The Chronic Angioedema Registry – CARE

Charter and Statutes

Introduction

The Chronic Angioedema Registry (CARE) is an open-ended registry for all types and forms of recurrent angioedema. CARE collects quality, real-world data, providing further understanding of recurrent angioedema and its treatment. CARE is a project of the Global Asthma and Allergy European Network (GA^{2}LEN) and Hereditary Angioedema International (HAEi) network of angioedema centers of reference and excellence (ACARE) and the urticaria network e.V. (UNEV). Care will seek endorsement by national and international medical and scientific societies. The aims and objectives of CARE are detailed in the CARE project plan, which can be obtained from the CARE Office and the CARE website.

This charter outlines the statutes of CARE, its structure, governance, bodies, and processes. Changes to the structure of CARE and its key processes require the approval of the CARE International Steering Committee (majority vote).

CARE governance and bodies

CARE is academia-driven, international, and peer-governed. Its bodies include the CARE International Steering Committee (CARE ISC), the CARE Management Team (CARE MT), and the CARE Office.

International Steering Committee

The CARE ISC is the decision-making body of CARE. The aims and responsibilities of the ISC are to:

- Decision on CARE variables and changes of CARE variables
- Oversee the scientific integrity and output of CARE
- Propose and help to develop scientifically important and clinically relevant publications
- Advise on publication proposals by CARE investigators
- Oversee and promote the dissemination of CARE results
- Decide on the addition of variables to the registry
- Work with the CARE MT and office to promote and continuously improve CARE
- Recruit and help CARE investigators
- Obtain endorsements of CARE by regional, national, and international societies
- Help to obtain funding and support for CARE
- Present CARE data at regional, national, and international meetings and congresses

- Invite new CARE ISC members

The CARE ISC is comprised of CARE investigators, a UNEV delegate, gold sponsor delegates (one per gold sponsor), and a non-voting consulting HAEi delegate. All ACARE steering committee members are CARE ISC members for the duration of their ACARE steering committee term. CARE investigators are invited to become CARE ISC members by the CARE ISC (majority vote) for a term of 4 years. CARE ISC membership may be renewed, by the ISC (majority vote). CARE investigators can apply to become CARE ISC members, and the CARE ISC votes on applications (majority vote). The ISC appoints, by majority vote, a chair and co-chair.

The CARE ISC meets at least twice a year, face to face or by video conference. Members who are not able to attend a CARE ISC meeting can be represented by another investigator from their site. Decisions are made by voting, at CARE ISC meetings or online. Voting, at CARE ISC meetings, can take place only if at least half of the ISC members or their substitutes are present. The majority vote decides. At least the chair or co-chair and the Principal Investigator or Chief Scientific Coordinator must be present for a valid vote to be cast. Online voting requires participation of more than half of the CARE ISC members, the chair or co-chair, and the Principal Investigator or Chief Scientific Coordinator. The majority vote decides. Members of the CARE Management Team and the CARE Office are invited to all CARE ISC meetings. They do not have voting rights unless they are also CARE ISC members. CARE ISC members will not receive honoraria or other fees for serving on the CARE ISC. Reasonable travel expenses for attending CARE meetings may be reimbursed, depending on the funding obtained for CARE.

The CARE Management Team

The CARE management team (CARE MT) manages, oversees, and directs the operation of CARE. Its responsibilities include:

- Development of CARE variables and changes of CARE variables
- Oversee and coordinate the eCRF development of CARE (IT-backbone)
- Communication with IT-team of the IT-backbone (eCRF and CARE data base)
- Implement and maintain CARE ethics approval and data security
- Oversee data entry, management, quality, and analyses
- Oversee the development and maintenance of the CARE website
- Coordinate and help with CARE investigator publication proposals
- Oversee and coordinate social media activities

- Obtain funding for CARE
- Coordinate data exploration, analyses, peer-reviewed manuscripts, abstracts and other publications generated from the CARE database.
- Recruit new CARE partners and coordinate cooperations with CARE partners
- Communication with the legal support (together with the CARE office)
- Communication with supporters and partners (together with the CARE office)

The CARE MT includes the Chief Scientific Coordinator (Thomas Buttgereit), the Principal Investigator (Karsten Weller), the Chief Statistician (Annika Gutsche), the CURE liaison officer (Pavel Kolkhir), the UNEV liaison officer (Frank Siebenhaar), the ACARE liaison officer (Markus Magerl), and the HAEi liaison officer (Marcus Maurer).

