

Improving the quality of consent to randomised controlled trials by using continuous consent and clinician training in the consent process

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Improving The Quality Of Consent To Randomised Controlled Trials Using Continuous Consent And Clinician Training In The Consent Process

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Key words: neonatology, continuous consent, ethics, RCT, clinician training.

Special note: We have been unable to embed the tables where cited in the text. This is because the tables are in landscape layout whereas the text is portrait. We apologise for this and hope you will bear with us. The tables are at the end of the text, after the references and appendix.

Improving The Quality Of Consent To Randomised Controlled Trials Using Continuous Consent And Clinician Training In The Consent Process

ABSTRACT

Objectives: To assess whether continuous consent, a process whereby information is given to research participants at different stages in a trial, plus clinician training in that process was effective when used by clinicians gaining consent to the TOBY trial. The TOBY trial is a randomised controlled trial investigating the use of whole body cooling for neonates with evidence of perinatal asphyxia. Obtaining valid informed consent for TOBY is difficult; as such, it is a good test of the effectiveness of continuous consent.

Methods: Semi-structured interviews were conducted with 30 sets of parents who gave consent to TOBY and with 10 clinicians who sought it using the continuous consent process. Analysis focused on the validity of parental consent based upon the consent components of competence, information, understanding and voluntariness.

Results: 19/27 (70%) couples had no significant problems with consent validity at the point of signature. Problems lay mainly with the parents' competence and understanding. Mothers particularly had competence problems in the early stages of consent. The understanding problems were primarily to do with side effects.

Problems in both areas (competence and understanding) reduced markedly, particularly for mothers, in the post signature phase when further discussion took place. Randomisation was generally understood but unpopular. Clinicians did not always give information in stages during the short period of time available before parents gave consent. However, most clinicians were able to give follow up information.

Discussion: The consent validity compares favourably with similar trials examined in a comparable study (the Euricon study).

Conclusion: Researchers should consider adopting elements of the continuous consent process and clinician training in RCTs, particularly where they have concerns about the quality of consent they are likely to obtain using a conventional process.

INTRODUCTION

The TOBY-QUAL study aimed to evaluate the process of continuous consent used during the MRC funded TOBY trial. TOBY is a randomised controlled trial (i.e. a research study in which patients are allocated at random to receive one of two or more clinical interventions) in which babies born with evidence of perinatal asphyxia are randomised either to receive conventional care or conventional care plus whole body cooling (to 34°C) on a special mattress for 72 hours. It presents a challenge for clinicians to obtain valid, informed consent from parents of neonates for at least three reasons: first, the trial involves very sick infants; second, the trial treatment needs to be started within six hours of birth; and third, treatment is not blind, even to the parents, and yet babies in the control group born away from specialist treatment centres will need to be transferred to one of these centres. The stress for parents is compounded by the fact that perinatal asphyxial encephalopathy is almost always unexpected. Such circumstances threaten the validity of consent (1, 2).

The continuous consent approach to obtaining informed consent for RCTs has been proposed as a method for ameliorating this difficulty (3). It involves giving parents information at more than one point in the trial in the hope that they will assimilate it better. Such an approach is used in the TOBY trial. It has three main elements (4):

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Element 1: If born in a non-cooling centre, while the baby is assessed for eligibility, parents are given preliminary information about the trial, including a preliminary information leaflet. (If deemed appropriate, the leaflet may also be given to parents of babies born in a cooling centre or preliminary information may be offered more informally.)

Element 2: If the baby is eligible, a second, more comprehensive, information leaflet is given to the parents and further discussion takes place. At this point, parents are asked for their written consent and randomised.

Element 3: During the intervention period the consultant neonatologist meets with the parents to ensure that they understand the trial procedures and wish to continue to participate in the trial. It is made clear that the parents remain free to withdraw their baby from the trial.

In addition, clinicians are given training in obtaining informed consent for TOBY and at all times, a senior investigator is available to discuss concerns raised by parents during the trial. As the trial took place during the critical opening 72 hours of the neonate's life, the availability of a senior investigator (who was also a senior clinician involved in the baby's care) was fairly reliable although there may have been some delay at times (e.g. in the middle of the night).

Continuous consent aims to obtain the best possible informed consent in a situation of urgency. However, it has not been evaluated. The objective of 'TOBY-QUAL', the qualitative sub-study reported here, was to evaluate the process of continuous consent used in TOBY.

