Home Tele-Monitoring of Non-Invasive Ventilation in Chronic Obstructive Pulmonary Disease – HOmeVent Connect

Prospective, non-interventional, observational multicentre study

Title	Home Tele-Monitoring of Non-Invasive Ventilation in Chronic Obstructive Pulmonary Disease
Acronym	HOmeVent Connect
Type of study	Non-interventional, observational, prospective, European, multicentre clinical study on marketed medical devices Relevant regulatory document: ISO 14155 (as far as possible in NIS)
Protocol version identifier	Version no. 2.0 dated 2020-01-10 (replaces previous version 160422)
Medicinal product(s)	ResMed non-invasive ventilation (NIV) devices and tele-monitoring solution for home care use available in clinical routine care
Product reference	CE 161c, 122, 125, 129, 161b, 161a,167b, ResMed connectivity module: CE 169a
Registry number	NCT02811588
Sponsor	ResMed Germany Inc, Martinsried, Germany
CRO	CRI – The Clinical Research Institute, Munich, Germany
Countries of study	European countries (e.g. Germany, Spain, UK)
Research question and objectives	**Primary Objective** ▪ Incidence of unplanned all-cause hospitalisations in routine clinical care in patients treated with NIV therapy who are continuously monitored by telemetric data **Secondary Objectives** ▪ Incidence of unplanned COPD-caused hospitalisations ▪ Predictors of unplanned all-cause hospitalisations ▪ Predictors of unplanned COPD-caused hospitalisations ▪ Predictors of compliance and persistence to NIV therapy

Marketing authorisation of devices

Marketing authorisation holder(s)	ResMed Ltd,1 Elizabeth Macarthur Drive, Bella Vista, NSW 2153 Australia Legal representative in Europe: ResMed Germany Inc., Fraunhoferstr. 16, 82152 Martinsried, Germany Phone: +49 (0) 89 99 01-001 Fax: +49 (0) 89 99 01-10 08
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2. List of abbreviations

AE	Adverse Event
ADE	Adverse Device Effect
CAT	COPD Assessment Test™ questionnaire
CDISC	Clinical Data Interchange Standards Consortium
CTMS	Clinical Trial Management System
CFR	Code of Federal Regulations
COPD	Chronic Obstructive Pulmonary Disease
CRF	Case Report Form
CRO	Contract Research Organisation
e-CRF	Electronic Case Report Form
e-TMS	Electronic Trial Management System
EDC	Electronic Data Capture
ERC	Endpoint Review Committee
FU	Follow-Up
GCP	Good Clinical Practice
HMV	Home Mechanical Ventilation
IFU	Instruction For Use of a medical device
NIV	Non-Invasive Ventilation
PID	Patient unique identifier in the e-TMS
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SOP	Standard Operating Procedure
SRI	Severe Respiratory Insufficiency
USADE	Unexpected Serious Adverse Device Effect

3. Responsible parties

Steering Committee Members:

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Representative of the sponsor:

Katrin Pucknat
President, ResMed Germany Inc.,
Fraunhoferstr. 16, 82152 Martinsried, Germany

3.1 Signatures

The undersigned have read this protocol and agreed to conduct this study in accordance with all stipulations of the protocol and in accordance with the Declaration of Helsinki.

Date	**Signature**
_____	_____ Professor Michael Dreher (International Chief Investigator and chair of Steering Committee)
_____	_____ Dr Claudio Rabec
_____	_____ Professor Nicholas Hart
_____	_____ Katrin Pucknat (sponsor representative)
_____	_____ Janina Haug (study statistician)
_____	_____ Signature of Principal Investigator
	_____ (Name of Principal Investigator in block letters)

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Date	Signature
	Professor Michael Dreher (International Chief Investigator and chair of Steering Committee)
12/01/2020	Dr Claudio Rabec
	Professor Nicholas Hart
	Katrin Pucknat (sponsor representative)
	Janina Haug (study statistician)
	Signature of Principal Investigator
	(Name of Principal Investigator in block letters)

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Date	Signature
13.1.2020	UNIKLINIK RWTH AACHEN Medizinische Klinik V Klinik für Pneumologie und Internistische Intensivmedizin Univ.-Prof. Dr. med. Michael Dreher Pauwelsstraße 30, D-52074 Aachen Professor Michael Dreher (International Chief Investigator and chair of Steering Committee)
	Dr Claudio Rabec
	Professor Nicholas Hart
14.01.2020	Katrin Pucknat (sponsor representative)
	Janina Haug (study statistician)
	Signature of Principal Investigator
	(Name of Principal Investigator in block letters)

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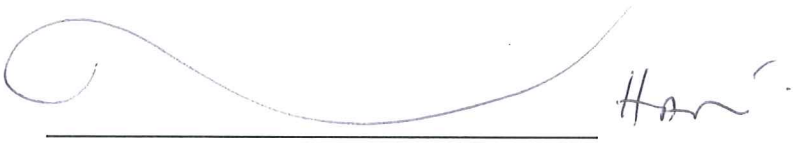
	Dr Claudio Rabec
29-1-20	 Professor Nicholas Hart
	Katrin Pucknat (sponsor representative)
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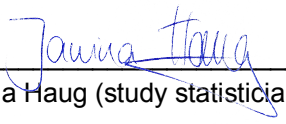
15.01.2020	 Janina Haug (study statistician)
_____	_____ Signature of Principal Investigator
	_____ (Name of Principal Investigator in block letters)

4. Synopsis

Title	Home Tele-Monitoring of Non-Invasive Ventilation in Chronic Obstructive Pulmonary Disease – HOmeVent Connect Prospective, non-interventional, observational multicentre study
Rationale and Background	There is robust scientific evidence that non-invasive ventilation (NIV) therapy is an effective option for most COPD patients hospitalised with acute hypercapnic respiratory failure secondary to an acute disease exacerbation [3]. More recently, NIV has been shown to significantly improve survival and quality of life in COPD patients with chronic stable hypercapnic disease [4] and in patients with persistent hypercapnia after an acute chronic respiratory failure [11]. Over the past two decades, the utilisation of NIV has become one of the most important developments in the field of mechanical ventilation. However, unsuccessful NIV was found to be independently associated with death [5] and poor NIV compliance was associated with higher risk of repeat acute NIV use [6]. There is a paucity of useful predictors of poor patient compliance and the performance of conventional algorithms for detecting COPD exacerbations is still weak. Detection of NIV failure is crucial in patient management in view of its negative effect on quality of life and prognosis and the fact that it often leads to hospitalisation. In addition, 70% of COPD-related healthcare costs are consequences of emergency and hospital stays for the treatment of exacerbations [7]. Recently, tele-monitoring emerged and unfolded differently among various healthcare organisations and countries. Evidence regarding its impact on the management of COPD patients is still insufficient to draw firm conclusions. Assumption has been made that remote monitoring of home NIV treatment could help to identify novel predictors of the early detection of NIV failure and deteriorations in patients with COPD. The incidence in routine clinical care of unplanned all-cause and COPD-caused hospitalisations in patients treated with NIV therapy who are continuously monitored by telemetric data in several European countries needs evaluation. In addition, predictors of unplanned all-cause and COPD-caused hospitalisations as well as of compliance and persistence to NIV therapy should be assessed in this patient population with special respect to continuous tele-monitoring.
Research questions and objectives	**Primary Objective** ▪ Incidence of unplanned all-cause hospitalisations in routine clinical care in patients treated with NIV therapy who are continuously monitored by telemetric data **Secondary Objectives** ▪ Incidence of unplanned COPD-caused hospitalisations ▪ Predictors of unplanned all-cause hospitalisations ▪ Predictors of unplanned COPD-caused hospitalisations ▪ Predictors of compliance and persistence to NIV therapy
Study design	Non-interventional, observational, prospective, European, multicentre clinical study on marketed medical devices

