NORACT

Nordic randomized trial on laparoscopic versus vaginal cerclage

ClinicalTrials.gov No.: Not yet available

Trial Sponsor: Aarhus University Hospital, Professor Niels Uldbjerg

Independent Data Monitoring Committee (IDMC) Charter

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Developed from DAMOCLES IDMC Charter Template v1. February 2005 (1)

Authorised by:			
Name:	Niels Uldbjerg	Role:	Trial Sponsor
Signature:		Date:	14-06-2023
Prepared by			
Name:	Lea Kirstine Hansen	Role:	Trial Coordinating Investigator
Signature:		Date:	09-05-2023

CONTENT	CHARTER DETAILS
1. Introduction	
Name of trial	Nordic randomized trial on laparoscopic versus vaginal cerclage (NORACT)
Clinicaltrials.gov number	Not yet available
Sponsor name	Niels Uldbjerg (Aarhus University Hospital)
Principal Investigator	Julie Glavind
Trial Coordinating Investigator	Lea Kirstine Hansen
Website	www.noract.dk
Objectives of trial	To compare laparoscopic versus vaginal cerclage in women at risk of preterm birth (PTB) due to cervical insufficiency. Primary outcome is delivery ≤32 weeks. Secondary, powered neonatal outcome is baby death (any death between 14+0 weeks of gestation and 28 days post discharge).
PICO	P: Women in whom the clinician has equipoise as to whether an elective vaginal or laparoscopic cerclage will be the best intervention to prevent preterm birth I: Laparoscopic cerclage pre-pregnancy or in early pregnancy C: Vaginal cerclage in early pregnancy O: Delivery before 32 weeks of gestation
Interventions being investigated	Intervention: Laparoscopic cerclage Control: Vaginal cerclage
Outline of scope of charter	The purpose of this document is to describe the roles and responsibilities of the independent data monitoring committee (IDMC) for the NORACT trial, including the timing of meetings, methods of providing information to and from the IDMC, frequency and format of meetings, statistical issues and relationships with other committees.
2. Roles and responsibilities	
A broad statement of the aims of the committee	To safeguard the interests of NORACT participants, assess the safety and efficacy of the interventions during the trial, and monitor the overall conduct of the clinical trial.
Terms of reference	The IDMC should receive and review the progress and accruing data of NORACT and provide advice on the conduct of the trial to the Trial Steering Committee (TSC). The IDMC should inform the Chair of the TSC if, in their view:

CONTENT	CHARTER DETAILS
	(i) the results are likely to convince a broad range of clinicians, including those supporting the trial and the general clinical community, that one trial arm, or a subset of trial population, is clearly indicated or contraindicated, and there was a reasonable expectation that this new evidence would materially influence patient management; or (ii) it becomes evident that no clear outcome would be obtained.
Specific roles of IDMC	Review of the trial's progress including updated figures on recruitment, data quality, and main endpoints including safety data. A selection of specific aspects could be compiled from the following list: • assess data quality, including completeness (and by so doing encourage collection of high quality data) • monitor recruitment figures and losses to follow-up • monitor compliance with the protocol by participants and investigators • monitor evidence for treatment differences in the main efficacy endpoints • monitor evidence for treatment harm (e.g. serious adverse events (SAEs), deaths) • review the report of suspected unexpected serious adverse reaction (SUSAR) provided by the management group whenever occurs • decide whether to recommend that the trial continues to recruit participants or whether recruitment should be terminated either for everyone or for some of the predefined obstetric risk subgroups • suggest additional data analyses • advise on protocol modifications suggested by the NORACT board (e.g. inclusion criteria, trial endpoints, or sample size) • monitor planned sample size assumptions, preferably with regards to a priori assumptions about the control arm outcome • monitor compliance with previous IDMC recommendations • consider the ethical implications of any recommendations made by the IDMC • assess the impact and relevance of external evidence • maintain confidentiality of all trial information that is not in the public domain • protect validity and scientific credibility of the trial
3. Before or early in the trial	
Whether the IDMC will have input into the protocol	All potential IDMC members will have sight of the protocol/outline before agreeing to join the committee.

