998; Nuffield Council on Bioethics 2006, p. 101, Case 7; Rennie and Leigh 2008)). But if it is not in Henry's best interests to provide life-sustaining treatment it seems highly problematic to allow its continuation. It suggests that treatment withdrawal should be obligatory rather than optional in such cases?

There are different ways to respond to these challenges. We might question whether withdrawal of life support *should* be permitted from infants with severe impairment like Henry. Perhaps we are wrong to let them die? Alternatively, we may be wrong in our judgement about the quality of life of surviving children like Michael with severe impairment. They *would* have been better to die in infancy. Perhaps we are wrong to allow the continuation of life support? But there is another possible response. Where a critically ill newborn infant is predicted to have severe and irremediable impairment, such that they

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[24] Based on a prevalence of very adverse outcome in infants with severe HIE of 80% and the sensitivity/specificity of MRI changes in the first week of 91/86% the positive predictive value is 96% (CI 95-97%) (see chapter 4 p51).

will not be able to take part in and realise many of the good features of life, it is permissible for parents and doctors *either* to allow them to die or to continue treatment. This may be the case even if it is anticipated that the child would have some overall benefit from life.

In this penultimate chapter I set out and defend such a view. I will focus on the practical policy question that has been the focus for the second half of this thesis – in what circumstances should we permit parents and doctors to allow an impaired newborn infant to die? I start by relating the concept of a life-worth-living and a life not worth living to future wellbeing. I point out some similarities between debates about neonatal treatment decisions and debates about 'wrongful life' in conception decisions. I draw on that literature and define two opposing views of the permissibility of treatment withdrawal: the Zero Line view, and the Threshold View. I then outline four arguments in favour of the Threshold View for the permissibility of withdrawal of life support. One reason for adopting the Threshold View is that it gives some weight to the interests of parents (following on from the previous chapter). But I also outline arguments based on uncertainty, and on the extent of parental duties or rights. I explore and reject several potential objections. I conclude by setting out how the Threshold View might relate to magnetic resonance imaging and decisions about life-sustaining treatment. The Threshold View would not necessarily lead to major changes in end-of-life care for newborns. But it would provide a better rationale for decision-making in a number of important ways.

## *9.2 Wellbeing and a life worth living*

In chapter 7, I provided a definition of a life worth living – one that will contain more intrinsically good experiences than intrinsically bad experiences; there is positive net future wellbeing. There are two other possibilities.

> **A Life Not-Worth-living (LNWL):** A life that will contain more intrinsically bad experiences than intrinsically good experiences. There is negative net future wellbeing (Buchanan et al. 2000, p. 224; Garrard and Wilkinson 2006, p. 485)
>
> **The Zero Point**: A life that will contain equal amounts of intrinsically good and bad experiences.

The zero point is a philosopher's abstraction (Glover 2006, p. 57). But it represents a useful way of conceptualising decisions about life and death. Some people reject the idea of a zero point because they deny that the negatives of life can ever outweigh the positives (Wyatt 2005; Garrard and Wilkinson 2006, p. 486). As noted in chapter 6 there are also substantial epistemic and conceptual hurdles to determining exactly where it is. I will assume in what follows that there is a zero point of wellbeing even if it is hard to identify.

As the concept of a life worth living is controversial and sometimes confusing (Garrard and Wilkinson 2006, p. 485), it will be worthwhile briefly setting out some competing meanings of the term. There is an *internal* sense to a life worth living: life is of sufficient value for the individual whose life it is to be worthwhile. This should not be confused with

an *external* sense of the worth of a life, and the value of that life to others (Buchanan and Brock 1986, p. 74). A second distinction is between the level of a *life worth starting* (for an individual who does not yet exist), and the level of a *life worth continuing* (for an existing individual) (Benatar 2006, pp. 22-3). Critical level theories (as discussed in chapter 7, p116) typically set the level of a life worth starting above the level of a life worh continuing. It is also possible to distinguish two ways of determining whether a life is above or below the zero point. The *objective* approach involves an attempt to impartially balance the intrinsically good states against the bad in an individual's future life. And there is the *subjective* judgement of the individual that the positives outweigh the negatives of life and that it is worthwhile continuing to live (McMahan 1998, pp. 226-8). The Intolerability and Balance Sheet approaches to best interests (discussed in chapter 6) can be mapped (more or less) on to the subjective and objective senses of a LWL respectively. Another overlap between these different ways of conceptualising a LWL is the suggestion that the level of a life worth starting reflects the level of an objective LWL, while a life worth continuing corresponds to a subjective LWL (McMahan 1998, p. 227). This approach has some plausibility, but as McMahan notes, it is difficult to identify conditions that are objectively not worth living, yet subjectively worth living (McMahan 1998, p. 228).

In this chapter, when I discuss a LWL I refer exclusively to the *internal* sense of a life worth *continuing*. The subjective sense of a LWL I believe represents the most common view of a LWL, and is the way that most courts and bioethicists have approached the question of treatment withdrawal. The arguments below, however, apply equally to subjective or objective senses of a LWL. I will also assume in what follows that some, perhaps many, individuals with very severe impairments have lives that are above the zero point, albeit not by much. Some may be tempted to set the zero point higher than this, but the arguments that I outline in the first half of this chapter are not dependent on the absolute position of the zero point.

## *9.3 Two views about the permissibility of conception*

The idea of a LWL has been central to some debates about artificial reproduction and conception decisions. Is it permissible for parents to decide to implant an embryo that they know will develop into a child with significant impairment? One view, as expressed by John Harris, is that it *would* be permissible for parents to do this, as long as the child's future wellbeing were predicted to be above the zero point (Harris 2000b). The child has not been harmed since they have net positive wellbeing, and since they would not otherwise exist. This has been referred to as a 'zero line' view (Glover 2006, p. 53).

This view conflicts, however, with common-sense morality as expressed by Bonnie Steinbock:

> "It's … a question of whether to create a child who is likely to have a life marked by pain and severe limitations. ... What reason could be offered in justification of an affirmative answer? That the child's life, while miserable, is not so awful that he or

> she will long for death? That is not the kind of answer a loving parent could give." (Steinbock and McClamrock 1994, p. 18)

Steinbock and several other philosophers have rejected a zero line view for conception decisions (Kavka 1982; Steinbock and McClamrock 1994; Archard 2004). They have argued that instead of the zero point of net wellbeing, a higher standard should be applied. On this view it is not permissible to undertake acts of deliberate conception like artificial reproduction unless the child will have at least a minimum level of wellbeing - their life will be above a certain *threshold*.

## *9.4 Two views about treatment withdrawal and newborn infants*

These views about conception decisions have some similarities with views about treatment for newborn infants. The setting for treatment withdrawal decisions is different - the judgement is inverted, but a view that parallels the Harris view of permissible conception is as follows:

> **The Zero Line View**: Life support may be withdrawn from a newborn infant *if and only if* their net future wellbeing is predicted to be below the zero point, ie they are predicted to have a life not worth living.

What I am here calling The Zero Line View overlaps with the view that treatment may be withdrawn only when it would be in the *best interests* of the infant to die. This view was endorsed by many of the guidelines discussed in chapter 2. Whether a best interests judgement necessarily means adopting this view is a further question that I will return to in section 9.6.4.

There is a second view about treatment withdrawal that is similar to the Archard/Steinbock view about conception:

> **The Threshold View**: Life support may be withdrawn from a newborn infant *if and only if* their net future wellbeing falls below a certain minimum Threshold. This Threshold is above the zero point of a life worth living. Life support may be continued for newborn infants predicted to have wellbeing above a Lower Threshold.

These two views are summarised in Figure 9.1

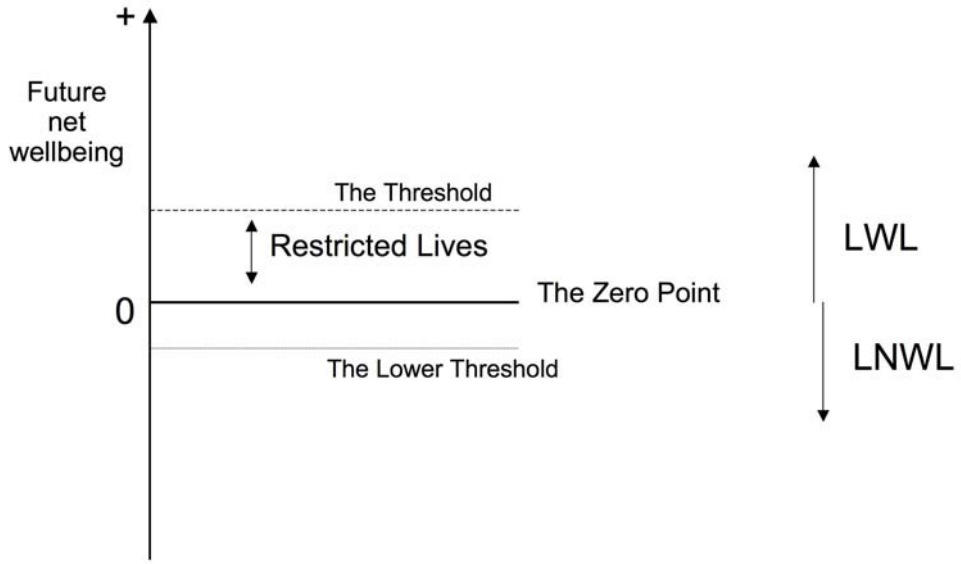


*Figure 9.1: The permissibility of treatment withdrawal from newborn infants based upon predicted future wellbeing*

In discussion of the Threshold View the following definitions will also be useful.

> **Restricted Life**: A life in which net wellbeing is above the zero point but below the Threshold (Kavka 1982, 103).
>
> **The Threshold**: A positive (supra-zero) level of net wellbeing defining the upper border of permissibility of treatment withdrawal. It is obligatory to continue life support for newborns with predicted wellbeing above this level.
>
> **The Lower Threshold**: A negative (below zero) level of net wellbeing defining the lower border of permissibility of treatment continuation. It is obligatory to withdraw life support for newborns with predicted wellbeing below this level.

In the discussion below I will focus almost exclusively on the (upper) Threshold. The arguments I cite provide reasons why the Threshold should be above the zero point. But they also provide reasons why the Lower Threshold should be below the zero point. The argument from uncertainty and asymmetry (section 9.5.1.1) gives rise to the idea (illustrated in the figure) that the Lower Threshold should be closer to the zero point than the (upper) Threshold.

There are two key features of the Threshold View. Firstly, it explicitly permits newborn infants to be allowed to die who are predicted to have a LWL. And secondly, it stipulates that below the Threshold treatment may be permissibly *continued*. This second feature marks a difference between the Archard/Steinbock views about conception and the Threshold View for treatment withdrawal as I have defined it. David Archard argues that parents should not be permitted to deliberately conceive a child whose predicted wellbeing lies below the threshold (Archard 2004, p. 420).

Various writers discussing treatment withdrawal for newborn infants have articulated views with some similarity to the Threshold View. They have argued that it may be permissible to allow newborns to die who lack certain key capacities (for example the capacity to develop

relationships, to appreciate life or to engage in minimal social interaction), or whose lives are not going to be meaningful (McCormick 1974; Engelhardt 1978; Kohl 1978; Arras 1984; Kipnis and Williamson 1984; Doyal and Durbin 1998). These authors do not talk explicitly about wellbeing, and whether such lives would be worth living. They are also somewhat unclear about whether (on their view) it would be permissible to *continue* life support for an infant lacking those key capacities.[25]

The above view also has some similarities to a classification of treatment decisions for extremely premature infants elaborated by Tyson and colleagues and by John Paris (Tyson et al. 1996; Paris et al. 2007). They argued that treatment could be divided into a set of normative categories: Mandatory, Optional, Experimental and Unreasonable. The upper threshold would correspond to the point at which treatment becomes 'Mandatory', the lower Threshold corresponds to the point of 'Unreasonable' treatment. Between the two thresholds treatment is 'Optional'. The Threshold View articulated in this chapter can be seen as an attempt to relate these categories to the concept of a LWL, as well as to provide a robust defense of such a categorisation. It extends the categorisation to infants with predicted impairment.

