Statistical analysis plan

Increase Level of Physical Activity and Decrease Use of Health Care for People With COPD

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Revision of Statistical analysis plan

Revisions in SAP v1.0

Revisions compared to previously described statistical analysis plan, published in the study protocol in BMJ Open.(1)

Due to the COVID-19 pandemic, the recruitment and retention of participants to the COPD Web RCT have not proceeded as planned. Recruitment through healthcare centres was almost stopped due to the pandemic, why an ethical amendment was search for and approved (Dnr 2019-05572).

The amendment made recruitment possible through advertisement in newspapers and the Internet. Another issue is the high dropout rates and many participants has raised the effects of the pandemic as a reason for not continuing in the study. We included the aimed number of participants (144) but instead of the expected 20% dropout, we ended up with approximately 30% dropout at 3 months.

- The primary statistical analysis has been changed from a mixed effects models to an ANCOVA analysis at 3 months follow-up, adjusting. In this analysis we will use age and sex as co-variates for the physical activity level.(2): The motivation to change to 3-months as primary analysis is the larger than expected dropout rate. The adjustments of age and sex is intended to increase power and precision in treatment effect estimates, as they are considered predictive covariates for outcome.

- For evaluation of the effect at 12 months follow-up we will use mixed model repeated measures, incorporating the measurements at baseline and 3-months follow-up. However, the model will not include random effects of subjects and primary health care units. Instead, repeated measurements will be modelled using an unstructured covariance matrix for the error terms. The updated model is motivated partly by that data on primary health care units is not available and partly that the new model will be more robust against misspecification, if model assumptions is found not fulfilled.

Content

Introduction

The use of adequate self-management strategies for people with chronic obstructive pulmonary disease (COPD) may increase the level of physical activity, improve health related quality of life and reduce health-care use. Whether web-based support, in addition to prompts (e-mail and SMS), could be used to promote self-management strategies to facilitate behaviour change in people with COPD is not clear.

Objectives

This clinical trial aims to generate evidence on the effect of a web-based solution, the COPD-web, in a cohort of people with COPD in primary healthcare context.

Outcomes

Primary outcome:

Physical activity (PA) level measured objectively (steps/day measured with DynaPort, McRoberts) and subjectively (questionnaire from the Swedish National Board of Health and Welfare).

Secondary outcomes:

Health-related quality of life measured with self-administered Chronic Respiratory Questionnaire (CRQ-SA)

COPD-related symptoms measured with COPD Assessment Test (CAT)

Dyspnea measured with modified Medical Research Council Dyspnea scale (mMRC)

Self-reported health-care contacts related to COPD.

Sample size calculation

The sample size was calculated with the premises that a total of 144 participants with COPD would be required to detect a mean difference of 1131 steps with a standard deviation of 2193 steps(3), α = 0.05, β = 0.20 (80% power), and a two-tailed test of significance including an estimated dropout rate of 20%.(4)

Randomisation and masking

A permuted block design with a random block size varying from 4 to 8 in a 1:1 allocation ratio will be computer generated to randomise participants. This approach is chosen to achieve balanced and evenly distributed samples. A third party, not involved in data collection or analysis of the results, will perform the randomisation and the result will be stored in sealed envelopes. Due to the character of the intervention, blinding of trial participants will not be applicable. Furthermore, as all data are self-reported, neither is blinding of outcome assessors applicable.

Data management and monitoring

To ensure confidentiality, participants with COPD will get a unique identification (ID) when included in the study. The code list linking participants and ID number will be kept separate from the data. Data will be analysed by ID only. All records that contain names or other personal identifiers, such as locator forms and informed consent forms, will be stored separately from study records identified by the ID number. The local database will be secured with a password-protected access system. All data will be coded and reported on group level. Thus it will not be possible to identify specific participants in the trial. We will use two-pass verification to ensure correct data entry. No interim analyses or stopping guidelines are pre-specified. Only the researchers will have access to the final trial dataset.

Statistics and analysis

Analysis population

The primary analysis will be an intention-to-treat analysis (including all participants randomised). In addition, a complete case population (participants with full outcome measurements independent on adherence to intervention), and a per-protocol analysis (defined as at least one login besides creating an account on the COPD Web or answering that the SMS and email with referral links have been used at least rarely (1-3 times) at the follow-ups) will be performed. No sub-group or adjusted analyses other than the pre-specified complete case and per-protocol analysis will be performed.

Missing data

Missing data will be imputed in the intention-to-treat analysis using multiple imputation assuming data is missing at random conditional on participants' severity of disease and self-reported history of

exacerbations. This is because the severity of disease and history of exacerbations are known risk factors for future exacerbations and may affect adherence to PA interventions.(5)

Analysis methods at 3 month follow up

The difference in the primary outcome between the intervention and control group will be estimated using an ANCOVA analysis with 3 months follow up as dependent variable, and group (experimental group vs control group) and baseline measurement as independent variables In this analysis we will use age and sex as covariates.

Analysis methods at 12 month follow up

For the analyses of 12 months follow-up, we will use Mixed model repeated measures with an unstructured co-variance matrix for error terms. Fixed effects will be time point (baseline, 3-months or 12 months), group (experimental group vs control group) and a Timepoint*group interaction. To judge the model assumptions of normality, we will analyse model residuals using qq-plots and histograms.

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