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# The impact of a graduated response to advanced COPD with enhanced support (GRACE) on unmet palliative care needs: study protocol for a single-center pilot randomized controlled trial

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# Abstract

Background

Inequality in access to Specialized Palliative Care persists, favoring patients with cancer despite complex needs being evident in many other patient groups, including patients with Chronic Obstructive Pulmonary Disease (COPD). Integrated models aimed at underserved patient populations are needed to rectify this inequality.

Objective

This article describes the protocol for a randomized controlled pilot trial of Graduated Response to Advanced COPD with Enhanced support (GRACE) compared with usual care. The study examines criteria for progression.

Methods

The GRACE intervention comprises systematic identification, ongoing and systematic needs assessment and goal setting, cross-sectoral virtual conferences between a respiratory specialized palliative team and community nurses, and competence development for the clinicians involved. Outcomes of this open-label single-center pilot study include feasibility metrics, quality of life assessed with ICECAP-SCM and SF-12, caregiver burden, cross-sectoral healthcare use, and costs. During the study period, 100 persons will be included. Analyses include mixed models and poisson regression.

Discussion

This study will provide an indication of the effectiveness, feasibility, and mechanisms of the GRACE intervention. The study is explorative and will support the development of hypotheses for further confirmatory evaluation.

**Clinicaltrials.gov ID**: NCT06967324


# 1. Introduction

As the composition of the world population shifts to a larger ratio of older adults than young ones, the healthcare system needs rethinking to continuously ensure the efficiency of funds and personnel (1). The prevalence of people living with chronic and life-threatening illnesses will inevitably increase with longevity and continuing medical advances (1). This is estimated to significantly increase the global need for specialized medical treatment, including palliative care (2).

A palliative care approach is aimed at alleviating physical, psychological, spiritual, or social suffering for patients with life-threatening disease and their families (3). Palliative care services are organized into two levels: general palliative care, conducted by general practitioners, community nurses, and hospital departments that are not dedicated solely to palliative care; and specialized palliative care (SPC),

provided by dedicated hospices and palliative hospital departments (4). SPC is recommended for patients with refractory or complex symptom burdens that are not adequately addressed by other treatment options (4). Historically, SPC has been integrated with oncology, creating well-defined care pathways for patients with cancer but leaving other populations underserved (4) despite clinical justification.

Patients with Chronic Obstructive Pulmonary Disease (COPD) exemplify the inequity in SPC access. COPD is one of the most prevalent diseases worldwide, with more than 200 million cases globally, and accounting for 3.3 million deaths in 2019 alone (5). It is associated with high morbidity, resource utilization, and mortality (6), and patients can experience debilitating symptoms, including severe breathlessness, pain, and persistent cough (6). Patients with COPD are often stigmatized by themselves and society due to the etiology of the illness (7), and they have a high prevalence of comorbid depression and anxiety (8). They often suffer from multimorbidity, and some research shows they have a higher treatment burden than patients with lung cancer, particularly due to fragmented treatment pathways (9). Fragmented healthcare, characterized by disjointed communication and coordination among multiple providers, further exacerbates challenges for patients with complex, life-threatening conditions like COPD. Yet, access to SPC remains limited, with only 5% of those dying with COPD in Denmark receiving SPC before their death in 2024 (10). Care fragmentation results in redundant tests (11, 12), medication overuse (11, 12), communication errors (11, 13), and preventable hospitalizations (12). For patients, this fragmented approach increases treatment burden, undermines continuity of care, and impedes personalized healthcare (11–15).

Integrated care (IC) models offer a solution to these challenges. IC focuses on holistic health needs rather than disease-specific interventions, emphasizing enduring patient-provider relationships and active patient involvement in care decisions (12, 16). Integrated Care interventions often include personalized care plans and transmural collaboration across community, primary, and hospital-based care providers (17), making them particularly compatible with the aims of palliative care. A meta-analysis investigating the effectiveness of transmural team-based palliative care in the prevention of hospitalizations in patients at the end of life showed an effect on lowering hospital admissions and an increase in the number of patients dying at home (18).