I have not, so far, provided a definition of the Threshold itself. I will return in section 9.7 to the application of the Threshold View to treatment decisions in HIE. But it may help for what follows to give some idea of the types of conditions that I believe would fall below the Threshold but above the Zero Point. I gave an example earlier of Michael (Case 2); his impairments would fit within many of the descriptions of a Restricted Life (Kavka 1982, p. 105; Archard 2004, p. 406). His cognitive, physical, and sensory impairments fundamentally diminish his access to things that are good in life. His life is *restricted* by his impairments in ways that cannot be overcome no matter how much support his parents or society provide to him. An example of a guideline based upon the Threshold is given in Box 9.1.

Treatment may be withdrawn when a newborn is predicted to have severely restricted future net wellbeing, close to the level of a life not worth living.

This could be, for example, because of severe functional limitation affecting most aspects of life. These limitations would lead to dependency on others for the activities of daily living throughout life, and prevent or substantially diminish the capacity to communicate, interact and develop goals. The limitations are unlikely to be able to be relieved or compensated for by medical or social intervention.

*Box 9.1: A guideline for decision-making based on the Threshold View.*

[25] For another defence of parental discretion in "borderline cases" see Duff (1981).

Now that we have a clearer idea of what the Threshold View might entail I will consider the arguments in favour of adopting such a view.

## *9.5 Arguments in favour of the Threshold View*

### 9.5.1 Arguments from uncertainty

In earlier parts of the thesis I have highlighted the nature and extent of uncertainty in treatment decisions for infants with HIE. *Prognostic uncertainty* arises from various factors, including the plasticity of the developing brain, variable resilience to injury, the influence of the environment and potential treatments, as well as imperfection in clinical assessment and prognostic tests (Shevell et al. 1999). The way that previous research has been performed also contributes to prognostic uncertainty (see chapter 4). There is further uncertainty relating to the future experiences of individuals with significant cognitive impairment. Even if we were certain of the degree of their future impairment we would remain unsure how aware the child would be of positive or negative experiences (see chapter 6). This *experiential uncertainty* makes it difficult to know whether such life would be above or below the zero point.

There are two ways in which uncertainty may justify the Threshold.

#### *9.5.1.1 Uncertainty and asymmetry of harms*

In a state of uncertainty, if we choose the zero-line as the criterion for the permissibility of withdrawal of life support, it is inevitable that some infants who survive will actually have lives below the zero point. Imagine, for example, an infant predicted to have future net wellbeing of zero. (Set aside for the moment the doubts that we may have about quantifying wellbeing or about determining the zero point). We make this prediction based upon median wellbeing in a group of past infants with relevantly similar prognostic features. On the Zero Line View this is the upper limit of permissible withdrawal. We should not allow a newborn to die with greater wellbeing than this. But given the problems of prognostic and experiential uncertainty this infant has, approximately, a 50% chance of actually having wellbeing above the zero point, and a 50% chance of wellbeing below this point. But should we weigh these possibilities equally? One reason to reject this idea and consider adopting a *higher* threshold is an asymmetry between harms.

A newborn who survives in a state of such severe impairment and suffering that they have a LNWL has been harmed by a decision to prolong their life (Feinberg 1986; McMahan 1998; Benatar 2006, pp. 20-22). Indeed many would consider this one of the most serious harms imaginable. On the other hand a newborn who would have had a LWL but who dies in the newborn period has also been harmed. They have been deprived of future wellbeing. As argued in the previous chapter, however, the degree of this harm depends upon how much future wellbeing they would have experienced. If, for example, they would have lived a Restricted Life, the amount of net positive wellbeing that they have lost is relatively small.

What is more, they were not, and are not, conscious of this loss. They will never be in a position to regret the decision that led to their death. Arguably, because of the ongoing nature of the harm and the consciousness of suffering, we should give greater weight to the harm of a LNWL, than to the harm of death for an infant who would have had a LWL. We should set the threshold for withdrawal of LST above a median of zero wellbeing.

The idea of asymmetrical harms has been widely discussed in relation to conception decisions (McMahan 2009a). It is generally accepted that an individual can be harmed by coming into existence, and that it is good to avoid bringing into existence someone who would have a LNWL. On the other hand there *is no individual who is harmed* if an individual (who would have had a LWL) is not conceived; there is a general intuition that it is not bad (or minimally bad) to fail to bring such an individual into existence. The asymmetry of harms for newborn infants above is related to this conundrum. But it is different in one important way. There is an individual existing (the newborn) to whom harm could be attributed if they die. However, as argued in the previous chapter, the nature of that harm is attenuated because of their limited awareness.

In response to this argument it could be argued that there are also asymmetrical benefits at stake.[26] If an infant with a LNWL dies they benefit from not experiencing the harm in their future. But they are not likely to be aware of or experience this benefit. Yet, if an infant with a LWL survives they will experience and, (potentially at least), be aware of this benefit. If harms and benefits are considered equally, and if there is a parallel asymmetry in benefits to the one that I have described for harms, then it would seem to undermine my argument for the Threshold. Positive utilitarians (ie those who believe that what is important is the promotion of happiness or preference-satisfaction) may reject the asymmetry argument. There is, however, widespread intuitive support for at least some degree of asymmetry between harms and benefits (Benatar 2006, pp. 30-36; Kamm 2007, p. 17; Alm 2009). Most parents and doctors, I suspect, have greater concern for the potential future harms to infants than for their future benefits. Such concern is sometimes expressed in the principle of non-maleficence (Beauchamp and Childress 1999, pp. 120-93).

There are different possible versions of the asymmetry argument. I do not claim that there is *no* harm to an infant who is allowed to die (but would have had a LWL). (I rejected such a view in the previous chapter). Nor do I claim that *any* risk of a LNWL outweighs the risk of allowing an infant to die with a LWL. To support the Threshold View I need only make the more moderate claim: it is a worse mistake to allow a newborn to live with a LNWL, than to allow a newborn to die who would have had a LWL – where they would have a Restricted Life.

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[26] I am grateful to Tom Douglas for this point.

#### *9.5.1.2 Uncertainty and liberalism*

Some may reject the asymmetry argument. They may believe, contrary to the above claims, that death (for an infant who would have had a LWL) is one of the worst possible harms, and that the threshold should perhaps be *below* the zero point (Kon 2008, p. 28). But uncertainty provides a second argument in favour of the Threshold View. I have described above the prognostic and experiential uncertainty that makes it difficult to know whether or not an individual infant will have wellbeing above the zero point. There is also significant *moral uncertainty* about how to evaluate future benefits and burdens. It is unclear which theory of wellbeing we should apply, and how we should weigh up different harms. There is significant disagreement about the chance of a LWNL that would justify a decision to allow a newborn to die.

The problem of moral uncertainty is complicated (Lockhart 2000), and beyond the scope of this thesis. But one plausible approach to policy in the face of different normative beliefs is to give individuals the freedom to decide for themselves which policy to apply to their own lives. This principle is often extended to include decisions by parents on behalf of their children. As noted in the previous chapter, the state will usually only interfere with parental choices where there is a significant risk of substantial harm to the child (Diekema 2004). One plausible liberal response to decision-making for newborn infants would be to allow parents to decide whether or not to continue life support when there is genuine uncertainty about whether a child will have a life above or below the zero point. The upper boundary of parental decision-making would be set at the Threshold.

Others have made this claim about uncertainty and parental freedom. See for example (Shelp 1986; Boyle et al. 2004; Diekema 2004; Jonas 2007). As noted, this claim also has some similarities with the idea of a 'grey zone' for decisions (Paris et al. 2005; American Academy of Pediatrics Committee on Fetus and Newborn 2007; Harrison 2008). The Threshold View differs from conventional accounts of the grey zone in several ways. Firstly I have argued that this zone will extend above and below the zero point (whereas some accounts of the grey zone seem to extend only below the zero point). Secondly the Threshold View explicitly acknowledges that it may be permissible to withdraw life support from infants who *will probably have* lives above the zero point. Third, the threshold is based upon both prognostic uncertainty and moral uncertainty. And fourth, there may be reasons to support a supra-zero threshold even where there is certainty about outcome.

I have argued that we are not obliged to keep a child alive if there is a significant uncertainty about whether the child will have a LNWL. But what if we were certain that an infant *would* have a LWL? Imagine an infant with a genetic disorder uniformly associated with profound cognitive impairment (they have the cognitive capacities of a 3 month old infant). Children with this condition usually have good physical health, and do not suffer from illness or require painful medical interventions. (Call this the Harmless Case). If we believe that there is no (or a negligible) chance of this infant having a LNWL is it still permissible to withdraw life-sustaining treatment?

### 9.5.2 The Argument from other interests

Some may still be tempted in such a case to think that the zero point is above this level and that perhaps it would be better for the infant to die in such a case. But there are at least two problems with such a view. Firstly, we do not generally think that the lives of 3 month-old infants are bad lives. (We may be glad that they subsequently develop, especially if we are their sleep-deprived parents, but that is a separate issue) Secondly, such a view would appear to imply that the lives of many nonhuman animals (with cognitive capacities no greater than a 3 month old human infant) are bad, and that it would be better for them to die. This seems highly implausible.

One reason why we may not be obliged to continue life support even in the hypothetical Harmless Case is because of the burden of care and the effect on the interests of parents. In the previous chapter I detailed some of the potential costs for families in terms of psychological and physical illness as well as marital discord and break-up. I argued that continuing treatment for an infant with severe impairment could have a substantial negative impact on the interests of parents, while providing a relatively small benefit to the infant. Although parents are expected to be willing to make some sacrifices for their children, the sacrifice involved in such cases is much more than most parents ever have to make. Perhaps it is more than should be required of them?

Commonsense morality endorses the view that some actions, while good and praiseworthy, go above and beyond the call of duty. Where aiding another individual would require substantial personal sacrifice and effort, that action is sometimes referred to as *supererogatory* rather than obligatory (Wolf 1982; Kamm 1985; Rawls 1999, p.100). There are various accounts of the level of personal sacrifice that would make an act supererogatory (Flescher 2003, p. 54, p. 72 fn 74; Heyd 2008). On most accounts, however, an action that involves substantial imbalance in the consequences, such that the costs to the individual are great, while the benefits achieved are small would be so classified.

In the previous chapter I suggested that the possibility of adoption limited the weight given to the interests of parents. Yet this may not extend to infants with severe impairment. In the hypothetical Harmless Case, the infant will certainly have a life worth living, and on that basis it would be good for the state, in its *parens patrie* role, to adopt the infant if parents do not wish to care for him. Finding adoptive parents for severely impaired infants is not easy, however. Furthermore, supporting the infant involves considerable cost, while providing only a small benefit to the child. When resources are limited the provision of life-saving treatment to an infant with a Restricted Life may mean that other children or adults are denied surgery or medical treatment, or other children with impairment denied educational and supportive care. From the point of view of society, as well as from the point of view of parents, continuing life-sustaining treatment may go above and beyond what is morally required, may be supererogatory. In the words of American bioethicist

Norman Fost, "No patient is entitled to infinite resources from his or her family or from society." (1999)

On the Zero Line View there is no scope for taking the interests of others, either parents, or the broader community, into account. But even if it is not accepted that the interests of others can outweigh the interests of the infant, the *argument from overlapping interests* provides a reason to take into account parental views and interests. One point to note is that if parental or family interests are to have *any* role in decisions about withdrawal of treatment this would necessarily support some version of the Threshold View. After all, if these interests could only be taken into account when the child's life were below the zero point, they would actually be playing no role at all in determining the permissibility of withdrawal of treatment.

