CONTRAST DATAMANAGEMENT PROTOCOLS, SOPs AND DOCUMENTS

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Authorized by	CONTRAST steering committee, PI's and study coordinators of MR ASAP, MR CLEAN-NO IV, MR CLEAN-MED, MR CLEAN-LATE, DIST pilot study
Purpose of document	To combine all the available data management protocols, SOPs and documents applicable for the CONTRAST consortium, CONTRAST investigators/collaborators, and external parties requesting data.
Contents	- CONTRAST Data Management Plan - **SOP1**: Workflow from data-request through dataset-issuing to sharing your publication for CONTRAST substudies: 1. Data application and issuing. 2. Publication policy 3. Required texts and acknowledgments - **SOP2**: Biobank materials & Imaging data request procedure - **SOP3**: Policy for Access to and Sharing of Data with external (non-CONTRAST) parties - Committees and members - Appendices

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CONTRAST Data Management Plan template

Author(s)	Workpackage 6 (WP6): Jasper Daems, Vicky Chalos, Olvert Berkhemer, Hester Lingsma, Diederik Dippel
Authorized by	Scientific committee of the CONTRSAT consortium and PIs of the [INSERT STUDY NAME]
Name of group/project	Collaboration for New Treatments of Acute Stroke (CONTRAST) consortium
Description of research	The overarching aim of CONTRAST is to improve outcome of patients with stroke by merging translational research and pragmatic randomized clinical trials, with a firm view of the future of Dutch Stroke Research beyond the coming five years. There are 4 large multicenter randomized acute stroke trials (almost) completed within CONTRAST. Future RCT's will be embedded within CONTRAST including [INSERT STUDY NAME]. Data management is facilitated by WP6 within the CONTRAST collaboration.
international trial identification numbers	[INSERT STUDY NAME]: [INSERT NUMBER]
Sponsor	Erasmus MC University Medical Center
Funding body(ies)	Disclosure: the CONTRAST consortium is supported by Netherlands Cardiovascular Research Initiative (CVON), an initiative of the Dutch Heart Foundation, by the Brain Foundation Netherlands, Medtronic and Cerenovus. AMC and Erasmus MC received additional unrestricted funding on behalf of CONTRAST, for the execution of MR CLEAN NO-IV from Stryker European Operations BV. [ADD ANY STUDY SPECIFIC FUNCERS]
Partner organizations	Lygature
Project duration [INSERT STUDY NAME]	Start: […], End: […]
Date written	06-01-2020
Date last update	23-03-2022

Version	2.0
Name of researcher(s) with roles/responsibilities for data management	Researchers of WP6 (Jasper Daems, Olvert Berkhemer, Hester Lingsma, Diederik Dippel), PI's and study coordinators of the trials, central research nurses, local PI's, local research nurses

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*** For the sections and details that are applicable to all CONTRAST trials we refer to the most recent version of the CONTRAST DMP, which can be found at the CONTRAST plaza. ***

1. Data collection

Clinical data

Randomization will be through a web-based, allocation service which will also allocate a unique study number to each patient. For the trials embedded in CONTRAST, data on patient eligibility and the treatment allocation that were entered into this allocation service will be sent to the study coordinators of the specific trial via an encrypted message. This encrypted message will be decrypted by the study coordinator via a specific decryption program. Only study coordinators and data managers are authorized to fill out data decrypted by the study coordinators into a web-based trial management system (i.e., Castor, see "2. Study database" below). To ensure that the treatment allocation cannot be changed, this part of the database will be locked directly (i.e., becomes read-only). Data on patient eligibility will be required before a randomization can take place in order to prevent randomization of non-eligible patients. Once a randomization has occurred, the data filled out in the application will be stored in its back-office. Access to the back-office will be given to study coordinators by logging into the system with their personal email and password. Central personal data storage is necessary to make centralized follow up possible. This procedure has to be mentioned in the study protocol. This procedure needs approval by the national Ethics Board (METC).

Data will be collected at several points in time throughout the study periods for each trial. Required data, apart from the randomization data, are to be obtained from the subject's medical notes/source documents where the information was first recorded and then entered into the electronic Case Report forms (eCRFs). Data will be collected from the medical records by trained local research nurses and entered into Castor by the local trained research staff. This process may be facilitated by using paper facsimile CRFs to make notes, but all source data should be in the medical record and the paper notes need not be retained. All eCRF data should be verifiable to a source at the investigational site or accessible by the site staff.

Source documents may include but are not limited to the following original documents, data, and records:

- Ambulance and hospital records
- Medical histories and narrative statements relating to the subject's progress
- Clinical and office charts
- Reports of surgical and interventional procedures
- Laboratory notes/reports
- Memoranda and telephone notes/records
- ECG recordings
- Pharmacy dispensing records
- Recorded data from automated instruments
- Copies of transcriptions certified after verification as being accurate copies

Imaging data

Imaging data in DICOM format that will be collected include baseline imaging, consisting of cranial CT and cervical and head CTA or alternatively, head MRI, and cervical and head MRA. Periprocedural imaging includes complete series of pre- and postprocedural DSA in at least lateral and anteroposterior views, showing arterial and venous phases of the contrast injection, and finally, after each device placement a non-contrast radiograph and one view of the contrast angiogram. Follow up imaging should include NCCT at 5-7 days, and CTA at 24-48 hrs or alternatively, MR and MRA at 24 hours. Technical requirements and specifications are listed in appendices of the trial protocols.

2. Study databases

Clinical data and imaging metadata

Castor is a fully web-based system that meets all ICH-GCP-E6 (R2) requirements for electronic data entry with respect to safeguarding data integrity and data security. The Castor database can only be accessed by those specifically granted access to the database and specific rights can be issued (e.g., data-entry, monitoring, admin) and are customizable. Permission to access Castor will be granted to trained research staff by the principal investigator of the study. The study coordinator indicates the role/authorization that should be applied to the specific user account. User accounts are personal, and access is protected with Two-Factor Authentication. Castor allows for audit trails. All actions carried out in Castor (i.e., all changes in the study structure, data collection and study management) will be captured via an electronic audit trail. Data can only be archived and not deleted. The audit trial records at least date and time of change, the individual that made the change and the new data value.

For each study phase (baseline, clinical information during hospital stay, clinical outcome assessments, imaging assessments) separate eCRFs will be created. Access to each study phase / eCRF can be regulated with user-roles (e.g. clinical data-entry, imaging data-entry, monitor, admin). And institute rights can be granted for each individual user. Therefore, specific parts of the study (e.g. primary outcome assessments) and specific records (from other institutes) can be hidden for certain roles or users on a predefined and customizable basis. New user-roles can be created, and rights can be specified (e.g. editing, viewing, signing, verifying, locking, archiving, exporting rights).

This way all staff can be blinded to the primary outcome according to the PROBE (Prospective Randomized Open, Blinded End point) design. Blinding for the randomisation eCRF is also possible. The eCRFs of the trials embedded in CONTRAST are mostly identical, with the exception of the randomization eCRF and any trial specific eCRFs, to enable future data pooling. The variable names within the eCRFs are uniform for all trials. The eCRFs themselves will not be changed during the conduct of the trials. When additions to the eCRFs themselves are necessary, additional eCRFs will be added to the database, without changing the CRFs that are already being used.

Imaging data

The collection of imaging data will be handled by imaging Work Package 10 through another central web-based database (i.e., XNAT Health-RI). All imaging data will be pseudonymized and stored under an unique number that is also used in the clinical database. Assessments of imaging by the imaging committee will be stored in CRFs and entered into a separate Castor eCRF. Imaging will also be stored locally at the investigational site on a secure data system.

Imaging Metadata

Imaging metadata, i.e. assessments by core lab, will be stored in the eCRF.

Biobank blood samples and metadata

Blood samples are stored at -80 degrees Celsius in monitored freezers at the central Biobank of the Erasmus MC. All biobank data will be pseudonymized and stored under a unique number that is also used in the clinical database. Work Package 5 handles the collection and processing of blood samples.

Biobank thrombi and metadata

Thrombi and aspirated thrombus material are kept in formaldehyde for no longer than two weeks and then embedded in paraffin. The material is stored under a unique number that is also used in the clinical database. Work Package 5 handles the collection and processing of thrombi and aspirated thrombus material.