Population	**Inclusion criteria:** ▪ Age ≥18 years ▪ COPD eligible for NIV treatment (according to applicable medical guidelines and local policy in routine clinical care) ▪ Prescription of an adequate ResMed NIV device with tele-monitoring option (according to Annex 1, 3.) as part of routine clinical care ▪ Acceptance of tele-monitoring and corresponding data handling ▪ Naive to long-term NIV treatment with initiation of NIV either ≤7 days before or after enrolment into study ▪ Able to fully understand information on data protection and provide written informed consent for use of corresponding medical and telemetric data. **Exclusion criteria:** ▪ Invasive ventilation therapy ▪ Another life-threatening disease with estimated survival < 12 months (other than COPD, e.g. cancer) ▪ Further exclusion criteria according to IFU of the device intended and prescribed.
Variables	All clinical variables are documented in a web-based e-CRF. Study relevant data available in routine clinical care will be entered into the e-CRF by adequate site staff members: demographic data, medical and treatment history and co-morbidities, physical status, and current medication as well as data on the aetiology of COPD, diagnosis parameters to determine the reasons for NIV therapy prescription. The patient will be asked to fill out SRI and CAT questionnaires.

Data sources	Data documented by study sites: Data will be derived from routine clinical care records and findings, observations or other sources (e.g. hospital records, clinical and office charts, electronic patient records, laboratory notes, recorded data from automated devices, patient files, laboratories and medico technical departments). In cases where data are collected while speaking to the patient, the e-CRF is the source document (if the patient's answer is documented there without prior documentation in other media). Data obtained from patients: Baseline and follow-up data derived from quality of life questionnaires SRI and CAT. Every six months of follow-up short questionnaires asking for hospitalisations and other potential SAEs since last contact will be sent by mail to all patients Data imported from devices: All ResMed devices to be used for NIV therapy within this study (refer to Annex 1, 3.) are CE-certified, marketed devices. All are used for NIV treatment in line with the corresponding instruction for use. Tele-monitoring data of the devices will be sent remotely to a central tele-monitoring server managed by an independent certified health data hosting service provider, located in France. Pre-defined technical and usage monitoring data will subsequently be transferred to the CRO as coded (pseudonymised) data for scientific analysis together with data derived from the e-CRF.
Study size	About 25 NIV expert centres in several European countries, e.g. Germany, Spain, UK are expected to participate in the study. In addition, data of comparable patients included by NIV expert centres in France in the "Cohorte de l'ANTADIR" (ANTADIR registry) will be used for joined analysis. Approximately 550 adult female and male patients with COPD eligible for NIV treatment will be enrolled, out of which 231 patients have been enrolled within the phase 1 of the study.
Data analysis	Data from all sites will be pooled for analysis. Standard statistical methods will be used to analyse all data. Continuous variables will be summarised using the number of observations, mean, median, standard deviation, minimum and maximum values. Categorical variables will be summarised using the number of observations and percentages. Two-sided, 95% confidence intervals will be used to characterise the major parameters. Demographic variables will be tabulated and summarised using descriptive statistics.

5. Amendments and updates

Amendment no. 1, dated 2019-12-30

After 231 patients being enrolled within 1.5 years in this observational study (phase 1) a review of feasibility was performed by the Steering Committee. As a consequence, modifications to protocol for subsequent phase 2 have been made primarily for the following aspects:

- Focus on NIV treatment and the use of tele-monitoring device data
- In- and exclusion criteria slightly broader according to routine clinical care
- More concise definition of primary and secondary endpoints
- Extension to study sites in other European countries

Details of the amendment:

Section of study protocol	Amendment or update	Reason
Marketing Authorisation Holder (MAH)	MAH contact person modified	New contact person nominated by MAH.
3. Responsible parties and representatives of the sponsor	List and addresses modified	Updated
6. Milestones	Milestone dates adapted	Updated to new planned schedules
7. Rationale and background	Text adapted to modified major aspects of the study, like tele-monitoring data, and to recent literature	Wording updated according to latest published references
8. Research question and objectives	The objectives have been adapted to modified major aspects of the study, like tele-monitoring data, and to a more concise definition	Adaptation to more concise and tele-monitoring focused objectives, also ensuring higher level of feasibility of the study in phase 2
9.1. Study design	Use of more up-to-date terms with reference to routine clinical care and IFU.	Routine clinical care should be the major factor for definition of the study design.
9.1.1 Type / design of study	Enrolment to the study clarified (NIV centres only) and HMV definition adapted. Flowchart adapted to study visits (e.g. inclusion of pre-screening) and procedures (e.g. informed consent for telemetric monitoring).	Procedures should reflect routine clinical care processes in all potentially participating countries, therefore, office-based pulmonologists will not be part of phase 2. Improved consistency with regulatory wording regarding pre-screening.
9.1.2. Primary Outcome	Primary outcome has been adapted to modified major aspects of the study and to the more concise definition “all-cause Hospitalisations”	Adaptation to more concise objectives, also ensuring higher level of feasibility of the study in phase 2

Section of study protocol	Amendment or update	Reason
9.1.3 Secondary Outcomes	Secondary outcomes have been adapted to modified major aspects of the study, like tele-monitoring data, and to more concise definitions	Adaptation to more concise objectives, also ensuring higher level of feasibility of the study in phase 2
9.2.1. Study sites	Study will be conducted in several countries in Europe and in NIV sites, only. Cooperation with French ANTADIR registry is defined.	A higher level of feasibility should be ensured and a better representation of routine clinical care in different European countries. A clinical study structure in this field of indication is existing in France, thus, this study will cooperate with the existing ANTADIR registry to avoid doubled infrastructure with competing efforts
9.2.2. Study population	Total number of patients defined in addition to those already enrolled in phase 1. Use of tele-monitoring added as prerequisite and corresponding process of informed consent defined. Maximum of data from ANTADIR registry defined In- and exclusion criteria slightly broader defined according to routine clinical care	Definition of patients still to be enrolled in phase 2 and limitation of those coming from the French ANTADIR registry. Adaptation of definitions and procedures to routine clinical care situation regarding usage of these devices.
9.2.3. Study duration	Extension of end of study and estimate of individual follow-up period added.	Adaptation according to new planned schedules in phase 2.
9.2.4. Withdrawal from consent of use of medical data	Reference to ISO 14155 and information on use of data before withdrawal added.	Editorial changes.
9.3. Study visits	More detailed description of visit procedures and data items added. Several patient questionnaires deleted.	Updated in accordance with the requirements of the GDPR. Improvement with respect to feasibility.
9.3.1 Pre-Screening and check of eligibility	More detailed description of visit procedures added.	Updated in accordance with the requirements of the GDPR.
9.3.2. Prescription of treatment	Definition on diagnosis, prescription of therapy and use of devices with referenced to IFU added.	Adaptation to routine clinical care and clarification of procedures in this observational study.

Section of study protocol	Amendment or update	Reason
9.3.3 Screening and enrolment visit	Consenting to the study elaborated. More detailed description of visit procedures and data items added.	Updated in accordance with the requirements of the GDPR.
9.3.4 Initiation of treatment	Reference to medical guidelines added.	Adaptation to routine clinical care and clarification of procedures in this observational study.
9.3.5 Follow-up visits	More detailed description of visit procedures and data items added.	Adaptation to routine clinical care and clarification of procedures in this observational study. Updated in accordance with the requirements of the GDPR.
9.3.6 Follow-up questionnaires	Detailed description of procedures for FU questionnaires and corresponding exceptions added.	Updated in accordance with the requirements of the GDPR. Exception for data from France necessary to meet feasible processes there.
9.3.7 Visit table	Visit table adapted.	Update to modified procedures and schedules.
9.4 Variables	More precise definition and description added.	Updated in accordance with the requirements of the GDPR.
9.5 Data sources	Editorial changes	More concise wording.
9.5.2 Data obtained from patients	Editorial changes	More concise wording.
9.5.3 Data transferred from NIV devices	Detailed description of data transfer processes from devices.	Updated in accordance with the requirements of the GDPR.
9.6 Study size	Adaptation of number of patients and sites to new definitions.	Updated in accordance with the content of the protocol.
9.7 Data management	Editorial changes	More concise wording.
9.8 Data analysis	Editorial changes	More concise wording.
9.9 Quality control	Editorial changes	More concise wording.
9.9.4 Direct Access	Editorial changes. No copy of the signed informed consent form has to be send to the CRO	More concise wording. Updated in accordance with the requirements of the GDPR.
9.10 Limitations of the research methods	Editorial changes	More concise wording.
9.11 Other aspects	Details on funding added.	Updated in accordance with requirements of ISO 14155.
10. Protection of human subjects	Reference to ISO 14155 added and editorial changes.	More concise wording.