METHODS

One researcher (PA) conducted semi-structured interviews with parents who gave their consent to the TOBY trial and clinicians who sought it using the above process. The interview questions were open-ended and based around the four components of informed consent: competence, information, understanding and voluntariness (5). The transcripts were analysed using a well-established, qualitative process (framework analysis) (6). The validity of consent was assessed against the four components of the consent listed above. A scoring system was used on each component as follows:

1 = perfect

2 = valid with minor problems

3 = equivocal: significant problems

4 = validity in doubt: serious problems with the standard.

A score was given for each parent both for the point at which they gave formal signed consent and for the point at which they had further discussion with the clinician after the signature but during the

treatment phase. These scores were then assimilated and an overall score was given first, for each parent and then for the couple as a whole. The interviews were also analysed with a view to discerning common themes.

Determining in which category to place the components involved judging the interviews against the criteria for informed consent that has developed across a wide range of ethical and legal literature. For example, the Re. C UK legal judgement gives several criteria by which to judge competence (7). Thus, were a mother to have received opiates to the extent that she were no longer able fully to retain the necessary information to give informed consent then this would be deemed either a significant or a serious problem (depending on how impaired she was). In a similar way, we would judge parents to have a problem with understanding if, for example, they were unable to give a description of how treatment was randomly assigned. To ensure reliability of analysis, the two investigators analysed each interview independently.

RESULTS

Background data

Between January 2003 and July 2004, there were 55 eligible TOBY-QUAL babies. Five sets of parents were excluded: one because of poor English, the rest because the consultant asked us not to approach the parents. In all these cases the baby had died and the consultant felt

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it inappropriate to approach the parents, for example, because he or she thought it would be unduly upsetting to talk about the study. The remaining 50 were asked to take part in TOBY-QUAL. 20 refused or did not respond to the request; 30 were interviewed. Of the parents interviewed, the split between those whose babies received the trial treatment and control was 17/13. 4/30 (13%) interviews were with the mother alone, the rest with both parents. In all but one case, both parents were available to give consent to TOBY. Ten clinicians were interviewed. Demographic information is provided in table I.

Use of the continuous consent process

Many parents did not recall the process being used precisely as set out above (Table II). The first information sheet is envisioned mainly for use when babies are to be transferred from an outlying hospital; as such, its absence was not considered a deviation from the continuous consent process if it was not given in cooling centres. We deemed more significant any deviations from elements 2 or 3. Overall, the process was followed fully in 17 cases, mostly in seven, but was not followed in six cases.

Validity of consent

At the point of signature, the overall consent validity for the couple, taking the best score of either parent was as follows: 19/27 (70%) had a validity score of 1 or 2 (i.e. perfect or with minor problems); 8/27 (30%) had a validity score of 3 or 4 (i.e. significant or serious

problems). For three sets of parents there were missing data for the father (e.g. where the mother was interviewed alone).

A key finding was the improvement in consent validity at signature to that post signature for each parent (Table III). At signature 22/30 (73%) of mothers and 8/27 (30%) of fathers had significant or serious problems with the validity of their consent. In the post signature phase (element 3) the respective figures were 7/29 (24%) and 4/26 (15%) (data missing from four sets of parents). Thus there was a general improvement for both mothers and fathers from element 2 to element 3 of the consent process. This was more marked for mothers, perhaps because they had the greater problem in the first place. 19/29 (66%) of mothers showed an improvement as against 9/26 (35%) of fathers. Taking each consent component in more detail:

A) Competence: See Table IV. 18/30 (60%) mothers had impaired competence (scored 3 or 4) at signature. This was due largely to the anaesthesia, opiates and other problems associated with a traumatic birth.

“I just, I really can’t remember anything at the time; ... I was smacking myself on the nose to keep myself awake because I was just like this [gestures sleepy] my head was spinning; most of the day is a blur anyway, most of the labour’s a blur ... they give you morphine...”

[Mother: 24] (The interview number at the end of each quote shows the variety of sources used.)

