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Parental perspectives about information and deferred versus two-stage consent in studies of neonatal asphyxia

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ABSTRACT

Objective The ALBINO Trial (NCT03162653) investigates effects of very early postnatal allopurinol on neurocognitive outcome following perinatal asphyxia where prenatal informed consent (IC) is impossible. Ethically and legally, waiver of consent and/or deferred consent (DC) is acceptable in such an emergency. Short oral/two-step consent (SOC, brief information and oral consent followed by IC) has recently been investigated.

Methods Mixed-methods analysis of parental opinions on DC versus SOC in the context of neonatal asphyxia in a survey at two German centres. Prospective parents (ProP), parents of healthy newborns (PNeo) and parents of asphyxiated infants (PAx) born between 2006 and 2016 were invited.

Results 108 of 422 parents participated (ProP:43; PNeo:35; PAx:30). Most parents trusted physicians, wanted preinterventional information and agreed that in emergencies interventions should begin immediately. Intergroup and intragroup variability existed for questions about DC and SOC. In the ALBINO Trial situation, 55% preferred SOC, and 26% reported DC without information might adversely affect their trust. Only 3% reported to potentially take legal action after DC. PAx were significantly more likely to support DC. PAx more frequently expressed positive emotions and appreciation for neonatal research. In open-ended questions, parents gave many constructive recommendations.

Conclusion In this survey, parents expressed diverse opinions on consent, but the majority preferred SOC over DC. Parents who had experienced emergency admission of their asphyxiated neonates were more trusting. Obtaining parental perspectives is essential when designing studies, while being cognisant that these groups of parents may not represent the opinion of all parents.

WHAT'S IS ALREADY KNOWN ON THIS SUBJECT

⇒ Obtaining parental consent for investigations in emergencies (eg, perinatal asphyxia) is ethically complex and sometimes impossible.

⇒ Deferred/waiver of consent is a controversial topic where parental/stakeholders' perspectives are scarce.

WHAT THIS STUDY ADDS

⇒ Stakeholders can have diverse opinions. In the context of asphyxia, the majority of parents preferred short oral consent followed by informed consent over deferred consent.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Considering parental perspectives when designing studies including waiver/deferred consent is essential.

⇒ Two-(or multi-)stage consent with the opportunity to opt-out may be a good approach and following participants in those studies for their perspectives is recommended.

OBJECTIVE

According to current legislation, guidelines on Good Clinical Practice and the Declaration of Helsinki[1] ethically justified research in humans requires informed consent (IC).[2 3] In paediatrics, parents/guardians provide consent for their children.[4]

In emergencies, 'deferred consent (DC)' can be used[1] and interventions started with later IC for continuing participation and data analysis.[2]

In neonatal research, this may be considered in trials on delivery room management,[5] where DC has been used before,[6] but is deemed ethically and legally complex.[7] The alternative, prenatal consent, was reported to negatively impact on validity and representativeness.[8 9] Recently, short oral/two-step consent (SOC) has been described, where researchers seek oral opt-out assent for participation during time-critical periods, followed by later IC.[10]

The ALBINO Trial (NCT03162653) investigates the effects of early allopurinol versus placebo, administered ≤45 min after birth, on neurocognitive outcome following perinatal asphyxia,[11 12] where prenatal and detailed IC before enrolment is not feasible because birth asphyxia is unpredictable and parents are burdened in such situations.[13] Nevertheless, research in these situations is essential to improve outcomes.[14]

Designing the ALBINO Trial, investigators, ethicists and parent advocates discussed the consent methodology and sought guidance by surveying parental perspectives about DC and SOC in perinatal emergencies.

METHODS

Questionnaire

The anonymous semistandardised questionnaire was co-developed by clinicians and experts in parental perspectives and qualitative healthcare research. The original questionnaire was in German (online supplemental appendix 1, online). Data were collected from October 2016 to October 2017.

In the standardised section, parents were asked about their general trust in physicians/paediatricians, decisions about medical interventions for their child, decision-making during emergencies, and consent in the context of ALBINO and other pharmaceutical trials. Answers were given on a 4-point Likert-Scale ('I fully agree' to 'I fully disagree') or, alternatively, 'I don't know/cannot judge this'.

Additionally, open-ended questions inquired parental perspectives on their child's participation in trials (eg, ALBINO), their reaction after DC and recommendations for the ALBINO team.

Subjects and recruitment

Three parent groups were invited:

1. Prospective parents (ProP) recruited during routine prenatal outpatient appointments.
2. Parents of healthy newborns (PNeo) recruited during inpatient maternity care.
3. Parents of neonates treated for perinatal asphyxia (PAx) in 2006–2016 (meeting ALBINO Trial inclusion criteria), invited by letter and reminded once.

ProP and PNeo received a brief verbal explanation before receiving the study documents.

Formal sample size calculation was not performed due to the exploratory and qualitative character of the study. The initial sample size was determined based on the prevalence of perinatal asphyxia in the preceding 10 years at Dresden and Tübingen, and an expected response rate of 30% in PAx.

Data analysis

Analyses of the standardised questions were descriptive using percentages, means and SDs. Couples were treated as independent observations. Likert-Scale results were dichotomised (positive vs negative). The neutral answer ('I don't know/cannot judge this') was set to 'missing'. Associations between answers (positive vs negative) and parent groups, gender, religious affiliation and education were evaluated exploratively by χ^2 test for questions with (predefined) differences of >10%. χ^2 tests were done with SPSS (Statistics V.25; IBM Corp.; Armonk, New York, USA). Significance level for alpha was <0.05 without adjustment for multiple comparisons.

Answers to open-ended questions were analysed using descriptive content analysis.[15 16] Themes were developed simultaneously and independently by three investigators. After reaching consensus on codes/definitions, answers were coded independently by two investigators, resolving discrepancies with a third.

Ethics

Parents signed a consent form before participation. The anonymity of respondents was preserved by having an evaluation-independent person open the return envelopes, file the consent forms and hand the sealed, anonymous questionnaires to the investigators.

RESULTS

Demographics

There were 108 participants (ProP: 43/120; PNeo: 35/114; PAx: 30/188; figure 1); overall return rate was 25.6%; mean age was 34 years (SD 4.9); 63% were mothers; 57% were Christians, 41% non-religious or stated that religion had no influence on their decisions; 58% had a university degree.

Standardised answers

The following section summarises the main results (all answers detailed in online supplemental appendix 1, online).

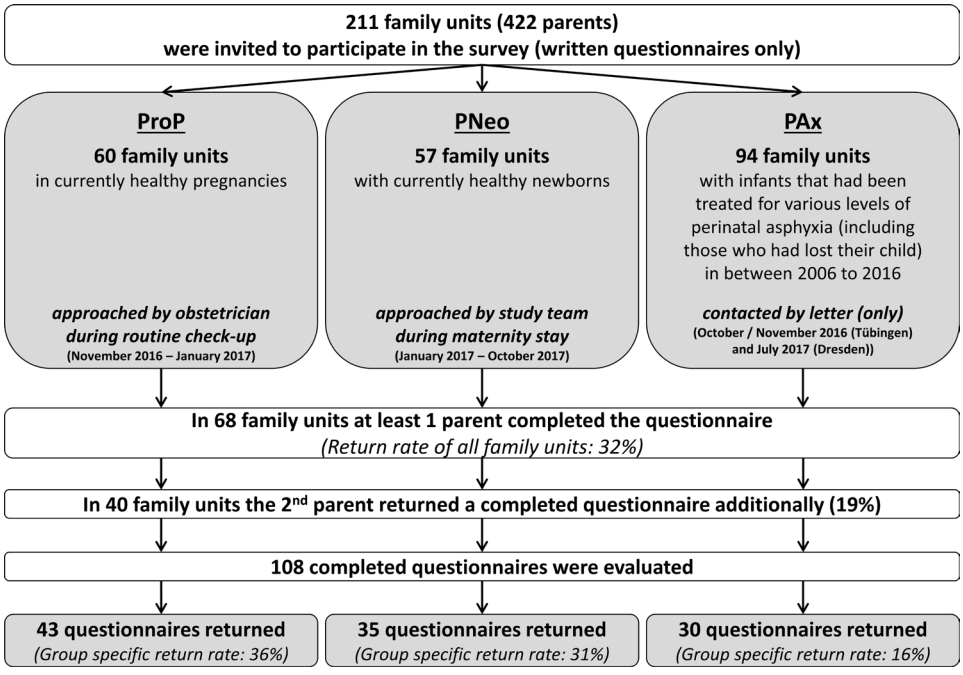

Figure 1 Trial flow chart. PAx, parents of neonates treated for perinatal asphyxia; PNeo, parents of healthy newborns; ProP, prospective parents.