Would this argument justify allowing an infant to die whose future life would be *above* the Threshold? In theory, if the impact on others were great enough they might outweigh the benefit to a child even where it is predicted that the child would have high levels of wellbeing. However, as argued in the previous chapter, it is *most likely* that the benefit to the child would be outweighed where that benefit is predicted to be very low. It would be reasonable, as a general rule, to consider the effects on parents and the future costs of care only where an infant is predicted to have a Restricted Life. Where the current and future care of an infant imposes substantial burdens on caregivers and where the benefit to the child is very small, it would be permissible to allow the infant to die.

What if there were no opposing interests and no costs? If we imagine a version of the Harmless case such that the care of the child will not cause a burden on parents and will not divert needed health and educational resources away from others, there would no longer be a positive reason to allow the child to die. Though they will be severely impaired there is no reason for the sake of the child, nor for the sake of others to withdraw life-saving treatment. Correspondingly, we should not permit withdrawal of life support in a Harmless Costless case. But in practice such cases will rarely if ever occur. Infants who are predicted to have very severe impairment have a real risk that their future wellbeing will fall below the zero point, and their care substantially affects the interests of others. These reasons converge to support allowing infants to die where they are predicted to have Restricted Lives.

### 9.5.3 The deontological argument for the Threshold

Arguments in favour of a threshold view for conception decisions are often based upon parental duties or rights. Steinbock refers to a 'principle of parental responsibility' (Steinbock and McClamrock 1994). She argues that when parents make a decision to bring a child into the world they should take into account the kind of life that the child will live. Parents should refrain from conceiving a child unless certain minimum conditions are likely to be satisfied. David Archard justifies a threshold in a different way; he argues that a 'minimally decent life' provides a constraint on parental reproductive rights (Archard 2004).

Both accounts seek to explain why it would be wrong to deliberately conceive a child with a Restricted Life. But these arguments do not extend to treatment withdrawal decisions. Steinbock explicitly focuses her principle of parental responsibility on situations where the child does not yet exist. Archard's central argument is about a limit to parental reproductive freedom.

Nevertheless, the Threshold could be seen as providing a constraint to a different duty. Parents and doctors have a strong prima facie duty to do what they can to preserve the life of a newborn infant (call this the *Duty of Preservation*). In the previous section I discussed the possibility that other duties may outweigh the duty to preserve the life of the infant. But perhaps there are limits to this duty. Many people do not believe that doctors and parents are obliged to keep a child alive who is dependent on life support and in a permanent vegetative state. A life of permanent unconsciousness offers no benefit to the child, and therefore dissolves the normal duty that the parent has to their child. But it may also be the case that where a child's future life is predicted to contain a very low amount of positive net wellbeing that the duty of preservation is significantly attenuated or absent. On this basis it would be permissible for parents and doctors to elect not to preserve the life of a newborn predicted to have a Restricted Life.

(A version of this argument is expressed by John Arras "In the absence of certain distinctly human capacities… the duty to sustain life loses its hold on caregivers"(Arras 1984, p. 32). This articulation of the deontological argument implies that the reason that treatment withdrawal is permissible is because of a lack of human capacities. The arguments given in this chapter are based on wellbeing rather than human-ness.)

A complementary way of justifying the Threshold View would be in terms of the *right* of parents to make decisions about their children. As noted previously, for most decisions there is a rebuttable presumption that parents have such a right. This might be justified by parents' right to autonomy, but also by the value of preserving intimate family relationships, and in the avoidance of undue state interference in family life. Again, if such a right has any relevance for decisions about life-sustaining treatment, it would necessarily support the Threshold View.

The deontological argument in favour of the Threshold View, either in a limit to parents' duties to the child, or in parents' right to make decisions, captures an intuitive sense that there is more to such decisions than the Zero Line View would indicate. To avoid begging substantive questions, however, we need to justify *why* parents' rights should apply, or why parental duties are limited or outweighed. The arguments in the above sections and in the previous chapter provide such justification.

## *9.6 Counterarguments to the Threshold View*

The Threshold View will be controversial to some. What arguments might be presented against it?

### 9.6.1 The scope of the Threshold

I have referred in the above exclusively to newborn treatment decisions. But there might be a concern that the Threshold View would justify the withdrawal of life-sustaining treatment from older children or adults with LWL.

There are several reasons for applying the Threshold View to newborn infants and not older individuals. The principal reason is, as argued in chapter 8, that a newborn's interest in her future wellbeing is diminished by her reduced awareness of herself and of that future. This affects how that interest should be weighed against other interests and other considerations (section 9.5.2) and gives rise to the asymmetry in harms noted above (section 9.5.1.1). Secondly, there is greater uncertainty for newborn treatment decisions than for older children and adults. This arises from the greater degree of plasticity and thus variability in response to injury, and from their greater developmental immaturity, which makes clinical assessment difficult. It gives more weight to the arguments from uncertainty. Thirdly, there is often a long period of time before the extent of an infant's impairments is known. By the time that it is clear that she is destined for a LNWL an infant may no longer be dependent upon life-sustaining treatment. Prolonged survival in a harmed state is possible. These three reasons would not usually apply, or would apply less forcefully for older children or adults. It would be appropriate to use the Zero line, (or something close to it) for determining the permissibility of withdrawal of treatment outside the newborn period.

It may be helpful to clarify how I see the relationship between wellbeing and moral status. It is not that future low levels of wellbeing warrant different moral consideration. Rather, the moral status of an individual determines how we should take into account their future wellbeing. The moral status of a competent adult would remain unchanged following a prediction that their future contains only a very slight positive balance of wellbeing or even net negative wellbeing. Similarly, a newborn's moral status is not altered by predicted future impairment. The view that I have defended in this chapter is that in newborn infants (compared to older children or adults) it is legitimate to use a different wellbeing threshold for deciding whether or not to continue to keep them alive.[27] In the final chapter I will briefly consider variants of the Threshold View that might hold on other views of the moral status of newborn infants.

The other question about the scope of the Threshold View is about the period during which it should be applied. I do not propose in this thesis to defend a specific time limit for the applicability of the Threshold View, but one approach might be to limit it to the first month of life (or to one month corrected age for infants born prematurely). Such a

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[27] I set aside here the question of whether a supra-zero threshold should be applied to decisions about life support for older individuals whose awareness of themselves and of their future is no greater than newborns.

time limit would be in one sense arbitrary, but also defensible. (The application of different criteria for termination of pregnancy at different stages of gestation provides an analogy for how this could work in practice.) I will return shortly to the question of arbitrariness and the Threshold View.

### 9.6.2 The Threshold and discrimination

It may be objected that the Threshold View represents a form of discrimination against disabled infants.

The first response to this objection is that the Threshold View justifies treatment withdrawal on the basis of future wellbeing – *not* primarily based on impairment. If an infant were predicted to be impaired, but to have future wellbeing significantly higher than the zero point, it would not be permissible to allow them to die. The Threshold View would also, in theory, permit treatment withdrawal from an infant who did not have a physical or cognitive impairment, but who was predicted to have levels of wellbeing only just above the zero point. I have not discussed such examples previously in this thesis, but imagine, for example, an infant with a very limited life expectancy (for example a matter of days or weeks), but who appears to be suffering little if at all. Their brief future life may well contain a positive balance of wellbeing. If so, the Zero Line View would appear to mandate that treatment continue. On the Threshold View, however, it would not be obligatory to continue life support for such an infant.

In practice, the majority of infants with Restricted Lives *would* be infants with predicted impairment. Yet it does not follow that this represents a form of wrongful discrimination (Arneson 2006). Treatment withdrawal on the Zero Line View is not thought to be discriminatory even though it, too, largely affects impaired infants. As highlighted in the previous section, future impairments do not change the moral status of an individual. The question is whether they affect wellbeing. Some types of impairment, for example severe cognitive impairment, necessarily reduce the amount of wellbeing in an infant's future life because they diminish the benefits available to them (see chapter 6, also (Kahane and Savulescu 2009)). Other impairments only contingently reduce wellbeing, for example depending upon the amount of support provided to the impaired individual and the social context in which they live. Such impairments, would not warrant withdrawal of life support. I will return shortly to the relationship between impairment and the Threshold.

### 9.6.3 Arbitrariness of the threshold

One concern that has been expressed about threshold views of conception decisions is that there is no non-arbitrary way of arriving at a threshold (Garrard and Wilkinson 2006). Similarly it could be objected that the Threshold that I have suggested for treatment withdrawal decisions is arbitrary. This is hard to deny, and the objection has some force.

There are three responses to the arbitrariness objection, however. Firstly, there are different senses of arbitrariness. A distinction may be arbitrary in the sense that it could be defensibly drawn at a different point. Or it could be arbitrary in the sense that there is *no reason* to make the distinction. A law that allows people to apply for a driving license after the age of 18 is arbitrary in the first sense. The line could have been drawn elsewhere. But there is good reason to draw a line somewhere, and there are a variety of reasons why a point in the late teenage years is an appropriate place. It is not arbitrary in the second sense. Similarly, we might think that there are multiple plausible places to draw a threshold for treatment withdrawal. But I have provided reasons why the threshold should be set a short distance above the zero point.

Secondly, the main alternative to the Threshold View is also arbitrary in the first sense. There is profound uncertainty about how to define the zero point for infants whose subjective experiences are presently unknowable, and may remain so. And even if we could define this point there is substantial prognostic uncertainty about whether or not an infant will fall above or below it. Furthermore, it is simply unclear, on the Zero Line View, what level of certainty (that an infant will live a LNWL) would justify treatment withdrawal. A decision, on the basis of the Zero Line View, that a newborn should or should not be allowed to die may also be criticized on the grounds of arbitrariness.

Third, even if the Threshold is arbitrary there is a further question about whether this should lead us reject the Threshold View. Given the important practical need to determine whether or not treatment withdrawal is permissible, and the reasons that I have outlined in favour of a supra-zero threshold, it may be that the disadvantages of greater arbitrariness are outweighed by the other advantages of the Threshold View.

### 9.6.4 The best interests of the infant

Another potential objection to the Threshold View is that it would be contrary to the best interests of the infant to permit withdrawal of life support from an infant predicted to have a LWL.

There are various ways of construing this objection. If the objection is that withdrawal of life support from an infant with a predicted Restricted Life would be contrary to the *legal* best interests principle it may have some traction. Previous legal judgments about withdrawal of life support in the UK (see chapter 2) have often used the concept of Intolerability, which appears to be a stringent subjective version of the Zero Line View. But the arguments in this chapter are about what the law should be – not about what is currently permitted.

Alternatively, the objection might be that the Threshold View is inconsistent with the *ethical* principle of the best interests of the child. If, as sometimes appears to be assumed, the best interests principle is consonant with the Zero Line View, the Threshold View will diverge from best interests. But if that is the case, the arguments that I have provided above would

serve as reasons for either rejecting or modifying the best interests principle for newborn treatment decisions.

It might also be argued that the Threshold View *is* consistent with the best interests principle. I discussed the argument from uncertainty in terms of the risk of a LNWL. But we could also express it as the newborn having an *interest* in not living a LNWL. This would be balanced by the infant's potential interest in a future LWL. The arguments above would give us reason to weigh the former interest as potentially stronger than the latter – particularly where the infant's future wellbeing is predicted to be low. Furthermore, at least some descriptions of best interests allow a role for the impact of an infant surviving on parents and other siblings (Kopelman 1997), in a way that I have suggested supports a supra-zero Threshold. It could be *in* an infant's best interests to be allowed to die, though they are predicted to have a LWL.