However, fathers were able to compensate; all but one father (whose first language was not English) scored 1 or 2 for competence at the point of signature. Nonetheless, some fathers did find consent difficult due to factors such as the speed and suddenness of events combined with the emotional trauma. Where fathers were more competent at the time of signature they usually signed the consent form. On a few occasions less competent mothers were asked to sign because the couple weren't married. One unmarried father signed on behalf of his incompetent partner. The competence of the mothers generally improved in the post-signature phase and they were usually able to play an active role in the third element of the continuous consent process.

B) Information: See Table IV. The main problem in the pre-signature phase was that 4/30 (13%) sets of parents did not recall receiving a main information sheet. In the post signature phase, 6/30 (20%) did not recall receiving follow up information although in half of these cases the baby died (and, therefore, follow up information would have been inappropriate).

C) Understanding: See Table IV. At the point of signature 19/30 (63%) mothers and 7/27 (26%) fathers had poor understanding

(scored 3 or 4). In the post signature phase there was a marked improvement: the respective figures were 10/29 (34%) and 5/26 (19%). The problems of understanding for the mothers seemed largely to result from their competence problems. However, a number of themes emerged across the range of parents.

1) *Treatment.* Following element 3 of the consent process, almost all parents grasped the general idea of whole body hypothermia, the procedure and its basic rationale. The main reason parents gave for their consent was the hope that trial entry would improve their baby's prospects. One or two also mentioned the hope that it would contribute to future knowledge.

2) *Side effects.* The main TOBY information sheet says the following:

“...there is a possibility that cooling may lead to problems with blood pressure control, abnormal heart rhythm, bleeding and clotting problems and chemical and sugar imbalances in the blood.”

Some clinicians highlighted this point (whilst others said they played down the side effects). Table V summarises the parental awareness of side effects. Surprisingly up to 48% of parents interviewed, despite being given the main information sheet (and

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usually verbally informed about side effects) did not seem to have knowledge of them at interview. 6/30 (11%) did not recall being informed of side effects (e.g. some said they were explicitly told that there were none, others did not recall being given the main information sheet). Some parents said that they only gave consent because they believed that the treatment could not harm the baby.

“Our main concern was whether it would have side effects, that was our main concern; any side effects and we wouldn’t have given our consent.” [Father: 11]

For other parents, the situation may have seemed so severe that side effects were of little import to them.

“We fully understood what he wanted to do in terms of treatment ... we fully understood the side effects if there was going to be any, or the risks involved, but obviously whatever anyone tells you all you listen to is that your child is damaged...” [Mother: 2]

3) *Randomisation*. In 3/30 (10%) interviews it seemed that the parents had not grasped the fact that treatment would be chosen randomly. For example, one parent thought it was used in order to allocate a scarce resource. In the remaining interviews at least

one parent in each couple had a reasonable understanding of randomisation. However, many parents disliked the method. Generally, those who received control were disappointed whilst those who received cooling were relieved.

“I remember saying to him, ‘Oh great, great, like some effing placebo’ is what I said to him; so, no, I totally understood that idea, so I was kind of glad [because the baby received cooling.]” [Mother: 4]

D) Voluntariness. See table IV. Clinicians showed concern about the voluntariness of parents’ consent:

“... it’s easy for someone to put a gun to your head and say it’s your decision. And the gun being that their baby is born and is damaged and is needing a lot of resuscitation and here we are saying, look there’s a trial happening and this is the only thing available, and there’s nothing else available...” [Clinician: 6]

And it was certainly something many parents spoke about:

“Interviewer: What made you say yes?

Father: Desperation, I suppose, there was no other option and it was worth a shot, and that is the truth.” [Father: 15]

Nonetheless, only two parents had a significant or serious problem in relation to voluntariness; the vast majority of parents were clear that the decision was theirs, that normal treatment was available outside the trial and that they could withdraw. Some parents mentioned this withdrawal option as a reason for giving their consent in the first place. Thus voluntariness seems to have been achieved at the point of signature despite the short period of time available and the desperation of the parents.

Attitudes to the consent process

26/27 (96%) sets of parents said they felt it was right that clinicians sought their consent for the trial (missing data from three sets of parents). Some parents talked of their right to decide on behalf of their child. Other parents said that being asked for consent enabled them to feel involved in their child's care, perhaps for the first time. Clinicians also generally viewed consent as valuable or necessary. However, at least two pointed to the scientific cost involved in delaying randomisation and trial entry whilst obtaining consent.