Section of study protocol	Amendment or update	Reason
11. Management and reporting of Adverse Events/Adverse Reactions	Definitions updated to meet wording of the ISO 14155. Adverse Events of Special Interest no longer defined.	To reflect ISO 14155 requirements.
13. References	Editorial changes	For consistency with updated protocol.
Annexes	Editorial changes	For consistency with updated protocol.

6. Milestones

Milestone	Planned date
Start of enrolment of phase 1, i.e. start of data collection	September 2016
End of enrolment of phase 1	June 2017
End of follow-up of phase 1	Mar 2018
Check of feasibility of phase 1, i.e. end of data collection phase 1	Sept 2018
Start of enrolment of phase 2, i.e. start of data collection	March 2020
End of enrolment of phase 2	March 2021
End of follow-up of phase 2	March 2022

7. Rationale and background

The prevalence of chronic respiratory disease continues to increase in industrialised countries, mainly because of tobacco use and improved overall survival.[1, 8] Currently it is estimated that 65 million people globally are affected by moderate-to-severe COPD, and over the next decade deaths from COPD are projected to increase by more than 30% resulting in COPD becoming the third leading cause of death worldwide by 2030.[2] In addition to being an important cause of mortality, COPD is also associated with significant morbidity. The symptom burden of COPD is similar to that of cancer,[9] and the negative impact of COPD on health status is greater than that of self-reported cardiovascular disease or diabetes.[10] In addition, the chronic nature of COPD and associated morbidities mean that this disease is associated with significant disease-related economic and healthcare costs.[7]

There is robust scientific evidence that non-invasive ventilation (NIV) therapy is an effective option for most COPD patients hospitalised with acute hypercapnic respiratory failure secondary to an acute disease exacerbation [3]. More recently, NIV has been shown to significantly improve survival and quality of life in COPD patients with chronic stable hypercapnic disease [4] and in patients with persistent hypercapnia after an acute chronic respiratory failure [11]. Over the past two decades, the utilisation of NIV has become one of the most important developments in the field of mechanical ventilation. However, unsuccessful NIV was found to be independently associated with death [5] and poor NIV compliance was associated with higher risk of repeat acute NIV use [6]. There is a paucity of useful predictors of poor patient compliance and the performance of conventional algorithms for detecting COPD exacerbations is still weak. Detection of NIV failure is crucial in patient management in view of its negative effect on quality of life and prognosis and the fact that it often leads to hospitalisation. In addition, 70% of COPD-related healthcare costs are consequences of emergency and hospital stays for the treatment of exacerbations [7].

Recently, tele-monitoring emerged and unfolded differently among various healthcare organisations and countries. Evidence regarding its impact on the management of COPD patients is still insufficient to draw firm conclusions. Assumption has been made that remote monitoring of home NIV treatment could help to identify novel predictors of the early detection of NIV failure and deteriorations in patients with COPD.

The incidence in routine clinical care of unplanned all-cause and COPD-caused hospitalisations in patients treated with NIV therapy who are continuously monitored by telemetric data in several European countries needs evaluation. In addition, predictors of unplanned all-cause and COPD-caused hospitalisations as well as of compliance and persistence to NIV therapy should be assessed in this patient population with special respect to continuous tele-monitoring.

8. Research question and objectives

The study will determine in several European countries the incidence in routine clinical care of unplanned all-cause and COPD-caused hospitalisations in patients treated with NIV therapy who are continuously monitored by telemetric data. Clinical and telemetric predictors of unplanned all-cause and COPD-caused hospitalisations and of NIV therapy compliance and persistence will be assessed in those patients.

The study will target adult individuals with COPD eligible for home NIV therapy according to applicable medical guidelines who agree to continuous telemetric monitoring. Medical data from routine clinical care will be documented in an electronic case report form (e-CRF), e.g. patient demographics, diagnostic information (including primary diagnosis and quality of life), and blood gas analysis at baseline and in follow-up. Telemetric data on NIV treatment (e.g. type of ventilator, modes and settings, usage times, usage profiles) will be added to e-CRF medical data.

Primary Objective

- Incidence of unplanned all-cause hospitalisations in routine clinical care in patients treated with NIV therapy who are continuously monitored by telemetric data

Secondary Objectives

- Incidence of unplanned COPD-caused hospitalisations
- Predictors of unplanned all-cause hospitalisations
- Predictors of unplanned COPD-caused hospitalisations
- Predictors of compliance and persistence to NIV therapy

9. Research methods

9.1 Study design

Non-interventional, observational, prospective, European, multicentre clinical study on marketed medical devices.

The study protocol does not define any specific study procedure for enrolled patients. Therapies and procedures during the course of this study will be performed according to the individual decision of the treating physician based on current applicable medical guidelines and on local policy in clinical routine care. This includes the indication and the use of the NIV device and possible follow-up examinations according to routine clinical care. All devices will be prescribed and used according to the corresponding Instruction for Use (IFU), only.

9.1.1 Type / design of study

This clinical study is a prospective observational study.

Patients will be diagnosed and evaluated for eligibility of NIV therapy by NIV expert centres and will be consecutively enrolled into the study provided that all inclusion and exclusion criteria are met and written consent is given to use their clinical routine data according to data privacy regulations.

NIV therapy refers to the application of ventilatory assistance without the use of an invasive airway. Home mechanical ventilation (HMV) is defined as NIV administered daily, primarily delivered in the user's home or other long-term care facility (not a hospital). It does not include treatment of patients with obstructive sleep apnea alone, or those with a tracheostomy not requiring mechanical ventilation.

Further follow-up of the patient according to clinical routine care will be performed by the NIV expert centre and by health care provider.