Addressing health inequities in palliative care requires the development of cost-effective and sustainable integrated care models tailored to underserved populations, such as patients with COPD. These models must enable systematic referrals to SPC when needed and provide care at the minimum effective intensity, ensuring that all patients with severe illness receive appropriate and person-centered support.

This article describes the protocol for an IC model; a stepped, sector-integrated palliative care intervention titled GRACE - Graduated Response to Advanced COPD with Enhanced Support. The primary aim of this intervention is to assess the feasibility and potential impact of the new GRACE model, compared with usual care, in addressing unmet palliative needs among patients with severe COPD.

## 2. Methods

This protocol has been developed in accordance with the SPIRIT 2025 guidelines. The completed SPIRIT 2025 checklist is provided as Additional File 1, and the SPIRIT figure illustrating the participant timeline is included in the manuscript (19). The study follows the Medical Research Councils framework for complex interventions (20).

# 2.1. Design

This study is a non-blinded, Randomized Controlled Pilot Trial with a 1:1 allocation ratio comparing the GRACE intervention with usual care. The GRACE intervention was developed through an extensive co-production process inspired by the framework outlined by Hawkins et al. 2017 (21), and in collaboration with healthcare professionals from partners in hospital and home nursing. This process is currently being described in a separate publication and includes an organization steering group and an intervention development group, amongst other involvement processes. The same partners will participate in the pilot trial of the GRACE intervention. The model of the intervention was developed to be pragmatic (22), utilizing existing resources, and transferable across regions and settings through local adjustments. The intervention will be assessed in terms of being worthy of progression to a full confirmatory trial. This article will focus on the GRACE intervention protocol.

# 2.2. Setting and usual care

The Danish healthcare system is divided into five geographical regions with a total of 98 municipalities who provide community nursing, rehabilitation and manage long-term care facilities. The trial takes place in one region and is being tested in two out of the regions' 29 municipalities. The two municipalities represent different sizes, with one covering approx. 300.000 citizens and the other 60.000, providing diversity to the intervention's feasibility results. Denmark offers fully tax-funded access to primary and hospital care for all residents, and the trial is in collaboration with Copenhagen University Hospital Hvidovre, covering 600,000 citizens.

Patients with severe COPD in Denmark are usually treated in the respiratory outpatient clinic of their local hospital, and patients with mild or moderate COPD are treated in general practice. Standard care is a yearly checkup. However, if acute exacerbations or other problems occur, the frequency of outpatient visits will be adjusted accordingly. If the patient has been stable for an extended period, they may revert to follow-up with their general practitioner. Patients with respiratory illness are rarely offered specialized palliative care before death. Still, select hospitals do have a respiratory specialized palliative care team consisting of doctors and nurses, operating with limited capacity and sometimes integrated with full specialized palliative care.

Furthermore, some patients with COPD already have contact with community nurses and home care staff who provide support in their daily lives and with their illness.

# 2.3. Participants

The potential participants are elderly patients with severe COPD. They are community-dwelling patients and are being followed at the Outpatient Respiratory Medicine Clinic, Copenhagen University Hospital Hvidovre-Amager. Therefore, their in-charge physician for their respiratory illness is the clinic's specialists. This is an essential prerequisite for the intervention, as it enables collaboration between community nursing and the respiratory specialized palliative care team and is utilized as an indication of more severe COPD due to the natural organization of care, as described previously.

