

## Additional File 3 Full tabulated findings

### The ethical basis of parental informed consent for neonatal/perinatal research

Where children are unable to give or decline consent, parents should do so

- Based in autonomy
  - Parental autonomy/parents' own rights (12, 13)
    - Making decisions about a child is part of what it is to be a parent (14)
    - +/- as a 'privacy' right (15)
    - Parenting decisions is part of deciding how to conduct one's own life (13, 15)
    - Fetal rights as a function of maternal autonomy (16)
- Objections
  - Does parents' interest in autonomous parenting outweigh child's interests? (15)
  - Parents are no longer 'owners' of their children' (17)
- Parents as surrogate decision-makers (13)
  - When a child is not yet autonomous the parent is the most appropriate 'proxy' (18)
  - May have knowledge of personality, values and beliefs (older children) (18)
  - Not appropriate to think of 'autonomy' of a neonate (17, 18)
  - 'Family decision-making' – not appropriate to consider the child's decision in isolation (14)
  - Not appropriate to think of 'informed consent' for a child (14)
  - Parents will bear the consequences of the decision (13)
  - Legal 'rights' not appropriate for family law (15)
- Beneficence – purpose of informed consent is to protect best interests of child (12, 17)
  - Responsibility of parents to make decisions as a way of promoting child's best interests (13, 19)

- Parents most likely to have best interests at heart (15, 20)
  - Parents are best judge of best interests (15, 17, 18, 20)(Objection to this – justification is prudential and therefore insecure (15))
  - Parents should only be allowed to make the decision when it is in the best interests of the child (13, 14, 17, 20)
    - Protection of best interests should not rest entirely on informed consent (12, 17)
- Never ethically obligatory to consent to research (16)
  - Because this would conflict with altruistic motivation (17)
- Determining what is meant by best interests of neonate is not simple (mental state account vs desire-satisfaction account vs objective list account) (21)
- Triangle of paediatric ethics – child on top, parents and clinicians to lend support (17)
- Parental consent is a misnomer – should be parental permission (17)
- Parents (not courts) should make decisions to promote pluralism (15)

## The validity of parental consent

### Potential barriers (22)

- Time limitation - simply not possible to ask for consent
  - Time limit affects information given (23, 24)
  - Time limit affects understanding (24)
- Stress, anxiety, pain, sedation (23, 24)
  - Affecting understanding (23, 24, 25)
  - Affecting capacity (23, 25)
  - Contributing (positively) to autonomous decision process (13)
- Desperation, fear (23, 24, 26)
  - Affecting voluntariness (15, 24, 25)
  - Does not affect voluntariness if there was no 'right' to receive the unproven treatment (23)
- Consent process increases parental anxiety (24)
- Researcher as a figure of authority/power
  - Affecting voluntariness (28)

Undermining individuals' appreciation of their own competence is an obstacle to autonomy (25)

### Implications of barriers to informed consent

- Principle of autonomy
  - Violated if there is a defect in the consent process (24)
  - Parents used as a means to an end in the consent process (24)

Beneficence becomes a more important principle in research with neonates because informed consent is not possible (therefore autonomy/respect for persons should be applied with caution) (27)

Must strive for improvement/best possible consent even where perfect informed consent not possible (17)

Deprived/uneducated parents more likely to consent

- Conclusion cannot be generalised (24, 29)
- Not a just allocation of burden (24, 29)

## **Risk and double standard/disanalogy/asymmetry between consent for research and consent for clinical treatment**

- Ambiguities of risk
  - If context is potentially life-threatening and outcome is unknown this should be viewed as significant risk (30)
  - If context is potentially life-threatening this is a risk of the disease/situation and not the trial, so should not be viewed as a risk of the trial intervention (31)
- Fully informed consent not possible for clinical trials because the very information needed for informed consent is that which is uncertain and under investigation (32)
- Beneficence trumps in clinical decisions (33)
- Autonomy trumps in research decisions (24)
  - Because the two types of consent evolved separately (29)
  - Because equipoise means appeals to beneficence in research are less convincing (13, 16, 17)
- Where there is genuine equipoise therapeutic research is not significantly different from treatment (33)
  - There should be no difference in principles between the two (32, 33)
- If there is inclusion benefit should research be any different to treatment? (34)
- Stricter ethical guidelines in research acknowledge the altered doctor/patient relationship (34)
- RCTs needed to protect patients from the use of untested treatments (23, 35)
  - Using unproven treatments is in itself a violation of autonomy (31)

## Other options for gaining consent

Waiver of consent in emergency situations (18, 36, 37, 38)

- With provisional assent at time (37)
- With community involvement at design stage (30)
- Principle of autonomy not violated (30)
- Aim is to make research possible for benefit of patients (30)

Antenatal notification and consent (36, 38)

- Advantages
  - Extra time (24)
    - Aids understanding (36)
    - Reduces anxiety (36)
- Disadvantages
  - Logistical problems (30, 37)
  - Unnecessary burden on those who are not eligible (34, 37, 38)
  - Parents may not listen properly if assuming they may not be affected (34)

These disadvantages can be mitigated by good communication skills (34)

Deferred/continuing consent (18, 24, 37)

- Full consent when they are capable of taking in the information and making decision (18)
  - 'Permission to continue' (18, 36)
  - Irrelevant if the trial is a one off intervention (30, 36)
- Justification for not obtaining initial full consent
  - Parents absent (18)

- Situational incapacity (18)
- Objections
  - No-one actually consents to enrolment (18, 24)

#### Proxy consent (18)

- Difficult finding truly independent proxy (18)
- Doesn't feel as if it honours autonomy in the same way (18)
- Needs truly independent proxy to ensure that interests of participants are not conflated with interests of research team or society (18)

#### Zelen method (12, 39)

- No need to inform patients if the 'intervention' does not affect them (39, 41)
- Avoids distress (41)
  - Of consent process itself (12, 40)
  - Of knowing they were in the control group (40)
- Still respects rights of family to know what is happening (12, 39)
- Statistical/methodological problems (35)
- Circumvents consent requirement (35)

#### Retrospective consent

- Logically incongruent (18)

#### Opt-out

- Advantages
  - May lessen burden on parents (34)
  - May increase recruitment (34)

- May increase understanding (34)
- Objections
  - Autonomy overridden (34)
    - If fails to exercise opt-out right by default rather than autonomously (34)
    - This could be minimised by good communication (34)
    - Loss of autonomy at that stage could be 'offset' by continued discussion after the event (34)
  - 'Restore autonomy' by giving more time for information processing (34)

Antenatal notification + opt-out + continuing consent = 'presumed consent' (24, 34)



### **Miscellaneous themes**

- Father has moral interest in health of fetus and pregnant woman (29)
- Fetal interventions have physical risks and implications for pregnant women (29)
  - Consent must be based on pregnant woman's assessment of her own interests (29)
- Pregnant women are subject to advice, influence and pressure from partners/mothers/in-laws/healthcare providers/the media, and it is therefore difficult for a pregnant woman to make her own decisions (28)