Table 1 Most relevant questions for the ALBINO scenario

% agreement	Total	ProP	PNeo	PAx
5.8 'I think that I would make the right decision even in this emergency. Therefore, I would prefer to only be informed in a few sentences and to be asked for short (oral) consent before administering the study medication.'	55 %	54 %	60 %	50 %
5.9 'In the emergency described, I would be glad not to have been asked for permission to give the study medication, because I would have felt helpless and unable to make decisions, and I would probably have followed the advice of the physicians anyway.'	43 % (disagree: 47 %)	40 % (disagree: 54 %)	34 % (disagree: 54 %)	57 % (disagree: 30 %)
5.16 'If my child has been given study medication in an emergency without my prior consent, I would decide afterwards as follows (after detailed information):'				
'I would agree to participate afterwards.' (deferred consent)	48 %	40 %	43 %	67 %
'I would refuse to participate afterwards.' (deferred consent)	4 %	7 %	0 %	3 %
'I would have refused to participate before the birth.' (prenatal consent)	2 %	2 %	3 %	0 %
'I do not know/ I am not sure for any scenario.'	46 %	51 %	54 %	30 %
5.17 'I think that giving a study medication in this situation without my knowledge is so inappropriate that I would take legal action against the investigators.'	8 %	14 %	0 %	10 %

PAx, parents of neonates treated for perinatal asphyxia ; PNeo, parents of healthy newborns; ProP, prospective parents.

Trust in physicians

The majority (88%) trusted their own physicians to make the right decisions/recommendations. Only 27% would generally seek a second opinion. Parents with university degree tended to rely less on the opinion of their child's physician than those without (76 vs 92%; p=0.028).

Medical interventions (in general)

The majority (95%) wanted to be informed before agreeing to a medical treatment for their child. Half insisted on information beforehand, even if this delay would reduce the intervention's benefit (50%); Some (44%) favoured starting treatment immediately.

Emergencies

Almost all (97%) agreed that in emergencies treatment must begin immediately and no time should be wasted on information; most (84%) reported that, especially in emergencies, more research should be done in order to better prevent serious harm (3% disagreed).

DC in the context of perinatal asphyxia

The majority thought they would be able to cope better with a situation of perinatal asphyxia and administration of study medication without prior information/consent if they had already heard about this (eg, by community engagement; 78%).

When asked for their preferences in the ALBINO Trial context, 55% preferred SOC, while 43% preferred DC. PAx more frequently favoured DC over SOC (54% vs 30%; p=0.032) (table 1).

In the ALBINO scenario, 91% would wish the medication to be given even without their prior consent, provided its therapeutic effect had been proven in previous studies. Administration of study medication in an emergency was acceptable without consent for 80%, provided it was safe (minor side effects only).

If the study medication had been administered without prior information/consent, 26% responded that it might adversely affect trust in their paediatrician. Men (40% vs 18%; p=0.029) and non-religious parents (36% vs 18%, p=0.040) reported this more frequently. Twenty-three per cent would later suspect that new health problems of their child might have been caused by the study medication. 74% would not consider legal action against the study team, whereas 3% would and 6% would at least consider it (table 1).

Concerning DC, 57% of respondents thought that information about such a study with flyers or posters in the delivery area and/or information in the media would be sufficient. PAx more frequently agreed with this point (70% vs 52%; p=0.149).

An 'emergency card' indicating the intention to participate in a study for perinatal asphyxia (yes/no) was considered helpful by 83%, while only 41% would use such a card.

Contemplating the 'ALBINO situation', 48% would consent to continued participation following detailed information in a DC scenario; 4% would not consent and 2% would have refused participation before birth if they had had the chance, for example, by community engagement; 46% were uncertain (table 1).

Pharmaceutical studies (in general)

Almost all (94%) agreed to participate in pharmaceutical trials, if there was a good chance for benefit and a low risk for harm.

Some (40%) would prefer a safe treatment with a proven small therapeutic effect over an experimental treatment with a potentially greater therapeutic effect.

Open-ended answers

When parents were asked which factors would impact on their decision to give consent in a study, 87 answers in the following main themes emerged: information and transparency of study (24%); side effects of study medication (23%); benefits of study (22%); risk-benefit ratio (16%); condition of the child (15%); relationship with the study team (14%); personal views regarding the necessity for study participation (14%); safety of/experience with the drug (11%); burden of the study intervention (9%); time needed to participate (8%) and reputation/commitment of the study team (7%).

Parents often invoked multiple themes. Examples of parental responses (each from a different participant) included:

- *'If there were the (smallest) possibility of a "cure" or improvement, I would take part. The side effects shouldn't be too bad either.'* (ProP-mother)
- *'[…] Do I have the feeling that I know exactly what is being done, what is being observed, what the goals are?'* (ProP-mother)

Table 2 Examples of parental quotes and emotions. When asked the following question: 'If a study drug was administered to your baby as part of an emergency trial without informing you; please tell us what would be your reaction when you would be informed later and asked for consent for continued participation in that trial.' (examples associated with only one emotion, for the complete list see online supplemental appendix II)

Parent group	Example of parental quotes and emotions associated with them		
	Positive (total: 19%)	Neutral (total: 55%)	Negative (total 26%)
ProP (n=36)	(17%) 'Positive thoughts: it's good that the doctors thought of the possibility; Hopefully the drug will work for my child; What would it have been like without it?' 'I would be glad that everything possible was done for my child.'	(53%) 'Assuming prior information: I would try to remain calm, thinking that by doing so you have done everything possible to help the child.' 'Possibly confusion; good or bad depends on the situation' 'Uncertainty at first, but if someone would explain to me what it's about, then it would be ok.' 'Concern and the right to be informed in detail afterwards. Side effects. What if the drug had not been administered.' 'I'd probably be fine with that, if it successfully helped. In the event of complications, I cannot judge how I will react. In general, I have to trust the knowledge and actions of the doctors in such a situation.'	(31%) 'Aggravation. After all, it is a drug that has not yet been approved.' 'Doctors ask why there was no brief explanation beforehand! There was enough time!' 'I wouldn't like that, it's still a study drug. A tested drug would be more ok! Especially in the case of study drugs, prior information would be particularly important to me!' 'That would probably depend very much on the success of the treatment. A certain feeling of deceit would probably not be avoidable, even if it is irrational.'
PNeo (n=23)	(13%) 'If the application brings a positive result, this would lead to joy. It's better to try something than to refrain from helping.' 'It's good that my child was given the best possible help. I am grateful because I know the sequalae and damage that can happen after a lack of oxygen' I would think: 'The doctors did everything they could to help my child.'	(67%) 'I would like a full explanation and exact reasons why the doctors chose this drug and why they acted the way they did.'	(21%) 'Disappointment, possibly anger because I wasn't asked in advance!' 'I would lose confidence in the doctors and possibly take legal action against them'
PAx (n=25)	(28%) 'I would hope that this would be as helpful to my child as possible, and even if not, that there would be a sense of progress that would help other children in a similar situation.' 'This triggered so much relief in me. The hope that my child could do well is irreplaceable!' 'I would be grateful if I knew that everything is being tried to save my child. I also expect that from a university hospital, which is why I go there and not to a birth center'	(48%) 'I would first get clarification from the doctor. But basically, I would trust his expertise.'	(24%) 'I would be shocked! Extremely angry. Depending on the side effects my child would have afterwards. If there were no adverse effects, I would probably just be shocked that something was done without permission.' 'Incomprehension, anger, doubts about legality; Would rate the approach as arrogant and high-handed.' 'That would harm my trust and my confidence. I would then question everything and suspect several things about which I was not informed.'