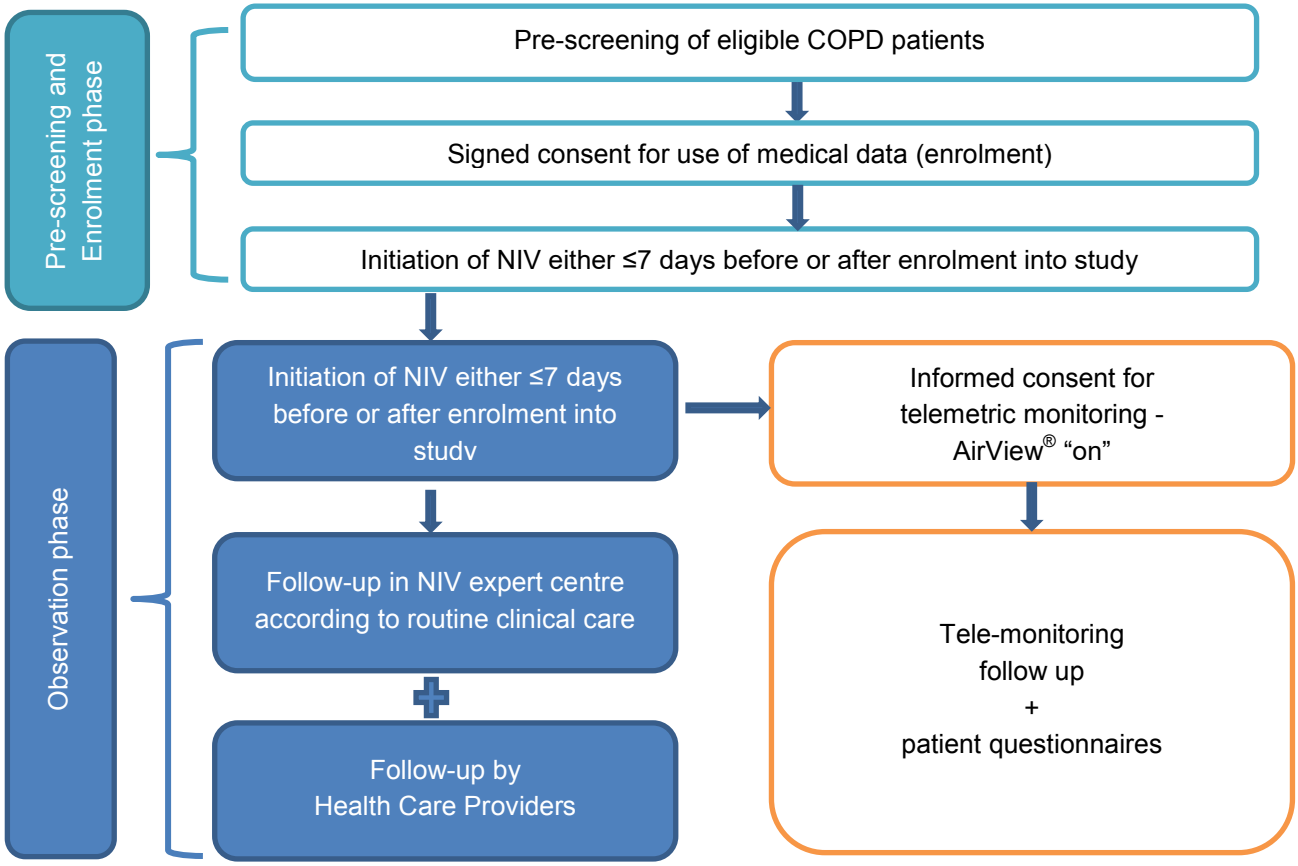


Figure 1: Flowchart of study visits and procedures

9.1.2 Primary Outcomes

- Rate of unplanned all-cause hospitalisations in the study population normalised to one year of FU

9.1.3 Secondary Outcomes

- Rate of unplanned COPD-caused hospitalisations in the study population normalised to one year of FU
- Prediction model with all-cause hospitalisation as independent variable and medical and telemetric data of the NIV devices as depending variables
- Prediction model with COPD-caused hospitalisation as independent variable and medical and telemetric data of the NIV devices as depending variables

- Prediction models with mean hours of device usage (compliance) and percentage of days with device usage related to total number of days potentially under therapy (persistence) as independent variables and medical and telemetric data of the NIV devices as depending variables

9.2 Study settings

9.2.1 Study sites

About 25 NIV expert centres in several European countries, e.g. Germany, Spain, UK are expected to participate in the study. In addition, data of comparable patients included by NIV expert centres in France in the “Cohorte de l'ANTADIR” (ANTADIR registry) will be used for joined analysis.

NIV expert centres are defined as those with any hospital or outpatient and/or co-ordinated HMV services, i.e. clinics having expertise in prescribing, initiating and monitoring HMV. NIV expert centres in the defined countries will be identified by the Steering Committee members and will be invited to participate to the study.

The prospective, non-interventional, observational study titled “Cohorte de l'ANTADIR - Database of Patients Registered as Treated With Respiratory Support in a Multicentre Homecare Federation for Patients With Respiratory Problems” (NCT01181869) is currently being conducted in France under sponsorship of ANTADIR (Association Nationale pour les Traitements A Domicile, les Innovations et la Recherche). Data set, basic procedures and in- and exclusion criteria of a cohort of COPD patients will be comparable to the settings of the HOmeVent Connect study for the period when both studies are running in parallel. It was agreed between ResMed and ANTADIR not to establish another observational study in France with focus on comparable patients but to join data of comparable patient cohorts for joined analysis. Adequate data of patients in France treated with corresponding ResMed devices will be transferred to CRI as coded (pseudonymised) data. These data will be joined with data of patients of the HOmeVent Connect study and analysed as part of a joined analysis to increase patient sample size, power of analysis and reliability of the results. Details will be given in a Statistical Analysis Plan (SAP).

9.2.2 Study population

Approximately 550 adult female and male patients with COPD eligible for NIV treatment will be enrolled, out of which 231 patients have been enrolled within the phase 1 of the study. Patients’ written informed consent to use their routine clinical data according to data privacy standards must be obtained prior to documentation of patients’ data in the e-CRF.

With regard to tele-monitoring as a pre-requisite in phase 2 the patient is also required to consent on the handling of the tele-monitoring data.

If a patient is enrolled into the study but is never using the prescribed device (i.e. refusal of prescribed therapy) he/she will be replaced.

If a patient, who has already started NIV therapy, is enrolled, the start of therapy must not be longer than 7 days before enrolment.

All patients using the device will be followed during routine clinical practice and will visit a site only in the course of their routine clinical care. No treatment or medical examinations additional to routine clinical care will be performed.

Within this study population, data of a maximum of about 100 patients will be added by the French ANTADIR registry in line with in- and exclusion criteria of this observational study.

Inclusion criteria:

- Age ≥18 years
- COPD eligible for NIV treatment (according to applicable medical guidelines and local policy in routine clinical care)
- Prescription of an adequate ResMed NIV device with tele-monitoring option (according to Annex 1, 3.) as part of routine clinical care
- Acceptance of tele-monitoring and corresponding data handling
- Naive to long-term NIV treatment with initiation of NIV either ≤7 days before or after enrolment into study
- Able to fully understand information on data protection and provide written informed consent for use of corresponding medical and telemetric data.

Exclusion criteria:

- Invasive ventilation therapy
- Another life-threatening disease with estimated survival < 12 months (other than COPD, e.g. cancer)
- Further exclusion criteria according to IFU of the device intended and prescribed

9.2.3 Study duration

The duration of the study is scheduled to be about 2 years with an enrolment phase of about 12 months after initiation of the first site in the first country as competitive enrolment in all participating countries. After about 12 months of follow-up of the last patient enrolled and subsequent final data cleaning global end of study will be declared.

The mean duration of patient's participation will be about 16 months. Every patient stays in follow-up until the global end of the study or death or withdrawal of consent.

9.2.4 Withdrawal from consent of use of medical data

Patients are free to withdraw from their consent of use of medical and telemetric data at any time. In this event the date of withdrawal will be documented in the electronic case report form (e-CRF). According to ISO 14155 section 6.10, the reason(s) for withdrawal shall also be recorded in the e-CRF. In addition, all reasonable efforts should be made by the responsible investigator to complete assessments and retrieve any outstanding data. Those patients will not have drawbacks in treatment, healthcare supply or in the relationship to the sites or the sponsor.

Data collected and documented until withdrawal will be included in the analysis.

Patients cannot be withdrawn from this observational study by investigators for medical or any other reasons.

9.3 Study Visits

9.3.1 Pre-Screening and check of eligibility

Routine clinical care patients are diagnosed and checked for potential eligibility of study participation based on existing data generated in routine clinical care which is not part of this observational study.

9.3.2 Prescription of treatment

The decision of prescription of NIV therapy to the individual patient lies with the treating physician during the course of routine clinical care and is not part of this observational study. Diagnosis of COPD and indication of NIV therapy as well as initiation of treatment should follow applicable medical guidelines and local clinical care policy. Prescription and use of adequate ResMed NIV devices with tele-monitoring option according to Annex 1, 3. have to follow the current instructions for use (IFU) of each device.