3. Data quality assurance and monitoring

The local principal investigator(s) of each trial will be responsible for ensuring eCRF data completeness and accuracy. The eCRFs will be reviewed by a monitor from the Sponsor or its designee for completeness and accuracy. Source document verification (SDV) will be performed. Study monitors performing SDV will be able to mark entire study phases or parts of eCRFs as verified. The eCRF data may also be reviewed internally by the Sponsor's Data Management, Medical and Scientific staff, or their designee and, if necessary, the investigational sites will be queried for corrections and/or clarifications.

The trials will be monitored by an independent monitor according to ICH-GCP guidelines and relevant national regulations. Before initiation of the trial, the monitors will receive training about stroke, the trial protocol, and the eCRF. This training will also include training for the site (initiation) visit procedures and monitoring forms to be used during the study conduct. Trained monitors will perform monitoring activities according to the Monitoring Plan and will supervise the maintenance of the Investigator Site File (ISF). Monitoring of the trials will be done according to the criteria laid down in the Monitoring Plan of each trial, which have been developed by the project leaders in collaboration with the monitoring organization. All monitoring activities will be on-site. All sites will

be initiated in person to ensure that all national, international and study-related requirements are met. Each of the active sites (i.e., open and enrolled at least one patient in the previous year) will be visited at least once a year during the trial. On-site data monitoring will include the verification of data with source documents, considering critical aspects of the trial such as: informed consent, inclusion and exclusion criteria, and (serious)AEs. A monitoring report will be written at the end of each monitoring visit. The last monitoring visit will also be the close-out visit. In addition, continuous remote monitoring with telephone and web-based monitoring 'visits' will be performed to assure resolution of all queries.

For the CONTRAST trials, based on pre-assessed risk evaluation and following the NFU guidelines, an independent monitor will perform 2 to 3 monitoring visits per center per year (depending on the inclusion speed and the previousprotocol deviations). The first 3 included patients in each center will be verified concerning in- and exclusion criteria followed by 25% of all subjects. Informed consent and source data verification will also take place for 25% of all subjects. For all trials, the monitored data will compriseage, time of onset, time of randomization, NIHSS at baseline and performance of baseline and follow up imaging. A screen for occurrence of study-related SAE, and 3-month assessment of primary outcome will also take place, as well as a verification of the presence of a study log and documentation.

All other data will be monitored by the study coordinators.

Checks on completeness of the data are performed by (automated) data checks in Castor.

Automated checks of SAE entries will be run (daily) and will be reported back to the study coordinators (on a daily basis).

Once data are concluded to be complete and accurate, the eCRF data will be locked, meaning that the data will become read-only. The local principal investigator or delegated personnel are required to approve the eCRF data of their site through provisioning of an (electronic) signature before the data is used for final analysis.

Imaging and biobank workpackage leaders will issue at least three-monthly flash reports on the completeness and quality of the data to the scientific committee.

4. Data security, access, storage and back-up

The principal investigators are responsible for ensuring data security. Patient records are coded by a unique study number. The local investigators will keep the key (i.e., a list showing codes and names). Unique documents with identifying information will be stored separately from the processed study data in digital files, categorized by study number on the secure Erasmus MC data storage system, only accessible to the principal investigators, study coordinators, and Work Package 10, Data Management section (WP10(DM)). Personal identifying data will not be made available to other persons, including researchers who are not member of the research team. Any data storage and handling procedures will ensure patient data protection and confidentiality under the direct responsibility of the principal investigators of the specific trials. The principal investigators can delegate this task to a data manager. Results of research will be published without any reference to individual subjects.

Data will be managed and stored according to the FAIR principles (Findable, Accessible, Interoperable and Reusable) according to the Handbook for Adequate Natural Data Stewardship (HANDS) developed by the Federation of Dutch UMCs that also includes Erasmus MC (http://data4lifesciences.nl/hands/handbook-for-adequate-natural-data-stewardship/).

Clinical data

Copies of pertinent records in connection with the study, including CRFs and queries, as well as subject charts, laboratory data, will be stored locally, at the investigational site. They are accessible to the research staff of each specific trial. If it becomes necessary for the Sponsor or the appropriate regulatory authority to review any documentation relating to this study, the principal investigator will permit access to such reports. On request the investigator shall grant the Sponsor access to any required background data from the study documentation or clinical records. This is particularly important when errors in data transcription are suspected. In case of special problems and/or regulatory queries or requests for audit or inspections, it is also necessary to have access to the complete study records, provided that subject confidentiality is protected. Subject records or other source data will be kept for the maximum period of time mandated by the hospital, institution, or private practice, but for at least 15 years. Data from the eCRFs will be encoded and stored in Castor during the conduct of the trials. Backups are made twice daily by Castor and stored encrypted in different physical locations. After the database-lock (as mentioned under the Castor database will be exported and stored on a secure data system of the Erasmus MC University Medical Center (i.e., University networked fileserver) and for long-term durability we will export the data to csv-format, as well as to SPSS-format. The final database includes clincial data as gathered by the local investigators, laboratory data, imaging and outcome assessments by local investigators and core lab. The database will be made available to the principal investigators and study coordinators of the specific trials in anDREa, an online research platform developed by Radboud UMC, UMC Utrecht and Erasmus MC. Here the data will be combined and processed by the study coordinators and principal investigators in SPSS/R/STATA using annotated syntax.

Processed data

The principal investigators will ensure that eCRF data is accessible and verifiable by the investigational site in anDREa and prevent unauthorised access to the data. A copy of the processed data will be retrieved from the study database in anDREa by WP10(DM) under direct responsibility of the principal investigators. It will be stored in a folder that will only be accessible to the WP10(DM) to prevent loss of data and unauthorized access to the data. Processed study data will be stored and backed up daily on a secure data system of the Erasmus MC University Medical Center (i.e., University networked fileserver) to prevent loss of data. This copy will be used for issuing datasets for future research proposals. The processed data will be stored in csv-format, SPSS-format, STATA-format and R-format.

Access to the processed data will be granted based on a research proposal including information on the background, research questions and methods, variables that are needed, a plan for publication and authorships, planning and if necessary, a budget. This research proposal should be submitted through the CONTRAST website. This procedure is open for CONTRAST collaborators only, until a specified time point after closure of the trial. Approval of the proposal depends upon the topic and the quality of the proposal and will be reviewed by the CONTRAST publication committee (see CONTRAST Publication and Authorship Policy). Feedback or approval will be sent to the researcher within 4 weeks, but generally not earlier than 2 months after the trial main publication has been submitted, after which the researcher will receive the requested data from WP10(DM). Data will be issued via a workspace in anDREa. Data will be made available in SPSS, R and/or STATA-exports, as requested by the researcher, and analyses will only be performed in anDREa. Two WP10(DM)WP10(DM)-members will be added to the workspace as “owner”, thereby regulating

data-access and dataflow of the workspace, preventing any unauthorized access or data-transfers out of the workspace. Researchers will be added as “member”, thereby granting them access to the workspace and data to perform their analyses. To extract documents / results from the workspace, researchers can submit a data request to WP10(DM). Data requests are regulated and checked by WP10(DM). No study data will be allowed to leave the workspace. Only data requests containing results from the analyses (tables/figures), paper manuscripts, and analysis-scripts (R/STATA/SPSS) will be approved for download. Data requests will be checked at least once weekly (Wednesday). Further details about data issuing procedures are described in a separate SOP.

5. Data Sharing and Reuse

The database will be closed within one month after the last scheduled follow-up date of the last included patient. The data that will be collected, will be suitable for reuse. When the database is closed, all CONTRAST investigators will be given access to the data, after their research proposal has been reviewed and accepted by the CONTRAST Data Access and Writing committee (DAWC). The final database will consist of clinical data as described above, and imaging database. The imaging material will be made available for further assessment and analysis to the CONTRAST investigators, after their research proposal has been reviewed and accepted by the CONTRAST Publication Committee. An additional requirement is that the resulting data will be added to the imaging database, for further use and analysis by the CONTRAST investigators. External parties, i.e. academic investigators will also be allowed access to the data through anDREa. For data requests by private parties and request for raw imaging data and lab specimens, the appropriate agreements need to be in place (e.g.Data Transfer Agreement) to secure confidentiality, obligations and protection of the data. A separate SOP (No.3) will be in place for data-transfers with external parties.

Data sharing

Data (clinical data and imaging data) will be made available for replication of the main study results upon reasonable request to the after publication of the main paper. Data, including imaging material may also be shared with non-commercial parties for scientific purposes, including individual patient meta-analyses, and with commercial parties for FDA approval. Access to study data is covered in the informed consent procedure. Only de-identified datasets will be made available upon specific request by removal of the study ID. In the absence of this ID, researchers cannot identify the individual subjects. Biobank material and thrombi will not be shared with third parties. Raw imaging data can be shared, but requires a data transfer agreement between CONTRAST management and investigators.