PAx, parents of neonates treated for perinatal asphyxia ; PNeo, parents of healthy newborns; ProP, prospective parents.

- *'Are the doctors concerned with the well-being of my child or just with participating in the study? […]'* (PNeo-mother)
- *'Follow-up examinations: time required, travel routes? […] child-friendly setting? […]'* (PNeo-mother)

Many of the 84 answers to the question on how parents would react after DC in an emergency trial were emotional: 19% reported only positive emotions (gratitude, satisfaction, relief, trust, etc), 26% only negative (anger, irritation, mistrust, frustration, sadness, etc), while about half answered without expressing emotions (table 2). Some parents also answered in a positive and negative manner, for example:

- '*Fear and hope, anger or gratitude depending on success of the drug*' (ProP-father)
- '*Worry about whether it might harm the child. Reassurance because everything has been done that is possible according to current research*' (ProP-father)

PAx more frequently reported positive feelings (28% vs 15%).

Fifty-six parents made recommendations for the ALBINO investigators, generally on 'information' and 'communication'. Many encouraged researchers to continue with the ALBINO Trial:

- *'I think flyers are great! Also, to inform parents in advance about the consequences of a lack of oxygen. […] because the public is not sufficiently informed and educated about rare conditions or disabilities. Always talk plainly, it can be difficult at first, but it is the best solution. […]'* (ProP-mother)
- *'Information brochures with the essential facts for expectant parents, as well as an emergency card on the maternity booklet are definitely helpful to avoid misunderstandings/conflicts […].'* (ProP-father)
- *'Humanity comes first, followed by honesty, openness, respect and professional competence. Don't make us feel like a lab animal! Child-friendliness must be a prerequisite.'* (PAx-mother)

DISCUSSION

To our knowledge, this is the first investigation on parental perspectives on consent for a trial in the context of neonatal asphyxia in a high-income country, and the only one asking a variety of parents with different pregnancy and birth experiences.

Previous poststudy surveys or hypothetical research studies indicated that parents may initially be upset by a study intervention started without their prior consent or short verbal information,[17 18] although this can often be mitigated by further explanations.[17] Parents wanted to be involved and asked for consent (even in an emergency),[19] and they were more willing to accept DC in an emergency.[18] We confirmed these findings

in our survey. In contrast, after the randomised controlled PREMOD Trial, a low risk comparison between two standard-of-care interventions (cord-milking vs delayed cord-clamping), parents reported to be generally satisfied with the use of DC.[20] However, in this online survey, several parents reported that physicians spoke about the study *before* delivery, and only half the respondents explicitly recalled that they had been informed *after* their baby's inclusion. Another successful DC example might be the 'milking in non-vigorous' trial.[21]

Seeking parental perspectives for an investigation about neonatal asphyxia raises the question which parents should be asked. ProPs (whose unborn child is at risk of asphyxia), parents of newborns (at the time when detailed IC would be obtained in the ALBINO Trial), parents of children who met ALBINO inclusion criteria in the past (both bereaved and non-bereaved parents)? When involving stakeholders, researchers generally seek the information of parents of living children who met inclusion criteria, generally those engaged in support groups. Such stakeholders may be more positive towards research. However, when consent is obtained in a suddenly evolving emergency (like perinatal asphyxia), parents are in a different frame of mind and acutely anxious whether their child will survive. This distinguishes them from parents of premature infants, who frequently have some time to prepare for the upcoming situation. Perhaps the best way to obtain stakeholders' opinions is to ask a variety of stakeholders.

In our case, participants agreed about some issues: almost all parents, when placing themselves in the ALBINO scenario, wished medication of proven efficacy to be given, even without their prior consent, and they were also in favour of research. However, when asked about DC and SOC, parents within and between groups were far from unanimous, for example, a large proportion favoured SOC over DC. However, parents of children having experienced perinatal asphyxia were different: Although their response rate was lower (presumably because of the method of contact), they preferred DC more often, were more often positive about emergency research and expressed more positive feelings and gratitude. Possibly, their experience resulted in a different understanding of the need for such research procedures and the limitations to judicious decision making in acute emergencies, whereas the purely hypothetical idea of a DC situation led to more emotional rejection/distrust.[22]

This survey has several limitations. The generalisability of the findings is limited by the low response rate, even if comparable to other surveys.[20 23] Additionally, predominantly well-educated parents participated with little diversity concerning religious background, which limits our findings to this group of parents. Possibly, German parents may also have a different ethical approach to DC than others. In other contexts, where parental decisions about participation are guided by unreserved trust in physicians, parental perspectives about the most appropriate consent procedure may differ.[24] Additional challenges for SOC have also been identified in low-income settings.[25]

Questionnaire studies have inherent biases, which we tried to reduce by asking different groups of parents. Because of their variety of perspectives and demographic factors, the results may represent the range of perspectives of parents in our centres. We even asked parents of children who had died of neonatal asphyxia, as their opinions were deemed to be particularly valuable, hoping that the chance for benefit from their potential participation, in the memory of their child, would exceed the risk of harm.[26] Another limitation is that we did not ask what information parents needed for their decision to participate in an emergency study, for example, legislation and ethics committees insist on detailed information about data protection, whereas this may not be important to parents.

Supported by these results, the ALBINO investigators asked national ethics committees to choose between DC and SOC.[11] DC was approved in Austria, Belgium, Estonia, Finland and Norway, whereas SOC was approved in Germany, Italy, the Netherlands, Portugal, Spain and Switzerland. In Poland, the leading ethics committee insisted on written IC from both parents before enrolment. Ethics committees considered the validity of parental consent in an emergency situation, burden to parents and legal requirements (eg, the European clinical trial regulation 536/2014 had not yet entered into force[2]). During the ongoing ALBINO Trial, parental satisfaction with the SOC/DC process will be evaluated.

CONCLUSION

The vast majority of parents wanted to be informed about study participation in an emergency such as perinatal asphyxia. SOC may improve parental satisfaction and safeguard their autonomy (parents can opt-out if they have concerns after receiving at least the most relevant information), while enabling emergency studies that are representative and valid. SOC could be complemented by prior study-related information such as provided in the delivery room. Parents' perspectives on these issues are essential for future research and should be sought in trials using DC or SOC. Additionally, future trials may compare these consent approaches by randomly allocating the consent process prior to a randomised-controlled trial.

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Correction notice The licence for this article has been updated to Open Access.

