NORACT

Nordic randomized trial on laparoscopic versus vaginal cerclage

ClinicalTrials.gov No.: Not yet available

Trial Sponsor: Aarhus University Hospital, Professor Niels Uldbjerg

Trial Steering Committee (TSC) Charter

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Developed using MRC Clinical Trials Unit template TSC Charter version 1.02, 13-Mar-2006 (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:	13-06-2023

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 $\leq$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 abdominal 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 Trial Steering Committee for the NORACT trial, including the timing of meetings, methods of providing information to and from the TSC, frequency and format of meetings, statistical issues, and relationships with other committees.
2. Roles and responsibilities (2, 3)	
A broad statement of the aims of the committee	To act as the oversight body for the NORACT trial on behalf of the Sponsor.
Terms of reference	The TSC should provide overall supervision for the trial on behalf of the Trial Sponsor and Trial Funder and ensure that the trial is conducted to the rigorous standards set out in the Guidelines for Good Clinical Practice. It should be noted that the day-to-day management of the trial is the responsibility of the Principal Investigator and the NORACT management group. The TSC should also provide advice through its independent Chair to the NORACT Board on all aspects of the trial.
Specific roles of TSC	The TSC will concentrate on the progress of the trial, adherence to protocol, patient safety and consideration of new information of relevance to the research question.

CONTENT	CHARTER DETAILS
	• Approve the trial protocol, sanctioning and/or proposing protocol changes. • Decide how to proceed with the full trial once the pilot trial has ended. • Receive letters of feedback from the Independent Data Monitoring Committee (IDMC) and consider its recommendations • Monitor completion of data collection and comment on strategies to encourage satisfactory data completion. • Monitor recruitment rates and recruitment related issues and comment on strategies to encourage the most favorable recruitment approach. • Monitor follow-up rates and review strategies to handle losses to follow-up. • Approve / comment on the statistical analysis plan • Approve / comment on the publication policy for the main trial • Approve / comment on the main trial manuscript • Assess the impact and relevance of any accumulating external evidence
3. Before or early in the trial	
Whether the TSC will have input into the protocol	All potential TSC members will have sight of the protocol/outline before agreeing to join the committee.
Whether the TSC will meet before the start of the trial	The TSC members will have their first meeting before the start of the trial to discuss the protocol, the trial, the statistical plan, future meetings and to clarify any aspects with the principal investigator, the sponsor, the trial coordinating investigator and the NORACT Board.
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 TSC will have a contract	TSC members 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 TSC 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 or 2. 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 3).
4. Composition	

CONTENT	CHARTER DETAILS
Membership and size of the TSC(2)	Membership will consist of three independent and voting members, one non-independent voting member and two non-independent non-voting members to ensure 75% independency in case of voting. Consideration has been made to reflect the international collaboration of the NORACT trial. The independent members have not been involved with the trial in any other way or have 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 TSC members to the trial coordinating team (Annexe 1 or 2). The independent members of the TSC for NORACT trial are: 1. Mr. Nigel Simpson, Consultant Obstetrician and Gynaecologist, Leeds Teaching Hospital NHS Trust and senior lecturer at the University of Leeds. 2. Dr. Caroline Fox, Consultant in Maternal and Fetal Medicine, Birmingham Women's and Children's NHS Foundation Trust. 3. Mrs. Catherine Moakes, Senior Medical Statistician, Birmingham Clinical Trials Unit, University of Birmingham. Non-independent, voting member of the TSC for the NORACT trial is: 4. Dr. Julie Glavind, Consultant Obstetrician, Ph.D., Associated Professor, Aarhus University Hospital Non-independent, non-voting members of the TSC for the NORACT trial are: 5. Professor Niels Uldbjerg, Consultant Obstetrician, Aarhus University Hospital 6. Dr. Lea Kirstine Hansen, Specialty Registrar in Obstetrics and Gynaecology, phd-student and trial coordinating investigator in the NORACT trial.
The Chair, how they are chosen and the Chair's role	The Chair has previous experience of serving on TSCs and experience of chairing meetings and can facilitate and summarise discussions. The Chair has been agreed by the NORACT board. The TSC chair is: Mr. Nigel Simpson, Consultant Obstetrician and Gynaecologist, Leeds Teaching Hospital NHS Trust and senior lecturer at the University of Leeds. The chair's responsibility include: • Chairing the TSC meetings and summarizing discussions. • Being familiar with the role of the IDMC. • Leading the TSC to provide regular, impartial oversight of the trial. • Being available to provide independent advice as required, also outside of scheduled TSC meetings.