The CARE Office

The CARE Office assists the CARE ISC and MT. Its responsibilities include:

- Preparation of ISC and MT meetings
- Management of the CARE website and social media activities
- Publicizing CARE activities and outcomes
- Preparing and sending out CARE newsletters and communication
- Data entry and query management
- Processing of CARE investigator applications and collaboration agreements
- Processing of CARE manuscript proposals
- Processing of cooperation agreements with sponsors
- Collection and documentation of required documents for participation, e.g. ethics approvals
- Communication with and coordination of the legal support (together with the CARE MT)
- Communication with partners and supporters (together with the CARE MT)
- Organisation and secure transmission of raw data for CARE sites/centers who ask for their own data for their own use
- Maintaining of the CARE codebook

The CARE Office includes a member of the ACARE team (Reinhardt Britz), a member of the UNEV team (Diana Siekierka), a project manager (NN), two data entry and query managers (NN, NN), and a CRUSE (chronic urticaria self evaluation app) liaison (Anja Lingnau).

Processes for Data Analyses and Interpretation and Publications

CARE aims to improve the knowledge on recurrent angioedema, by CARE data analyses, interpretation, reporting and publication. Reports containing descriptive information as well as the results of analyses of CARE patient data will be provided for information to CARE ISC members, CARE investigators and eligible partners at regular intervals. In addition to these regular descriptive data summaries, specific analyses of scientific or clinical interest are conducted. For this, the following rules apply:

- Specific analyses of CARE data and publications can be proposed by any CARE investigator who has entered at least 30 baseline data sets and corresponding follow up data sets (ANNEX 1). This requirement is subject to annual review by CARE ISC.
- Proposals are processed by the CARE office and put forward for consideration by the CARE MT. The MT may seek CARE ISC advice.
- The analyses will be overseen by the CARE MT, by a CARE ISC member, or an appointed biostatistician.
- For publications that result from data analyses of global CARE data, the number of co-authorships for each CARE site/center is not limited and based on the number of data sets, other contributions, and ICMJE criteria.
- When equal or more than 50 baseline and corresponding follow up data sets were entered, the respective CARE site/center is automatically asked for co-authorship (one co-author). If equal or more than 100, 200, 400, and 800 baseline and corresponding follow up data sets were entered, the CARE site/center is automatically offered 2, 3, 4, and 5 co-authorships, respectively. If only baseline data sets are used for the analysis, then the same co-authorship criteria apply but only baseline data sets are taken into account for the number of co-authors that can be included per CARE site/center.
- It is the responsibility of the CARE sites/centers to discuss the co-authorship within their team and to provide this information to the CARE Office.
- The CARE ISC members will be asked whether they are interested to contribute to CARE manuscripts and become coauthors (ICMJE criteria must be fulfilled). CARE ISC members are not automatically included as coauthors of CARE manuscripts.
- For being part of the author team of a CARE publication, the criteria of authorship (as described below) have to be met. CARE investigators who are not co-authors are included in the acknowledgement section of CARE publications.
- CARE investigators may request information on the patients they entered (raw data) from

the CARE database, for their own use including publications, by the use of the Proposal for CARE Data Analysis and Publication form (ANNEX 1).

- CURE data may be used for CARE publications, in line with CURE and CARE rules and regulations.

The details of the scientific publication activities including the publication development process for global and individual CARE site/center publications as well as guidelines for authorship are specified below.

Global CARE publications

The CARE ISC develops and maintains the overall CARE publication plan, together with the CARE MT and with the help of the CARE office. The overall CARE publication plan is based on an evaluation of the available data within the CARE database, expected timelines for further data to accrue/analyses to become available, and assessments of the current scientific literature. The CARE ISC proposes scientifically and/or clinically relevant analyses and publications (manuscripts, abstracts) and helps to develop them. The CARE ISC has oversight of all concepts and proposals for publications to ensure scientific accuracy and appropriateness. The CARE publication plan is shared with all CARE investigators regularly (e.g. annually). Copies of published CARE manuscripts are made available to the CARE investigators by the CARE office.

Publications by individual CARE investigators/sites

Each CARE investigator/site is free to use and publish their own data, and also has the right to veto pooling of their data for scientific publications (apart from regular descriptive data summaries, which cannot be vetoed). A standardized Proposal for Analyses and Publication form for CARE investigators to request specific analyses is available from the CARE office and website and should be used (ANNEX 1). A copy of any publication/abstract developed by an individual CARE investigator/ site using CARE data must be sent to the CARE office for review prior to submission at least twenty-one (21) days prior to submission. All publications/presentations of individual CARE investigator/site results shall appropriately acknowledge that the publication/presentation benefitted from the work of the ACARE network and CARE, reference relevant previous CARE publications, and state that the individual CARE investigator/site results are derived from a subset CARE data.