Table 1

*Inclusion and exclusion criteria*

| | | |
|---|---|---|
| **Primary screening – from the electronic patient record** | **Inclusion criteria** | **Exclusion criteria** |
| | **• Aged 65 and above.**<br><br>**• Speaks Danish.**<br><br>**• Cognitively relevant.**<br><br>**• Diagnosis of COPD (ICD10: DJ44*).**<br><br>**• Has had an exacerbation of COPD within the last year.**<br><br>**• Lives in either Høje-Taastrup Municipality or in Copenhagen Municipality (Amager or Valby, Kgs. Enghave and Vesterbro).** | **• Has, within the last 6 months, been in touch with the health system with regard to one or more of the following diagnoses:**<br><br>**o Dementia (ICD10: F00-F03 eller F051)**<br><br>**o Psychotic states (ICD10: F20-F29)**<br><br>**o Mental illness caused by substance abuse (ICD-10: F10-F19)**<br><br>**o Cancer (ICD10: DC01*-DC9***<br><br>**• Enrolled in a similar research project.**<br><br>**• Enrolled in "Tele-COPD" either in the municipality or the hospital.**<br><br>**• Receives specialized palliative care.**<br><br>**• Has a severe hearing or speech impairment.**<br><br>**• Patient is imminently dying.** |
| Secondary individual screening by research staff | • An ICECAP-SCM* score, which indicates palliative care needs. Operationalized as being the following: If the respondent answers one of the following answers to two or more items in ICECAP-SCM:<br><br>1.1, 2<br><br>2.1, 2<br><br>3.1, 2<br><br>4.1, 2<br><br>5.1, 2, 3<br><br>6.1, 2<br><br>7.1, 2 | |

**As described by Coast et al. 2016* (23)

A score of 6 + on the Clinical Frailty Scale (24) was an original inclusion criterion in the primary screening, but was removed before any participants were included. We assessed that a recent COPD exacerbation alone was a sufficient marker of life-threatening condition. The change was approved by the project's steering group and by the ethics committee. Inclusion is ongoing in March 2026.

*2.4. Drop-out criteria after inclusion*

- Admission to full specialized palliative care
- Moving away from the intervention municipalities
- Patient rejecting all care from either the municipality or the hospital
- Caregivers drop out if the patient drops out or the patient dies

# 2.5. Inclusion procedure

There are two total possible recruitment pathways for patients based on the outlined criteria.

## 1) The hospital – patients will be systematically assessed at the in- and out-patient respiratory clinics

The research staff will screen the electronic patient record before approaching the patient. The initial contact will occur either in person or via email, depending on the patient's place of care. If the patient is scheduled for a checkup in the outpatient clinic, they will receive a letter in their e-boks (a secure system for official emails) before their appointment, informing them that they will be contacted by the research team soon. The research staff will contact them by phone, as stated in the letter, to ask whether they would like to hear more.

If the patient is hospitalized, the research staff will ask their nurse to inquire if they are willing to receive information about the project. If the patient is interested in participation after hearing more about the project, they will be screened for eligibility and included if relevant. At inclusion, they will be asked if they have any caregivers, defined as "someone who supports you in terms of your illness", who would like to participate too.

## 2) Referral by community nurses

The community nurses have the option to identify participants, but without any systematic efforts to do so. Should they wish to include a patient, they will provide the patient with written and oral information about the study and obtain the patient's consent for the research team to access their electronic patient record. Then, the patient data will be sent to the research team, who will perform the primary and secondary screening, inform them of their eligibility status, and include them if eligible. The research staff will also inquire about possible caregivers.

If patients are eligible and willing to participate, consent and baseline information will be obtained either electronically, by phone collection (except consent), or by mail. Patients who are exempt from using e-boks due to difficulty navigating technical solutions may use paper forms. Patients will always be offered time as needed to consider their participation. After the baseline measures are completed, the patient will be randomly assigned to either the control or intervention group and informed of the outcome, either in person, if still hospitalized, or by phone.

# 2.5. Number of participants and randomization

In total, 100 patients, along with their caregivers if applicable, will be included in the study. The pilot study is exploratory and there is no power calculation. The patients will be randomized into an intervention and control group with a 1:1 ratio. The block size will be concealed during the inclusion process and generated by a fellow researcher using a random number generator, who is not otherwise involved in the study. Randomization will be conducted via the Research Electronic Data Capture (REDCap) system (25), and the sequence will not be known to staff who recruit or randomize patients via REDCap. Furthermore, patients will be stratified by municipality to ensure we gather feasibility data from both.