Nevertheless, the most plausible understanding of the relationship between the Threshold View and best interests is that they are distinct. On the view that I have defended the best interests of the child are a *primary* consideration though not *the paramount* consideration (Archard 2008). Although I have criticised the use of the best interests principle for determining treatment decisions on epistemic and conceptual grounds, it should remain a central concern and normative *ideal* for doctors and parents (Kopelman 1997). It remains the case, on the Threshold View, that treatment *should be provided* if it would be in the best interests of the child to do so. Yet, for the reasons outlined above, it would be permissible not to do so if the child's future wellbeing falls below the Threshold, if they would have a Restricted Life.

## *9.7 Where is the Threshold?*

In the first part of this chapter I have argued in favour of a Threshold View for treatment decisions in newborn infants – treatment withdrawal may be permissible within a range of cases above and below the level of a LWL. In this last section I will defend a particular level for the Threshold, and set out the implications of this for treatment decisions in HIE.

In a sense, this task is harder than the preceding one. The arbitrariness objection points to the difficulty in setting out boundaries for decisions other than the zero line. There is no clear dividing line that separates Restricted Lives from those above the Threshold. If there are epistemic problems in determining which conditions fall above or below the zero point, there are likely to be similar or greater epistemic problems in relation to the Threshold.

Nevertheless, the arguments above may prove useful in setting out the necessary and sufficient conditions for Restricted Lives and for the Thresholds.

Treatment withdrawal is permissible for infants with conditions that

C1. Reduce future wellbeing, either by reducing benefits or by imposing substantial burdens on the child (or both) AND

C2. Are expectably close to the level of a LNWL, AND EITHER

C3. Involve a significant risk of a LNWL (in view of prognostic, experiential or moral uncertainty) OR

C4. Impose a substantial burden of care on others

*Box 9.1: Normative criteria for the Threshold*

Treatment continuation is *not* permissible for infants with conditions that

C1. Reduce future wellbeing, either by reducing benefits or by imposing substantial burdens on the child (or both) AND

C5. Render it highly likely that the infant will have a LNWL and be harmed by continuing treatment

*Box 9.2: Normative criteria for the Lower Threshold*

Of these criteria, C2 is the most important, since in all actual cases conditions that are close to the zero point involve a significant risk of LNWL (C3), and thus lead to the arguments from uncertainty. It is also in cases close to the zero point where the benefits to the child are relatively small, and it is most likely that the benefits to others will outweigh the benefits to the infant (C4). In addition, as noted in the previous chapter, in genuine borderline cases (ie where the infant's future life is close to the zero point), the overlapping nature of interests would justify giving some weight to parental interests and views.

The criteria set out in box 9.1 are potentially just as difficult to apply to practical decisions as the guidelines discussed (and criticised) in chapter 2. What is a 'significant' risk, or a 'substantial' burden of care? Which conditions are close to the level of a LNWL? For this reason it would be important to provide clinicians, and parents, with some idea of the sorts of conditions that would fall into the different normative categories that I have described. Figure 9.2 represents an attempt to apply the Threshold View to prognostication in HIE.

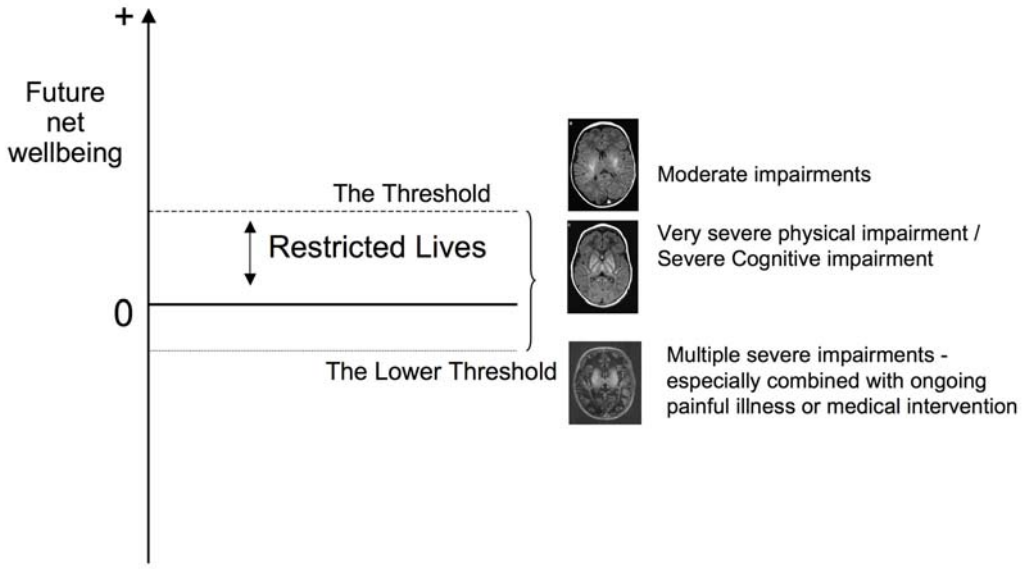


*Figure 9.2: The Threshold View and predicted impairment in HIE*

Why draw the Threshold at the level of severe cognitive impairment or very severe physical impairment? Moderate physical impairment (GMFCS 3) means that children are usually able to walk with assistive mobility devices, though often have limitations on their walking outside or in the community (Himmelmann et al. 2006). Individuals with moderate cognitive impairment (IQ 35-50) are usually socially interactive and able to communicate at least to the level of basic needs, and often can carry on simple conversations (Harris 2006, p. 54). Both types of impairment would be consistent with a broad range of goods on either subjective or objective theories of wellbeing. It is not usually thought that such individuals have lives that are not-worth-living, nor that there is a significant risk of this befalling them. (Although, as noted in chapter 7, some authors have argued that infants with this level of impairment should be allowed to die – they do not claim that this is for the sake of those infants nor because there is a serious concern that they have a LNWL).

In contrast, for individuals with very severe physical impairment (GMFCS 5) or with severe cognitive impairment (IQ ≤ 35) it is more questionable whether their lives fall above the zero point, and more reasonable to worry that they may have a LNWL. It is for infants with this level of impairment that there is most debate about whether or not treatment may be in their best interests. Recall the infant Henry (p. 139), predicted to have a future life that is similar to that of Michael with severe physical and at least moderate cognitive impairment. In his case, although he may be expected to have a life that is worth living, there is a risk that in fact his impairments will be more severe than anticipated, or that other medical problems arise, meaning that his life falls below the zero point.

It is also for such infants, particularly those with severe cognitive impairment, that the benefits of life appear uncontroversially diminished (McMahan 2009b). Many objective list theories of wellbeing include elements that are related to cognitive function, including

communication, knowledge, aesthetic appreciation, the development of deep reciprocal relationships, the achievement of goals or ambitions (Parfit 1984, pp. 493-502; DeGrazia 1995; Veatch 1995; McMahan 2009b). (As noted in chapter 6, the benefits of life for individuals with profound physical impairment may or may not be diminished, but such conditions are usually also associated with substantial burdens for the individual). Some subjective theories of wellbeing would potentially yield a different answer. It is not necessarily the case that an individual with severe cognitive impairment would have less pleasure or more pain than an unimpaired individual, nor that less of their desires or preferences would be satisfied. Consequently, on those views, they would have no less wellbeing in their life than a cognitively normal individual. Such a view, however, would also imply that there is *nothing* bad for the infant and nothing to regret for their sake about a medical condition in infancy that causes brain damage and leaves them severely cognitively impaired. This seems highly implausible. Furthermore, even if some hold this view and are prepared to accept its counterintuitive implications, the objective view outlined above represents a reasonable alternative accepted by many. (It fits with the importance of independence noted by clinicians interviewed in chapter 3, and with the emphasis in guidelines and in case law of severe cognitive impairment noted in chapter 2). On the basis of the argument from uncertainty and liberalism (section 9.5.1.2), we should permit those who hold the objective view to apply it to their own lives and those of their children.

I mentioned earlier in the thesis that I would return to clarify the relationship between uncertainty and treatment decisions, and attempt to resolve the ambiguity present in current guidelines. As noted in chapter 6, uncertainty is unavoidable in neonatal treatment decisions. The Threshold View, as outlined above, includes reference to uncertainty in criteria C2, C3 and C5. It provides a major part of the justification for parental discretion in treatment limitation decisions. I have not indicated a specific statistical threshold, but the arguments from uncertainty outlined earlier in the chapter would suggest that it is appropriate to give weight to at least modest chances of significant harms. Is it possible to be more specific? One way of capturing this idea without using specific numerical thresholds would be by borrowing the language of the law. Civil cases are often settled on the basis of the *balance of probabilities,* while criminal conviction is usually required to establish guilt *beyond reasonable doubt* (Murphy 2007, p.111). The latter is unsatisfactory for the Threshold, since there is always some doubt about prognosis. Stipulating the former would permit treatment withdrawal in infants with a slightly less than 50% chance of survival without severe impairment, which may give too great a weight to survival with a restricted life. In the absence of a better standard, I suggest that it would be permissible to withdraw treatment if there is *clear and convincing* evidence that an infant will have severe impairments as described above. (The clear and convincing evidence standard is used in some American legal cases, and indicates a high degree of probability – more than 50%, but less stringent than *beyond reasonable doubt* (Murphy 2007, p.111)). Similarly, if there is *clear*

*and convincing evidence* that continuing treatment would harm an infant, it should not be provided even if parents request it.

### 9.7.1 Avoiding the technical criteria fallacy

The above attempt to relate the results of imaging and predicted impairments to normative thresholds for treatment or non-treatment has some similarity with the way in which neonatologists have in the past developed criteria for treatment, for example on the basis of gestational age (Wilkinson et al. 2009a), or on the basis of specific medical features in infants with spina bifida (Lorber 1972). American bioethicist Robert Veatch criticised the latter attempts on the basis of what he called the 'technical criteria fallacy'.

> "In principle it is a mistake, so I would claim, 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" (Veatch 1977, p. 15)

Are the criteria for the Threshold guilty of this fallacy?

Veatch objected to the criteria advanced by John Lorber and others on the grounds that they appeared to medicalise questions that are fundamentally value judgements. Those who outlined such criteria provided no ethical argument for adopting their criteria rather than an alternative set. Moreover, such criteria appeared to leave no place for other values, such as those of parents.

However, the Threshold criteria outlined above resist all of Veatch's criticisms. They are openly based on normative judgements, and I have outlined a set of reasons why the Threshold should be placed at the level that I indicate above. Furthermore, the Threshold View makes explicit the importance of taking into account parental views, albeit within limits. Finally, the examples given above are intended to serve as guides for decisions, not as rigid rules that doctors or parents must follow. There are likely to be other relevant factors in individual cases that should be taken into account.

## *9.8 Conclusion*

In this chapter I have developed and defended a novel account for the permissibility of treatment limitation in newborn infants. The aim has been to determine the policy that we should use for treatment decisions in neonatal intensive care,.

The conventional view of the permissibility of withdrawal of life support is a view that I have labeled the Zero Line View – treatment may be withdrawn only where an infant is predicted to have a life-not-worth-living. I have argued for an alternative model - the Threshold View, according to which it is not obligatory to continue life support for infants who will have very low levels of wellbeing and Restricted Lives. Recall the infant Henry described at the start of this chapter. It is simply unclear whether or not his future life will be so bad that it would be better for him to die than to live. But we can be reasonably certain that if he survives his capacity to experience the goods of life will be severely

constrained. To keep Henry alive risks a very serious harm – that of being harmed by life. Treatment will impose serious burdens on Henry's family while yielding relatively little benefit to Henry. His parents have a right to decide about treatment given reasonable disagreement about how to weigh up the risk of a LNWL and because they will ultimately bear the costs of that choice.