Publication development process

CARE follows Good Publication Practice 2 (GPP2) guidelines (www.gpp-guidelines.org). ISC members may be authors of CARE publications, but ISC membership does not automatically

confer authorship (BMJ 2009;339:b4330; doi: 10.1136/bmj.b4330.)

ACARE and UNEV may facilitate professional writing and editorial assistance from a third party, which can, under the direction of the CARE MT, assist with:

- the drafting or editing of publications (manuscript, abstract, poster)
- drawing figures and graphs,
- performing literature searches,
- manuscript submission

Guidelines for authorship of publications arising from CARE

Authorship is attributed according to the International Committee of Medical Journal Editors (ICMJE) Uniform Requirements for Manuscripts Submitted to Biomedical Journals (http://www.icmje.org/). All authors of CARE publications will be required to provide full disclosures of their financial interests in line with the international Good Publications Practice 2 (GPP2) guidelines for reporting medical research.

To be an author of a CARE publication/abstract, all 3 of the following criteria must be met:

- Substantial contributions to design, acquisition of data, or analysis and interpretation of data
- Drafting the publication/abstract or revising it critically for important intellectual content
- Final approval of the version to be published

Positions of administrative leadership, however important to the research, are not by themselves criteria for authorship. The author group of each CARE manuscript/abstract will determine, prior to the initiation of the development, which authors are first, last, and corresponding authors, and who has the lead for writing and managing each publication or presentation (i.e. lead author). The lead author has overall responsibility for the integrity of publication/abstract.

Declaration of Conflicts of Interest

The members of the CARE ISC, CARE MT, and CARE Office should not undertake any other activity which could affect their independent judgment in the performance of their CARE duties, or which conflicts with (or could reasonably give the appearance of conflicting with) the interests of CARE. This does not preclude membership on advisory boards of pharmaceutical companies, receiving honoraria for lectures or consulting, membership on the executive boards of other

disease registries or other scientific committees, but such activities should be declared as potential conflicts of interest.

Confidentiality

All CARE ISC, CARE MT, and CARE Office members shall be aware that information they receive on CARE may be of confidential nature, and that they may not make use of or disclose such confidential information for any other purpose than for performing their CARE duties.

Role of ACARE and UNEV

CARE is the ACARE registry. All ACAREs are expected to contribute to CARE. Participation in CARE does not require ACARE membership. The ACARE network and steering committee support CARE. CARE results are disseminated by ACARE activities and meetings.

UNEV developed and maintains the CARE database. UNEV has the right and the obligation to use the information in the database in relation to the authorities. Participation of investigators and sites in CARE requires completion of a collaboration agreement with UNEV (available from the CARE office and website).

UNEV and ACARE retain the right to evaluate CARE data and may perform any such evaluations with the approval of the ISC. UNEV has overall responsibility for all statistical work on CARE data.

Role of CARE partners

CARE aims to partner with regional, national and international medical and scientific societies and networks, patient organizations, industry and other stakeholders, to promote CARE participation and dissemination of results. CARE is funded via donations, collaboration, and sponsoring by partners. The terms and conditions of financial support by partners are detailed in the Partner Collaboration Agreement, available from the CARE office.

Annex 1

Proposal for CARE Data Analysis and Publication

Name / E-mail: …… Date: ……

HYPOTHESIS / RESEARCH QUESTION:	
BACKGROUND/ RATIONALE:	
REQUESTED ANALYSES:	
POPULATION(S) OF INTEREST: (e.g. all patients/ children/ adults/ treated/ untreated)	**1.**
	2.
	3.

The analysis should be done on data from:

☐ **All CARE countries** ☐ **Selected CARE countries** ☐ **My CARE patients**

Data needed by (DD/MM/YYYY): ……

(Normally at least 3 months are needed for answering a request)

Purpose:

☐ Manuscript
☐ Abstract
☐ Other ……

Additional information: ……
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All publications that use CARE data require pre-submission review by the CARE management team. Publications that use CARE data entered by other CARE investigators must be approved by the CARE management team. The rules outlined in the CARE charter apply. In case of any questions please contact thomas.buttgereit@charite.de and karsten.weller@charite.de