CONTENT	CHARTER DETAILS
Whether the IDMC will meet before the start of the trial	The IDMC members will have their first meeting approximately 6 months into the pilot study unless an earlier meeting is requested. The chair of the IDMC will attend the first TSC meeting, which is held prior to trial start,
Any issues specific to the disease under study	The protocol describes issues specific to the disease under study.
Any specific regulatory issues	None
Any other issues specific to the treatment under study	The protocol describes issues specific to the treatment under study.
Whether members of the IDMC will have a contract	IDMC member will not formally sign a contract but should formally register their assent to join the group by confirming (1) that they agree to be on the IDMC and (2) that they agree with the contents of this Charter. Any competing interests should be declared at the same time. Members should complete and return the form in Annexe 1. Observers attending any part of the meeting should sign a confidentiality agreement on the first occasion they attend all or part of a meeting (Annexe 2).
4. Composition	
Membership and size of the IDMC	Membership will consist of three members with clinical trial experience. Consideration has been made to reflect the international collaboration of the NORACT trial. The members have not been involved with the trial in any other way or have some competing interest that could impact on the trial. Any competing interests, both real and potential, should be declared. Although members may well be able to act objectively despite such connections, complete disclosure enhances credibility. A short competing interest form should be completed and returned by the IDMC members to the trial coordinating team (Annexe 1). The members of the IDMC for this trial are: 1. Mr. Paul Seed, Reader in Medical Statistics, Department of Women and Children's Health/Unit for Medical Statistics, School of Life Course & Population Sciences, King's College London & King's Health Partners 2. Dr Martijn Oudijk Professor of Obstetrics, University of Amsterdam 3. Dr Victoria Hodgetts Morton Associate Professor and Honorary Consultant in Obstetrics University of Birmingham

CONTENT	CHARTER DETAILS
The Chair, how they are chosen and the Chair's role	The Chair has previous experience of serving on IDMCs and experience of chairing meetings and is able to facilitate and summarise discussions. The Chair has been chosen by the NORACT board. The IDMC chair is: Paul Seed, Reader in Medical Statistics, Department of Women and Children's Health/Unit for Medical Statistics, School of Life Course & Population Sciences, King's College London & King's Health Partners
The responsibilities of the IDMC statistician	The IDMC membership will include a statistician to provide independent statistical expertise. The IDMC statistician will not prepare the IDMC report. The IDMC statistician is: Paul Seed, Reader in Medical Statistics, Department of Women and Children's Health/Unit for Medical Statistics, School of Life Course & Population Sciences, King's College London & King's Health Partners
The responsibilities of the trial statistician	The trial statistician will have the overall responsibility for producing the report to the IDMC and will participate in IDMC meetings, guiding the IDMC through the report, participating in IDMC discussions and, on some occasions, taking notes. The trial statistician is: Erik Thorlund Parner, Professor Department of Public Health - Biostatistics, Aarhus Univeristy
The responsibilities of the NORACT trial coordinating investigator	The NORACT trial coordinating investigator will help the trial statistician to produce the non-confidential sections of the IDMC report. The trial coordinator may attend open sessions of the meeting.
The responsibilities of the trial coordinating investigator and other members of the trial management group (TMG)	The Principal Investigator or the sponsor may be asked, and should be available, to attend open sessions of the IDMC meeting. Other NORACT Board members will not usually be expected to attend but can attend open sessions when necessary (See Section 6. Organisation of IDMC Meetings).
5. Relationships	
Relationships with committees (TSC, NORACRT board, TMG), sponsor and regulatory bodies	See Figure 1