Only two parents noted problems with the use of continuous consent itself. Both related to receiving additional information at a later stage. For example, one father said,

“We were told a hell of a lot more on the [element 3 stage] than we were on the [element 2, day of birth].” [Father:10]

DISCUSSION

Interpretation of the study requires discussion of its limitations. First, we relied on the memory of participants, which may be flawed (8). This problem applies to any interview-based study of a phenomenon. It is obviated in our study by the fact that 12/30 (40%) interviews were conducted within one month of the baby’s birth, and 22/30 (73%) within three months; all were conducted within 12 months. Furthermore, flawed memory should, if anything, worsen the results because parents, for example, lose their understanding of randomisation. Therefore, flawed memory does not undermine our generally positive findings on continuous consent.

Perhaps it might be argued that interviewees were inclined to give a positive assessment of the consent process as the immediate memory faded, particularly in the presence of a kindly interviewer; a type of Hawthorne effect. However, three points make this unlikely. First, many of our questions probed objective measures, such as knowledge of randomisation; a kindly interviewer cannot create this knowledge. Second, parents were willing to criticise elements of the consent process, particularly randomisation. Third, it would be odd for there to be a Hawthorne effect in the TOBY-QUAL study that was not

present in the many other studies of consent to RCTs that found poorer quality consent.

Another limitation relates to our sample. Twenty sets of parents either declined or did not respond to our interview request. There were a higher proportion of deaths in the non-respondent group (40% against 13%). However, one should bear in mind that many of the babies that survived were impaired to varying degrees. Their parents would not necessarily have a particularly rosy view of the TOBY trial compared with those whose babies died. Another issue is that we interviewed only parents who gave consent to TOBY. There were some parents who refused it. Our reason for excluding this group is that they did not go through the continuous consent process and, therefore, could not comment on it.

TOBY-QUAL's chief aim was to judge whether or not the standardised, continuous consent process used in the TOBY trial was successful at getting valid informed consent from parents. The time available for consent is short and the research is looking at a treatment for a life threatening condition in the neonate. The Euricon study (1) interviewed 30 sets of parents who had given consent to similar studies. In the Euricon study, at the point of signature, there were significant or serious problems with consent validity in at least 17/30 (57%) cases. (This is the lowest possible estimate; it may have been

higher.) The equivalent figure in the TOBY trial is 8/27 (30%) parents: this is a marked improvement on the Euricon figures. It suggests that TOBY clinicians using the continuous consent process had done well in difficult circumstances. Perhaps more importantly, in the post-signature phase (element 3) the validity scores often improved, particularly for mothers. This is one of the successes of continuous consent. With conventional consent procedures, mothers whose competence is impaired up to the point of signature can be sidelined from consent, with continuous consent they are not.

What explains this relative success? In the first place, TOBY trial clinicians were offered training and support in the process of obtaining consent (including role-play and workshops). The success in obtaining a relatively good quality of consent at the point of signature is presumably partly down to this training and partly down to element 1 (formal or informal) and element 2. The improvement post signature shows the benefit of the formal follow-up discussion (element 3) and, presumably, again the training of clinicians.

This has implications for other trials. Numerous empirical studies have uncovered a poor standard of informed consent to RCTs (9, 10, 11). It is tempting to conclude that valid informed consent cannot be obtained, particularly in difficult situations (12). TOBY shows that careful attention to consent can, at least to some extent, overcome the difficulties. Researchers should consider using aspects of the

continuous consent process particularly where they believe that obtaining valid informed consent might be difficult.

One such aspect is formal training of researchers in obtaining informed consent. Presently, clinicians have very little, if any, such training (3). This may change as ethics and communication enter medical curricula. However, the training for clinicians in the TOBY trial is geared specifically at gaining informed consent for that trial; such an approach could be more helpful than a generic one.

A second aspect is treating informed consent as a process rather than a point (i.e. the point where a signature is given). This recommendation has been made before (13). In TOBY it is done through graded information (element 1, followed by element 2) prior to signed consent and formal follow-up discussion (element 3). We found element 3 to be most helpful to mothers who are unwell after the birth. As such it might be of particular use where consent is obtained from people with acute illnesses. However, many of the fathers also seemed to benefit from the follow-up; hence its use should not necessarily be restricted to the acutely ill. Element 1 may be particularly helpful in non-urgent situations where there is a lot of complex information to convey.