CONTENT	CHARTER DETAILS
	• Commenting in detail (when appropriate) regarding the continuation or stopping of the trial.
Arranging meetings and communication between the different bodies	The NORACT trial coordinating investigator is responsible for arranging meetings of the TSC, coordinating reports as well as producing and circulating minutes and action points. The trial coordinating investigator will be the central point for all communication between the TSC and other bodies, will be copied into all correspondence among TSC members, and will be kept aware of trial issues as they arise.
Reports	The NORACT trial coordinating investigator will produce a detailed report on the trial before each TSC meeting (figure 1).
5. Relationships	
Relationships with committees and other bodies (IDMC, NORACT board, the trial management group (TMG))	The responsibilities of each trial committee are detailed in the protocol and in the respective Charters. The relationship between these groups are summarised in Figure 2.
Clarification of whether the TSC 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 TSC makes decisions about the trial, following recommendations from the IDMC.
Payments to TSC members	Members will be reimbursed for travel and accommodation where required. No other payments or rewards are given.
6. Organisation of TSC meetings	
Expected frequency of TSC meetings	The TSC will have its first meeting prior to trial start. Hereafter the meeting frequency will be every 6 months, which can later be increased to once a year. The chair of the IDMC will be invited to the first TSC meeting. The exact frequency of meetings will depend upon any statistical plans specified and otherwise on trial events. The wishes of the TSC and needs of the management group will be considered when planning each meeting. An unplanned TSC meeting may be called by the Chair or requested by the NORACT board 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 TSC members.
How TSC meetings will be organised	A mixture of open and closed sessions is recommended. Only TSC members and others whom they specifically invite, e.g. the trial statistician, are present in closed sessions. In open sessions, all those

CONTENT	CHARTER DETAILS
	attending the closed session may be joined by 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: TSC discussion of "closed" parts of the report 3. Closed session: TSC 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
Can TSC members who cannot attend the meeting input	As the report is circulated before the meeting, TSC members who will not be able to attend the meeting may pass comments to the TSC Chair or NORACT Trial coordinating investigator for consideration during the discussions.
What happens to independent members who do not attend meetings	If an independent member does not attend a meeting or provide comments when requested between meetings, it should be ensured that the independent member is available for the next meeting. If an independent member does not attend the next meeting or provide comments when next requested, they should be asked if they wish to remain part of the TSC. If an independent member does not attend a third meeting, strong consideration should be given to replacing this member.
7. Trial documentation and procedures to ensure confidentiality and proper communication	
Intended content of material to be considered during meetings	A short report will be prepared by the NORACT trial coordinating investigator. This will report on accrual and any matters affecting the trial. Additionally, the material may include a report from the IDMC, requests from the NORACT Board or draft publications. No trial outcome measure data will be presented by arm unless explicitly authorised by the IDMC. Where relevant, accrual, compliance with follow-up and adherence to treatment may be presented by site.
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.