9.3.3 Screening and enrolment visit

Patients will be screened and enrolled by contracted study sites only, i.e. NIV expert centres.

Screening of potentially eligible patients will be performed within routine clinical care using data created within routine clinical care. Adequate staff members of the study site will inform potentially eligible patients about the potential use of their medical and telemetric data within this observational study by information documents which have been approved by the responsible Ethics Committee. Within this study medical care of the patient is not in any way touched by protocol definitions but an individual decision by the treating physician in routine clinical care. Only use and handling of medical and telemetric data for scientific purposes defined in this protocol are elements of informed consent. The patient will be given sufficient time to consider informed consent to data handling and to get answers to his questions. If the patient agrees, the informed consent form for data use will be provided for signature.

After patients' signing, patients are screened and checked for eligibility according to in- and exclusion criteria by the participating sites, either on every day consecutively or at pre-defined schedules (e.g. on defined days of the week, only) to minimise selection bias. Medical screening includes check of COPD according to medical guidelines.

Study relevant data will be reported in the e-CRF. The system will automatically display the patient ID as consecutive number across all participating study sites, i.e. without reference to the recruiting site.

The following data items will be documented of each participating patient:

- Demographic data
- Patient's physical status
- Patient's social status
- Medical history
- Concomitant medication and diseases
- Data regarding COPD diagnosis
- Spirometry results (no older than 1 month)
- Blood gas analyses (carbon dioxide and bicarbonate concentration) during spontaneous breathing (pH>7.35) at date of decision making on initiation of NIV therapy
- Date of NIV therapy prescription
- Telemetric data of NIV device settings will be recorded as soon as the device has been delivered to the patient and was used for the first time
- Amount of supplemental oxygen during NIV (if needed)

The patients will further be asked to answer the SRI questionnaire (refer to Annex 2), and the CAT questionnaire (refer to Annex 3).

9.3.4 Initiation of treatment

Initiation of NIV therapy (the device has been delivered to the patient and was used for the first time) after prescription should start according to local routine clinical care before or as soon as possible after enrolment into the study (with a maximum of 7 days before enrolment). Current medical guidelines and recommendations apply, however, they might differ in participating countries, and thus, prescription and initiation of NIV therapy is the decision of the treating physician and will follow local policies. Data on initiation of NIV therapy will be recorded by telemetric data as soon as the device has been delivered to the patient and was used for the first time.

9.3.5 Follow-up visits

In routine clinical care, a first control visit of the patient at the site after NIV therapy initiation should take place within the first 6 months together with nocturnal assessment of ventilator therapy [12]. It is recommended that subsequent control visits at the site should be performed at least 1–2 times a year [12]. To ensure comparability of FU data, at least one follow-up visit at the site within 12 months of follow-up should be performed (if in line with routine clinical care).

At the FU visit at the site the following data from routine clinical care data should be documented in the e-CRF:

- Patient status
- Concomitant medication and diseases
- Spirometry results (no older than 3 months)
- Body plethysmography (if available)
- Blood gas analyses (carbon dioxide, pH and bicarbonate concentration) during spontaneous breathing
- Serious adverse events since last site visit.
- History of exacerbations not leading to a hospitalisation

The patient will again be asked to answer to the SRI and CAT questionnaires.

NIV device settings and other device data will continuously be transferred in FU as tele-monitoring data.

9.3.6 Follow-up questionnaires

Every six months of follow-up short questionnaires asking for hospitalisations and other potential SAEs since last contact will be sent by mail to all patients. Closed envelopes with PID outside including the questionnaire and a free return envelope will be prepared and sent to site by the CRO. Site staff will forward the envelope to the corresponding patient who is asked to return the completed questionnaire (which contains pseudonymous data only) directly to CRI using the free reply envelope. In case of missing answer after one written reminder the study site should contact the patient by phone in order to obtain the required information.

Data regarding hospitalisations or SAEs reported by the patient will be documented in the e-CRF primarily by the CRO on the basis of available medical data. In case a patient reports a hospitalisation or other SAE, the responsible study site will be informed by the CRO and will subsequently contact the patient's family doctor respectively the hospital where the patient was treated and ask for supportive documents (i.e. hospital discharge letter, diagnostic reports) as applicable. The study site is subsequently responsible for completion of event data.

These procedures will not be performed in study patients enrolled in the ANTADIR registry in France and used for joined analysis in this study. Thus, analysis of hospitalisations will therefore be performed for patients enroled in Germany, Spain, UK and other potentially participating countries but not for patients from France.

9.3.7 Visit table

Assessments	Screening and enrolment visit	FU visits	FU questionnaire	Tele-monitoring data
Data privacy consent	X			
Demographic data	X			
Medical history	X			
Patient's status	X	X		
Spirometry*	X	X		
Blood gas examination*	X	X		
Medication	X	X		
Quality of life questionnaires	X	X		
Serious Adverse Events		X	X	
NIV settings & other device data				X

* If data are available in routine clinical care.

9.4 Variables

All clinical variables are documented in a web-based e-CRF. Study relevant data available in routine clinical care will be entered into the e-CRF by adequate site staff members: demographic data, medical and treatment history and co-morbidities, physical status, and current medication as well as data on the aetiology of COPD, diagnosis parameters to determine the reasons for NIV therapy prescription. The patient will be asked to fill out SRI and CAT questionnaires.

9.5 Data sources

9.5.1 Data documented by study sites

Data will be derived from routine clinical care records and findings, observations or other sources (e.g. hospital records, clinical and office charts, electronic patient records, laboratory notes, recorded data from automated devices, patient files, laboratories and medico technical departments). In cases where data are collected while speaking to the patient, the e-CRF is the source document (if the patient's answer is documented there without prior documentation in other media).

Serious Adverse Events during FU will be assessed by the treating investigator.

9.5.2 Data obtained from patients

Baseline and follow-up data derived from quality of life questionnaires SRI and CAT.

Every six months of follow-up short questionnaires asking for hospitalisations and other potential SAEs since last contact will be sent by mail to all patients and replied to the CRO for documentation in the e-CRF.

9.5.3 Data transferred from NIV devices

All ResMed devices to be used for NIV therapy within this study (refer to Annex 1, 3.) are CE-certified, marketed devices. All are used for NIV treatment in line with the corresponding instruction for use. Tele-monitoring data of the devices will be sent remotely to a central tele-monitoring server managed by an independent certified health data hosting service provider, located in France. Pre-defined technical and usage monitoring data will subsequently be transferred to the CRO as coded (pseudonymised) data for scientific analysis together with data derived from the e-CRF.

Tele-monitoring data of study patients are recorded and transferred to a central server located in France as part of routine clinical care settings. Treating physicians have in routine clinical care secured access to a web platform provided by the manufacturer of the NIV devices which reports in dashboards and other report formats usage and technical data of the corresponding patients on NIV therapy to be used for monitoring and individual management of the out-hospital patients.

9.6 Study size

A total of about 550 patients will be enrolled across Europe, out of which 231 patients have already been enrolled in the phase 1 of the study.

About 25 NIV expert centres in several European countries, e.g. Germany, Spain, UK are expected to participate in the study. In addition, data of comparable patients included by NIV expert centres in France in the “Cohorte de l'ANTADIR” (ANTADIR registry) will be used for joined analysis.

9.7 Data management

Study and site management as well as data cleaning, data management and statistical analysis was delegated by the sponsor to CRI – The Clinical Research Institute, Munich, Germany, as responsible CRO.

