Non-Interventional Study Protocol	
Drug Substance	NA
Study Code	NIS-RSE-DUM-2010/1
Edition Number	1.0
Date	[redacted]

A Retrospective Epidemiological Study to map out patients with Chronic Obstructive Pulmonary Disease (COPD) and Describe COPD health care in Real-Life Primary Care during the first ten years of the 21th century - PATHOS

Sponsor:

AstraZeneca Nordic
[redacted]

The following Amendment(s) and Administrative Changes have been made to this protocol since the date of preparation:

Amendment No.	**Date of Amendment**	**Local Amendment No:**	**Date of Local Amendment**

Administrative Change No.	**Date of Administrative Change**	**Local Administrative Change No.**	**Date of Local Administrative Change**

PROTOCOL SYNOPSIS

A Retrospective Epidemiological Study to map out patients with Chronic Obstructive Pulmonary Disease (COPD) and Describe COPD health care in Real-Life Primary Care during the first ten years of the 21th century - PATHOS

Investigators

[redacted]

Objective

The objective of the study is two-fold:

- To describe the development of the COPD health care structure in a primary care setting and,
- To describe the COPD population in primary care with special reference to treatment, co-morbidity and mortality during last decade.

Study Design

This is a retrospective epidemiological study to map out patients with COPD and describe COPD health care in real-life primary care during the first ten years of the 21th century. Data will be extracted anonymously from electronic patient journals in primary care. In addition, data regarding morbidity and mortality will be collected from the Hospital Discharge Register (Slutenvårdsregistret) and the Cause of Death Register respectively and information on prescribed drugs will be collected from the Prescription Register. The merging of data will be performed by the National Board of Health and Welfare.

Study population and inclusion criteria

The population will consist of adult patients diagnosed with Chronic Obstructive Pulmonary Disease.

Number of patients planned

All COPD patients from approximately 60 primary care centers, estimated to approximately 18.000 patients.

Assessments

Through use of patient unique identifiers the following data will be registered:

- COPD disease from medical records and the national registers.
- Admittances, discharges and deaths from the national registers.
- Prescriptions of drugs from medical records and the national registers.
- Lungfunction assessments from medical records.
- Health care consumption (assessed as contacts with primary care center, in-hospital time periods for COPD (e.g. Intensive Care Unit and General Ward) and pharmacological treatment).
- As available in medical records, information on COPD rehabilitation, smoking status/cessation and employment status.

Structure

Size of population in catchment area, availability of spirometer and smoking cessation program and Asthma/COPD nurse and physician, will be assessed by a questionnaire that will be answered by each participating centre.

Statistical methods

Events will be analyzed with survival methods (Cox regression models, Kaplan-Meier curves). Costs of healthcare resource utilization will be estimated through models incorporating unit costs.

Statement of Compliance

This study will be performed in accordance with the ethical principles that are consistent with the Declaration of Helsinki, ICH GCPs and the applicable legislation on Non-Interventional studies.

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STUDY ADMINISTRATION

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1 BACKGROUND INFORMATION AND SCIENTIFIC RATIONALE

1.1 Background

Chronic Obstructive Pulmonary Disease (COPD) is a chronic slowly progressive disorder characterized by airflow limitation, reduced FEV_1 and FEV_1/FVC ratio. Most of the lung function impairment is fixed, although some reversibility can be produced by bronchodilator and/or other therapy. The chronic airflow limitation characteristic of COPD is caused by a mixture of small airway disease (obstructive bronchiolitis) and parenchyma destruction (emphysema), the relative contributions of which vary from person to person.

COPD is a major cause of chronic morbidity and mortality throughout the world. Many people suffer from this disease for years and die prematurely from it or its complications (1). COPD is the fourth greatest cause of death, according to estimates of World Health Organization (WHO) and an important source of disability (2). The prevalence of COPD is 8% in a Swedish population above 50 years of age (3).

Even though we know much about underlying pathology and treatment, the “best practice” and the most effective COPD management is under debate. Today, there are different health care approaches available and the therapy comprises several medications e.g. short- and long-acting beta-agonist, anti-cholinergics, mucolytics and inhaled corticosteroids. In the last ten years combined treatment options i.e. fixed combination of ICS and LABA, has become also more widely used.

In 2004 the Swedish National Board of Health and Welfare published national guidelines for treatment of asthma and COPD (3). In this guideline there is a discussion about prioritization and quality assurance in the disease management and care of patients with asthma and COPD.

Patients with moderate-severe COPD account for more than 80% of the total healthcare cost of COPD due to the propensity for repeated acute exacerbations leading to hospitalizations (4).