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Contributors CAM conceptualised the study, designed the survey, recruited parents on the maternity ward in Tübingen and drafted the first version of the manuscript (including translation of the survey and the answers). CAM approved the final version of the manuscript and agreed to be accountable for all aspects of the work. CR contributed to the design of the survey, recruited parents on the maternity ward in Tübingen and coordinated the data collection in the obstetric practices and in Dresden. CR revised the manuscript, making important contributions, approved the final version of the manuscript and agreed to be accountable for all aspects of the work. MR coordinated data collection in Dresden. MR and CFP supervised the project as heads of the neonatal departments involved and critically reviewed the manuscript for important intellectual content and translations. Both authors revised the manuscript, making important contributions, approved the final version of the manuscript and agreed to be accountable for all aspects of the work. HS and MM assisted in the design of the survey from a perspective of healthcare research and critically reviewed the manuscript. Both authors made important contributions and approved the final version of the manuscript. AJ encouraged this study by critically commenting on 'deferred consent' for ALBINO as member of the ALBINO Ethics Advisory Board. AJ revised the manuscript critically for important intellectual content and with regard to the English language as a native speaker. AJ agreed to the final version of the article and agreed to be accountable for all aspects of the work. GM made important contributions as member of the ALBINO ethics advisory board. GM revised the manuscript critically for important intellectual content, agreed to the final version of the article and agreed to be accountable for all aspects of the work. H-JE made important contributions as member of the ALBINO ethics advisory board. H-JE revised the manuscript critically for important intellectual content, agreed to the final version of the article and agreed to be accountable for all aspects of the work. ARF conceptualised the study and designed the survey and was coordinator of the project. ARF was responsible for concept and design and supervised assessment of the data. ARF revised the manuscript, making important contributions, approved the final version of the manuscript and the translations and agreed to be accountable for all aspects of the work. ARF and CAM are guarantors.

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Online supplemental material:

- **Appendix I: Results of answers to all closed-ended questions, according to parental demographics**

Category 1: Demographics	Total n = 108	ProP n = 43	PNeo n = 35	PAx n = 30
1.1 Gender:	68 Female; 40 Male	25 Female; 18 Male	22 Female; 13 Male	21 Female; 9 Male
1.2 Age in years (mean, ±SD):	Women: 33 (±4) Men: 35 (±6)	Women: 32 (±3) Men: 33 (±4)	Women: 33 (±5) Men: 37 (±5)	Women: 35 (±5) Men: 37 (±8)
1.3 Nationality:	98 German; 1 Italian; 1 Ugandan; 1 Croatian; 1 Romanian; 3 Bosnian-Herzegovinian; 1 Dutch; 2 Russian and German	40 German; 1 Italian; 1 Croatian; 1 Bosnian-Herzegovinian;	30 German; 1 Romanian; 2 Bosnian-Herzegovinian; 1 Dutch; 1 Russian and German	28 German; 1 Ugandan; 1 Russian and German
1.4 Religion:	60 Christians; 3 Orthodox; 43 no religion or don't care about religion; 2 invalid answers	22 Christians; 0 Orthodox; 20 no religion or don't care about religion; 1 invalid answers	25 Christians; 1 Orthodox; 9 no religion or don't care about religion; 0 invalid answers	13 Christians; 2 Orthodox; 14 no religion or don't care about religion; 1 invalid answers
1.5 Highest education:	38 Vocational training; 62 University degree/PhD; 8 Other	9 Vocational training; 33 University degree/PhD; 1 Other	12 Vocational training; 20 University degree/PhD; 3 Other	17 Vocational training; 9 University degree/PhD; 4 Other

Main text: a) Trust in physicians Written on questionnaire: Category 2: "The following questions relate to your general attitude towards medicine and your physicians"			Number of evaluable answers / cannot judge / missings
2.1 "I believe, my physicians to make the right decisions for me and my health. "	88% agreed ProP: 98% vs. PNeo: 77% vs. PAx: 87% 88% females vs. 88% males 87% religious vs. 93% non-religious 92% ≥ university degree vs. 85% else	8% disagreed ProP: 0% vs. PNeo:20% vs. PAx:7% 9% females vs. 8% males 10% religious vs. 2% non-religious 7% ≥ university degree vs. 10% else	104 / 3 / 1
2.2 "I always get a second medical opinion before I give my consent to treatment."	27% agreed ProP: 26% vs. PNeo: 34% vs. PAx: 20% 27% females vs. 28% males 28% religious vs. 21% non-religious 24% ≥ university degree vs. 31% else	71% disagreed ProP: 72% vs. PNeo: 63% vs. PAx: 80% 72% females vs. 70% males 70% religious vs. 78% non-religious 74% ≥ university degree vs. 67% else	106 / 2 / 0
2.3 "I prefer alternative medical methods to conventional medicine."	24% agreed ProP: 12% vs. PNeo: 29% vs. PAx: 37% 31% females vs. 13% males 20% religious vs. 27% non-religious 15% ≥ university degree vs. 39%	72% disagreed ProP: 79% vs. PNeo: 71% vs. PAx: 63% 68% females vs. 80% males 75% religious vs. 71% non-religious 81% ≥ university degree vs. 62% else	104 / 4 / 0

Main text: a) Trust in physicians and b) medical interventions (in general) Written on questionnaire: Category 3: "The following questions relate to your attitude towards the physicians who would treat your child."			Number of evaluable answers / cannot judge / missings
3.1 "I would rely completely on the opinion and decisions of my child's physicians."	81% agreed ProP: 86% vs. PNeo: 74% vs. PAx: 80% 79% females vs. 83% males 82% religious vs. 80% non-religious 76% ≥ university degree vs. 92% else	17% disagreed ProP: 12% vs. PNeo: 23% vs. PAx: 17% 16% females vs. 18% males 15% religious vs. 18% non-religious 21% ≥ university degree vs. 5% else	105 / 1 / 2
3.2 "I would be more critical of the physician who treats my child, than I would be if it was my own treatment/physician."	76% agreed ProP: 63% vs. PNeo: 80% vs. PAx: 90% 77% females vs. 75% males 68% religious vs. 84% non-religious 74% ≥ university degree vs. 77% else	22% disagreed ProP: 35% vs. PNeo: 20% vs. PAx: 7% 22% females vs. 23% males 28% religious vs. 16% non-religious 23% ≥ university degree vs. 23% else	106 / 1 / 1
3.3 "Before the physicians start to treat my child, I always want to know what they want to do and why."	95% agreed ProP: 95% vs. PNeo: 94% vs. PAx: 97% 96% females vs. 95% males 95% religious vs. 96% non-religious 98% ≥ university degree vs. 90% else	4% disagreed ProP: 2% vs. PNeo: 6% vs. PAx: 3% 3% females vs. 5% males 5% religious vs. 2% non-religious 2% ≥ university degree vs. 8% else	107 / 1 / 0
3.4 "I always would like to be informed before my child is treated. I always want to be able to give my consent, even if this delay could reduce the success of the treatment."	50% agreed ProP: 51% vs. PNeo: 46% vs. PAx: 53% 49% females vs. 53% males 43% religious vs. 59% non-religious 45% ≥ university degree vs. 54% else	44% disagreed ProP: 42% vs. PNeo: 49% vs. PAx: 40% 44% females vs. 43% males 48% religious vs. 39% non-religious 48% ≥ university degree vs. 39% else	101 / 4 / 3
3.5 "There will probably be situations where I wish to follow my child's physician's advice because I lack the expertise to question their decision."	91% agreed ProP: 91% vs. PNeo: 89% vs. PAx: 93% 88% females vs. 95% males 95% religious vs. 84% non-religious 95% ≥ university degree vs. 82% else	7% disagreed ProP: 7% vs. PNeo: 9% vs. PAx: 3% 9% females vs. 3% males 3% religious vs. 11% non-religious 5% ≥ university degree vs. 10% else	105 / 2 / 3

Main text: c) Emergencies Written on questionnaire: Category 4: "Your perspective to treatments in emergencies"			Number of evaluable answers / cannot judge / missings
4.1 "I believe that in emergencies, treatment must start immediately. No time should be wasted on detailed information given."	97% agreed ProP: 98% vs. PNeo: 94% vs. PAx: 100% 97% females vs. 98% males 97% religious vs. 100% non-religious 100% ≥ university degree vs. 98% else	2% disagreed ProP: 2% vs. PNeo: 3% vs. PAx: 0% 2% females vs. 3% males 2% religious vs. 0% non-religious 0% ≥ university degree vs. 0% else	107 / 1 / 0
4.2 "Especially in emergencies, I rely on physicians to make the best decisions for me and my child."	100% agreed ProP: 100% vs. PNeo: 100% vs. PAx: 100% 100% females vs. 100% males 100% religious vs. 100% non-religious 100% ≥ university degree vs. 100% else	0% disagreed ProP: 0% vs. PNeo: 0% vs. PAx: 0% 0% females vs. 0% males 0% religious vs. 0% non-religious 0% ≥ university degree vs. 0% else	108 / 0 / 0