# 2.6. Intervention

Figure 1

*Components of the GRACE intervention vs usual care*

| Component | Usual care | The GRACE Intervention |
|---|---|---|
| Identification of target group of palliative care | Ad hoc | Systematic screening<br><br>Formal inclusion criteria (See Table 1) |
| Palliative care needs assessment | Ad hoc | Systematic and ongoing needs assessments using ICECAP-SCM |
| Cross-sectoral communication methods | Reactive<br><br>Written one-way communication | Proactive<br><br>Systematic virtual cross-sectoral conference between community nurses and the respiratory palliative team (two-way) |
| Setting goals with the patient | Ad hoc | A tool designed to go from values and needs to well-defined goals<br><br>Goals shared across sectors |
| Competence development | Driven by personal interest | 1-day session<br><br>Virtual cross-sectoral conferences with insights and small teaching session |

The intervention was designed to serve as an intermediate step between general palliative care provided by community nurses and specialized palliative care. This approach is a stepped care model for managing patients with severe COPD.

The target population consists of patients who show an indication of palliative care needs. This refers to individuals who have unmet palliative care needs, as assessed by responses to the ICECAP-SCM, but their problems may be manageable within the community nursing framework. Refractory symptoms are addressed during virtual conferences with the specialized palliative care respiratory team, and if they persist, the patient may be transferred to specialized respiratory palliative care services. General practitioners will provide medical treatment at home and coordinate with community nurses as per usual care. See core components in supplemental Fig. 1.

Table 2
*Guidelines for cross-sectoral virtual conference*

| | |
|---|---|
| **Before the conference** | **• Community nurses conduct the first needs assessment with the patients**<br>**• Community nurses report to the research team how many patients they have for the conference**<br>**• Everyone reads the guidelines for the conference** |
| During the conference | • A research group member participates as moderator<br>• Each patient is allocated an estimate of 10 minutes<br>o Community nurses present the patient using ICECAP-SCM and the needs assessment (3 min)<br>o Follow-up questions from the group (1 min)<br>o The Respiratory Specialized Palliative Care team presents their viewpoint, experiences, and suggestions for the presented patient (2 min)<br>o Follow-up questions from the group (1 min)<br>o The other community nurses offer further perspectives (1 min)<br>o Follow-up questions (1 min)<br>o Plan and sum-up of individual responsibilities (2 min) |
| After the conference | • Everyone executes their respective tasks<br>• Everyone goes back to their respective (and separate) record systems and update the medical records with the long-term palliative plan for the patient<br>• If relevant, the community nurse contacts the patients and suggests further measures or adjustments to the treatment plan. |

# 2.7. Data

The GRACE intervention pilot study data are stored in accordance with the requirements of the General Data Protection Regulation and registered in the Capital Region database (p-2024-15665). The following demographic information is collected from health administrative databases: Age, gender, sex, and municipality of residence. Furthermore, the latest FEV1 (%) will be collected if available. As comorbidities are likely to affect the goal of decreasing care fragmentation, data will be collected on the presence of the top 10 non-communicable, and non-injury related causes of disease burden in 2019 for the ages of 50–74 years according to the Lancet Global Burden of Disease Project (1) (excluding COPD, hearing loss, vision loss and cancers per exclusion criteria as well as musculoskeletal pain, oral disorders and lower back pain which are unlikely to appear in the health records). See Supplementary Table 1.

Patient-reported outcomes will be collected and managed using REDCap electronic data capture tools (25) hosted by the Capital Region and administered online via e-boks. If this is not possible, they will be administered either in person, by letter, or by telephone interview. Figure 2 provides an overview of the participant timeline and the primary and secondary outcomes inspired by the SPIRIT 2025 statement (19).

Marked in **bold** is the primary outcome.

All outcomes are exploratory but the focus is on the ICECAP-SCM score at 6 months. Healthcare usage include costs and contacts in primary care, hospital care, and community nursing.

# 2.8. Measures

ICECAP-SCM

ICECAP-SCM is a patient-reported outcome developed to evaluate palliative care. It exists in both patient- and proxy-oriented formats. The questionnaire has seven items, and responses are rated on a 1–4- point Likert scale, with lower scores indicating greater unresolved needs and lower quality of life (26). The current study is utilizing the version by Coast et al 2016 (23), which omits the examples “having your funeral planned” and “saying goodbye to family and friends” in the seventh item, to ensure that end-of-life references are less overt. ICECAP-SCM has been backwards- and forwards translated to Danish.