CONTENT	CHARTER DETAILS
The people who will see the accumulating data	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.
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 TSC members. The NORACT Board and the trial management group will collate any such information for the presentation in an open session.
To whom the TSC will communicate the decisions/ recommendations that are reached	See section 9.
What will happen to the papers after the meeting	TSC members would be expected to delete, destroy or store securely copies of the reports to and from the TSC, agenda and minutes, as well as copies of communications between meetings. All documentation should be considered confidential. The NORACT trial coordinating investigator will keep a central record of all minutes, reports and correspondence by the TSC.
8. Decision making	
What decisions/recommendations will be open to the TSC	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 • Stopping recruitment within a predefined obstetric risk subgroup • Extending recruitment (based on actual control arm response rates being different to predicted rather than on emerging differences) or extending follow-up • Sanctioning and/or proposing protocol changes Based on other factors, possible decisions include the decisions above and: • Censuring sites for poor recruitment/poor data quality • Approving requests for early release of (subsets of) data • Approving presentation of results during the trial or soon after closure
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.

CONTENT	CHARTER DETAILS
How decisions or recommendations will be reached within the TSC	Every effort should be made to achieve consensus. The role of the Chair is to summarise discussions and encourage consensus; therefore, it is usually best for the Chair to give their own opinion last. It is important that the implications (e.g. ethical, statistical, practical, financial) for the trial to be considered before any decision is made.
When the TSC is quorate for decision-making	All voting members of the TSC must be present including the Chair.
9. Reporting	
To whom will the TSC report their recommendations/decisions, and in what form	The TSC will report their decisions (via the NORACT trial coordinating investigator) to the NORACT Board who will be responsible for implementing any actions resulting. The TSC may also provide feedback to the IDMC and, where appropriate, to the Sponsor.
Whether minutes of the meeting be made and, if so, by whom and where they will be kept	Notes of key points and actions will be made by the NORACT trial coordinating investigator. This will include details of whether potential competing interests have changed for any attendees since the previous meeting. The draft minutes will be initially circulated for comment to those TSC members who were present at the meeting. The TSC Chair will sign off the final version of minutes or notes.
What will be done if there is disagreement between the TSC and other trial committees	The TSC is the oversight body for the trial. However, the TSC should have good reason before deciding not to accept requests from the NORACT Board or trial management group and recommendations from the IDMC. If there are serious problems or concerns with the TSC decision following an IDMC recommendation, a joint meeting of the TSC and IDMC should be held. The information to be shown would depend upon the action proposed and each committees' concerns. Depending on the reason for the disagreement confidential data and/or data by trial may have to be revealed to all or some of those attending such a meeting: this would be minimised where possible. The meeting would be Chaired by an external expert who is not directly involved with the trial.
10. After the trial	
Publication of results	The TSC will oversee the timely analysis, writing up and publication of the main trial results. The independent members of the TSC will have the opportunity to read and comment on the proposed main publications of trial data prior to submission and abstracts and presentations during the trial. This review may be concurrent to that of the trial investigators and IDMC.

CONTENT	CHARTER DETAILS
The information about the TSC that will be included in published trial reports	TSC members will be named and their affiliations listed in the main report, unless they explicitly request otherwise.
Any constraints on TSC members divulging information about their deliberations after the trial has been published	The TSC 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