Embargo period for data sharing

In order to allow the PIs and PhD students involved with the study first access and opportunities for substudies, they will have the first and immediate right to propose substudies. A short embargo period follows for CONTRAST collaborators, and a slightly longer embargo period will be in effect for othernational and internatiomnal academic investigators. For details, see SOP 1.

6. Data Preservation and Archiving

In compliance with ICH-GCP guidelines, local investigators will maintain all source documents supporting data collected from each subject, as well as all study documents as specified in ICH-GCP

Section 8, Essential Documents for the conduct of a Study, and all study documents as specified by the applicable regulatory requirement(s). Subject records or other source data must be kept for the maximum period mandated by the hospital, institution, or private practice, but for at least 15 years. Processed data will be stored as described under “4. Data security, access, storage and back-up”. After locking the database and ending the study, Castor will store the study data for 15 years at no additional costs. This is done for GCP traceability purposes. Even if no users are left in the Castor study, data will remain stored.

SOP1: Workflow from data-request through dataset-issuing to sharing your publication for CONTRAST substudies

Version: 10-04-2025 (v1.6)

Introduction

The aim of this document is to provide an overview of the different steps between a data request, actual issue of the dataset and sharing your manuscript and publication, for CONTRAST substudy proposals.

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1. The first part concerns the procedure for data issuing and sharing for CONTRAST studies.
2. The second part concerns the procedure for publication approval of a manuscript.
3. The third part provides required standard text samples, to be included in your manuscript or in your presentation.

Part 1: procedure for data application and issuing

This workflow is applicable to all CONTRAST research proposals by consortium members and collaborators. Consortium members are investigators who are affiliated with an institute that is part of the CONTRAST consortium and is represented in the board of governors. Collaborators are affiliated with the clinical department of a center that participates in the CONTRAST clinical trials of which data are requested. SOP3 addresses additional requirements for data issuing for parties outside CONTRAST. Practical aspects in this SOP are also applicable for parties outside CONTRAST.

Application

1. To request data for a research proposal / substudy proposal of one of the CONTRAST clinical trials, a **data request form** (Appendix 2) needs to be completed and submitted. The data request form can be found and submitted on the CONTRAST website under the heading “data requests”.
2. For every research question and project, a separate data request form needs to be submitted.
3. After completion, the data request form should be sent to to the data access and writing committee A data request form can be attached to that email.
4. Data request forms for external (CONTRAST non-members are the same as for CONTRAST members. However, if imaging data are needed by external parties, a data transfer agreement has to be drawn up and signed (contact the program managers after approval of your data request, at the CONTRAST website). Private parties that require access to the data should first contact one of the research leaders of CONTRAST, before submitting any requests.
5. The secretary of the DAWC will notify the Data access and writing committee (DAWC) about the new data request.

6. Within 14 days the DAWC will evaluate the request and give a verdict, including any comments or recommendations. PIs and PhD students leading the study will have access to the data immediately, but should nevertheless apply for substudy approval by the DAWC. CONTRAST collaborators may apply for data from finished study, but the DAWC will start the evaluation only 3 month after the main publication is published.
7. Applications for data of a particular study from investigators outside CONTRAST will be taken into consideration 12 months after publication of the main paper of that study. Applications from academic researchers will generally be granted, if:
    a. the DAWC considers the scientific rationale and design of sufficient quality,
    b. the application's research question does not conflict with projects submitted by CONTRAST consortium members
8. For data issuing to private parties a reasonable compensation will be requested and negotiated by representatives of the CONTRAST financial committee and the involved workpackage leaders. Applications should first be addressed to the CONTRAST leaders (see website.
9. The applicant will be notified by email about the decision. In case of approval. The clinical datamanager of WP 10(DM)will be notified by the secretary of the DAWC to initiate the dataset-issuing.
10. WP10(DM) will perform the data issuing under direct responsibility of the principal investigators. Data will be issued via the online research platform anDREa.
11. Appeals against a decision of the DAWC should be directed to the Scientific Committee, within 4 weeks.
12. Upon approval, **WP10(DM)** will **request** a substudy-specific **anDREa workspace** with 1 standard virtual machine. For the workspace-request an accountable needs to be specified, this will by default be (one of) the principal investigator(s) of the main study who is also collaborating on this substudy.
13. Members of the CONTRAST consortium will receive two-step pseudonymized data to be used in anDREa.
14. Note: Workspaces and datasets will be issued as soon as possible after the DAWC decision has been made, starting from 1 month after publication of the main article.
15. WP10(DM) will also **request myDRE-accounts** for the investigators in case they do not have a myDREaccount yet. By default, this will be for the applicant, first author and last author.
16. When the workspace has been created, WP10(DM) will install a standard set of programs (e.g., Rstudio, SPSS, Office, R-packages) in the virtual machine. This process is described in more detail in a separate manual, stored by WP10(DM)
17. Then, WP10(DM) will create the substudy-specific **dataset** based on the **requested variables** in the data request form (which can be found in the CONTRAST Plaza) and upload the dataset to the workspace.
18. The workspace is now complete, and the dataset is available. The applicant will be notified by WP10(DM) and receive a codebook for the dataset, and the **anDREa user manual** with instructions on the use of anDREa and responsibilities for CONTRAST investigators/collaborators (Appendix 1).
19. Finally, all requested/contributing investigators will be added to the workspace, thereby granting them access to the dataset within the virtual machine. By default, this will be the applicant (first author) and accountable (principal investigator). Investigators will be added

in the role of a “member”. Therefore, they can analyze the data in the virtual machine, but cannot extract or download the data from the virtual machine to a local storage. The supervisor of the applicant will be held responsible and accountable for budget overruns. The applicant will be held responsible for any misconduct, scientific or otherwise. A WP10(DM)-member (DD) and the CONTRAST data manager will be added to the workspace as “owner”, thereby regulating data-access and data-flow of the workspace, preventing any unauthorized access or data-transfers out of the workspace.

20. To extract documents / results from the workspace, investigators (“members”) can submit a data request to the “owner” of the workspace (i.e., WP10(DM)). Data requests are regulated and checked by WP10(DM). No study-dataset and/or pseudonymized data will be allowed to leave the workspace. Only data request containing results from the analyses (tables/figures), paper manuscripts, and analysis-scripts (R/STATA/SPSS) will be approved for download. Data download requests will be checked at least once weekly (Wednesday).

Archiving and closing of workspaces after publication of the substudy article:

21. When they plan to submit the manuscript to a journal, investigators send their manuscript to the DAWC via email for approval. An approval email will be sent within 2 weeks afte receipt of the manuscript. The manuscript will be checked marginally for criteria published in SOP 2.
22. The DAWC will notify the investigators and WP10(DM) about the approval for Submission. In this email, the investigators are requested to notify the DAWC once their manuscript is accepted for publication, with mention of journal and the publication date. From date of publication, investigators have 1 month to archive the workspace (scripts, results). It is the investigators' responsibility to archive all relevant scripts and documents of their substudy, in accordance with the applicable guidelines at their institution. The dataset will remain archived in the Erasmus MC on the local storage of the department of Neurology (as described in the CONTRAST Data Management Plan), in a WP10(DM) folder with limited access to WP10(DM) members.
23. The DAWC will notify WP10(DM) about the publication date. WP10(DM) will note the date of publication.
24. After 1 month, WP10(DM) will close and delete the workspace, and the dataset will be archived in the Erasmus MC as described above. Requests to extend the availability of the workspace can be directed to the DAWC.
25. Abstracts and preliminary results presented at scientific meetings will be shared by the investigators by reference to conference proceedings on the CONTRAST plaza, by the secretary of the DAWC.

Part 2: Publication policy CONTRAST

The overall aim of the publication policy is 1) to stimulate, harmonize and streamline high-quality scientific output from the CONTRAST project and 2) to fulfil the contractual commitments done to partners and funders.
This procedure is applicable to all studies, from single or multiple workpackages, that concern the CONTRAST consortium, or will be submitted on behalf of the CONTRAST collaborators. This includes studies using patient data collected within CONTRAST, but also experimental studies, reviews, protocols and opinion papers.