Another factor researchers might take from the TOBY trial is the attitude to informed consent. The decision to use continuous consent

was a reflection of the fact that the trial investigators viewed consent as important; much attention was paid to the design of the process; clinicians were trained in its use. Some of the positive findings of this study, such as the overwhelming voluntariness of parental consent, may reflect the attitude of the clinicians to consent as much as the process itself. Overall, the TOBY-QUAL study suggests that a process view of consent, reflected in a design such as continuous consent, can help clinicians obtain valid informed consent.

Conflict of interest: None declared

Ethics approval: North West Multi-centre Research Ethics Committee (UK) granted approval for this study on 27th March 2003. The number is MREC 03/8/9. Appropriate local approval was given by all necessary LRECs and Trust Research and Development Departments.

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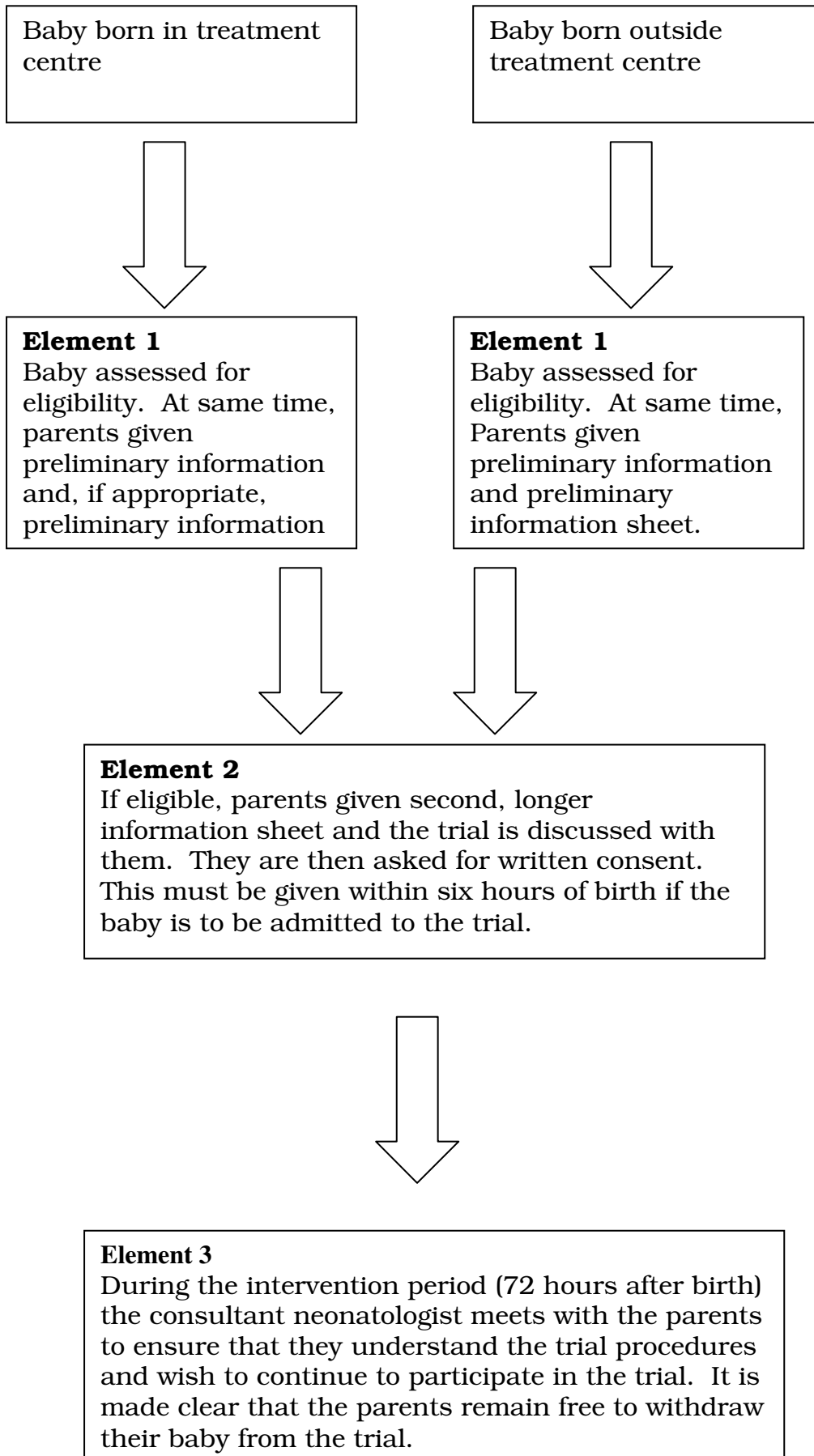
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Appendix: Flow chart of continuous consent process



TABLES

Continuous consent in the TOBY trial.