The idea that life support may be permissibly withdrawn from newborn infants who are predicted to have lives worth living may seem striking, even shocking to some. Yet in fact the proposal is not a radical suggestion. The Threshold View, as I have outlined it, is broadly consistent with current practice in many neonatal units. On the basis of the guideline outlined above, it would be permissible to withdraw life support from newborn infants with predicted severe cognitive deficits including infants like Henry with HIE, those with congenital brain malformations such as lissencephaly, and infants with trisomy 13 or 18. It would also potentially include infants with overwhelming physical impairments such as spastic quadriplegic cerebral palsy, severe spina bifida or spinal muscular atrophy. It would not permit withdrawal of life support from infants with Down syndrome or milder forms of spina bifida.

One advantage, however, of the Threshold View is that it does not commit us to saying that the lives of children with the severe impairments outlined above are not worth living. It thus has potential advantages for the care of older individuals with impairment. Furthermore, unlike the Zero Line View, it does not commit us to the judgment that if parents refuse to allow withdrawal of life support from the infant they, and by extension any doctors who go along with their request, are harming the infants. It is consistent with the approach adopted currently in many neonatal units. In cases like those listed above doctors do not force parents to agree to withdrawal of life support. In my experience they often do not even try to *persuade* parents that treatment should be withdrawn. On the contrary, as described in the interviews in chapter 3, withdrawal of life support is offered to parents as an alternative that they may choose to embrace. With rare exceptions doctors do not oppose parental requests to continue treatment.

A second advantage is that it makes it possible to separate judgements about what *ought* to be done – for the sake of the child alone, and what should be *permitted*. It provides scope for recommendations about decisions, but permission for alternative decisions to be made. It is consistent with the Threshold View for a doctor to believe that, for the sake of Henry, life-sustaining treatment *should* be continued, even to recommend that it be provided, and yet ultimately, to respect his parents' decision to allow him to die.

The third advantage of the Threshold View is that it potentially provides more practical assistance with decision-making than the Zero Line View. Guidelines for treatment decisions have been vague about the severity of impairment that would warrant treatment withdrawal partly because of the epistemic and conceptual problems in determining the zero point, and partly because of potential expressivist concerns. The Threshold View, as noted above, does not express objectionable judgements about the lives of older

individuals with severe impairment in the way that the Zero Line View does. The Threshold is also defined in a way that makes it easier for the permissibility of withdrawal to be determined. It raises the possibility of more consistent decision-making between doctors and between hospitals.

# PART 3: CONCLUSIONS

## CHAPTER 10

### Neuroethics and neonatal prognostication

### *10.1 Introduction*

In this thesis I have outlined some of the ethical issues arising from the use of magnetic resonance imaging for prognostication in HIE. My main contention has been that there is a need for better guidelines relating to prognostic tests and decision-making in this group of patients. There is a need to clarify the relationship between treatment withdrawal and impairment, and to more clearly define the role and limits of parental involvement in treatment decisions. In this last chapter I draw together conclusions from the preceding chapters and summarise the practical suggestions arising from the analysis. I return to some of the case examples discussed earlier and look at what the proposed model for decision-making (The Threshold View) would imply for them. I highlight some of the broader potential implications of my analysis.

### *10.2 Neuroethics*

Neuroethics as a field of enquiry is a relatively recent offshoot of applied ethics. It involves the analysis of ethical and philosophical issues arising from developments in neuroscience (Levy 2007). Examples include the use of neuroimaging to detect when a witness is lying, or to detect consciousness in apparently vegetative patients.

There are a number of recurring themes in neuroethics. One of them is skepticism about the capacity of current technology to do the things that it is claimed to do. A second is the anticipation of problems and questions. Once we have sorted out the technical problems how should such technology be applied, what practical questions are going to be raised by these developments, what will be the implications for guidelines or for the law? A third theme relates to the deeper philosophical or ethical questions that are sometimes highlighted by new technology. These are often not new questions, but developments in neuroscience may bring novel insights or perspectives, or simply bring them back to academic attention and debate.

Neuroethics has, to date, largely focused on adults, for the simple reason that most research and most of the interesting technological applications have been in adults.

Detection of different brain states is far more challenging in patients who are non-verbal or pre-verbal. But there have been developments in neuroscience for newborns that raise a number of ethical questions.

One such development is the use of magnetic resonance imaging for prognostication. MRI of the brain in newborn infants has been available for 20 years. It is only in the last 5-10 years, however, that it has reached widespread clinical use. The distinctive feature of this new technology compared to previous technologies (ultrasound and CT, for example) is its ability to provide detailed images of the brain, and to distinguish between different patterns of injury, and different types and degrees of future impairment. There have been no previous attempts to look at the potential ethical issues arising from developments in prognostic technologies in newborn infants.

## *10.3 Themes and guidelines*

The first conclusions that I reached in this thesis are related to skepticism about new technology and science. My review of the published scientific literature relating to MRI and HIE (chapter 4) reveals that predictions from MRI are limited by uncertainty. Some of this uncertainty is likely to be intrinsic to the technology and to the nature of predictions in newborn infants. But I also identified a number of significant weaknesses in existing research that contribute to uncertainty. Previous studies have failed to focus on the most important prognostic question. I proposed a number of ways in which research into prognostic tests in HIE could and should be improved (Box 10.1).

One of the problems with previous research that I discussed relates to potential self-fulfilling prophecies. SFPs are inevitable for decisions about life-sustaining treatment that are made in setting of uncertainty. I highlighted some ways to reduce the epistemic problems related to SFPs. One important normative issue is the way in which patients and parents can be misled when given information about the chance of survival. When talking to patients and families about prognosis doctors should distinguish between survival rates *if treatment is continued*, and survival rates in populations *where treatment is sometimes limited*. For HIE, there is little or no existing data on survival rates in patients where life-sustaining treatment is continued, again highlighting the need for more research.

1. Studies of prognosis in HIE need to be adequately powered and prospective
2. They should measure multiple different prognostic factors and regression or propensity analysis should be used to determine the independent value of new tests for prognostication
3. They should focus on ventilated infants with moderate to severe encephalopathy in the first days of life
4. Cut-off points for continuous variables should be generated in a data-independent way
5. Follow-up should use validated, blinded outcome measures, present results in detail, and avoid overly inclusive outcome groups
6. Research into new prognostic tests should ensure, where possible, that test results are not used to influence treatment limitation decisions
7. Patients whose treatment is continued despite a poor prognosis should be followed-up and reported separately

*Box 10.1: Improving prognostic research in HIE*

A second broad theme emerging from the analysis relates to practical questions arising from the current or future use of new technology. One issue raised by the clinicians who I interviewed, was the timing of testing and the influence of the potential window of opportunity for treatment withdrawal. In chapter 5, I addressed some of the objections that might be raised to the window of opportunity. I applied decision theory as a way to tease out the important considerations for parents and doctors to consider when making a decision about the timing of testing. This gave rise to a number of recommendations for practice (Box 10.2)

In particular, I suggested that MRI should be available (and reported) urgently in neonatal units caring for infants with severe HIE. This is not presently the case in many places. For such infants there is a strong case that imaging should be performed early (within the first few days of life). Given the uncertainty around predictions MRI should not be used on its own to make a decision about treatment withdrawal. However, a *normal* appearance on MRI in an infant with severe encephalopathy and abnormal aEEG would raise serious questions about the underlying diagnosis and prognosis, and would often justify treatment continuation. I also argued that improvements in palliative care for infants with predicted severe impairment would reduce (to some extent) the problems created by the window of opportunity.

1. Neonatal intensive care units that care for ventilated infants with HIE need to have the ability to organise and obtain reports for MRI urgently (within 24 hours)
2. For infants with severe encephalopathy early prognostic testing should be seriously considered because of the high pre-test probability of severe impairment if the infant survives.
3. If testing is equivocal or reassuring parents should consider repeating it subsequently.
4. If the pre-test probability of severe impairment is high and testing is going to be delayed parents should be given the option of withdrawing intensive care without further tests.
5. Clear guidelines should be developed relating to withdrawal of artificial nutrition in infants with predicted impairment
6. If artificial nutrition is withdrawn, parents and infants should be supported as part of a coordinated palliative care program

*Box 10.2: Recommendations relating to the timing of testing and the window of opportunity for treatment withdrawal.*

In chapter 6, I highlighted the practical problem facing clinicians using existing guidelines to determine the permissibility of treatment withdrawal. Even where prognostic uncertainty is removed there are substantial epistemic and conceptual obstacles to determining whether or not, for a given degree of impairment, it would be in the best interests of the infant to withdraw treatment. This may be one reason why existing guidelines are vague. I argued that vagueness in guidelines creates significant problems in practice, and that this should motivate an attempt to generate more specific guidance.

In the ensuing chapters, I addressed a question that has faced those working in newborn intensive care for more than 35 years (Duff and Campbell 1973). When is it permissible to allow a newborn infant to die? In chapter 7, I analysed and rejected the view that there is a strong impersonal reason to replace impaired newborn infants. I suggested that there is, however, a stronger individual-affecting reason to allow an infant to die, based on the interests of parents. In chapter 8, I assessed how much weight should be given to this factor. I argued that parental interests *should* be taken into account, and that they should be given more weight for newborn infants than older children because of the attenuated nature of the newborn's interest in his future. However, I also argued that this would not justify the replacement of mildly or moderately impaired infants.

In chapter 9, I extended this argument to develop a different model for decision making – one that I called the Threshold View. I introduced the concept of a Restricted Life. For newborn infants who are predicted to have low levels of future wellbeing (below a defined

Threshold) it is permissible either to continue or to withdraw life-sustaining treatment. I defended the Threshold View on the basis of several discrete (though interrelated) arguments. Firstly, prognostic, experiential and conceptual uncertainty makes it difficult to know whether infants with severe patterns of injury will have a life that is above or below the zero point. Secondly, the argument from overlapping interests means that in such cases some weight should be given to parents' views about treatment, including their judgement about whether a given level of impairment would be worth living. Both of these factors mean that for a range of cases it may be permissible either to continue or to withdraw treatment. More controversially perhaps, I argued in chapter 8 that the interests of newborns in their future are reduced by their developmental immaturity. The strength of their interests, and consequently their moral standing, lies somewhere in between that of a fetus and that of an older child. I drew on this for two further arguments. There is an asymmetry in harms for newborn infants, such that it is a worse mistake to keep them alive with a life that is not worth living, than to allow them to die when they would have had a LWL – particularly where they would have a Restricted Life. Secondly, it is possible that the interests of others (particularly those of parents and siblings) outweigh the interests of the infant in continuing existence; this is most likely to be the case for infants with severe impairment.

Some may accept the first two arguments in favour of a Threshold View, but reject the latter arguments because they hold a different view of the interests of newborns and their moral status. Figure 10.1 illustrates other potential Threshold Views, based on different views about moral status.