Specific aims:

- Maximize the quality of scientific output, where appropriate harmonization of methods
- Increase efficiency and avoid duplication of research within CONTRAST
- Define authorship criteria, fostering the involvement of different entities participating in CONTRAST in the scientific outputs
- Maintain transparency within the consortium
- Ensure identification of the CONTRAST consortium and its members as the publication source where appropriate
- Ensure acknowledgements of the funders of the CONTRAST consortium
- Facilitate analyses on data from multiple work packages
- Share descriptions of common procedures, criteria and analyses
- Promote early sharing of detailed results of analyses, for others to anticipate on in follow-up publications.

Guidelines for publications

- For papers concerning solely content from 1 workpackage: WP leaders from that work-package suffice as representation of the scientific committee.
- For papers on data from multiple workpackages: at least two collaborators, including the WP leaders from each of these workpackages should be invited to become author; they can propose other WP collaborators to replace them.
- Lead authors should be encouraged to invite collaborators from other workpackages as authors, to increase cohesion in the consortium and improve the quality of our output.
- Workpackage leaders should make clear and explicit agreements about the order of authors on the paper, particularly about first, second, last and shared first or last authorships.
- All authors should meet ICMJE criteria for authorship, please click this link and advise your co-authors about these criteria.
- Authors should be given the opportunity to adhere to the ICMJE criteria by involving them in an early stage (e.g. by sending abstract and tables and figures for review, or a first draft , with sufficient time to edit and respond, i.e,. 4 weeks at minimum.
- Lack of adherence to the ICMJE criteria means that authors should be removed from the author list and added as collaborators instead.
- All investigators that contribute to a particular study should be invited to become co-author on the paper that reports the results concerning the primary research question of that study. A list of all collaborators of the specific RCT should be available and up to date.
- On other papers using data from the aforementioned WP study, the collaborators of should be acknowledged as collaborators in such a way that they will be recognized and can be found

on Pubmed.gov. This is usually accomplished by providing the journal with an appendix, with all collaborators and their affiliations, to be published online and linked with Pubmed.

- The CONTRAST consortium should be acknowledged on all publications, using standard formulations on Plaza. Acknowledgments and disclosures are very important. See template for Acknowledgments and disclosures in part 3 of this document, which is the source document for the template on the Plaza.
- Standard texts on availability of data from CONTRAST studies for other parties can also be found in part 3 of this document.

*Collaborator lists should be made available by WP leaders for all studies in CONTRAST and MR CLEAN. This includes MR CLEAN, MR CLEAN Registry, MR CLEAN MED, MR CLEAN NOIV, LATE, the DIST and MR ASAP, including collaborators (executive committee, local PI's, outcome core, imaging core, statistician, labs, etc.) of the RCT, and made available through the contrast plaza.

Publication Checklist

- Study Plan was approved?
- Is "CONTRAST" recognizable in the title/subtitle/authorslist?
- Are the appropriate funding sources mentioned?
- Appropriate lists of authors and collaborators included reflecting contribution made to the manuscript?
- Data analytic methods agree with main CONTRAST publication on these data (handling of patient selection and missing data, multivariable approach, reporting of associations)
- Data analysis performed in anDREa?
- Sponsor informed if required?
- All authors meeting ICMJE criteria?

Procedure

1. Researchers send the final manuscript and the target journal to dawc.contrast@contrastconsortium.nl **before submitting to a journal.**
2. Publication committee checks content (marginal) and adherence to Guidelines for Publication
3. **Sponsor checks** on technical accuracy, error corrections or release of companies IP or confidential information
4. **Feedback** or approval is sent to researcher by DAWC secretary, **within 14 days** after receipt of the manuscript.
5. Only **after approval** the publication should be **submitted** to a journal
6. Publication will be **listed and accessible** for CONTRAST researchers on plaza

Part 3: Required texts to be included in scientific papers and presentations concerning data from the CONTRAST consortium

All publications need an acknowledgment of the CONTRAST consortium and its funders. We propose texts and these will often suffice. If you need to adapt the text, please consult the DAWC directly or highlight it when you send your publication to the DAWC prior to submission.

We additionally provide Dutch texts, to be used for national publications.

We distinguish between
1) General acknowledgments and disclosures to be used in all publications and presentations.
2) WP specific acknowledgements and disclosures
3) Statement concerning data-sharing
4) Acknowledgment of the CONTRAST WP leaders.

1. Acknowledgement & Disclosure on posters and presentations

Posters

At the bottom of the poster, insert all logo's of funders. At the top, include the CONTRAST logo. Alternatively, include the acknowledgment text.
Here you can find a poster template: 3. Poster format

Slides

Insert a slide with all logo's of funders as second or last. Use the CONTRAST format (2. Presentation format), or at least show the contrast logo on the first and last slide in the right upper corner.
A slide with the acknowledgment text is also allowed. We advise you to reserve the last slide for your conclusions & implications, and insert the acknowledgment slide as second.

Logos in presentations:

Include at least the Acknowledgement slide to your presentations with all logos: Logos.pptx

Manuscripts

For manuscripts, use this acknowledgement and disclosure text:

This research is funded by the Dutch Heart Foundation and The Brain Foundation Netherlands and is conducted in collaboration with and supported by the Dutch CardioVascular Alliance, 01-002-2022-0126 CONTRAST 2.0. In addition, this work was funded in part through unrestricted funding by Stryker, Medtronic and Penumbra. The funding sources were not involved in study design, monitoring, data collection, statistical analyses, interpretation of results, or manuscript writing.
Studies that make use of core-lab assessed CTP data should add the following sentence:
" Leading the Change/Healthcare Evaluation Netherlands provided funding for CTP analysis. "

In text (methods) statement about funding:

This study received unrestricted private/public funding through the CONTRAST consortium.

Dutch publications:

In Dutch publications a brief funding statement should be made in the text, and refer to a footnote.
Het onderzoek ontving publieke en private financiering van onder andere Hartstichting en Hersenstichting, via het CONTRAST Consortium.[1]

[1] Dit onderzoek wordt gefinancierd door de Hartstichting en Hersenstichting en wordt uitgevoerd in samenwerking met en ondersteund door de Dutch CardioVascular Alliance, 01-002-2022-0126 CONTRAST 2.0. Daarnaast werd dit werk gedeeltelijk gefinancierd door Stryker, Medtronic en Penumbra. De financierders waren niet betrokken bij het ontwerpen van het onderzoek, het monitoren, de gegevensverzameling, de statistische analyses, de interpretatie van de resultaten of het schrijven van het manuscript.

2. Additional workpackage-specific disclosure or acknowledgement on posters and presentations and in manuscripts.

Workpackages that received separate funding should acknowledge this and add the information to the standard text.

WP3A: MeVO

Check agreement met Basel

WP3B: Cases Benefit

"This report is independent research funded by Belgian Health Care Knowledge Centre and the Dutch Organisation for knowledge and innovation in health, healthcare and well-being (ZonMw): BeNeFIT2, Carotid artery stenting during endovascular treatment of acute ischemic stroke: A randomized multicenter clinical trial in patients with acute ischemic stroke and carotid artery stenosis undergoing endovascular treatment (CASES), 80-87700-98-21561]. The views expressed in this publication are those of the author(s) and not necessarily those of the funders."

WP3C: IRIS

AMC and Erasmus MC received additional funding on behalf of CONTRAST2 for the execution of this study from Stryker European Operations BV and from Boehringer Ingelheim.

The phrase, "on behalf of the IRIS Collaboration Investigators", will be included at the end of the author list on all publications. An appendix will be added to the manuscripts with the names of the IRIS Collaboration Investigators, as supplied by the collaboration Executive Committee after acceptance of a study proposal (see Appendix 1 Complete_with_DocuSign_202309278_reviewed_pr.pdf).

WP4: DIST

Radboud UMC and Erasmus MC received additional unrestricted funding on behalf of CONTRAST2 from Penumbra Inc and from ZonMw/Zorginstituut veelbelovende zorg.

3. Texts about data sharing

Data of this study will be made available upon reasonable request to the corresponding author, usually 12 months after publication of the main results.

4. Acknowledgement of the CONTRAST WP-leaders and collaborators

The starting point is that every publication that makes use of CONTRAST data or CONTRAST infrastructure, should acknowledge CONTRAST. The CONTRAST members do not need to be mentioned in the paper or in an appendix, but the paper should refer to the CONTRAST website (www.contrast-consortium.nl). Also consider adding "CONTRAST Investigators" to the authors list.