Applicable national and international legal requirements for data handling and data archiving will be met. All data will be collected using the web-based MARVIN system, a GCP and 21 CFR 11 compliant EDC and CTMS software based on CDISC data standards. Medical data within this study will be recorded directly in the e-CRF at the site without use of paper documents. The e-CRF system is available for all participants in the study 24 hours/7 days during the course of the study. After closure of the study, all participating sites will be provided media with PDFs of all e-CRF data ever entered in the corresponding site together with all related metadata (e. g. audit trail, data queries).

9.7.1 Electronic case reporting form

The e-CRF has been approved by the Steering Committee. It is identical for each country and is provided in local language. Data will also be collected about the site itself (e.g. type of institution and other administrative data), and basic, pooled details about their patients to allow for control of selection bias.

9.7.2 Personal Data and Data Protection

All data obtained in the context of this clinical study are subject to data protection. The storage of data for statistical assessment shall likewise be performed only under the patient’s study number. Only adequate staff members in each site can assign identifiers to personal data. If personal data are stored and processed, requirements for data protection will be followed. The study database is centrally stored on redundant servers in Germany provided by the e-CRF system vendor.

All recorded data will be pseudonymised for storage in the central database during the course of the study. As the decoding information is held only by the treating study sites, nobody else will know the identity of the participating subjects. After the end of the project, the data will be anonymised, deleted from the vendor’s servers and transferred to the sponsor where it will be stored for ten years.

Data will only be collected and processed to reach the goals of the study. Personal data of the patient are demographic data (e.g. height, weight, data on comorbidities, data on current medication intake), data on quality of life (section 9.5.2), serious adverse events (section 11) and therapy data (section 9.5.3). Data will be transferred to the CRO (database management, questionnaire data entry, data analysis), to ResMed subsidiaries within the EU and to the scientific Steering Committee.

The patient will be informed about the study and her/his rights in terms of data usage, data storage, correction of data and deletion of stored data.

9.7.3 Completion of Case Report Forms

All medical data in this study will be recorded directly in the e-CRFs without the use of paper documents. The investigator must ensure the accuracy, completeness, legibility and timeliness of data reported in the e-CRF and of all required clinical reports (e. g. in case of SAEs). Any change or correction to a data in the e-CRF must be explained as a prerequisite of the e-CRF system. Any change or correction to an e-CRF item will automatically be tracked (audit trail), recording the person logged-in as well as the time stamp of the change and the reason for change. The e-CRF system will not accept changes without given reason. The history of changes to a single item including original entries is always visible to the responsible local research team and to the CRO. Data reported in the e-CRF that are derived from source documents should be consistent with the source documents or existing discrepancies should be explained. After completion of a patient visit, the investigator should agree to have correctly completed by electronically signing the corresponding parts of the e-CRF. Upon entry into the e-CRF the data will be automatically stored in the central study database in pseudonymised form.

9.8 Data analysis

Data from all sites will be pooled for analysis. Standard statistical methods will be used to analyse all data. Continuous variables will be summarised using the number of observations, mean, median, standard deviation, minimum and maximum values. Categorical variables will be summarised using the number of observations and percentages. Two-sided, 95% confidence intervals will be used to characterise the major parameters. Demographic variables will be tabulated and summarised using descriptive statistics.

A separate Statistical Analysis Plan (SAP) will be prepared by the CRO and approved by the sponsor prior to the start of data analysis, detailing the statistical analysis methods that will be used.

9.9 Quality control

Quality control is defined as the operational techniques and activities undertaken within the quality assurance system to verify that the requirements for quality of the study-related activities have been fulfilled. Quality control should be applied to each stage of data handling to ensure that all data are reliable and have been processed correctly.

A site initiation visit will be performed by the sponsor when a new site joins the study.

Quality assurance is defined as the planned and systematic actions that are established to ensure that the study is performed, and the data generated, documented (recorded) and reported, in compliance with Good Clinical Practice (GCP) and the applicable regulatory requirements.

9.9.1 Source Data

Source data are defined as all information obtained in clinical routine care and stored in original records and certified copies of original records of clinical findings, observations or other activities in a clinical study necessary for the reconstruction and evaluation of the study. Source data are contained in source documents (original records or certified copies).

9.9.2 Source Documents

Source documents are defined as original documents, data and records in clinical routine care (e.g. hospital records, clinical and office charts, laboratory notes, memoranda or evaluation check lists, pharmacy dispensing records, recorded data from automated instruments, copies or manuscripts certified after verification as being accurate copies, microfiches, photographic negatives, microfilm or magnetic media, x- rays, patient files, records kept at pharmacy, at the laboratories and at medico technical departments).

9.9.3 Access to Source Data/Document

The investigator will permit, and participating subjects will consent for, potential study-related monitoring, audits, Ethics Committee review and regulatory inspections, providing direct access to primary patient data (i.e. source data) that support data in the e-CRFs, i.e. general practice charts, hospital notes, appointment books, original laboratory records, etc. Because this is a patient confidentiality issue, access to such data must form part of the Informed Consent Form to be signed by the patient.

9.9.4 Direct Access

Direct access is defined as the permission to examine, analyse, verify and reproduce any records and reports that are important to the evaluation of a clinical study. No identifiable subject data can be released from a site. Any party (e.g. regulatory authorities, the sponsor and/or authorised representatives of the sponsor such as monitors and auditors) with direct access should take all reasonable precautions within the constraints of the applicable regulatory requirements to maintain the confidentiality of patient identities and sponsor proprietary information.

9.9.5 Audits

An audit is a systematic and independent review of study-related activities and documents to determine whether the validated study-related activities were conducted and the data were recorded, analysed and accurately reported according to the protocol, designated Standard Operating Procedures (SOP), GCP and the applicable regulatory requirements. An independent audit at the site may take place at any time during or after the study.

9.10 Limitations of the research methods

This clinical study is purely observational. All procedures and therapies used within the study are routine clinical care based on individual decisions of the treating physician and are not defined in the study protocol. It is expected that observed variations in diagnosis and treatment of COPD will be larger compared to controlled clinical trials with given standards.

The data of this study represent clinical routine care of COPD patients without limitations normally given by protocol definitions of controlled clinical trials. Thus, the generalisability of results is deemed to be higher compared to those of controlled clinical trials. However, due to the expected larger range of variations in procedures and therapies the level of statistical significance is expected to be smaller but allowing for generation of hypotheses which might be investigated in subsequent clinical research projects.

9.11 Other aspects

This clinical study is industry funded and solely financed by the sponsor. The costs necessary to perform the study, i.e. to reimburse the time spent by site staff for documentation work, will be agreed upon with each study site and will be documented in a separate financial agreement which will be signed by the investigator and the CRO on behalf of the sponsor, prior to the study commencing.

10. Protection of human subjects

This clinical study is purely observational. No risks or benefits compared to routine clinical care will be added because all therapeutic decisions and procedures are performed in routine clinical care following all applicable medical guidelines, local policies, and ethical and regulatory standards. The study will be conducted in accordance with the principles laid down in the Declaration of Helsinki in its version of October 2013 (Fortaleza) and in accordance with ISO 14155:2011.

Before initiating the study at a site, approval of the corresponding Ethics Committees will be obtained.

11. Management and reporting of Adverse Events/Adverse Reactions

All Serious Adverse Events (SAEs) will be documented according to ISO 14155 and reported in accordance with applicable national standards. Since the study design is observational, all therapies and procedures are routine clinical care and in line with applicable medical guidelines, market authorisations and corresponding Instructions For Use (IFUs). Since no risks or benefits compared to routine clinical care will be added, the rate of non-serious adverse events (AEs) will be identical to routine clinical care, thus, AEs will not be documented within this study.

Definitions

Adverse Event (AE):

Any untoward medical occurrence in a subject. This includes any undesired symptom, sign, illness, or experience, which develops or worsens in severity and/or frequency during the course of the study (i.e. any undesired change from baseline).