It is the responsibility of the Primary care to diagnose, treat and follow-up patients with asthma and COPD. Astma/COPD nurse practice (ACP), were the nurse has adequate time for consultations, increases the opportunity to offer high standard care for Asthma/COPD patients.

The aim of this study is to describe COPD health care and to assess demographics, co-morbidity and mortality and the use of pharmaceuticals for a COPD population in real life in primary care during the last ten years.

1.2 Rationale for performing the study

- The development of treatment in relation to different outcomes for the COPD population in real life during the last ten years has never been studied before
- Describe the development of the COPD health care structure in a primary care setting
- Describe the COPD population in primary care
- Describe COPD co-morbidity and mortality
- Provide information about use of pharmacological therapy

2 OBJECTIVE

The objective of the study is two-fold;

- To describe the development of COPD health care structure in primary care and,
- To describe the COPD population in primary care with special reference to co-morbidity, mortality and pharmacological treatment during last decade

3 STUDY DESIGN

3.1 Design

This is a retrospective epidemiological study to map out patients with COPD and describe COPD health care in real-life primary care. Data will be extracted from medical records and from national health registers, see below. Additionally, each participating site will answer one questionnaire regarding their health care structure.

3.2 Data collection method

3.2.1 Data on primary care centers structure

The following data will be collected by a questionnaire answered by participating primary care centers covering each year of the study:

- Size of the population in the catchments area of the primary care centre
- Availability of asthma/COPD physician
- Availability of asthma/COPD nurse
- Number of hours allocated per week for the asthma/COPD nurse

- Availability of spirometer
- Availability of smoking cessation program

3.2.2 Patient journals at primary care centres

Data from electronic patient journals enables the detailed assessment of:

- Date of birth and gender
- Diagnoses (ICD-10 codes)
- Number of patient contacts with the primary care centre
- Lungfunction assessments
- Drug prescriptions (date, drug name and ATC-code, strengths, dosage, number of iterations)
- As available in medical records, information on COPD rehabilitation, smoking status/cessation and employment status

The software program Pygargus Customized eXtraction Program (CXP) will be used to extract the patient data from the electronic patient journals of the participating primary care centres for all patients with a diagnosis of COPD (ICD 10: J44) and/or prescription of drug within the ATC class R03 (pharmaceuticals for obstructive lung diseases). The social security number of identified patients will immediately be replaced with a study ID-number for further processing of data. The key file linking the study ID-number and social security number will be stored in a locked safe by the principal investigator.

The Swedish National Board of Health and Welfare will perform the merging of data from primary care and hospital registers. No identification of patients is made elsewhere.

3.2.3 National registers

3.2.3.1 Data from the Cause of Death Register

The following data will be extracted:

- Date of death
- Underlying cause of death
- Multiple causes of death

3.2.3.2 Data from the Hospital Discharge Register

The following data will be extracted:

- Date of admission and discharge
- Main diagnosis
- Secondary diagnoses
- DRG-codes set by the discharge hospital

3.2.3.3 Data from the Prescription Register

The following data will be extracted:

- Date of prescriptions
- Type of drug
- Strength

4 STUDY POPULATION

Eligible subjects are all COPD patients, found in medical records at the participating centres. Primarily patients with diagnosis code J44 (ICD-10) stated in the medical record will be investigated. Patient data from the period [redacted] will be included in the observation.

4.1 Inclusion criteria

COPD diagnosis according to medical record.

4.2 Exclusion criteria

None.

5 DATA SOURCES

5.1 Primary Care Centers

Approximately 60 primary care centers will participate in this study. This selection is estimated to be a representative sample reflecting the targeted COPD population and the COPD health care. If necessary to ascertain sufficient data, the number of centers can be increased during the sampling period.

5.2 Lung function

In this study the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines (5) will be used to classify the severity of COPD.

Lung function data from any source within the electronic patient electronic journal can be incorporated in the source data set.

5.3 Health care consumption

Health care consumtion will be assessed as contacts with primary care center, in-hospital time periods for COPD (e.g. Intensive Care Unit and General Ward) and pharmacological treatment.

5.4 Health care provider contacts

Contacts will be recorded for the complete observable period for each patient. Out of hospital contacts will only be obtained from primary care centre records. Outpatient contacts with hospitals will not be part of the source data set.

5.4.1 Primary care centre contacts

These will be recorded as number of contacts without recording time duration of the visit.