However, the main publication of a project, trial or study should list all collaborators who directly contributed to the study and were not included as an author. This collaborator list should be attached to the publication as a supplementary appendix. These collaborators should be made known in PubMed. This includes local PIs of the centers, local coordinators, but also research nurses involved in follow-up, laboratory coordinators, and not to forget, core lab members who assessed the baseline and follow up imaging, and the blinded outcome assessors. Names can be found in the list on the CONTRAST plaza.

SOP2: Biobank materials & Imaging data request procedure

Version: March 2020

Proposals using CONTRAST materials

The use of materials (blood, thrombus, DNA, tissues etc.) and medical images that are collected within the CONTRAST clinical trials and preclinical studies is restricted to projects that fall within the aims and targets of the CONTRAST studies. We encourage suggestions for research utilizing these materials, if the embedding within the CONTRAST consortium is protected.

Proposals for extra materials

In addition to using materials and images that are collected within the CONTRAST studies, projects may also be proposed that include the collection of additional materials or images from the patients participating in the studies. For these studies it may be interesting to use the CONTRAST logistics procedures. Such requests may not be covered by the CONTRAST METC approval, may need extra time from CONTRAST PhD or technicians, and may require extra budget, which needs to be covered by the applicant.

Ownership of data

Data derived from analyses of CONTRAST materials or images becomes available for all members of the CONTRAST consortium. Also, extra materials and images that are collected, using the CONTRAST infrastructure, will remain available to the CONTRAST studies. The group that performed the measurements will be involved in any future analysis that uses the data. All measurements involving any materials, data or images from the patients in the trials will in principle only be processed upon completion of the clinical trial and in agreement with the steering committee of the trial. For use of animal-derived materials or images, the planning of the measurements is independent of the completion of the clinical trials.

All materials, images or data will be made available **only** for use under the terms specified in the application.

When measurements or the analysis of biomarkers from materials or images involves industrial partners, the negotiations always must involve the CONTRAST financial committee.

Procedure

1. Exploratory discussions need to take place prior to application; for projects concerning the blood and plasma biobank, or imaging databank approach the appropriate work-package leaders, and/or the leaders of a clinical work package, we refer to the work packages info, and ongoing studies and closed studies information on the CONTRAST website.
2. Next, an application can be submitted through the CONTRAST website, at least 2 months before the start of the study using the available form. The full application will be evaluated with 4 weeks by a small access committee based on scope and technical feasibility. All requests will be handled by the DAWC in case biomaterials will be needed the appropriate WP leaders will be consulted. .

SOP3: Policy for Access to and Sharing of Data with external (non-CONTRAST) parties
Version: 14-04-2025

1. Introduction

Background
Endovascular thrombectomy (EVT) with the use of a retrievable stent improves outcome in selected patients with acute ischemic stroke (AIS) and a proximal intracranial artery occlusion. Still, major challenges in the treatment of acute stroke remain. First, about 15% of all strokes are intracerebral hemorrhages (ICH), for which treatment options are very limited. Second, only few patients with AIS eligible for EVT. And third, even after successful intraarterial treatment, in active treatment arms of recent EVT trials one to two thirds of patients still had a poor outcome.

Incomplete microvascular reperfusion despite recanalization of the occluded artery is a major contributor to poor outcome after AIS. Possible mechanisms are distal microembolization and distal microthrombotic occlusion through activation of platelets and pro-coagulatory pathways and possibly also through microvascular occlusion through cellular swelling by activation of the innate and adaptive arms of the immune system.

Mission
All data gathered by the CONTRAST consortium serve our mission, which is to improve the effectiveness and safety of acute treatment for stroke and to increase the number of eligible patients by expanding indications for treatment.

Aims
Our major aim is to improve microvascular reperfusion, and thereby improving outcome for our patients. A second, just as important aim is to increase the number of patients who potentially benefit from treatment, by extending the indications for thrombectomy, bringing new treatments into the ambulance, and by testing new treatments for intracerebral hemorrhage.

Consortium
The CONTRAST consortium is a unique nationwide collaboration of clinical and translational scientists from all academic and large clinical centers in the Netherlands who want to act together to improve the treatment of acute stroke.

Randomized clinical trials
We performed five large acute stroke trials to test novel treatment strategies, aimed at preservation of ischemic tissue and improving outcome by including:

- pre-hospital augmentation of collateral blood flow and blood pressure reduction: MR ASAP
- antithrombotics to prevent microvascular occlusion after EVT: MR CLEAN MED
- immediate EVT without preceding thrombolysis: MR CLEAN NO IV
- EVT in the 6 to 24 hour-time window: MR CLEAN LATE
- microsurgical hematoma evacuation in patients with ICH: DUTCH ICH pilot

Translational research
Apart from providing direct answers to pressing clinical questions, the trials provide a wealth of prognostic and etiologic information. The trials have similar designs and data structure. Biomarker information from serial blood samples, neuro-imaging and thrombus material have been gathered and stored centrally.

- We aimed to identify patients who will benefit from these interventions through advanced imaging;
- We elucidated mechanisms of incomplete microvascular reperfusion with the aim to develop novel stroke treatments with data from our clinical biobank, which stores blood, plasma and extracted thrombi;
- We applied discrete event modelling (DES) with data from the trials, to optimize stroke care.

Experimental research
The CONTRAST collaboration hosts porcine and rodent studies to investigate the effect of vascular and medical interventions on vessel wall and infarction. With a focus on incomplete microvascular reperfusion.

2. Data access policy

This access policy presents three areas of guidance:
- ethical principles;
- governance procedures; and
- practical procedures for access.

Together with existing legal frameworks, these three areas provide the ethical and legal framework and practical procedures to guide access to and use of Data, Images and Samples. This policy is a binding document for Requesters, who are seeking access to Data, Images and Samples of CONTRAST.

3. Definition of Terms

Data
Data = descriptive parameters from clinical observations, biosamples and neuroimages, collected in a database, which have been collected by the consortium, as specified in the Project plan and (clinical) Protocols.

Materials
Neuroimages (typically Dicom files) – biosamples (tissue, thrombi and blood) from translational studies, animal experiments and clinical studies. Note that biosamples are of limited availability.

Database
The database containing all the Data of which the Coordinating Center (= Erasmus MC, Rotterdam, the Netherlands) acts as custodian. Any database rights shall be owned by Coordinating Center.

Consortium

The involved research groups at the **Public Parties executing the project** as defined by the CONTRAST Consortium agreement entered between the Parties. The consortium consists of several workpackages (WPs), each led and represented by two Work Package (WP) leaders.

Site Party
Data Provider as described in "DATA TRANSFER AGREEMENT FOR CONTRAST"

Requester
A qualified person requesting Data or Material. Needs to be registered as specified in Step-1 and -2 of section 7.

Bona Fide Researcher
A researcher:
1. with an intention to generate new knowledge and understanding by using rigorous scientific methods;
2. with an intention to publish the research finding in open access journals without restrictions and with minimal delay, for wider scientific and eventual public benefit; and
3. who shall comply with legal and ethical requirements or widely recognized good research practice; and
4. who has a bona fide research project: in practical terms, a research project or proposal that has been approved by a recognized funder providing unrestricted funding, or a researcher that belongs to a research organization that has the capability to lead or participate in high quality, ethical research should normally be considered bona fide.

Private Party

A party:

1. with an intention to generate new knowledge and understanding by using rigorous scientific methods;
2. which shall comply with legal and ethical requirements or widely recognized good research practice; and
3. wants to use the data to for internal use, with a commercial purpose.

Data Transfer Agreement (DTA)
A contract between the Requester and CONTRAST specifying conditions under which Data are transferred to Requester.

Material Transfer Agreement (MTA)
A contract between the Requester and CONTRAST specifying conditions under which Materials are transferred to Requester. A distinction should be made between biomaterials and images.

Project Results
Can be published in the form research papers, patents, new therapies and other types of commonly acknowledged medical research achievements. This also includes a report on the use of Data.

Personal Data

'Personal data' means any information relating to an identified or identifiable natural person ('data subject'); an identifiable natural person can be identified, directly or indirectly, in particular by reference to an identifier such as a name, an identification number, location data, an online identifier or to one or more factors specific to the physical, physiological, genetic, mental, economic, cultural or social identity of that natural person (GDPR Article 4.1).

Pseudonymization and de-identification

'Pseudonymization' means the processing of personal data in such a manner that the personal data can no longer be attributed to a specific data subject without the use of additional information, provided that such additional information is kept separately and is subject to technical and organizational measures to ensure that the personal data are not attributed to an identified or identifiable natural person (GDPR Article 4.5 File. "De-identification" means that all records will be given a new unique number, that cannot be linked to the original database.