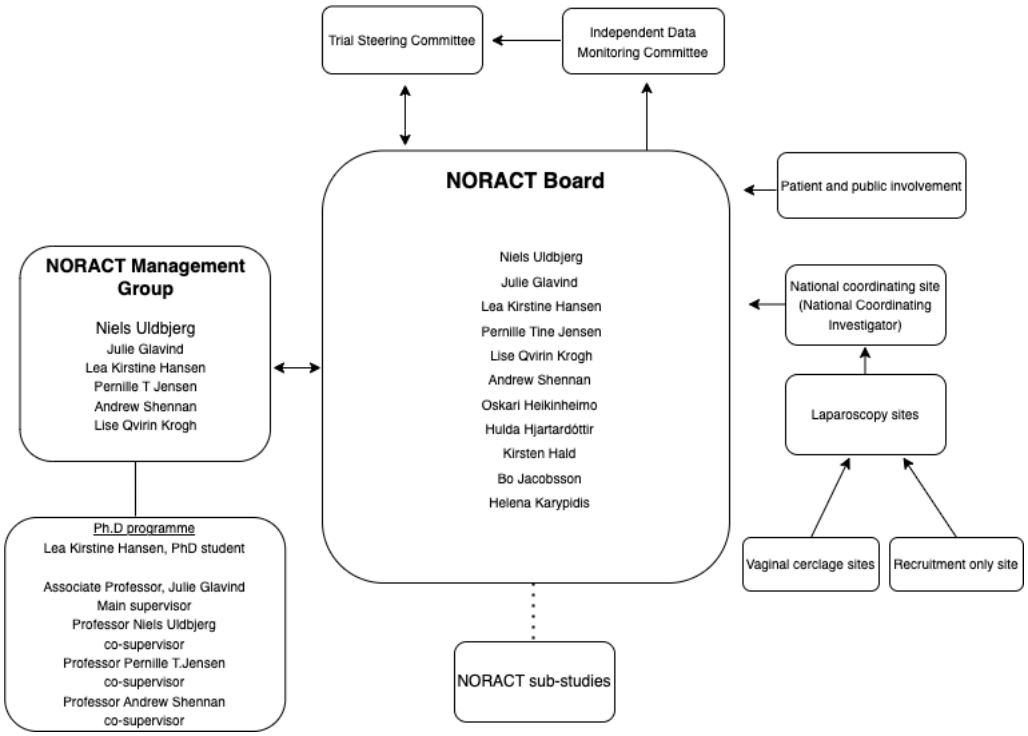
CONTENT	CHARTER DETAILS
Clarification of whether the IDMC are advisory (make recommendations) or executive (make decisions)	The TSC is oversight body of the trial and is delegated this role by the sponsor. The IDMC does not make decisions about the trial, but rather makes recommendations to the TSC.
Payments to IDMC members	Members will be reimbursed for travel and accommodation where required. No other payments or rewards are given.
6. Organisation of IDMC meetings	
Expected frequency of IDMC meetings	The IDMC will meet at least once a year. The exact frequency of meetings will depend upon any statistical plans specified and otherwise on trial events. The wishes of the IDMC and needs of the trial coordinating team will be considered when planning each meeting. An unplanned IDMC meeting may be called by the Chair or requested by the NORACT Board or Trial Steering Committee if there is an emergency concern on the safety of participants.
Whether meetings will be face-to-face or by teleconference	The meetings will be held virtually. Face-to-face meetings can be arranged according to need and wish from the IDMC members.
How IDMC meetings will be organised, especially regarding open and closed sessions, including who will be present in each session	A mixture of open and closed sessions is recommended. Only IDMC members and others whom they specifically invite, e.g. the trial statistician, are present in closed sessions. In open sessions, all those attending the closed session may be joined by the Principal Investigator or other members of the NORACT Board. The format of the meetings: 1. Open session: Introduction and any "open" parts of the report 2. Closed session: IDMC discussion of "closed" parts of the report 3. Closed session: IDMC members private meeting 4. Open session: Discussion with other attendees on any matters arising from the previous session(s). 5. Closed session: extra closed session as required
7. Trial documentation and procedures to ensure confidentiality and proper communication	