4.3 "I think, especially in emergencies, more research should be done to better prevent serious harm."	84% agreed ProP: 81% vs. PNeo: 89% vs. PAx: 83% 84% females vs. 85% males 87% religious vs. 80% non-religious 81% ≥ university degree vs. 87% else	3% disagreed ProP: 5% vs. PNeo: 3% vs. PAx: 0% 3% females vs. 3% males 2% religious vs. 5% non-religious 3% ≥ university degree vs. 3% else	93 / 14 / 1

Main text: d) DC in the context of perinatal asphyxia Written on questionnaire: Category 5: "Your perspective in the emergency of neonatal asphyxia, that your child will be harmed by oxygen deficiency during childbirth". (this was described to parents at the beginning of the questionnaire)			Number of evaluable answers / cannot judge / missings
5.1 "I would be better able to cope better with the described emergency if I could be informed about it before labor/birth".	79% agreed ProP: 84% vs. PNeo: 71% vs. PAx: 80% 77% females vs. 83% males 80% religious vs. 77% non-religious 81% ≥ university degree vs. 74% else	19% disagreed ProP: 14% vs. PNeo: 26% vs. PAx: 17% 19% females vs. 18% males 17% religious vs. 21% non-religious 18% ≥ university degree vs. 21% else	105 / 1 / 2
5.2 "I hope that in the emergency described, everything that is medically possible will be done for my child without my prior consent (to avoid sequelae and /or further damage)".	91% agreed ProP: 91% vs. PNeo: 94% vs. PAx: 87% 88% females vs. 95% males 95% religious vs. 86% non-religious 87% ≥ university degree vs. 95% else	5% disagreed ProP: 5% vs. PNeo: 3% vs. PAx: 7% 6% females vs. 3% males 2% religious vs. 7% non-religious 3% ≥ university degree vs. 3% else	103 / 2 / 3
5.3 "If, after the emergency described, I was informed about the use of the study drug in my child without my prior consent, this would have a negative impact on my faith in my child's physicians".	26% agreed ProP: 35% vs. PNeo: 17% vs. PAx: 23% 18% females vs. 40% males 18% religious vs. 36% non-religious 31% ≥ university degree vs. 15% else	67% disagreed ProP: 61% vs. PNeo: 74% vs. PAx: 67% 71% females vs. 60% males 73% religious vs. 57% non-religious 65% ≥ university degree vs. 72% else	98 / 3 / 7
5.4 "If my child had received the study medication, I would always suspect a side effect of the study medication if my child has health problems or long-term disabilities"".	46% agreed ProP: 44% vs. PNeo: 51% vs. PAx: 43% 40% females vs. 58% males 45% religious vs. 50% non-religious 50% ≥ university degree vs. 33% else	43% disagreed ProP: 47% vs. PNeo: 34% vs. PAx: 47% 49% females vs. 33% males 45% religious vs. 41% non-religious 39% ≥ university degree vs. 54% else	96 / 9 / 3
5.5 "I would also consider health problems to be side effects of the study drug, even if the physicians told me that these complications often occur after birth with oxygen-deficiency".	23% agreed ProP: 19% vs. PNeo: 23% vs. PAx: 30% 24% females vs. 23% males 22% religious vs. 27% non-religious 18% ≥ university degree vs. 31% else	69% disagreed ProP: 74% vs. PNeo: 66% vs. PAx: 63% 69% females vs. 68% males 68% religious vs. 68% non-religious 74% ≥ university degree vs. 62% else	99 / 5 / 4
5.6 "It is important to me that independent physicians and ethics committees have examined this study and find it reasonable and ethically justifiable".	92% agreed ProP: 95% vs. PNeo: 91% vs. PAx: 87% 88% females vs. 98% males 93% religious vs. 89% non-religious 97% ≥ university degree vs. 82% else	4% disagreed ProP: 5% vs. PNeo: 0% vs. PAx: 7% 6% females vs. 0% males 3% religious vs. 5% non-religious 8% ≥ university degree vs. 2% else	103 / 3 / 2

5.7 “It would reassure me to know that the study was recommended and developed by pediatricians, not by a pharmaceutical company”.	94% agreed ProP: 93% vs. PNeo: 91% vs. PAx: 97% 96% females vs. 90% males 93% religious vs. 93% non-religious 94% ≥ university degree vs. 92% else	5% disagreed ProP: 7% vs. PNeo: 6% vs. PAx: 0% 2% females vs. 10% males 5% religious vs. 5% non-religious 7% ≥ university degree vs. 3% else	105 / 0 / 3
5.8 “I think that I would make the right decision even in these emergencies. Therefore, I would prefer to only be informed in a few sentences and to be asked for short (oral) consent before administering the study medication.”	55% agreed ProP: 54% vs. PNeo: 60% vs. PAx: 50% 52% females vs. 60% males 48% religious vs. 64% non-religious 52% ≥ university degree vs. 56% else	34% disagreed ProP: 33% vs. PNeo: 29% vs. PAx: 43% 38% females vs. 28% males 38% religious vs. 30% non-religious 39% ≥ university degree vs. 28% else	96 / 10 / 2
5.9 “In the emergency described, I would be glad not to have been asked for permission to give the study medication, because I would have felt helpless and unable to make decisions, and I would probably have followed the advice of the physicians anyway.”	43% agreed ProP: 40% vs. PNeo: 34% vs. PAx: 57% 47% females vs. 35% males 42% religious vs. 43% non-religious 45% ≥ university degree vs. 39% else	47% disagreed ProP: 54% vs. PNeo: 54% vs. PAx: 30% 40% females vs. 60% males 48% religious vs. 48% non-religious 48% ≥ university degree vs. 46% else	97 / 9 / 2
5.10 “I think it is better to make a decision only in the acute emergency. I don't want to have to worry about such emergencies before giving birth.”	17% agreed ProP: 19% vs. PNeo: 20% vs. PAx: 10% 16% females vs. 18% males 17% religious vs. 18% non-religious 19% ≥ university degree vs. 13% else	78% disagreed ProP: 79% vs. PNeo: 71% vs. PAx: 83% 78% females vs. 78% males 78% religious vs. 75% non-religious 77% ≥ university degree vs. 77% else	102 / 4 / 2
5.11 “Information about the study via flyers, posters and newspaper articles are sufficient if more detailed information is provided later.”	57% agreed ProP: 51% vs. PNeo: 54% vs. PAx: 70% 62% females vs. 50% males 58% religious vs. 59% non-religious 53% ≥ university degree vs. 69% else	36% disagreed ProP: 47% vs. PNeo: 31% vs. PAx: 27% 29% females vs. 48% males 37% religious vs. 32% non-religious 40% ≥ university degree vs. 23% else	101 / 5 / 2
5.13 “For parents who don't want to participate, it's reasonable to develop an emergency card (similar to the organ donation card in some countries) that they can put into their pregnancy book and on which they can document their general rejection or approval of the study.”	83% agreed ProP: 86% vs. PNeo: 89% vs. PAx: 73% 87% females vs. 78% males 85% religious vs. 82% non-religious 87% ≥ university degree vs. 77% else	8% disagreed ProP: 12% vs. PNeo: 3% vs. PAx: 10% 6% females vs. 13% males 8% religious vs. 9% non-religious 8% ≥ university degree vs. 10% else	99 / 5/ 4

5.14 "I would actually use such an emergency card myself."	<u>41% agreed</u> ProP: 44% vs. PNeo: 34% vs. PAx: 43% 46% females vs. 33% males 37% religious vs. 50% non-religious 36% ≥ university degree vs. 54% else	<u>47% disagreed</u> ProP: 49% vs. PNeo: 51% vs. PAx: 40% 44% females vs. 53% males 53% religious vs. 36% non-religious 57% ≥ university degree vs. 26% else	94 / 8 / 6