Serious Adverse Event (SAE):

According to ISO 14155, SAE is an adverse event that has resulted in any of the following consequences or could result in the following consequences:

- Death
- A serious deterioration in the health of the subject that
  - resulted in a life-threatening illness or injury,
  - resulted in a permanent impairment of a body structure or a body function,
  - required in-patient hospitalisation or prolongation of existing hospitalisation,
  - resulted in medical or surgical intervention to prevent permanent impairment to a body structure or a body function
- Fetal distress, fetal death or a congenital abnormality or birth defect
- Any other medically important event

Medically important event

Medical and scientific judgement should be exercised in deciding whether other situations should be considered as serious reactions. Some medical events may jeopardise the subject or may require an intervention to prevent one of the above characteristics/consequences. Such important medical events should be considered as serious.

Life-threatening

The definition of an SAE refers to an event in which the patient was at risk of death at the time of the event. It does not refer to an event which hypothetically might have caused death if it was more severe.

Hospitalisation

- **Hospitalisation** is within this protocol defined as inpatient care of more than one calendar day (overnight stay) for any cause. Overnight survey visits (e.g. sleep lab) are not considered "hospitalisation".
- **Unplanned hospitalisation** is within this protocol defined as ill-defined hospital admissions in acute inpatient medical settings for any cause for more than one calendar day (overnight stay) where managing demand for unplanned admissions is a priority [13].
- **COPD-caused hospitalisation** is within this protocol defined as COPD exacerbation leading to hospitalisation as defined above.
- **COPD exacerbation** is defined as an acute worsening of respiratory symptoms that results in additional therapy with systemic steroids and / or antibiotics [14].

The investigator will document in the e-CRF each hospitalisation of study patients including a statement if he classifies it as "unplanned" and as "COPD-caused". As second source of information, patients will be asked to report hospitalisations and other potential SAEs every six months of follow-up using a short questionnaire (refer to 9.3.6).

Because hospitalisation decisions might be subject to local practices, social considerations, bed availability, and so on, all hospitalisations will be reviewed by an independent Endpoint Review Committee (ERC) based on coded (pseudonomysed) copies of corresponding medical files to assess the reason and appropriateness of each hospitalisation, i.e. whether it is "unplanned" and "COPD-caused".

Adverse Device Effect (ADE)

Any untoward and unintended response to a medical device. This includes any event resulting from insufficiencies or inadequacies in the instructions for use or the deployment of the device.

Serious Adverse Device Effect (SADE)

Adverse Device Effect that has resulted in any of the consequences characteristic of a Serious Adverse Event or that might have led to any of these consequences if suitable action had not been taken or intervention had not been made or if circumstances had been less opportune.

Unexpected Serious Adverse Device Effects (USADEs)

Are defined as any Serious Adverse Effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

Medical judgment should be exercised in deciding whether an AE/ADE is serious in other situations. Important AE/ADE that are not immediately life-threatening or do not result in death or unplanned hospitalisation of a planned hospitalisation but may jeopardise the patient or may require intervention to prevent one of the other outcomes listed in the definition above, should also be considered serious.

11.1 Recording and reporting Adverse Events/Adverse Device Effects

The investigator shall report in detail all serious adverse events (SAEs) and device deficiencies that could have led to serious adverse device effect. The investigator shall document any SAE in the e-CRF in the “SAE visit”. All items of the form should be filled in adequately and promptly.

The investigator should not wait to receive further information before reporting such an event. The initial report should carefully be followed until the event is resolved.

The sponsor of the study is responsible for reporting of Adverse Events/Adverse Device Effects to regulatory bodies according to his duties in routine clinical care.

12. Plans for disseminating and communicating study results

12.1 Publication policy

Study results will be pooled across all participating sites for the purpose of publication that will be coordinated by the sponsor. Preparation of the comprehensive publication will occur at the completion of the study, but the sponsor may, at its discretion, coordinate an additional, interim publication. The order of authorship will be determined by the sponsor and will be based in part on the number of qualified and completing subjects at each site.

An investigator intending to publish results of the study must provide the sponsor with a copy of any proposed publication, abstract, or presentation at least 60 days prior to submission for publication or presentation. The sponsor will have the right to object to the publication, abstract, or presentation if, in the sponsor’s reasonable opinion, such publication (i) contains confidential information; or (ii) will adversely affect any intellectual property or proprietary right of the sponsor. In the event of an objection by the sponsor, the investigator must either modify or delay the publication, abstract, or presentation for a period requested by sponsor not to exceed ninety (90) days to permit the sponsor to re-dress or mitigate risks.

Investigators and sites must acknowledge the sponsor in all publications or presentations resulting from this study and provide any required disclosures.

All relevant measures for transparency of clinical studies, and especially the recommendations of the editors of the major medical journals, will be met.

13. References

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Annex 1. **List of stand-alone documents**

Number	**Title**
1	Item list of e-CRF
2	List of participating investigators
3	List of adequate ResMed NIV therapy devices
4	Follow-up questionnaire (patient questionnaire on events and hospitalisations)

Annex 2. **SRI questionnaire**

Only sample – the form to be used throughout the study will be made available as a separate document.

Severe Respiratory Insufficiency Questionnaire

SRI

General Health Questionnaire for patients with Severe Respiratory Insufficiency

Dear patient!

We are treating you for your respiratory disorder. Please fill in this questionnaire so that we can assess your current state of general health. Please answer every question by marking the appropriate answer once with a cross. Participation is, of course, voluntary. All data is bound by the rules of patient/doctor confidentiality and will be treated in strict confidence. Your attending physician will be pleased to answer any questions you may have.

☐ Inclusion Visit ☐ FU Visit

HOmeVent Connect Centre-ID: _____ Patient-ID: |_|_|_|_|

☐ Inclusion Visit
☐ FU Visit

SRI

Centre-ID: _____
Patient-ID: |_|_|_|_|

The following question relate to your general condition. You will see statements related to various aspects of daily life.

How did you feel ***last week?*** For EVERY statement please mark the answer that best applies to you.

	completely untrue - 2	mostly untrue - 1	sometimes true 0	mostly true 1	always true 2
1. I find it difficult to climb stairs.	- 2	- 1	0	1	2
2. I suffer from breathing problems when I eat.	- 2	- 1	0	1	2
3. I can go out in the evening.	- 2	- 1	0	1	2
4. I often feel miserable.	- 2	- 1	0	1	2
5. I suffer from breathing problems even without physical exertion.	- 2	- 1	0	1	2
6. I often have a headache.	- 2	- 1	0	1	2
7. I have many friends and acquaintances.	- 2	- 1	0	1	2
8. I worry that my illness might worsen.	- 2	- 1	0	1	2
9. I go to sleep easily.	- 2	- 1	0	1	2
10. I can deal with other people easily.	- 2	- 1	0	1	2
11. I sometimes feel dizzy.	- 2	- 1	0	1	2
12. I wake up at night with breathing difficulties.	- 2	- 1	0	1	2
13. I am afraid of having breathing difficulties at night.	- 2	- 1	0	1	2
14. I often have neck pain.	- 2	- 1	0	1	2
15. I am largely confined to the house.	- 2	- 1	0	1	2
16. Housework is difficult for me.	- 2	- 1	0	1	2

☐ Inclusion Visit
☐ FU Visit

SRI

Centre-ID: _____
Patient-ID: |_|_|_|_|

How did you feel ***last week?*** For EVERY statement please mark the answer that best applies to you.