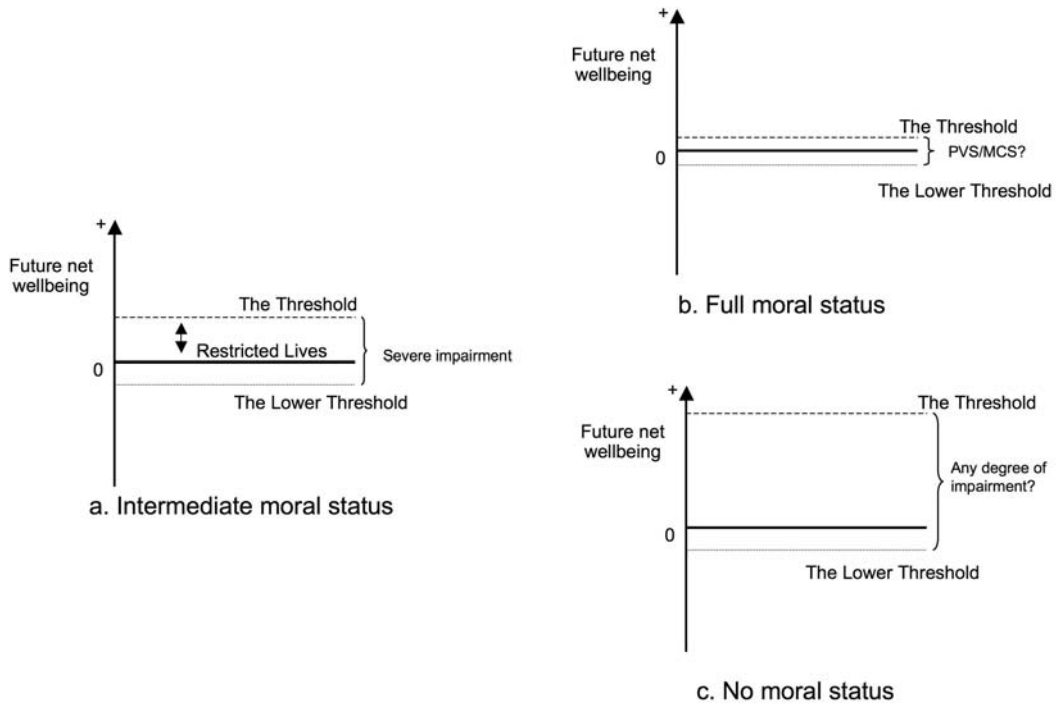


*Figure 10.1: Different Threshold Views*

If a newborn is believed to warrant identical treatment to an adult, then the range of cases in which parental discretion would legitimately hold would be small (Figure 10.1.b). Treatment continuation or withdrawal may be permissible for infants predicted to be in a persistent vegetative state (PVS), or possibly a minimally conscious state (MCS). But treatment could not be withdrawn on the basis of less severe impairments.

Alternatively, if a newborn is believed to warrant equivalent treatment to an early fetus there would potentially be no upper limit to the Threshold, and treatment might be withdrawn at any level of impairment (Figure 10.1.c.). (This may be limited by the possibility of adoption, as argued in chapter 8). The lower threshold would potentially still prevent treatment continuation for infants predicted to have substantial negative wellbeing, since the infant's interest in not suffering would be undiminished.

I rejected both of these views in chapter 8. In chapter 9, I proposed that the Threshold should be drawn at the level of severe cognitive or very severe physical impairment and outlined the way in which this would potentially relate to different patterns of injury from MRI (Table 10.1).

| Pattern on conventional MRI | Usual Outcome | Treatment limitation |
|---|---|---|
| Normal scans, mild basal ganglia or moderate white matter changes | Normal outcome (may include minor behavioural or learning problems) | Not permitted |
| Focal basal ganglia changes with bilateral signal abnormality in the PLIC | Moderate to severe motor problems (often dystonic/athetoid cerebral palsy), cognitive development may be normal | May be permitted (depending on likelihood of coexistent cognitive impairment and severity of predicted motor impairment) |
| Severe white matter changes | Moderate to severe motor impairment, as well as moderate to severe cognitive impairment | Permitted |
| Severe and diffuse basal ganglia changes | Severe motor impairment, severe cognitive impairment, microcephaly, often cortical blindness | Permitted. (If severe global injury and infant is ventilator dependent treatment continuation would not be permitted) |

*Table 10.1: Patterns of imaging and treatment limitation decisions.*

*(MRI findings should be interpreted in the context of other prognostic information including clinical assessment and aEEG)*

The reason for choosing to draw the threshold at this level of impairment is based on the risk of the infant having a LNWL, and the anticipated substantial reduction in wellbeing in the infant's future life. I argued that severe cognitive impairment, in particular, prevents or diminishes the infant's ability to access objectively valuable features of life.

## *10.4 Applying the Threshold View*

I referred to a number of cases during the course of the thesis. Figure 10.2 represents an attempt to relate these cases to the Threshold View developed in chapter 9. The figure is a simplification, since there are other factors that are relevant to decisions apart from the severity of impairment, for example the chance of death even if treatment is provided, the anticipated duration of survival, the need for painful medical interventions. But the Threshold View may help resolve some conflicting intuitions about previous cases.

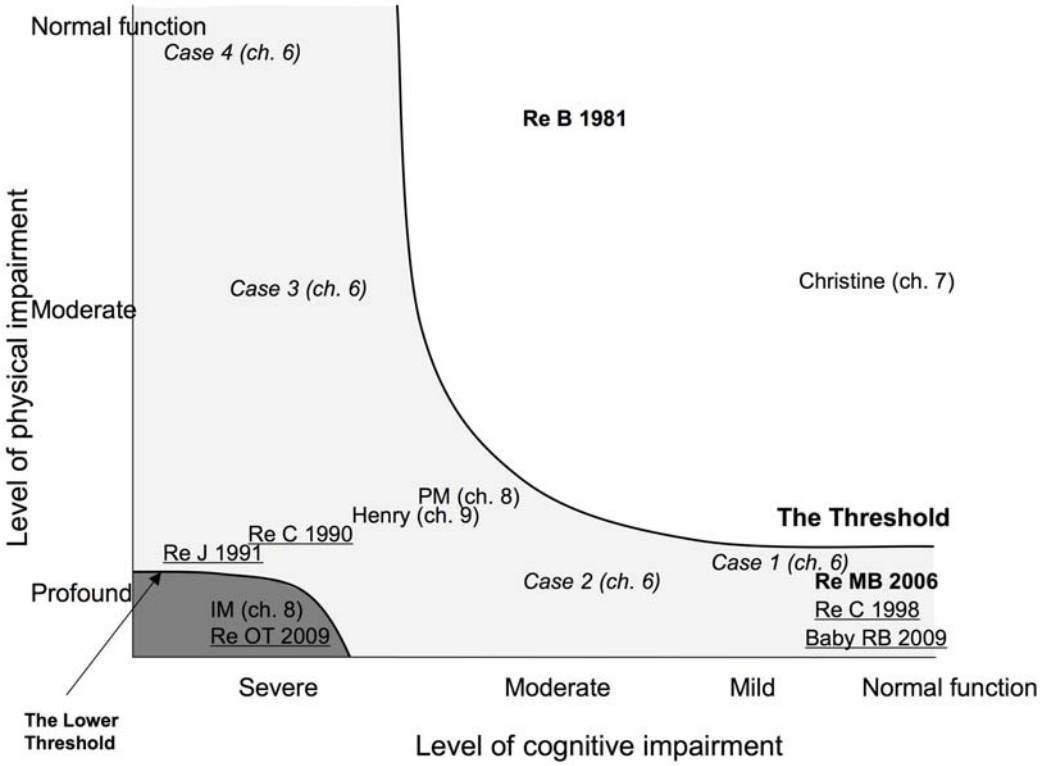


*Figure 10.2: The Threshold View in relation to previous legal cases and hypothetical cases discussed during the thesis*

> *Legal cases are discussed in chapter 2, summarised in Table 2.1. Other chapter locations are indicated in the figure. Cases in bold are those where courts ordered that treatment* not *be withdrawn/withheld. Those underlined are where courts approved of treatment withdrawal. The grey area indicates those cases that fall below the Threshold. The dark grey area indicates cases potentially below the Lower Threshold.*

In chapter 8, I discussed a pair of recent Canadian cases – those of IM and PM. Both were infants with severe HIE and severe predicted impairment. In IM's case doctors sought to withdraw treatment against the wishes of parents. In PM's case her parents' decision to withdraw treatment (supported by doctors) was overruled by the local clinical ethics committee. One difficulty for PM's parents (and legal team) was that they sought legal redress for the decision that led to their infant surviving, and yet they also now appeared to believe that PM's life was worth living despite her impairment. Full clinical details (not to mention MRI results) are not available from media reports. But it appears that IM's condition, given his need for ongoing mechanical ventilation and combined predicted

severe physical and cognitive impairment, falls below the Lower Threshold on the view that I have defended. Treatment continuation should not be permitted despite his parents' request. (His parents did, ultimately, consent to treatment withdrawal). In contrast, PM's current condition appears to be consistent with a Restricted Life. Her parents and doctors *should have been permitted* to withdraw LST, even though it was possible that she would have a LWL.

The Threshold View may also make sense of diverging judgements in those difficult cases where infants have profound physical impairments (quadriplegic or locked-in), are ventilator dependent, but are cognitively normal (Re C 1998; Re MB 2006a; Baby RB 2009a). In the case of MB the court ordered that treatment continue, while in RB and in Re C the court endorsed decisions to withdraw treatment. One reason why the court may have favoured continuation of treatment in Re MB is that it does not appear *necessarily* the case that such a life falls below the zero line. Some adult patients in a locked-in-syndrome report subjective wellbeing that is not substantially different from unimpaired individuals (Laureys et al. 2005). On the other hand, some adults who are locked-in request not to go on living (Fine 2005), and some request euthanasia (Kompanje et al. 2007). For infants who have no means of communication, who are likely to die in early childhood, and who require frequent painful interventions it is, in my view, more likely than not that the negatives of their lives outweigh the positives. On this basis treatment *should* be withdrawn from such infants, and it would be permissible to do so. It is appropriate that doctors attempt to persuade parents to change their minds if they insist that treatment be continued. And yet, it may also be permissible to continue treatment if parents are resolute in their desire and there are sufficient resources available to support the infant. If the infant is required to remain in intensive care for their respiratory support this latter question is likely to be critical.

The Threshold View would not prevent all conflict. Rather than disagreements about whether or not infants' lives would be above or below the zero line, disagreements may shift to whether or not infants' future lives would be above or below the Threshold (or Lower Threshold). There will always be borderline cases where guidelines are unclear. In this thesis I have largely focussed on the substantive questions relating to treatment withdrawal rather than procedural ones (Fost 1986, p. 151). I have not addressed how such decisions should be made (though I have argued that parents should have a key role in a range of cases), nor have I set out how disagreements should be resolved. Whether such disagreement would be more common or less common if the Threshold View were adopted is an empirical question that could be settled by future research. However, there is some reason to think that the Threshold View would lead to greater consistency in treatment decisions between neonatologists and between neonatal units.

## *10.5 Broader implications*

I have deliberately focused in this thesis on a small subgroup of critically ill newborn infants, term infants with HIE, and on one particular technology used in prognostication – magnetic resonance imaging. Nevertheless, the results of my analysis are highly relevant to other groups of newborn infants and other technologies. For example, the Threshold View would help explain why it is permissible either to treat or to withhold resuscitation for some extremely premature infants (within the so-called 'grey zone') (Paris and Schreiber 1996; Paris et al. 2005; Harrison 2008). It would answer those critics of the grey zone who argue that providing such scope for parental discretion is discriminatory since similar latitude would not be afforded to parents of older children (Janvier et al. 2007; Janvier et al. 2008a; Janvier et al. 2008b). The analysis of research into prognostic tests would also be relevant for this group, since there is considerable interest in the use of MRI to predict outcome in such infants (Woodward et al. 2006; de Vries and Cowan 2007).