CONTENT	CHARTER DETAILS
Intended content of material to be available in open sessions	Open sessions: Accumulating information relating to recruitment and data quality (e.g. data return rates, sample collection, treatment compliance) will be presented.
Intended content of material to be available in closed sessions	Closed sessions: In addition to all the material available in the open session, the closed session material will include efficacy and safety data by treatment group.
Will the IDMC be blinded to the treatment allocation	Open label trial.
The people who will see the accumulating data and interim analysis	The confidential accumulating data will be seen by the IDMC members and the trial statistician(s). IDMC members do not have the right to share confidential information with anyone outside the IDMC, including the Principal Investigator, coordinating investigator and the trial sponsor.
Responsibility for identifying and circulating external evidence (eg from other trials/ systematic reviews)	Identification and circulation of external evidence (e.g. from other trials/ systematic reviews) is not the responsibility of the IDMC members. The NORACT Board and the trial management group will collate any such information for the presentation in an open session.
To whom the IDMC will communicate the decisions/ recommendations that are reached	The IDMC will report its recommendations in writing to the TSC. This should be copied to the trial coordinating investigator in time for consideration at a TSC meeting. In its communications, the IDMC should be careful not to relay any unnecessary information to the TSC: the TSC has members from the trial management group.
Whether reports to the IDMC be available before the meeting or only at/during the meeting	It is usually helpful for the IDMC to receive the report at least 2 weeks before any meetings. Depending on the trial, it may sometimes be preferable for all papers to be brought to face-to-face meetings by the trial statistician; time would then be needed for IDMC members to assimilate the report.
What will happen to the confidential papers after the meeting	The IDMC members should store the papers safely after each meeting so they may check the next report against them. After the trial is reported, the IDMC members should destroy all reports.
8. Decision making	
What decisions/recommendations will be open to the IDMC	Possible recommendations could include: • No action needed, trial continues as planned • Early stopping due, for example, to clear benefit or harm of a treatment, futility, or external evidence

CONTENT	CHARTER DETAILS
	• Stopping recruitment within one of the predefined obstetric risk subgroups • Extending recruitment (based on actual control arm response rates being different to predicted rather than on emerging differences) or extending follow-up
The role of formal statistical methods, specifically which methods will be used and whether they will be used as guidelines or rules	Formal statistical methods may have been considered by the IDMC in making their recommendations to the TSC. These methods are usually used as guidelines rather than absolute rules. This is because they generally only consider one dimension of the trial. The IDMC will record reasons for disregarding a stopping guideline in the notes of their meetings and may choose to also note this in their report to the TSC if necessary.
How decisions or recommendations will be reached within the IDMC	Issues to be specified can include: • The decision-making methods and criteria that will be adopted for guiding deliberations • The process of decision making, will be via voting to achieve consensus. • The role of the Chair is to summarise discussions and encourage consensus; it may be best for the Chair to give their own opinion last. It is recommended that every effort should be made for the IDMC to reach a unanimous decision. If the IDMC cannot achieve this, a vote may be taken, although details of the vote should not be routinely included in the report to the TSC as these may inappropriately convey information about the state of the trial data. It is important that the implications (e.g. ethical, statistical, practical, financial) for the trial be considered before any recommendation is made.
Can IDMC members who cannot attend the meeting input	As the report is circulated before the meeting, IDMC members who will not be able to attend the meeting may pass comments to the IDMC Chair for consideration during the discussions.
What happens to members who do not attend meetings	If a member does not attend a meeting, it should be ensured that the member is available for the next meeting. If a member does not attend a second meeting, they should be asked if they wish to remain part of the IDMC.
	Equal weight will be given to maternal and fetal outcomes

CONTENT	CHARTER DETAILS
Whether different weight will be given to different endpoints (e.g. safety/efficacy)	
9. Reporting	
To whom will the IDMC report their recommendations/decisions, and in what form	This will be a letter to the TSC or Trial coordinating investigator, within 3 weeks. A copy of the IDMC recommendation will be stored in the trial master file.
Whether minutes of the meeting be made and, if so, by whom and where they will be kept	Minutes of the meeting will be kept by the designated minute keeper. Separate records will be kept for open and closed sessions. The IDMC Chair will sign off any minutes or notes.
What will be done if there is disagreement between the IDMC and the body to which it reports	If the IDMC has serious problems or concerns with the TSC decision a meeting of these groups should be held. The information to be shown would depend upon the action proposed and the IDMC's concerns. Depending on the reason for the disagreement confidential data will often have to be revealed to all those attending such a meeting. The meeting would be Chaired by an external expert who is not directly involved with the trial.
10. After the trial	
Publication of results	At the end of the trial there will be a meeting to allow the IDMC to discuss the final data with the key members of the NORACT Board and give advice about data interpretation
The information about the IDMC that will be included in published trial reports	IDMC members will be named and their affiliations listed in the main report, unless they explicitly request otherwise. A brief summary of the timings and conclusions of IDMC meetings should be included in the body of this paper.
Whether the IDMC will have the opportunity to approve publications, especially with respect to reporting of any IDMC recommendation regarding termination of a trial	The IDMC will be given the opportunity to read and comment on publications before submission. This will usually be concurrent with the trial investigators and independent members of the TSC reading and commenting. The commenting period will be 2 to 3 weeks.
Any constraints on IDMC members divulging information about their deliberations after the trial has been published	The IDMC may discuss issues from their involvement in the trial 12 months after the primary trial results have been published, or when permission is agreed with the overseeing committee TSC.