Data Access and Writing Committee

An independent committee with the mandate to review all applications for access to Data or Material derived from the conduct of CONTRAST studies. The Data Access and Writing Committee makes recommendations for approval and rejection of access requests to the CONTRAST Scientific committee. The composition of the Committee is specified in Section 9.

Financial committee

The financial committee will be called upon by the DAWC, after approval by the scientific committee, to negotiate a reasonable compensation for the issue of data to private parties.

4. Legal Premise

All proceedings related to access and sharing must be compliant with national and European legislation such as the Directive 95/46/EC and, as of 28 May 2018, the EU General Data Protection Regulation and Code of Conduct (GDPR Article 40). The processing of Data must be compliant with the provisions of the consent procedure and/or decision of an ethical review board, and/or a data protection authority/officer if applicable. If none of the above is applicable, it must be compliant with national legislation.

5. Governing Principles

CONTRAST will facilitate and support access to Data according to the following principles:

a) Scientific integrity:
   Requesters and providers are expected to act in an honest and transparent manner and uphold the highest standards of quality in scientific research.
b) Research questions:
   Data requests may be rejected if the research question is pre-specified in the CONTRAST

workplan, or if data will be published that may compromise the publication of the main papers on the primary research questions of CONTRAST. The use of data that are collected within the CONTRAST clinical trials and preclinical studies should agree with the general mission of CONTRAST.

c) Responsibility and accountability:
It is both the requesters' and providers' responsibility to ensure that they have read and understood the relevant CONTRAST policies and procedures (published as study protocols and procedures on www.contrast-consortium.nl) and that they act in accordance with these regulations.

d) Respect for responsible governance regarding data and research:
Requesters and providers are expected to take the necessary precautions and safeguards to avoid Data breaches. This entails protecting their Data and putting in place state-of-the-art safety measures for data security.

e) Accessibility to research results:
Requesters submit their research results to open access journal in a timely manner, I.e. within 12 months from data-issue.

f) Attribution of CONTRAST consortium:
The intellectual investment of investigators involved in the creation of CONTRAST is substantial, and should be acknowledged as CONTRAST collaborative. This should be specified in a DTA or MTA signed by Requester and Coordinating Center (=Erasmus MC, Rotterdam, The Netherlands) after approval of the Data Access and Writing Committee.

g) Respect for intellectual property:
Sharing of Data needs to be performed in a way that protects intellectual property rights of the parties involved. It also needs to address the requirements of institutions and third-party funders. In a case an external party wishes to develop IP using the data, TTO of Erasmus MC should be involved.

h) Equity and inclusivity of users:
Bona fide researchers who meet the relevant criteria should be granted access based on fair and non-discriminatory terms.

i) Reciprocity:
Stewardship also implies giving something back. Feedback regarding general results should be channeled towards institutions and patients.

j) Additional data collection:
In addition to using materials and images that are collected within the CONTRAST studies, projects may also be proposed that include the collection of additional materials or images from the patients participating in the studies. This can only be done in close collaboration with the responsible WP leaders, according to the CONTRAST logistic procedures. Such requests may not be covered by the CONTRAST METC approval, may need extra time from CONTRAST PhD or technicians, and may require extra budget, which needs to be covered by the applicant. Such additional data should be attached to the CONTRAST database, in order to be accessible and usable by CONTRAST researchers after a reasonable period of time, to be discussed and included in the agreement, see next point.

k) Ownership of data:

l) Data derived from analyses of CONTRAST material (bio-, imaging-, or clinical material) becomes available for all members of the CONTRAST consortium after a reasonable time

period. Also, extra materials and images that are collected, using the CONTRAST infrastructure, will remain available to the CONTRAST consortium and should be included in the CONTRAST database. The consortium will be involved in any future analysis that uses the data. All measurements involving any materials, data or images from the patients in the trials will in principle only be processed upon completion of the clinical trial and in agreement with the steering committee of the trial. For use of animal-derived materials or images, the planning of the measurements is independent of the completion of the clinical trials. Confidentiality:
CONTRAST shall treat all the access requests confidentially and will not use them for any purpose other than assessing the availability of the data and access provisions.

6. Procedures Governing Access to and Use of Data

~~a)~~ The data shall remain under the stewardship of the Site Parties as the original source, unless otherwise specified in a separate agreement

b) Requests for access to Data or Material issued by Requesters will be required to follow the request procedure for Data (see section 7 & SOP1) and will be taken into consideration 18 months after publication of the main paper of that study. This requirement does not pertain to the issue of data to private parties, for internal use.

c) The Data Access and Writing Committee advices the Scientific Committee (SC) of CONTRAST. The SC approves or rejects data transfer to a Requester based on this advice.

d) Data will be made available via the online research platform anDREa. Further details and procedures are described in SOP1 and Appendix 1.

e) If Data needs to be issued outside of anDREa, the Requester needs to ascertain that the requested Data provided are stored in a secure and operational facility accompanied by an appropriate access policy, including a description of who can access the facility and the time-period the requested Data are needed.

f) For all data issued to external parties, de-identification is mandatory.

g) Transfer of requested Data for research purposes to Requester outside the CONTRAST consortium should always be governed by a DTA or MTA. By signing the DTA or MTA, the consortium scientific committee mandates the Data Access and Writing Committee to coordinate and arrange the transfer of Data from the central Open Clinica and/or CONTRAST database to the Requester.

h) Materials: transfer of materials will be coordinated and arranged by the WP leaders who are responsible for the materials.

i) Data can only be used for academic or industrial research purposes, depending on the legislation of the Member State or international organization: the usage and limitations need to be specified in the DTA with Requester.

j) Access to data or materials should be cost neutral for provider. It is possible that CONTRAST requires the Requester to partially or fully cover the costs incurred in providing Data or materials. Cost aspects must be specified in the DTA/MTA.

k)

7. Request Procedure for Access to Data

The basic framework governing the request procedure for accessing Data via the CONTRAST portal comprises the following steps.

Step 0: Exploratory discussion prior to application; for all projects, particularly those concerning the blood and plasma biobank with WP5 (Moniek de Maat and Hugo ten Cate), for the thrombus biobank with van Beusekom and for materials from the animal studies with WP1 (Rick Dijkhuizen and Heleen van Beusekom). For the use of imaging data or the imaging infrastructure, discussions must take place with WP7 (Aad van der Lugt and Charles Majoie). Use of clinical and follow-up data should be discussed with WP10(DM) (Hester Lingsma and Diederik Dippel). When a request is made by a private party, DAWC will notify the financial committee which, is mandated by the Scientific Committee to negotiate a reasonable compensation from that party.
Internal and external requesters are advised to first contact one of the PIs of a particular study/trial before applying. This guarantees a smooth application.
Step 1: Registration of Requester
CONTRAST verifies the identity of each Requester and his/her institutional affiliation (employee status).

Step 2: Request for Data

A Requester files a request for access to data by mail to dawc.contrast@contrast-consortium.nl. The digital request form must be filled in (see Appendix 2 for questions on the digital request form). The Data Access and Writing Committee may request refinement of the request. In compliance with the governing ethical principles (section 5), the request is treated as confidential by the Data Access and Writing Committee. In case of identical research questions by two or more Requesters the Data Access and Writing Committee will bring Requesters together and encourages Requesters to jointly resubmit the research question.

Step 3: Access control & Data delivery
After receiving feedback from the Data Access and Writing Committee, the Requester follows up directly with the Data Access and Writing Committee in order to provide any additional information needed to assess whether access can be granted. As part of this process, the Data Access and Writing Committee must comply with the regulatory and ethical conditions (e.g., data protection regulations, assessment of compliance of informed consent with the approved/proposed project, assess whether the amount of extraditable data required is scientifically justified), assess the application on content and feasibility, prevent duplication and transfer liability to the Requester by using DTAs as deemed appropriate. The Data Access and Writing Committee advises the SC, which decides whether Data are released for the project requested. Review by the Data Access and Writing Committee will take at most four (4) weeks. At approval the DTA will immediately be provided. This DTA needs to be executed before Data are released to the requester.
WP10(DM) will coordinate the Data delivery under the direct responsibility of The Data Access and Writing Committee and Principal Investigators of the applicable trials.