The guidelines developed above for prognostic research are also relevant for other current and future prognostic technologies used in newborn infants. It is possible for example, that higher intensity MRI, functional magnetic resonance imaging, diffusion tensor imaging, or optical imaging may provide better prognostic tools for newborn infants with HIE or other conditions. Research into such technologies will be more useful for decision-making in newborn intensive care if it is focussed on the most important prognostic questions.

The analysis in this thesis is also highly pertinent to developments in neuroimaging for fetuses. There has been considerable interest in the use of MRI for prenatal diagnosis in fetuses (Dietrich and Cohen 2006; Al-Mukhtar et al. 2009; Rutherford 2009). But this development is likely to raise issues very similar to those addressed in this thesis. The epistemic problem created by self-fulfilling prophecies is likely to be even more challenging since large numbers of parents may elect for termination of pregnancy when abnormalities are detected, leaving a relatively small cohort of surviving infants on which to establish the validity of predictions. In jurisdictions where there are gestational cut-offs for termination of pregnancy there may be problems related to those of the window of opportunity for treatment withdrawal. Finally, for those jurisdictions where termination of pregnancy *is* permitted in the third trimester, new forms of imaging are likely to raise questions about whether predicted impairment is severe enough to permit termination. A Threshold View for late termination decisions might help set out the boundaries for parental discretion, and avoid expressivist objections. On the view that I have developed for newborns, a termination decision for a fetus with predicted severe impairment is consistent with the view that those who have such conditions have lives that are, on balance, worth living.

My analysis of the ethical issues arising from MRI in newborns reveals the same broad themes that are apparent in other areas of neuroethics. Firstly, a certain degree of scepticism is warranted on the basis of the science underpinning the prognostic use of

MRI; this points to the need for more, and better research studies. Secondly the development of new technology raises a number of practical questions that are not addressed by existing guidelines. Thirdly, these developments bring to the fore old questions about treatment decisions in newborn infants and the role of parents in such decisions.

In this thesis, I have criticized guidelines for treatment decisions that focus on the best interests of the infant, since it seems to me that such guidelines are unable to provide practical guidance to clinicians. In many cases it simply is not clear whether or not it would be in the best interests of the child to keep them alive. Nevertheless, the model that I have developed for decision-making retains a central role for best interests. Treatment decisions *should* be guided by what would be best for the patient. However, this is not the only consideration. It is the starting point, but not the finishing point for reflection about treatment withdrawal in newborn intensive care.

The model for decision-making that I have developed would not necessarily lead to a major change in practice in newborn intensive care. It would not lead to withdrawal of life support from infants with a reasonable chance of a good life. But it potentially provides a more consistent, more robust and more practical basis for the difficult decisions that are made daily in newborn intensive care units. It also accords with a sense, (that I suspect many parents and doctors share), that for us to be obligated to save the life of a newborn it must not only be a life worth living, it should also be a life worth giving.

## GLOSSARY:

**A Life Not-worth-living (LNWL):** A life that will contain more intrinsically bad experiences than intrinsically good experiences. There is negative net future wellbeing

**Balance Sheet approach to best interests**: Surrogate decision-makers are instructed to document the separate benefits and disbenefits of treatment. If the benefits outweigh the burdens treatment is in the best interests of the patient. If the burdens outweigh the benefits treatment is not in the best interests of the patient.

**Causing an Individual to Exist**: a decision to bring an individual into existence where there is no individual who thereby dies, or whose coming into existence is thereby prevented.

**Hypoxic Ischaemic Encephalopathy (HIE):** an illness marked by abnormal neurological behaviour in the newborn period as well as evidence suggestive of acute hypoxia/ischemia, including need for resuscitation at birth, and evidence of fetal compromise.

**Impairment**: reduction in physical, physiological or psychological capacities relative to species norm (Bickenbach et al. 1999; Buchanan et al. 2000, 285)

**Impersonal reason**: We have impersonal reasons to do something when wellbeing would be greater in one of two alternatives, but neither existing nor future individuals would be made either better or worse by such a choice.

**Individual-affecting reason**: We have individual-affecting reasons to do something, when a course of action will affect existing or future individuals for better or for worse.

**Intolerability test for best interests.** Treatment may be withdrawn if the condition that a patient will experience is intolerable.

**Intolerability (1)**. An *intolerable* condition is one that from the perspective of the individual patient P, involves extreme suffering or adversity and is more than they are able or willing to endure.

**Intolerability (2).** An *intolerable* condition is one that from the perspective of a reasonable third party (T), involves extreme suffering or adversity and is more than they (T) would be willing to endure.

**Intolerabilty (3).** An *intolerable* condition is one that from the perspective of a reasonable third party (T), involves extreme suffering or adversity and is more than they are able or willing for P to endure.

**Life worth living (LWL)***:* a life that contains or will contain overall more intrinsically good experiences than intrinsically bad ones

**Life-sustaining treatment (LST):** Treatment that is supporting vital functions, and without which the patient may die.

**Mild encephalopathy (Sarnat stage 1):** infants with HIE who are usually hyper-alert with normal muscle tone. They do not have seizures. Virtually all such infants survive without impairment.

**Moderate cognitive impairment:** intelligence quotient 35-50, (individuals usually are socially interactive and able to carry out basic conversations)

**Moderate encephalopathy (Sarnat stage 2):** infants with HIE who have reduced tone and conscious state. They often have seizures. They have about a 30% chance of severe impairment if they survive.

**Moderate physical impairment**: physical impairment at the level of GMFCS 2 or 3 (ie able to walk with aids, may require wheelchair in the community.

**Replacement**: a decision to kill or allow to die an existing individual in order to cause a different individual to exist, when that second individual *would not otherwise exist*

**Restricted Life**: A life in which net wellbeing is above the zero point but below the Threshold.

**Self-fulfilling Prophecy:** (SFP) A prediction (that a certain outcome is likely or inevitable) that has the potential to independently increase the probability of the outcome actually occurring.

**Severe cognitive impairment:** intelligence quotient ≤35, individuals may have elemental language and self-care skills see p 4

**Severe encephalopathy (Sarnat stage 3):** infants with HIE who are severely hypotonic (floppy), comatose, and have usually lost the drive to breath. They have at least an 85% chance of severe impairment if they survive.

**Severe physical impairment:** physical impairment at a level of GMFCS 4 or 5 or equivalent (ie wheelchair dependent) (Wake et al. 2003)

**Substitution**: a decision to cause one individual to exist rather than another individual (who does not already exist).

**The Lower Threshold**: A negative (below zero) level of net wellbeing defining the lower border of permissibility of treatment continuation. It is obligatory to withdraw life support for newborns with predicted wellbeing below this level.

**The Threshold View**: Life support may be withdrawn from a newborn infant if and only if their net future wellbeing falls below a certain minimum Threshold. This Threshold is above the zero point of a life worth living.

**The Threshold**: A positive (supra-zero) level of net wellbeing defining the upper border of permissibility of treatment withdrawal. It is obligatory to continue life support for newborns with predicted wellbeing above this level.

**The Zero Line View**: Life support may be withdrawn from a newborn infant *if and only if* their net future wellbeing is predicted to be below the zero point, ie they are predicted to have a life not worth living.

**The Zero Point**: A life that will contain equal amounts of intrinsically good and bad experiences.

**Tolerability Paradox:** Intuitively, the more severe a child's future impairment, the harder it will be for them to bear, and the more likely that their condition will be intolerable. There are, however, some reasons to think that beyond a certain point more severe degrees of cognitive impairment may make life *more* tolerable.

**Window of Opportunity**: the period of time during which infants with severe brain injury are dependent on life support, and consequently when withdrawal of LST is likely to lead to death.

# APPENDIX A

## *Topic guide*

### Introduction

Aim: to introduce the interviewer, explain the purpose of the interview and of the research, to explain how information from the interview will be used

- Introduce self and the Ethox Centre
- Discuss the purpose of research including objectives
- Explain nature of qualitative research, in-depth interviews, no right or wrong answers, interested in participants' views and practice
- Explain length of interview, reasons for recording
- Explain voluntary nature, free to withdraw, and free to choose not to answer any questions
- Ask not to use any identifying patient details
- Explain confidentiality, and how findings will be reported
- Ask if any questions

### Background and professional practice

Aim: to put the participant at ease, to highlight any key issues in the background of the participant that might affect their understanding of ethical issues, to understand the nature of the practice at the participant's institution

- Age, current role in unit,
- Training in UK and overseas, work in previous units
- Religious or spiritual background
- Research interests
- Personal research
- Other research within the unit
- Patient mix in the unit, frequency of infants with HIE
- Access to specialty services
- Neurology, EEG, imaging

**Prognosis for infants with HIE**

Aim: to explore the use of different prognostic tests for infants with HIE and rationale

- What does the term 'prognosis' mean to them
- Explore concepts raised by participant eg "uncertainty", "disability"
- Prognostic factors or prognostic tests they use in the setting of HIE
- Probe for detailed list of factors/tests used – *spontaneous list, then prompt if necessary for*
    - U/S
    - MRI
    - CT
    - EEG
    - Amplitude integrated EEG
- How often the test or factor is used
- Importance of different factors/tests
- Reasons why used
- How results from different tests are combined
- What they do if tests disagree
- How results are communicated with parents

**MRI for infants with HIE**

Aim: to explore the use of MRI for infants with HIE and ethical issues perceived

- Access to MRI
- Ease of access
- Transport
- Reporting
- Reasons for performing or not performing MRI
- Types of imaging used
- Timing of MRI
- How results are communicated
- Images/reports shown to parents or not
- Ethical issues associated with MRI – probe for how these affect decisions, how they are resolved
- Influence of MRI on treatment-limitation decisions

## Decisions to withdraw or withhold life-sustaining treatment in HIE

Aim: to explore the role of ethical concepts in decisions to limit or withdraw life-sustaining treatment

- Factors influencing decisions to withdraw treatment for infants with HIE in their practice
- Explore concepts raised – spontaneous, then prompt if necessary
- Certainty/Uncertainty – how dealt with
- Severity – what this means
- Different types of impairment/disability

## Role of parents in treatment-limitation decisions

Aim: to explore the role of parents in decisions to limit or withdraw life-sustaining treatment

- Role of parents in decision-making
- Limits to parental decisions
- Resolving disagreement between medical staff and parents

## Case vignette

Aim: to explore how decisions are reached and issues identified in specific case vignette

- Case 1:
- Brief clinical vignette presented
- MRI picture presented with report
- Outcome for the infant in their belief
- Basis for that belief, importance of different factors
- Other information that would be sought
- Advice that they would give to parents of this child
- Decisions to limit/withdraw treatment
- Basis for that decision

## General/closing issues

Aim: to elicit participants' thoughts on policies/guidelines for the use of MRI in HIE

- Ideas or suggestions for guidelines or policies in relation to MRI in HIE
- Anything else they would like to add

- Reiterate confidentiality, thank participant

## *Case example*

Case based on Micallef (2001)

A mother presents in labour at 41.6 weeks. CTG at presentation shows deep decelerations, and an emergency caesarean section is performed. There is thick meconium stained liquor, and a male infant is delivered.

Apgars are 4 at 1 minute, 4 at 5 minute, 4 at 10 minutes.

The infant is intubated within the first minutes of life.

Cord pH 6.76/7.02.

First blood gas at 90 minutes of age – pH 7.29, CO2 30, BE -11, lactate 11

He receives mechanical ventilation, though that is able to be reduced in the first 24-48 hours. He is cardiovascularly stable and does not require inotropic support; he has normal renal function.

He develops seizures at 48 hours of age that are treated with phenobarbitone. aEEG reveals continuous low voltage pattern.

On neurological examination on day 4 he was severely hypotonic, with absent gag reflex. An MRI is performed.