Figure 1


Trial Steering Committee
Independent Data Monitoring Committee
NORACT Board
Niels Uldbjerg
Julie Glavind
Lea Kirstine Hansen
Pernille Tine Jensen
Lise Qvirin Krogh
Andrew Shennan
Oskari Heikinheimo
Hulda Hjartardóttir
Kirsten Hald
Bo Jacobsson
Helena Karypidis
Patient and public involvement
National coordinating site (National Coordinating Investigator)
Laparoscopy sites
Vaginal cerclage sites
Recruitment only site
NORACT Management Group
Niels Uldbjerg
Julie Glavind
Lea Kirstine Hansen
Pernille T Jensen
Andrew Shennan
Lise Qvirin Krogh
Ph.D programme
Lea Kirstine Hansen, PhD student
Associate Professor, Julie Glavind
Main supervisor
Professor Niels Uldbjerg
co-supervisor
Professor Pernille T.Jensen
co-supervisor
Professor Andrew Shennan
co-supervisor
NORACT sub-studies

Annexe 1: Agreement and competing interests form for IDMC members

Agreement to join the NORACT Trial Independent Data Monitoring Committee and disclosure of potential competing interests

Please complete the following document and return to the NORACT Trial coordinating Investigator.

(please initial box to agree)

	I have read and understood the IDMC Charter version 1 , dated 09/05/2023
	I agree to join the Data Monitoring Committee for this trial as an independent member
	I agree to treat all sensitive trial data and discussions confidentially

The avoidance of any perception that independent members of an IDMC may be biased in some fashion is important for the credibility of the decisions made by the IDMC and for the integrity of the trial.

Potential competing interests should be disclosed via the NORACT trial coordinating investigator. In many cases simple disclosure up front should be sufficient. Otherwise, the (potential) independent IDMC member should remove the conflict or stop participating in the IDMC. Table 1 lists potential competing interests.

	No, I have no potential competing interests to declare
	Yes, I have potential competing interests to declare (please detail below)

Please provide details of any potential competing interests:

_____

_____

_____

Name: _____

Signed: _____ Date: _____

Table 1: Potential competing interests for independent members

- Stock ownership in any commercial companies involved
- Stock transaction in any commercial company involved (if previously holding stock)
- Consulting arrangements with the Sponsor/Funder
- Ongoing advisory role to a company providing drugs to the trial
- Frequent speaking engagements on behalf of the intervention
- Career tied up in a product or technique assessed by trial
- Hands-on participation in the trial
- Involvement in the running of the trial
- Emotional involvement in the trial
- Intellectual conflict e.g. strong prior belief in the trial's experimental arm
- Involvement in regulatory issues relevant to the trial procedures
- Investment (financial or intellectual) or career tied up in competing products
- Involvement in the writing up of the main trial results in the form of authorship

Annexe 2: Agreement and confidentiality agreement for observers

Agreement to attend the NORACT Trial Independent Data Monitoring Committee and treat all information confidentially

Please complete the following document and return to the NORACT trial coordinating investigator.

(please initial box to agree)

	I have received a copy of the IDMC Charter version 1.0
	I agree to attend the Independent Data Monitoring Committee meeting on ___/____/_____
	I agree to treat as confidential any sensitive information gained during this meeting unless explicitly permitted

Name: _____

Signed: _____ Date: _____

Abbreviations

TSC	Trial Steering Committee
PTB	Preterm Birth
IDMC	Independent Data Monitoring Committee
TMG	Trial Management Group
PI	Principal Investigator
SAE	Serious Adverse Event
SUSAR	Suspected unexpected serious adverse reaction

References

1. Damocles Study Group NHSHTAP. A proposed charter for clinical trial data monitoring committees: helping them to do their job well. Lancet. 2005;365(9460):711-22.