Main text: d) DC in the context of perinatal asphyxia (ALBINO-Scenario) Written on questionnaire: "Now imagine that your child has already received this medication and the treating physicians are asking you whether you would give consent for continued participation in the study."			Number of evaluable answers / cannot judge / missings
5.16 "If my child has been given study medication in an emergency without my prior consent, I would decide afterwards as follows (after detailed information):"	a. "I would agree to participate afterwards."	<u>48% agreed</u> ProP: 40% vs. PNeo: 43% vs. PAx: 67% 50% females vs. 45% males 50% religious vs. 46% non-religious 45% ≥ university degree vs. 56% else	101 / see answer d. / 7
	b. "I would refuse to participate afterwards."	<u>4% agreed</u> ProP: 7% vs. PNeo: 0% vs. PAx: 3% 3% females vs. 5% males 2% religious vs. 7% non-religious 5% ≥ university degree vs. 3% else	
	c. "I would have refused to participate before the birth."	<u>2% agreed</u> ProP: 2% vs. PNeo: 3% vs. PAx: 0% 2% females vs. 3% males 3% religious vs. 0% non-religious 3% ≥ university degree vs. 0% else	
	d. "I cannot judge"	<u>46% agreed</u> ProP: 51% vs. PNeo: 54% vs. PAx: 30% 46% females vs. 48% males 45% religious vs. 48% non-religious 47% ≥ university degree vs. 41% else	
5.17 "I think that giving a study medication without my prior consent is so inappropriate that I would take legal action against the physician investigators."	<u>8% agreed</u> ProP: 14% vs. PNeo: 0% vs. PAx: 10% 7% females vs. 10% males 5% religious vs. 14% non-religious 7% ≥ university degree vs. 8% else	<u>74% disagreed</u> ProP: 77% vs. PNeo: 74% vs. PAx: 70% 75% females vs. 73% males 75% religious vs. 71% non-religious 79% ≥ university degree vs. 69% else	89 / 10 / 9

Main text: e) Pharmaceutical studies (in general) Written on questionnaire: Category 6: "In the following questions, we would like to hear from you how you feel about drug studies in general."			Number of evaluable answers / cannot judge / missings
6.1 "I always prefer an appropriately tested treatment with a presumably safe but small therapeutic effect over an experimental treatment with a potentially greater therapeutic effect."	40% agreed ProP: 42% vs. PNeo: 40% vs. PAx: 37% 41% females vs. 38% males 37% religious vs. 48% non-religious 40% ≥ university degree vs. 44% else	34% disagreed ProP: 30% vs. PNeo: 40% vs. PAx: 33% 29% females vs. 43% males 35% religious vs. 30% non-religious 36% ≥ university degree vs. 28% else	80 / 22 / 6
6.2 "I disapprove of all drug studies."	5% agreed ProP: 7% vs. PNeo: 0% vs. PAx: 7% 6% females vs. 3% males 3% religious vs. 7% non-religious 7% ≥ university degree vs. 3% else	92% disagreed ProP: 93% vs. PNeo: 94% vs. PAx: 87% 88% females vs. 98% males 93% religious vs. 89% non-religious 94% ≥ university degree vs. 87% else	104 / 3 / 1
6.3 "I disapprove of all drug studies in children."	18% agreed ProP: 23% vs. PNeo: 9% vs. PAx: 20% 19% females vs. 15% males 20% religious vs. 14% non-religious 18% ≥ university degree vs. 13% else	77% disagreed ProP: 74% vs. PNeo: 86% vs. PAx: 70% 75% females vs. 80% males 77% religious vs. 77% non-religious 79% ≥ university degree vs. 77% else	102 / 4 / 2
6.4 "Studies are acceptable if there is a good chance of benefit and serious side effects are very rare."	94% agreed ProP: 93% vs. PNeo: 89% vs. PAx: 100% 93% females vs. 95% males 93% religious vs. 93% non-religious 95% ≥ university degree vs. 90% else	3% disagreed ProP: 2% vs. PNeo: 6% vs. PAx: 0% 3% females vs. 3% males 3% religious vs. 2% non-religious 2% ≥ university degree vs. 5% else	104 / 3 / 1
6.5 "If the study medication has previously been classified as "low risk for side effects" in other studies, I approve administration without my consent in an emergency."	80% agreed ProP: 72% vs. PNeo: 89% vs. PAx: 80% 81% females vs. 78% males 82% religious vs. 80% non-religious 82% ≥ university degree vs. 77% else	17% disagreed ProP: 26% vs. PNeo: 9% vs. PAx: 13% 13% females vs. 23% males 13% religious vs. 21% non-religious 18% ≥ university degree vs. 13% else	104 / 3 / 1

Category 7: open-ended questions
7.1 Please tell us what would make you allow your child to participate in research studies (including follow-up visits)?
7.2 If a study drug was administered to your baby as part of an emergency trial without informing you, please tell us what would be your reaction when you would be informed later and asked for consent for continued participation in that trial.
7.3 Do you have any recommendations for the investigators?

Appendix II: Results of answers to all open-ended questions

Open-ended questions	
7.1 Please tell us what would make you allow your child to participate in research studies (including follow-up visits)?	
ProP (n=39)	• If there were the (smallest) possibility of a "cure" or improvement, I would take part in a study. The side effects shouldn't be too bad either. The child should not suffer from the medication. • That my child notices as little as possible, that the study is promising and has no further influence on the child's development. • Depends on the procedure, location, time required and above all what the child has to contribute, e.g. blood samples etc. • From pre-birth counseling. • Whether a disease exists. • Information about the study beforehand. • Whether risks and side effects are excluded or known. Presentation of the study, i.e. (as a mother), do I have the feeling that I know exactly what is being done, what is being observed, what the goals are, etc. • I must be convinced that it has more benefits (for my own and other children) than disadvantages. • What the risks are of continued participation or whether continued participation will lead to further improvement in health. • see 5.11.1 • From danger to the child. • The safety of the drug, the procedure and the benefits of the study. • The benefits of the study for families who may later find themselves in a similar situation. • Trial stage of the drug. • It would have to be an “independent” unbiased scientific study, not only performed for economic reasons -> recommended by my pediatrician -> I would possibly get a second opinion; risk-benefit ratio” . • Prospects of success, side effects, possible alternatives. • I would probably let my child participate because I think research is extremely important. In a scenario where I have lost my trust in the doctors, I would probably find that very difficult. • Benefit to the child. Whether it restricts the child. • I wouldn't do it at all. • Is it the last option? What are the side effects? How many times already tested? • Trust in doctors, feeling of being sufficiently informed. • Trust, education and second opinion. • What is the disease, the chances of success and side effects. • Severity and number of side effects and the percentage chance of success. • From the drug, from the side effects, from the severity of the disease. • If there is no risk for my child, I would participate in such a study. At the follow-up, the question would not arise, since the drug has already been administered. So, I would participate! • Information and that I am convinced of the benefits of the study. • I need to be informed about the study and believe that the study is useful. • Difficult to answer. The information and the condition of the child. • From the prognosis without administration of the drug and from the risks and side effects of the drug. • It is important to have a basis of facts to decide this trade-off. What are the results so far? • Seriousness of the study. Seriousness and empathy of the physicians. Success of the treatment. • Very good chances of success, very few side effects -> If the doctor has my trust and is fully convinced by the study. • Condition of child after birth; detailed information about study; helpful but usually probably not possible: an interview with parents of participating children. • The condition of the child. • Confidence in the study -> Good/conclusive argumentation for sense and purpose -> Believability of the treating physicians of the study. • This would be an option for me if there were no other alternatives that promised a positive cure. • Existing long-term studies, samples of patients > 5000 without abnormalities. • It must not experience any side effects or problems from such a study and treatment.