MRI is reported as showing: Loss of grey-white matter differentiation; Diffuse high signal intensity in the basal ganglia with no myelin signal in the posterior limb of the internal capsule.

# APPENDIX B

| First Author and Year | Pattern on MRI used for classification | Very Adverse Outcome |
|---|---|---|
| (Barnett et al. 2002) | Mod or severe BG, severe WM | Death, SQCP, dystonic/athetoid CP |
| (Biagioni et al. 2001) | Mod or severe BGT, severe WM | Quadriplegic or dystonic CP or DQ<50 or CP unable to sit, or death |
| (El-Ayouty et al. 2007) | Mod or severe BG, severe WM | Dystonic or quadriplegic CP |
| (Gire et al. 2000) | 'Severe': changes involving WM or BG | Profound handicap: cerebral palsy, blindness, non-aidable deafness |
| (Jyoti et al. 2006) | >30% BG or >30% WM or PLIC abnormality | CP not expected to walk, or DQ <55 |
| (Kuenzle et al. 1994) | Severe WM, Moderate or severe BG | DQ<55 or SQCP |
| (Leijser et al. 2007) | Mod or severe BG, severe WM | SQCP or death |
| (Mercuri et al. 2000) | Mod or severe BG, severe WM, or WM with haemorrhage, | SQCP or DQ<55 |
| (Meyer-Witte et al. 2008) | absent (not equivocal) PLIC on T1 or diffusely abN grey/white differentiation | "Severe cognitive or motor deficit" |
| (Robertson et al. 2001) | Diffuse BG change or abN PLIC | DQ<55 or death |
| (Rutherford et al. 1996) | Abnormal BG, or multiple areas of WM infarction | dystonic/quad CP, 'severe dev delay' |
| (Rutherford et al. 1998) | bilaterally abnormal PLIC | DQ<50, death |
| (Rutherford et al. 2010) | Mod/severe BGT, severe WM, abN PLIC | MDI <70 or GMFCS 3-5 or bilateral cortical visual impairment with no useful vision |
| (van Schie et al. 2007) | Abnormal signal in the entire cortex and BG or abnormal PLIC | dystonic or quadriplegic CP or DQ<55 |

*Table B1: Patterns of MRI findings and outcome descriptions used in analysis*

*Studies were included from those in the metaanalysis by Thayyil and colleagues if they reported patterns of conventional MRI imaging and included individual patient data with indication of the severity of changes in basal ganglia or white matter, and outcome in sufficient detail that they could be classified into the following categories:*

*Severe patterns included at least one of: non-focal signal abnormality in basal ganglia, abnormality (not equivocal) in posterior limb of internal capsule, diffuse or widespread white matter abnormality*

*Very adverse outcome: death, spastic quadriplegic or dystonic cerebral palsy or severe developmental delay (>3 standard deviations from mean on standardised testing)*[28]

*Other outcome: all other outcomes*

| | Severe patterns | | Non-severe patterns | |
|---|---|---|---|---|
| First author and year | Very adverse outcome | Other outcome | Very adverse outcome | Other outcome |
| (Barnett et al. 2002) | 28 | 4 | 0 | 36 |
| (Biagioni et al. 2001) | 15 | 1 | 0 | 9 |
| (El-Ayouty et al. 2007) | 10 | 4 | 3 | 8 |
| (Gire et al. 2000) | 8 | 2 | 3 | 5 |
| (Jyoti et al. 2006) | 7 | 0 | 0 | 13 |
| (Kuenzle et al. 1994) | 7 | 0 | 1 | 35 |
| (Leijser et al. 2007) | 14 | 0 | 0 | 9 |
| (Mercuri et al. 2000) | 21 | 4 | 0 | 27 |
| (Meyer-Witte et al. 2008) | 9 | 3 | 2 | 12 |
| (Robertson et al. 2001) | 3 | 1 | 1 | 9 |
| (Rutherford et al. 1996) | 7 | 0 | 0 | 9 |
| (Rutherford et al. 1998) | 32 | 4 | 1 | 35 |
| (Rutherford et al. 2010) | 53 | 18 | 5 | 54 |
| (van Schie et al. 2007) | 2 | 4 | 6 | 20 |
| Totals | 216 | 45 | 22 | 281 |

*Table B2: Severe patterns on conventional MRI and relationship to very adverse outcome (as defined in table B1)*

[28] This definition is pragmatic, and based upon categorisation available in studies. None of the studies provided GMFCS classification (except Rutherford 2009), and many did not provide details of cognitive/developmental testing. However, if MRI patterns lack sensitivity and specificity for predicting this level of impairment, a fortiori the same patterns will lack specificity for predicting greater degrees of impairment.

| | Severe patterns | | Non-severe patterns | |
|---|---|---|---|---|
| First author and year | Very adverse outcome | Other outcome | Very adverse outcome | Other outcome |
| (Kuenzle et al. 1994) | 2 | 0 | 1 | 26 |
| (Leijser et al. 2007) | 14 | 0 | 0 | 9 |
| (Meyer-Witte et al. 2008) | 9 | 3 | 2 | 12 |
| (Robertson et al. 2001) | 3 | 1 | 1 | 9 |
| (Rutherford et al. 1998) | 24 | 3 | 1 | 32 |
| (Rutherford et al. 2010) | 29 | 8 | 1 | 21 |
| (van Schie et al. 2007) | 2 | 2 | 5 | 10 |
| Totals | **83** | **17** | **11** | **119** |

*Table B3: Severe patterns on conventional MRI in the **first week** of life and relationship to very adverse outcome (defined in table B1)*

| | Severe patterns | | Non-severe patterns | |
|---|---|---|---|---|
| First author and year | Very adverse outcome | Other outcome | Very adverse outcome | Other outcome |
| (Barnett et al. 2002) | 28 | 4 | 0 | 36 |
| (Biagioni et al. 2001) | 15 | 1 | 0 | 9 |
| (El-Ayouty et al. 2007) | 10 | 4 | 3 | 8 |
| (Gire et al. 2000) | 8 | 2 | 3 | 5 |
| (Jyoti et al. 2006) | 7 | 0 | 0 | 13 |
| (Kuenzle et al. 1994) | 5 | 0 | 0 | 9 |
| (Mercuri et al. 2000) | 21 | 4 | 0 | 27 |
| (Rutherford et al. 1996) | 7 | 0 | 0 | 9 |
| (Rutherford et al. 1998) | 8 | 1 | 0 | 3 |
| (van Schie et al. 2007) | 0 | 2 | 1 | 10 |
| (Rutherford et al. 2010) | 24 | 10 | 4 | 33 |
| Totals | 133 | 28 | 11 | 162 |

*Table B4: Severe patterns on conventional MRI **after** the first week and relationship to very adverse outcome (defined in table B1)*

| | Severe patterns | | Non-severe patterns | |
|---|---|---|---|---|
| First author and year | Very adverse outcome | Other outcome | Very adverse outcome | Other outcome |
| (Leijser et al. 2007) | 5 | 0 | 0 | 7 |
| (Robertson et al. 2001) | 2 | 1 | 0 | 6 |
| (Rutherford et al. 1998) | 13 | 3 | 1 | 11 |
| (van Schie et al. 2007) | 2 | 2 | 5 | 8 |
| Totals | 22 | 6 | 6 | 32 |

*Table B5: Infants with moderate or Sarnat stage 2 encephalopathy: severe patterns on conventional MRI in the first week of life and relationship to very adverse outcome (defined in table B1)*

# APPENDIX C

Modelling and sensitivity analysis for this chapter used Excel (Microsoft, Redmond, Mass. USA)

## *Abbreviations*

Pt = Pre test probability of poor outcome

P(sw) = probability of survival after late withdrawal of life support

$SN_e$ = Sensitivity of early testing

$SP_e$ = Specificity of early testing

$SN_l$= Sensitivity of late testing

$SP_l$ = Specificity of late testing

P (FN) = Probability of False negative test result (survival with poor outcome )

P (TP) = Probability of True Positive test result (death of an infant who would have survived with poor outcome)

P (TN) = Probability of True Negative test result (survival with good outcome)

P (FP) = Probability of False positive test result (death of an infant who would have survived with a good outcome)

V (D) = Value assigned to death = 0

V (POL) = Value assigned to survival with poor outcome

V (L) = Value assigned to life with good outcome = 1

V (LW) = Value assigned to late withdrawal

## *For Early Testing:*

The probability of Death (of infant with poor outcome) P (TP) = Pt x $SN_e$

P (FN) = (1- $SN_e$) x Pt

P (TN) = $SP_e$ x (1-Pt)

P (FP) = (1- $SP_e$) x (1-Pt)

Expected Utility = (P (TP) x V (D)) + (P (FN) x V (POL)) + (P (TN) x V (L)) + (P (FP) x V (D)) = 0 + (P (FN) x V (POL)) + P (TN) + 0

## *For Late Testing:*

P (TN) = $SP_l$ x (1-Pt)

P (FN) = (1- $SN_l$) x Pt

P (FP) = (1- $SP_l$) x (1-Pt)

P (TP) = Pt x $SN_l$

Survival after late withdrawal (good outcome) = P(sw) x P (FP)

Death after late withdrawal (good outcome) = 1-P(sw) x P(FP)

Survival after late withdrawal (poor outcome) = P(sw) x P (TP)

Death after late withdrawal (poor outcome) = 1-P(sw) x P(TP)

Expected Utility = P (TN) x 1 + (P (FN) x V (POL)) + (P(sw) x P (FP)) x 1 + ((1-P(sw)) x P(FP) x V(LW)) + (P(sw) x P (TP) x V (POL)) + ((1-P(sw)) x P(TP) x V(LW))

Disutility of late withdrawal is attached only to deaths, i.e. the value of death becomes V(LW) for those deaths rather than 0

For simplicity I have not discounted survival without impairment (following late testing), or changed the utility of survival with severe impairment (following late withdrawal)

## *One-way sensitivity analysis:*

The Expected Utility is calculated for Early Testing, Late Testing, No Testing, and Early Repeated Testing with different values of the variable in question. Since the probabilities and values are independent, Expected Utility is represented by a straight line when plotted against any individual variable.

The intersection of lines represents the points where testing strategies are equivalent

## *Two-way sensitivity analysis*

The intersection points for Early Repeated and Late testing are calculated using simultaneous equations derived from calculated Expected Utility

For example, using Pt as the dependent variable

Expected Utility (Pt) = a + b x Pt

Where a and b are constants

a = EU (0) [Calculated expected utility for Pre-test probability of 0]

b = (EU (0.1) – EU (0))/ 0.1

Intersection of Early Repeated Testing with Late Testing corresponds to the value of Pt when the expected utility of Early Repeated Testing and Late Testing are equal

$a_{ET} + b_{ET} \times Pt = a_{LT} + b_{LT} \times Pt$

$Pt = a_{LT}-a_{ET} / b_{ET}-b_{LT}$

# APPENDIX D

## *A costs model of replacement.*

The impersonal reason to bring an individual into existence is greater than the impersonal reason to replace

From Figure 7.2 p 115

The impersonal reason to replace is proportional to the difference in net value between the current and next child.

Net Value $V_1$=(b-c) –(a-c) = b-a

The reason to conceive a child (compared to not having a child) is equal to the difference in net value between the positive wellbeing in the life of that child, and the costs of bringing that child into existence

$V_2$= b-c

But if we assume that the current child's life is worth living, and that the benefits in her life outweigh the costs, this means

1. a-c>0
2. a>c
3. therefore b-a <b-c ie $V_1$< $V_2$

The impersonal reason to replace is less than the reason to conceive.

## *Critical level utilitarianism*

In such a model 'L' (the level of wellbeing at the threshold) would replace 'c' in the costs model. Since a-L>0, b-L >b-a

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