	completely untrue - 2	mostly untrue - 1	sometimes true 0	mostly true 1	always true 2
17. I often wake up at night.	- 2	- 1	0	1	2
18. I sleep through the night easily.	- 2	- 1	0	1	2
19. I am often short of breath.	- 2	- 1	0	1	2
20. I am optimistic about the future.	- 2	- 1	0	1	2
21. I feel lonely.	- 2	- 1	0	1	2
22. I have trouble breathing when I speak.	- 2	- 1	0	1	2
23. Visitors exhaust me.	- 2	- 1	0	1	2
24. I cough a lot.	- 2	- 1	0	1	2
25. There is often mucus in my airways.	- 2	- 1	0	1	2
26. I avoid situations where my breathing problems might embarrass me.	- 2	- 1	0	1	2
27. I feel good when I am with friends/ acquaintances.	- 2	- 1	0	1	2
28. I am afraid of having a bout of difficult breathing.	- 2	- 1	0	1	2
29. I have difficulties breathing during physical exertion.	- 2	- 1	0	1	2
30. I am irritated by the limitations caused by my illness.	- 2	- 1	0	1	2
31. My marriage/relationship is suffering because of my illness.	- 2	- 1	0	1	2
32. I can go shopping.	- 2	- 1	0	1	2
33. I can pursue all hobbies that interest me.	- 2	- 1	0	1	2

☐ Inclusion Visit
☐ FU Visit

SRI

Centre-ID: _____
Patient-ID: |_|_|_|_|

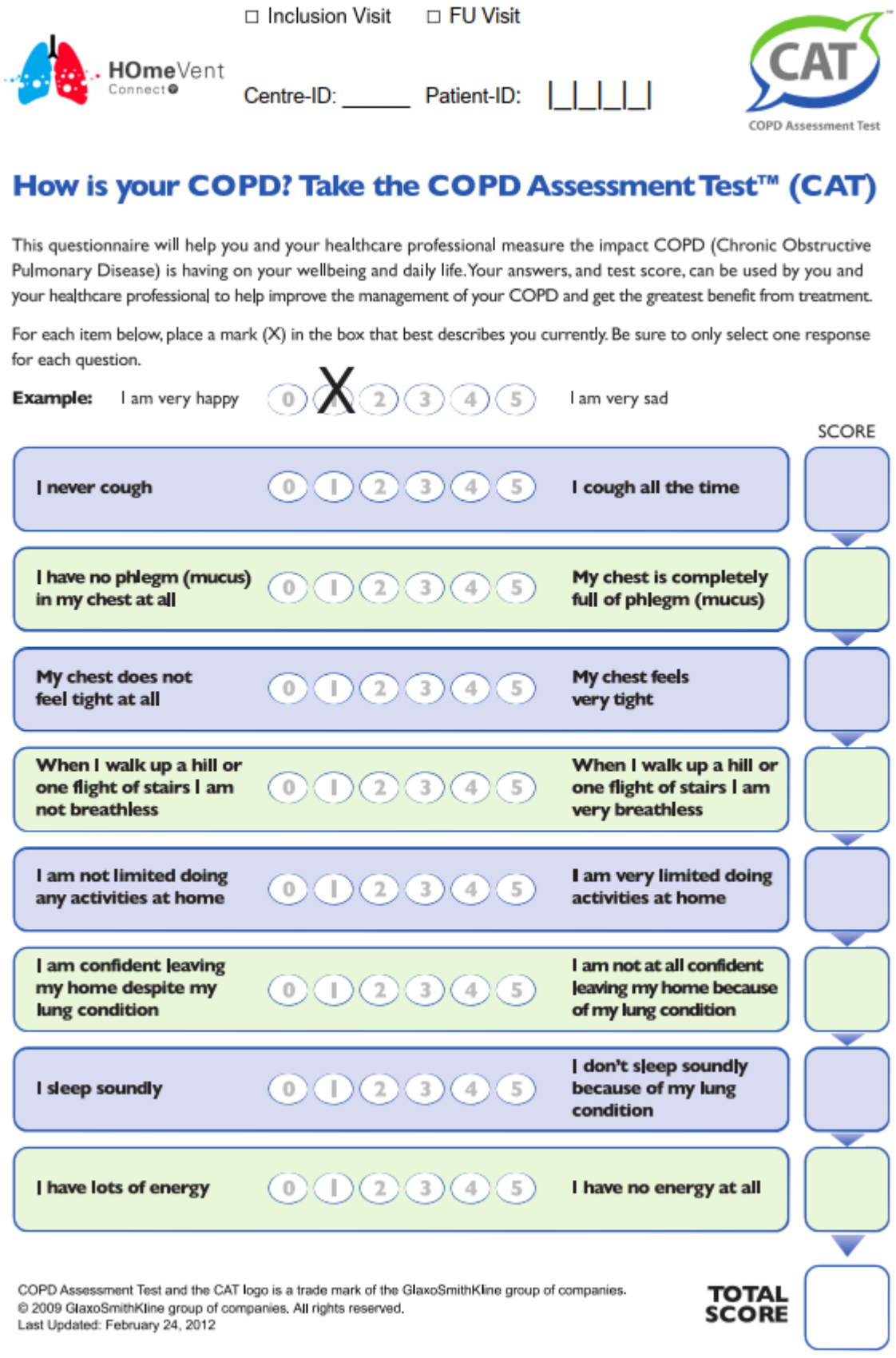
How did you feel ***last week?*** For EVERY statement please mark the answer that best applies to you.

	completely untrue - 2	mostly untrue - 1	sometimes true 0	mostly true 1	always true 2
34. I am often irritable.	- 2	- 1	0	1	2
35. My contact with friends/acquaintances is limited by my illness.	- 2	- 1	0	1	2
36. I am enjoying life.	- 2	- 1	0	1	2
37. I can take part in social events.	- 2	- 1	0	1	2
38. I am often sad.	- 2	- 1	0	1	2
39. My breathing difficulties bother me in public situations.	- 2	- 1	0	1	2
40. I am often nervous.	- 2	- 1	0	1	2
41. I can dress myself.	- 2	- 1	0	1	2
42. I am tired during the day.	- 2	- 1	0	1	2
43. I feel isolated.	- 2	- 1	0	1	2
44. I can cope well with my illness.	- 2	- 1	0	1	2
45. My breathing difficulties impair me in everyday activities.	- 2	- 1	0	1	2
46. My family life is suffering because of my illness.	- 2	- 1	0	1	2
47. I have broken off contact to other people because of my breathing problems.	- 2	- 1	0	1	2
48. My free-time opportunities are limited.	- 2	- 1	0	1	2
49. I am satisfied with life in general.	- 2	- 1	0	1	2

Thank you!

Annex 3. **CAT questionnaire**

Only sample – the form to be used throughout the study will be made available as a separate document.



☐ Inclusion Visit ☐ FU Visit

HOmeVent Connect

Centre-ID: _____ Patient-ID: |_|_|_|_|

CAT COPD Assessment Test

How is your COPD? Take the COPD Assessment Test™ (CAT)

This questionnaire will help you and your healthcare professional measure the impact COPD (Chronic Obstructive Pulmonary Disease) is having on your wellbeing and daily life. Your answers, and test score, can be used by you and your healthcare professional to help improve the management of your COPD and get the greatest benefit from treatment.

For each item below, place a mark (X) in the box that best describes you currently. Be sure to only select one response for each question.

Example: I am very happy 0 X 2 3 4 5 I am very sad

			SCORE
I never cough	0 1 2 3 4 5	**I cough all the time**	
I have no phlegm (mucus) in my chest at all	0 1 2 3 4 5	**My chest is completely full of phlegm (mucus)**	
My chest does not feel tight at all	0 1 2 3 4 5	**My chest feels very tight**	
When I walk up a hill or one flight of stairs I am not breathless	0 1 2 3 4 5	**When I walk up a hill or one flight of stairs I am very breathless**	
I am not limited doing any activities at home	0 1 2 3 4 5	**I am very limited doing activities at home**	
I am confident leaving my home despite my lung condition	0 1 2 3 4 5	**I am not at all confident leaving my home because of my lung condition**	
I sleep soundly	0 1 2 3 4 5	**I don't sleep soundly because of my lung condition**	
I have lots of energy	0 1 2 3 4 5	**I have no energy at all**	

TOTAL SCORE