Step 4: Request completion notification
For each request obtained via dawc.contrast@contrast-consortium.nl, where Step 3 has been completed, the Data Access and Writing Committee needs to be informed whether the request has been completed successfully. The Requester will have exclusive access to the requested dataset to perform the analyses solely for the research purposes as described in the data request form. After a period of six (6) weeks, the Requester reports the status of the analyses. If needed the analysis period can be extended. After request completion the Data Access and Writing Committee will publish the approved research question(s) including the contact information of the Requester on the CONTRAST website.

Step 5.: Data issuing
After approval of the Data Access and Writing Committee, WP10(DM) will issue the Data under direct responsibility of the DAWC and Principal Investigators via anDREa. Further details and procedures about data issuing are described in SOP1 and Appendix 1.

8. Publication and Authorship

General principles:

A. For each publication resulting from a Data delivery of CONTRAST:
    a. the Data Access and Writing Committee will form a writing group on behalf of CONTRAST; this writing group will be involved in the writing process and will be mentioned in the authors list if both parties have agreed and added this to the DTA.
    b. If the Provider and Requester have agreed that no authors of CONTRAST will contribute to writing or analysis, acknowledgments as described in SOP1 will suffice.
    c. the acknowledgements should refer to a list of collaborators. This list will be provided by the Data Access and Writing Committee.
B. On papers using data from the RCTs, the collaborators of the specific RCT should be acknowledged as collaborators. A collaborator lists will be constructed for MR CLEAN Med, No IV, Late, the DIST and MR ASAP, including collaborators (executive committee, local PI's, outcome core, imaging core, statistician, labs, etc.) of the RCT.
C. The CONTRAST consortium should be acknowledged on all publications, using standard formulations on CONTRAST Plaza, and will be provided to Requester by Data Access and Writing committee.

    Within six (6) months after accessing the dataset the Requester has the possibility to prepare material for public dissemination (e.g. publications, posters, presentations) based on a data delivery from CONTRAST. After six (6) months the 'exclusivity' of the data will be over. All material for public dissemination will be sent to the Coordinating Center and be globally reviewed by the Data Access and Writing Committee. Data analyses for internal (commercial) use will not be reviewed.
D. Publications based on data delivered from CONTRAST will be in accordance with international recognized scientific and ethical standards concerning publications and authorship, including the *Uniform Requirements for Manuscripts Submitted to Biomedical Journals*, established by the International Committee of Medical Journal Editors. Copyrights concerning Publications of the CATACITY remain with the authors of the Publication, regardless of any other provisions regarding intellectual property rights (see www.icmje.org).

E. All authors on a publication should meet ICMJE criteria for authorship. Those who do not meet these criteria, should be moved to the list of collaborators.
F. Authors should be given the opportunity to contribute by involving them in an early stage by: inviting them with an outline of the project and sending abstract and tables and figures for review) well in advance before the final draft.

9. The Data Access and Writing Committee

See section: “Committees and members”.

Committees and members

Members of the CONTRAST Scientific Committee, the Data Access and Writing committee, the CONTRAST scientific committee can be found on the CONTRAST website.

DAWC Contact information:
Contact Naziha el Ghannouti (dawc.contrast@contrast-consortium.nl) or rick.vannuland@lygature.org if questions remain.

Appendix 1: User manual anDREa: instructions for researchers of a CONTRAST substudy

Version: 20-04-2025 (v1.8)

First note

This is a working document. Information in this document is subject to change. Please verify you are using the latest version before proceeding with the steps mentioned below. If you encounter issues or have any suggestions, please let us know.

Introduction

Accessible network Digital Research Environment alliance (anDREa) is a platform in which different workspaces with virtual machines (VMs) can be arranged. All CONTRAST (sub)studies will be performed in an anDREa workspace, this includes giving out the data and performing the analyses. In short, a workspace can be seen as a digital office with 1 or more (as desired) virtual machines, which are essentially regular computers "virtualized". These can then be used to combine, modify, or analyze your data in a secure online environment from wherever you are. More info on workspaces can be found here.

Substudy approval

After the approval of a DAWC-request for a CONTRAST (sub)study, a workspace with virtual machine will be set up. Workspaces are hosted by the Erasmus MC University Medical Center. Data will be made available within the VM. An unlimited number of persons can be given access to the workspace, but only 2 persons can work in the same VM simultaneously. Hereby, access to the workspace is specifically only allowed for researchers specified in the approved DAWC-request.

Microsoft Remote Desktop

If you are accessing your virtual machine via macOS, the application "Microsoft Remote Desktop" is required. The newest version can be found in the apple app-store.

Activate new account

You will receive an email with the instructions to create a mydre-account when your workspace is ready. Detailed instructions on creating and activating your account can be found here. Briefly, go to mydre.org and click to log in. Click on "use a different account" and fill in your @mydre.org account. Click next and click on "forgot my password". Check if your alternate e-mail address is valid. You will receive a code via email, fill in the code. Create a new password. Note: @mydre.org accounts are personal accounts and for personal use only. Users shall keep all user IDs, passwords and access to the mydre-portal and workspaces within its own possession and control and shall keep those confidential and secure from unauthorized access or use. If you become aware of any unauthorized use of a @mydre.org account, please notify WP10(DM) as quickly as possible.

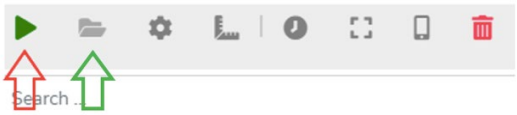
Authenticator

Now you have activated your account you will need to set up Multi-Factor Authentication (MFA). Log

in at mydre.org. A pop-up will appear asking for your preferred MFA-method. You can choose for MFA via the mobile Microsoft Authenticator app, or via a code sent to your phone via SMS.

Open and close VM

For access to the VM, log in to your workspace at mydre.org with your mydre-account. In this workspace, the prepared VM can be started by double clicking or single clicking on VM and clicking on start machine (red arrow). To open the VM, click on the folder-icon to the right (green arrow)



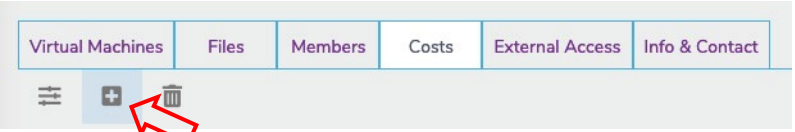
You will be asked to sign in with your credentials. Be sure to sign in with your @mydre.org account and not your institutions account (e.g., @erasmusmc.nl or @amsterdamumc.nl). A .rdp file will downloaded. Open this file (with Microsoft Remote Desktop on macOS) to access the VM. The following warning might show: “The certificate couldn’t be verified back to a root certificate. Your connection may not be sure. Do you want to continue?”. You can accept this warning (or mark as safe). Your connection is secure.

By default, all VMs will automatically shut down at 19:00 (+1 UTC), to prevent unnecessary costs from running VMs which have been forgotten to be deallocated. Be sure to save any changes in advance. The auto-shutdown can be adjusted or turned off manually (click here for instructions). Be aware that costs can accumulate rapidly if you forget to deallocate a VM and the auto-shutdown is turned off manually.
Currently, there is no warning-message in the VM prior to the auto-shutdown. The best solution at this moment is to set up an email reminder, which you will receive 30 minutes before auto-shutdown. We will enable this email-notification by default for the requesting researcher of the workspace. Via the email you will be able to postpone the auto-shutdown for 1 or 2 hours, or skip it entirely for this instance. For additional researchers, please request the email-notification via j.daems@erasmusmc.nl.
Please note: currently there is a bug with the time-zone settings inside the VM and time will be incorrectly 1 or 2 hours behind.

Costs

Disclaimer: No rights can be derived from cost estimations provided below. Costs are subject to change over time. For a more personalized and accurate estimate see the *cost-estimator* at mydre.org.
Per month, approximately 100 hours on a 2 cores 4GB RAM virtual machine with an E10 OS disk (1 per workspace) and 100gb storage will be subsidized by the Erasmus MC University Medical Center and is free of charge. Additional hours or a machine upgrade are at extra cost. These **extra costs** will be for the account of the **WP-leader** of the concerning substudy (**the accountable**). On a standard virtual machine, 10 hours of usage will cost approx. €0.54. Storage in the file-share of a workspace is charged per Gb per month: currently €0,064 per Gb per month. Therefore, the more data you store in the file-share, the more costs your workspace incurs (100gb storage = €6.40/month). It is advised to transfer/remove any files you don’t need any more to your local storage. Virtual Machines can be upgraded (more cores, more RAM) at increasing costs, but for regular workflow the standard 2 cores 4GB RAM (standard_B2S) should suffice. Upgrading VMs or OS disks can become very expensive rapidly and is therefore not advised. There is no automated halt if the free-of-charge subsidy is

reached, but users can set up reminders of the cost. By clicking the + symbol under the costs-tab, notifications can be turned on. The budget will be set to €20,- incl. BTW (this approximates the EMC-subsidy) by default by us, with reminders at 60% - 100%.