PNeo (n=23)	• How much is already known about the drug. • From risk and benefit. • The extent and time required for follow-up examinations. The condition of my child after birth. • Effort, side effects, information. • Provided that the further treatments/examinations do not pose any additional risk, I would always participate in the study. • Whether I see a benefit in the study. Whereas I am generally more of a supporter of studies. • Preliminary conversation + info! • Own conviction of the drug and active ingredient. • From the success. • Information • That it is not the first study with this drug in children. • How well advised and cared for I feel by the doctors. Are the doctors concerned with the well-being of my child or just with participating in the study? My feeling would decide. • Study content, i.e., what does our child need to do? is he or she suffering? are there side effects from follow-up? • Previous studies, stochastic data, physician's vote. • Whether the follow-up would involve invasive methods and thus be harmful to my child. In general, however, I see the great general benefit of the study. • Depending on whether that is the "last chance" for my child. • It depends on the situation and on the medication or study. • The chances of success of the therapy. • If there is no other option. • From health condition. • From the explanation of possible risks, trust in the physicians, anticipated success of the therapy. • Follow-up examinations: time required, travel routes? Appointments are usually stressful situations for babies and young families. Can something be absorbed by a very child-friendly setting (local doctor instead of hospital? Childcare for older siblings? etc.). For participation in the study, my impression of the investigators will be decisive: Do they take me seriously? Do they inform me? Do they have time for me? Are they empathetic? Which idea of humanity and patients do they have? • Good information and trust in the treating physicians.
PAx (n=25)	• From whether I have the feeling that the doctors respond to me and take me seriously, and from whether I have the feeling that they know their stuff. On the ward, I sometimes had the feeling that the nurses knew better than the doctors how the children were doing, what they needed, how they were being treated. • Whether it is deemed necessary and only if it is in the best interest of my child (including subsequent examinations). • A transparent approach to the issue. Pros & cons. And of course an important point: how extensive and time-consuming is it? • Aims of the study, side effects, risks and opportunities. • Kindness and understanding of the doctors and nurses. It depends on how stressful the investigations and examinations are for my child, whether the follow-up investigations are uncomfortable/painful and the frequencies. • I support studies in principle. • Above all, that the expected benefit for my child, as well as the common good, is greater than any harm to be feared (AND the study does not conflict with my religious certainties!). • It depends on whether the doctors have recommended this to me. • 1) Expected benefit for the child; 2) Potential risks to the child; 3) Benefit for the general public • Sufficient information about possible opportunities and risks. • Whether it contributes to the survival. • Detailed information about the benefits and opportunities of the drug and the importance of follow-up is important. • How few side effects the drug has and how well it works. • Would not let it participate if I am not convinced of it. • From the health condition of the child, the distance from home to the hospital, the side effects. • Prior informed consent and my consent for administration. • I would be advised on doctors (It is difficult) may also depend on the situation (no idea). Would have to discuss with my wife. • From the success of the study. • From faith: did the medication prevent worse in my child? 2. from the child: what is the condition and do I want to expect further hospital visits from him? • It depends on how important I recognize my child's participation in it and the benefit to my child and other children as well.

	• From what his health condition is, if after the discharge from the hospital he has suffered consequential damages from the birth, I would continue to have him examined. However, if it is healthy at the core, I am not sure about it. • There is nothing to think about for me. If this situation were to occur, my child would have already received the medication anyway and then I would also participate in the study to help other parents. • From the physicians. • Previous information, side effects. • After weighing risks and opportunities. Data collection for the purpose of research is basically okay.

7.2 If a study drug was administered to your baby as part of an emergency trial without informing you, please tell us what would be your reaction when you would be informed later and asked for consent for continued participation in that trial.			
	Positive	Neutral	Negative
ProP (n=36)	Positive thoughts: it's good that the doctors thought of the possibility; hopefully the drug will work for my child; what would it have been like without it? If the emergency really does call for immediate action without prior notice, I would be glad the doctors acted quickly, but as soon as there is time, I expect prior information. I would be glad that everything possible was done for my child.	First, I would like to have precise information about what the drug is and what side effects it has; What it can do for my child and what are the chances of success. Assuming prior information: would try to remain calm, thinking that by doing so you have done everything possible to help the child. Possibly confusion; good or bad depends on the situation. Depends on the effect. I cannot assess. Uncertainty at first, but if someone would explain to me what it's about, then it would be ok. Surprise, caution, need to get more information, skepticism. Uncertainty, which would be resolved if someone could show me that the medication is effective and is best for the child. Fear and hope, anger or gratitude depending on success of the drug. I would ask for precise information. First of all, I assume that the doctors will do everything possible to help my child. However, doubts may also arise that the child is above all a test subject. A stroke of luck for research. Provided the dosing was done under the assumption that there was a sufficiently high probability of no significant side effects, I would probably be grateful that everything was tried. In general, I trust the doctors that they will try everything possible to help my child in an emergency and weigh up the opportunities/risks to the best of their	I wouldn't like that it's still a study drug. A tested drug would be more ok! Especially in the case of study drugs, prior information would be particularly important to me! That would probably depend very much on the success of the treatment. A certain feeling of deceit would probably not be avoidable, even if it is irrational. Aggravation. After all, it is a drug that has not yet been approved. Insecurity, paternalism, distrust. I would definitely complain. Doctors ask why there was no brief explanation beforehand! There has to be so much time! Without prior clarification: panic, loss of trust If I hadn't received any information beforehand (i.e. during the pregnancy), I would have been irritated at first. Anger, fear, worry Anger, helplessness

		knowledge and current research. First, I would be surprised, but if the advantages outweighed, I would probably be glad to have gotten this chance. Shocked at first, after a brief explanation I would certainly understand. If everything goes well and my child gets better, I would be very grateful. Uncertainty; fear for the well-being of my child; My understanding and gratitude for trying to give my child the best possible treatment. How well tested is the drug? I would ask myself about the chances and risks. Concern for my child's health; great need for information. I would be grateful that the doctors did everything possible to help my child. Shocked at first, did this save the child from harm? --> Relief; Mood is definitely dependent on how the child is doing. Worry about whether it might harm the child. Reassurance because everything has been done that is possible according to current research. Concern and the right to be informed in detail afterwards. side effects. What if the drug had not been administered. I'd probably be fine with that, if it successfully helped. In the event of complications, I cannot judge how I will react. In general, I have to trust the knowledge and actions of the doctors in such a situation.	
PNeo (n=23)	It's good that my child was given the best possible help. I am grateful because I know the consequential damage to be feared due to lack of oxygen. I suspect that averting the danger would relieve me so much that I wouldn't think too much about the application of the drug. I would think: The doctors did everything they could to help my child. Gratitude for trying everything possible to help my child.	I think it's the side effects that matter. If it was a success I would be happy. If there are any side effects, I would worry about what would have happened without the medication. Concern, but also the hope that the desired effect (and no consequential damage) will occur. There may be concern, but it depends on the child's condition. What side effects does the drug have? (Consequential damage).	I would have liked to have known in advance that my child could potentially participate in the study. I would lose confidence in the doctors and possibly take legal action against them. Disappointment, possibly anger because I wasn't asked in advance! Breach of trust. Shock