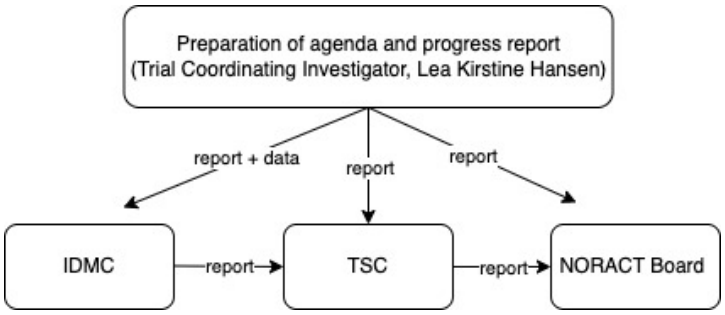
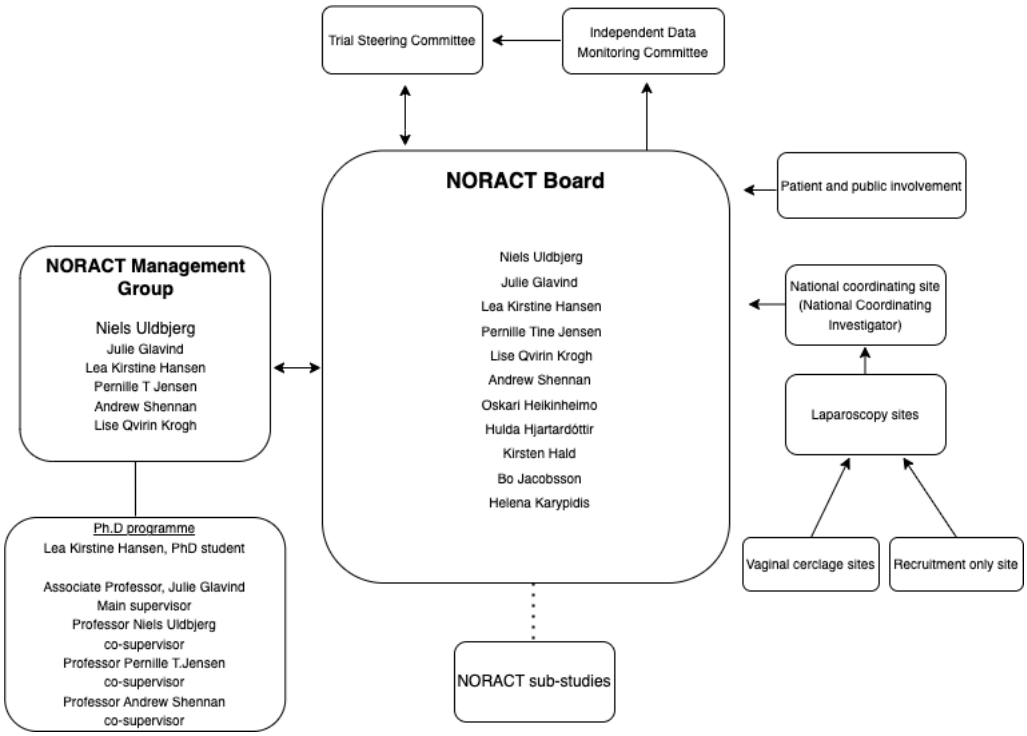


Figure 2



Annexe 1: Agreement and competing interests form for independent members

Agreement to join the NORACT Trial Steering Committee as an independent member 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 TSC Charter version 1,0, dated 13/06/2023
	I agree to join the Trial Steering 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 a TSC may be biased in some fashion is important for the credibility of the decisions made by the TSC 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 TSC member should remove the conflict or stop participating in the TSC. 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 competing interests form for non-independent members

Agreement to join the NORACT Trial Steering Committee as a non-independent member 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 TSC Charter version 1,0 dated 13/06/2023
	I agree to join the Trial Steering 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 a TSC may be biased in some fashion is important for the credibility of the decisions made by the TSC 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 TSC member should remove the conflict or stop participating in the TSC. 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

Annexe 3: Agreement and confidentiality agreement for observers

Agreement to attend the NORACT Trial Steering 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 TSC Charter version 1,0
	I agree to attend the Trial Steering 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

References:

1. Council MR. MRC Clinical Trials Unit at UCL Templates 2023 [updated 05-04-2023. Available from: https://www.mrcctu.ucl.ac.uk/our-research/other-research-policy/regulatory-information-toolkits-templates/.
2. Harman NL, Conroy EJ, Lewis SC, Murray G, Norrie J, Sydes MR, et al. Exploring the role and function of trial steering committees: results of an expert panel meeting. Trials. 2015;16:597.
3. The Medical Reserach Council. MRC GUIDELINES FOR

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HEALTH TRIALS 2017 [updated 2022. Available from: https://www.ukri.org/wp-content/uploads/2021/08/20220202_Guidelines-for-Global-Health-Trials-2017-v5-final.pdf.

Note: This TSC charter was developed using MRC CTU template TSC Charter version 1.02, 13-Mar-2006