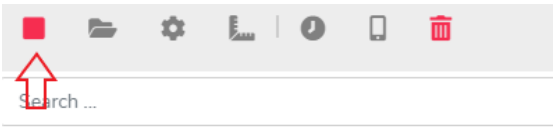


Costs can be estimated based on your preferred settings with this cost-estimator.

Analyses

R/Rstudio and SPSS will be available in the workspace. A standard set of packages will be available on the workspace (currently 467 packages), if additional packages are needed, please let us know. A VM can be programmed to shut down at a certain timepoint, which can be adjusted. This timepoint is standardly programmed to be 19:00 (+1 UCT). You can manually cancel the auto-shutdown, which might be needed for advanced analyses requiring the VM to run for an extended period of time. But be careful, the VM will continue to run until you deallocate it manually. You can run out of subsidized hours and costs will continue to increase! It is therefore advised to always enable the auto-shutdown and re-enable it after completing your advanced analyses. The only ways to shut down the VM are:

1. Auto-shutdown (default 19:00, +1 UCT)
2. Pressing deallocate in myDRE portal → (red square)



Saving data and files in a VM

It is not advised to save important data, files or analysis scripts on the C: drive of a VM for storage, as this drive is not snapshotted (backed up) and data might get lost. Therefore, save important data, files or analysis scripts on the Z: drive, also known as the shared disk drive (SDD) / file-share. The SDD will have a 30-day cycle back-up. Remember that storage in the file-share of a workspace is charged per Gb per month. Storage used on the C: drive of a VM is not charged per Gb per month, instead it is charged at a fixed price per OS disk per month (the standard E10 disk costs approx. €10.00 per month). For some advanced analyses it might be desirable to run your dataset from the C: drive, which runs faster than the Z: drive. It can therefore be useful to make a local copy of the dataset on the C: drive.

Folder-structure

The following standard folder-structure is used on the Z: drive.

- Datasets
  - Issued_datasets > folder with the issued core-dataset
  - Adjusted_datasets > here you can store your own adjusted datasets
- R-scripts
  - R-scripts_dataset > here you can store your own r-scripts
- Analyses_output > here you can store your analyses output
- WP10(DM)_files > this folder will be used by WP10(DM) for workspace configuration

Uploading/Downloading files

Analyses must be performed within the VM. It is not allowed to export the dataset or any identifying or indirectly identifying personal data from the VM. Under the GDPR/AVG pseudonymized data are considered as identifiable data and can't be exported out of the VM. Export requests such as output of statistical programs, documents or images must be approved by the owner of the workspace (study coordinator from the Erasmus MC and/or local institution). These requests will be reviewed every Wednesday. At this moment, no automated approval for figures/images can be applied. Therefore, if you need a figure/table immediately or on short notice, it is advised to take a screenshot.
Uploading data to the VM is possible without approval. Instructions on uploading files/data can be found here. Briefly, open the workspace and go to the "Files" tab. Click on the blue upload-cloud icon in the top left corner. Click on "Select and upload" and select your files. When the upload is finished, click on "Clear finished uploads". You will receive a confirmation mail when your files have been uploaded. Click on "Close", a pop-up will appear asking "Would you like to import the inbox?", click on "OK". The uploaded files/data will now be pushed to an inbox-folder in the Z: drive / file-share. After completion you can transfer the files from the inbox-folder to a folder of your preference.

Organization
Clinical data management is a core-task of CONTRAST Work Package 10. For CONTRAST (sub)studies anDREa is managed by the WP10(DM) leaders and members in collaboration with anDREa.
WP10(DM) members: Hester Lingsma (Erasmus MC) and Diederik Dippel (Erasmus MC)

anDREa: Elo Bosma (Erasmus MC), Sabine Reinink (Erasmus MC)

Final remark
Issued data is exclusively intended for researchers under the CONTRAST consortium agreement. For external / third party data-issuing a Data Transfer Agreement needs to be arranged with the CONTRAST consortium.

For further questions and practical instructions, we would like to refer you to the anDREa support site: https://support.mydre.org/portal/en/home. Of course, you can also always contact us if you have further questions or encounter any issues.

Appendix 2. DATA REQUEST FORM

Version: 20-04-2025

Form to request data for a CONTRAST research proposal, for use by consortium members and collaborators*, as well as non-CONTRAST members. An online version of this form is available on the CONTRAST Website (link)

For a data request, please complete this form and send to the Data access and writing committee (DAWC): dawc.contrast@contrast-consortium.nl

For more information see CONTRAST publication policy

Title of research proposal	
Applicant	*Name:* *Email address:* *Phone number:* *Affiliation:* *City and Country* *Contrast member: Yes/No*
First author:	*Name:* *Email address:* *Phone number:* *Affiliation:*
Co-authors	*Names, email addresses, affiliation:*
Last Author	*Name:* *Email address:* *Phone number:* *Affiliation:* Contrast member: Yes/No
Accountable†	*Name:* *Email address:* *Phone number:* *Affiliation:*

* Consortium members and collaborators are investigators who are affiliated with an institute that is part of the CONTRAST consortium and is represented in the board of governors.

† Costs of an anDREa workspace are for the accountable/principal investigator of the research proposal. This concerns the costs exciding the Erasmus MC subsidy. The accountable needs to be a WP-leader (preferably of the main study).

You are required to use anDREaeven when you are a non-CONTRAST member.

$ anDREa does not support analysis of imaging data, that will have to be done outside the andDREa environment.

Involved-WP Leaders	*Names, email addresses:*
Abstract	*Background (<200w)* *Aim (<100w)* *Approach (<200w)*
Planning (6 months after obtaining the data an update to the DAWC is required)	*Timeline for analysis and writing* *Milestones to be reached in 6 months*
What data is needed form the study (please specify in boxes below)	*Clinical data:* *Imaging data:* *Experimental data:* *Biomaterials:*
Clinical data (please consult of CRF-on-paper on trial sites through www.contrast-consortium.nl)	*From which trials:* *Which variables:* *Any specific patient selection:*
Imaging Data	*Meta data (already scored parameters):* *Raw Images:*
Experimental data	*Open text:*
Biomaterials	*Meta data (already scored parameters):* *Material:*
Statement of storage method by which access to data will be limited to research team members only[#$]	

* Consortium members and collaborators are investigators who are affiliated with an institute that is part of the CONTRAST consortium and is represented in the board of governors.

† Costs of an anDREa workspace are for the accountable/principal investigator of the research proposal. This concerns the costs exciding the Erasmus MC subsidy. The accountable needs to be a WP-leader (preferably of the main study).

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Appendix 3. DATA REQUEST FORM

Version: 20-04-2025

For a data request, please complete this form and send to the Data access and writing committee (DAWC): dawc.contrast@contrast-consortium.nl

For more information see CONTRAST publication policy

Private parties only need to fill out a., and i-m. They will be contacted by financial committee.

Title of research proposal/request	
a. Applicant	*Name:* *Email address:* *Phone number:* *Affiliation:* *City and country:* *CONTRAST member: Yes/No*
b. First author:	*Name:* *Email address:* *Phone number:* *Affiliation:*
c. Co-authors	*Names, email addresses, affiliation:*
d. Last Author	*Name:* *Email address:* *Phone number:* *Affiliation:*
e. Accountable	*Name:* *Email address:* *Phone number:* *Affiliation:*
f. Involved-WP Leaders (minimal 2)	*Names, email addresses:*
g. Abstract	*Background (<200w)* *Aim (<100w)* *Approach (<200w)*

h. Planning (6 months after obtaining the data an update to the DAWC is required)	*Timeline for analysis and writing* *Milestones to be reached in 6 months*
i. What data is needed form the study (please specify in boxes below)	*Clinical data:* *Imaging data:* *Experimental data:* *Biomaterials:*
j. Clinical data (check CRF-on-paper on trial sites through www.contrast-consortium.nl)	*From which trials:* *Which variables:* *Any specific patient selection:*
k. Imaging Data	*Meta data (already scored parameters):* *Raw Images:*
l. Experimental data	*Open text:*
m. Biomaterials	*Meta data (already scored parameters):* *Material:*