Table I: Social class, ethnicity and age of parents							
Social class¹		Ethnicity²			Age		
			Mother	Father		Mother	Father
1 – Higher managerial and professional	1	White UK	24	19	16-19	1	0
2 – Lower managerial and professional	8	White other	2	6	20-29	9	5
3 – Intermediate occupations	3	Pakistani	1	1	30-39	18	17
4- Small employers and own account workers	2	Black Caribbean	1	0	40+	1	5
5 – Lower supervisory and technical	5	Black African	2	3	Not known	1	3
6 – Semi-routine occupations	2	Not known	0	1	Total number	30	30
7 – Routine occupations	5	Total number	30	30			
8 – Never worked/ long term unemployed	3						
Not known	1						
Total number	30						

¹ Based on Office of National Statistics Classification [www.statistics.gov.uk – accessed 30/5/05].

² Based on Office of National Statistics Classification [www.statistics.gov.uk – accessed 30/5/05]. Ethnic groups not represented were: mixed, Indian, Bangladeshi, Other Asian, Other Black, Chinese, Other Ethnic.]

Continuous consent in the TOBY trial.

Table II Was the continuous consent process followed?	
<i>Element 1</i>	
First sheet given separately (transferral centre)	5
First sheet given separately (cooling centre)	3
First sheet given with main information sheet (cooling and transfer centres)	12
First information sheet not remembered being given (transferral centre)	3
First information sheet not remembered being given (cooling centre)	7
<i>Element 2</i>	
Main information sheet given with discussion	26
Main information sheet given after signed consent	1
Main information sheet not remembered being given but discussion took place	3
<i>Element 3</i>	
Follow up discussion took place	24
No follow up discussion remembered (baby died)	3 [all in control group]
No follow up discussion remembered (baby lived)	3 [2 in control group]

Continuous consent in the TOBY trial.

Table III: Consent validity at signature and post signature for each parent, plus validity improvement post signature				
<u>Validity score</u>	Mother		Father	
	At signature	Post signature	At signature	Post signature
1- Perfect	0	8	3	9
2- Minor Probs	8	14	16	13
3- Significant Probs	12	3	5	2
4- Serious Probs	10	4	3	2
Don't know	0	1	3	4
Total Number	30	30	30	30
Improved post signature	19		9	
Stayed the same post signature	10		17	
No information	1		4	
Total Number	30		30	

Table IV: Validity of individual components At sign and Post sign signature for each parent																
<u>Validity score</u>	Competence				Information				Understanding				Voluntariness			
	Mother		Father		Mother		Father		Mother		Father		Mother		Father	
	At Sign	Post sign	At sign	Post sign	At sign	Post sign	At sign	Post sign	At sign	Post sign	At sign	Post sign	At sign	Post sign	At sign	Post sign
1 – Perfect	3	24	13	22	20	23	21	23	1	8	5	8	23	27	22	25
2 – Minor problems	9	3	12	2	4	1	3	0	10	11	15	13	6	2	4	1
3 – Significant problems	10	2	1	1	3	2	1	1	9	6	4	3	0	0	1	1
4 – Serious problems	8	0	0	0	3	3	2	2	10	4	3	2	1	1	0	0
Don't know	0	1	4	5	0	1	3	4	0	1	3	4	0	0	3	3
Total number	30	30	30	30	30	30	30	30	30	30	30	30	30	30	30	30

Continuous consent in the TOBY trial.

Table V Parental recall of side effects of total body cooling (55 parents of 30 babies)	
Aware of side effects before signing consent form	19 (34%)
Aware of side effects after signing consent form	4 (7%)
Side effects not acknowledged although clearly informed about them (e.g. had read main information sheet)	18 (33%)
Not aware of side effects although given main information sheet (but this had not been read)	8 (15%)
Not properly informed of side effects	6 (11%)
Total Number	55