	I would be glad that action was taken.	If positive, I would be happy. Nothing at all. Uncertainty, personal discussion with the treating physicians is absolutely necessary. Concerns, but also hope. Mixed feelings: gratitude that my child was given the opportunity; Worry about side effects and late effects. Does that help or not? I would like to know why the drug was administered and what effects and side effects it has. I would like a full explanation and exact reasons why the doctors chose this drug and why they acted the way they did. Acceptance, the shock of the emergency would probably prevail.	
PAx (n=25)	I would be a bit worried because I would be afraid that the drug could harm my child. However, I would of course do everything to ensure that my child is healthy. If the doctors think it's the right decision to give the medication, then I can only trust that. I would hope that this would be as helpful to my child as possible, and even if not, that there would be a sense of progress that would help other children in a similar situation. If the application brings a positive result, then that would trigger joy. It's better to try something than to refrain from helping. Gratitude that everything is done for my child; fear of side effects; Hope for a normal life for my child. I basically trust the doctors to act to the best of their knowledge and belief. I would inform myself about the study drug to form an opinion. Relief was triggered in me; the hope that my child could do well is irreplaceable! I would be grateful if I knew that everything is being tried to save my child. I also expect that from a university hospital, which is why I go there and not to a birth center.	First, I would be irritated. However, if I look at the general situation after my two births, after the 1st spontaneous birth + the 2nd birth by caesarean section, I probably would not have been able to give my approval or rejection. If the doctors considered it necessary in this situation, I would probably (also out of trust in God) take note of the whole thing, but I would like to find out more about it. I wish for an open approach. Why was it necessary to give the drug? What risks does it entail? I desire openness and honesty of the medical team. I would first get clarification from the doctor. But basically, I would trust his expertise. If everything is ok, I wouldn't have any problems with it, since everything went well and my child survived the emergency. I would hope that there are no side effects. Initially surprised why no one informed about it. But this would give way to the relief that everything that seemed necessary was done for my child. I would decide that spontaneously.	I would be shocked! Extremely angry. Depending on the side effects my child would have afterwards. If the child were inconspicuous, I would probably just be shocked that something was done without permission. That would attack my confidence. I would then question everything and suspect several things about which I was not informed. Incomprehension, anger, doubts about legality; Would rate the approach as arrogant and high-handed. Speechless at first but glad that action has been taken. Stunned; Information from physicians. I would wonder why I wasn't informed beforehand. I would like some information before giving. Fright!

	Would everything be the same if my child had not received the medication and the birth had been normal? On the other hand, I would be grateful that the doctors would have reacted so quickly so that it wouldn't have gotten any worse.	I do not know. I would accept that.	

7.3 Do you have any recommendations for the investigators?	
ProP (n=24)	• I think flyers are great! Also, to inform parents in advance about the consequences of a lack of oxygen --> by flyer or in detail. Because the population is not sufficiently informed and educated about rare conditions or disabilities. Always talk plainly, it can be difficult at first, but it is the best solution. Do not beat around the bush. • Information brochures with the essential facts for expectant parents, as well as an emergency card on the maternity booklet are definitely helpful to avoid misunderstandings/conflicts • I think that all sounds very good. Expectant parents should be informed about the possibility, just as about toxoplasmosis or influenza, prevention or tests, etc. The idea with the emergency card in the maternity booklet should then be implemented. • You should provide information in advance in simple sentences. Also offer information evenings and flyers. • I would like to have the possibility to inform myself before the birth, so that I have at least heard something about such a study and that such a thing exists at all. • Hospitals that offer study participation should provide information about this in advance during registration, if possible. So the parents could decide in peace before the birth. Of course, only possible if the registration takes place a few days before delivery. • Informative talks as standard before a birth would still increase acceptance in my case. • I would inform the expectant mothers in detail before the birth. It should be known that there can be complications - for me it would be more reassuring to know all the treatment options beforehand. • Information about ALBINO already during pregnancy, possibly as part of the other information sessions with the gynecologist. Possibly additionally the "emergency card" with the options of consent & refusal. • Ask the parents in advance. The idea with the emergency card in the maternity booklet is a good one. • I think in the clinics where the drug is used, it is important and helpful to try to inform the parents in advance. • In case of emergency, ask for consent anyway. • Research very much. • Side effects should be communicated clearly. • Do not conceal risks. Provide honest information. • Detailed information during the prenatal check-up, at the gynecologist's office. • Expectant parents should be informed in detail about the ALBINO trial already during pregnancy. • Good arguments, more positive successes, to have an explanation for everything at least. • Transparency; publication of previous results create trust. • The widest possible range of information even before birth (flyers and posters are not enough). Extreme care in the study. Maximum independence from interest groups. • Better information: what are the consequences without medication; what are the consequences with medication; statistics; what exactly does the medication do? I would have liked more information about the drug in the questionnaire (I will now inform myself on the Internet). • To do a lot of advertising, in every possible way, so that expectant parents can deal with the topic before birth and actually clarify initial questions about "What does oxygen deficiency at birth mean" in advance. Then decisions in emergencies may be easier. • Basic information before birth about the gynecologist, if everything is still okay, then I know the medication and the procedure and can form an opinion beforehand. • It is important that new helping medications are developed and tested. But for new parents it is very scary, because nobody wants to use their child as a " laboratory rabbit".
PNeo (n=12)	• Test the side effect in advance. No influence of companies in the study. Test the drug in children only when the risks of administration are clear. • You should clearly contrast the consequences that may occur if the drug is not given (brain damage...) with the risks of giving it (drug vs. no drug). • Prior clarification of the parents. • Continue!!!!! • A short explanation with the most important things is enough.

	• Do not get discouraged. • Difficult topic. Unfortunately, no advice ready, except to enlighten the parents very gently afterwards. • Provide information about this option in advance. • Enlighten; do not act in the interests of the pharmaceuticals. • If the doctors are convinced of this drug and this certainty becomes clear in the discussion, parents can more easily decide to allow administration of study drugs. • Enlightenment should be given in a way that is appropriate and in simple language and, absolutely, in the language of the parents. Not when the birth has already begun, but during a preventive consultation, e.g. with a midwife. • Don't be "Mr./Mrs. Doctor anyway", be aware that the parents' world has probably collapsed. Empathy should take precedence over expertise and skills.
PAx (n=20)	• Be very careful with the parents, an emergency birth (as in our case) is a "borderline situation" in which parents also lose their calm quickly. Such "unsafe" administration of medication may cause additional anxiety. • I wish the physicians that they always have the human being in the foreground and that they are not only guided by the study itself in their actions. • Humanity comes first, followed by honesty, openness, respect and professional competence. Don't make us feel like a lab animal! Child-friendliness must be a prerequisite. • I recommend not only to the doctors but to all who are working on this study: "Imagine you are doing this for your own child." Only then you can do it right. • God's blessing! • You should continue to strengthen couples who are uncertain and give them hope by telling them about your successes so far. • Implement verbal consent in emergencies. Do not implement the emergency card. Assessment based on experienced situation with oxygen deficiency at birth of our child. • Provide good and comprehensive information and transparency. • Make expectant parents aware in advance through the gynecologists. • If possible, I would like to receive information about the study and the planned administration of the drug in the case of an emergency before birth. • Keep the essentials in mind! Is it really always necessary to give this drug? I wish you good luck and that your medicine helps the children as you hope! • Always keep looking for new methods. • I have never heard about this study. Therefore, I recommend to inform all expectant parents about it. I think that way you get the most approvals and the parents don't have to doubt etc. • Keep going. I have my fingers crossed that the ALBINO trial will be successful and help many babies. • Inform the parents beforehand! "If this and that were to happen, we would act immediately and do this and that; Would that be ok for you!?" Then parents are already prepared! And don't feel left out! And can have a say if they have been informed beforehand. • The study drugs, which will be administered in an emergency, should be addressed or discussed in advance." • To do as much preliminary work as possible (as described) with flyers and posters, so that it only has to be clarified afterwards in rare cases! • As long as you act on behalf of the child, I wouldn't worry too much about the parents. The life and health of the child always come first. • It's difficult to find a way. On the one hand, it is good to be informed beforehand about possible treatments. On the other hand, as a pregnant woman, you don't want to deal with such situations, as it can drive you extremely crazy... I wish the doctors a lot of strength to find the best way for everyone and good luck with the study. • Please take part in the study, it is always important. Thank you to the doctors who helped my child. Thank you, Dresden.