5.4.2 Hospital contacts

These will be recorded as time variables defined from the time point of admission to a ward until the time for discharge the same ward. A hospital stay is defined from admission to discharge from in-hospital care, either to home, to living at facilities outside the regional hospital system (e.g. community care and homes for retired people) or discharged as dead. A series of contiguous admissions and discharges to and from different hospital care givers will thus represent one single hospital stay, but several admission – discharge periods. Each such period will be associated with level of care of the ward in question.

5.5 Diagnoses, events and therapeutic interventions

Classification of diseases will, when incorporating diagnoses, be according to ICD-10.

6 STATISTICAL METHODS

6.1 Number of patients

With a COPD prevalence of 3% and a catchments area of approximately 10.000 persons, the number of patients is estimated to be approximately 18,000. The sample size is considered large enough to be representative for the COPD population in a primary care setting.

6.2 Descriptive statistics

Continuous and nominal variables will be described using standard statistical measures, i.e. number of observations, number of missing observations, mean, standard deviation, minimum and maximum value, median, 1st and 3rd quartile.

All categorical variables will be summarized with absolute and relative frequencies.
Time differences will have a resolution of one 24-hour day.

6.3 Survival analyses

All endpoints will be analyzed with methods for survival data (Cox regression models, Kaplan-Meier estimates).

It can be assumed that treatment groups will show unbalanced baseline characteristics.

To adjust for differences in baseline variables methods allowing for adjustment of Confounders or propensity-matching technique (5) will be used.

The adjustment of confounders will be done as follows. Univariate regression analyses of all confounders will be performed. All confounders with a p-value of 0.10 or less in the univariate analysis comparing the groups at baseline will be considered for inclusion in the multivariate regression model. The final multivariate models will include variables or interactions with p-values of 0.05 or less.

Variables of medical importance for the outcome will be included in the propensity matching technique.

Costs of healthcare resource utilization will be estimated through models incorporating unit costs, level of care, age, gender and study year.

Differences in health care consumption will be estimated through models incorporating normalised costs, level of care, age, gender and study year.

7 Ethical Conduct

This study will be performed in accordance with the ethical principles that are consistent with the Declaration of Helsinki, ICH GCPs and the applicable legislation on Non-Interventional studies.

7.1 Ethics review

The final protocol of this study must be approved or given a fabourable opinion in writing by the Ethics Committee. The Ethics Committee must also approve any amendment to the protocol.

7.2 Informed Consent

Normally, informed consent is needed when either the research imposes a risk for patients or the study requires data containing personal identifiers. Studies conducted entirely using administrative databases and which do not use any personal identifiers may require only abbreviated review or may not require formal review at the discretion of the Ethics Committee.

7.3 Patient anonymity

All data regarding the same patient will be collected using the personal identification number (personnummer). Investigators will ensure that personal identifiers will be removed from any study files that are accessible to non-study personnel in accordance with applicable laws and regulations. All personnel with access to data containing personal identifiers will sign a pledge to maintain the confidentially of study subjects, and will maintain an ability to verify the origin and integrity of data sets from which personal identifiers have been removed.

7.4 Protocol amendments

Any modification to the agreed protocol must be approved in writing by the Sponsor and the involved investigator(s).

The involvement of a new study centre, even after study start, will not be considered per se as a protocol modification requiring an amendment because it is part of the planned study procedures.

8 REPORTING AND PUBLISHING

AstraZeneca will ensure analysis and report of all data as described in the protocol. Authorship will be according to the principal criteria for eligibility that are detailed in the Uniform Requirements for Submission of Manuscripts to Biomedical Journals (ICMJE, 5th Edition, 1997).

9 TIMELINES

First data collection: March 2010

Last data collection: May 2010

Database lock: August 2010

Study Report: December 2010

10 REFERENCES

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4. Nationella vårdprogrammet. Version updated Sept.9, 2005. Available from http://www.slmf.se/kol/.
5. Global Initiative for Chronic Obstructive Lung Disease (GOLD): Global strategy for the diagnosis, management and prevention of chronic obstructive pulmonary disease. Version updated Sept. 2005. Available from http:// www.goldcopd.com
6. Lori S. Parsons, Ovation Research Group, Seattle, WA. Reducing Bias in a Propensity Score Matched-Pair Sample Using Greedy Matching Techniques. SUGI 26: Paper 214-26

11 SIGNATURES

The signature below constitutes the approval of this protocol and appendices.

Principal Investigator:

_____ Date:_____
[redacted]

Sponsor's project manager:

_____ Date:_____
[redacted]

Biostatistician:

_____ Date:_____
[redacted]