HADS

The Hospital Anxiety and Depression Scale (HADS) is a patient-reported outcome measure with 14 items, seven aimed at symptoms of depression and seven items covering symptoms of anxiety. Responses are rated on a 0–3-point Likert scale, with higher scores indicating higher symptom severity (27). The HADS is one of the most well-established and commonly used measures for adults with chronic illness. In patients with COPD, it is recommended for the measurement of anxiety symptoms, but the measurement of depressive symptoms is still missing high-quality evidence (28).

SF-12v2

SF-12v2 is a well-known patient-reported outcome measure with 12 items that assesses the impact of health on an individual's everyday life and is recognized as a quality-of-life measure. SF-12v2 is a shorter version of SF-36 (29).

GSE

The General Self-Efficacy (GSE) scale measures general perceived self-efficacy using ten items. The responses are on a 1–4 Likert scale, ranging from 1 (not at all true) to 4 (exactly true), with higher scores indicating higher self-efficacy (30). The total score ranges from 10 to 40, with higher scores indicating greater perceived self-efficacy. The scale has been used in studies of patients with COPD and has shown excellent internal consistency ($\alpha = 0.92$) (31).

WHO-5

The WHO-5 Well-Being index measures current mental well-being and consists of 5 statements about the past 2 weeks, with higher scores indicating better well-being. It is scored on a 6-point Likert Scale ranging from 5 (All the time) to 0 (At no time). The WHO-5 is used across countries by its developers, the World Health Organization, and has consistently demonstrated robust psychometric properties (32).

ZBI-22-SF

The Zarit Burden Interview – 22 items Short Form is derived from the original 29-item version. The instrument is developed for assessing the burden experienced by caregivers of older persons with dementia or other types of disability. Responses are scored on a 5-point Likert Scale from 0 (Never) to 4 (Almost always), with higher scores indicating a higher caregiver burden. High-quality evidence on the use of ZBI-22-SF in caregivers of patients with COPD is lacking; however, general evidence of shorter forms of the Zarit Burden Interview shows primarily strong content and construct validity as well as adequate internal consistency (33).

## 2.9. Analyses

Given that the current project is a pilot trial with only 100 patients, no power calculation has been performed for the outcomes and the trial is not powered for effectiveness. We will evaluate the GRACE intervention for merit of further testing using the following criteria:

- An overall judgement of feasibility and acceptability as described in Table 3 (34)

AND

- Indication of clinical change as defined by half a standard deviation change (35) in either ICECAP-SCM scores or SF-12 scores

OR

- Indication of a reduction in costs without a reduction in quality of life

Table 3
*Progression criteria on feasibility and acceptability*

| **Intervention fidelity** | **Red (Stop)** | **Amber (Discuss and amend)** | **Green (Go)** |
|---|---|---|---|
| | **< 75% of intervention elements were conducted as planned** | **75–85% of intervention elements were conducted as planned** | **> 85% of intervention elements (quarterly needs assessment and cross-sectoral conference discussion) were conducted as planned** |
| **Recruitment strategy** | < 30% of eligible patients are randomized and included | 30–50% of eligible patients are randomized and included | > 50% of eligible participants are randomized and included |
| **Decliners** | More decliners than accepters | Equal accepters and decliners | More accepters than decliners |
| **Dropouts (not caused by death or hospitalizations)** | > 40% dropouts | 20–40% dropouts | < 20% dropouts |
| **Staff acceptability** | Executing staff would not recommend the intervention to patients | Executing staff would recommend a modified version of the intervention to patients | Executing staff would recommend the intervention to patients |
| **Steering group acceptability** | The steering group do not find the intervention feasible | The steering group finds that a modified version of the intervention is feasible | The steering group finds the intervention feasible |

We estimate that 50 participants from each municipality will provide sufficient variation in gender, age, and comorbidities. The statistical data will be used to estimate the effect size, power, and sample size required to potentially conduct a full Randomized Controlled Trial (36).

Data will be analyzed using the intention-to-treat principle, and outcomes will be examined using generalized linear mixed models that account for autocorrelation and the assumption that missing data are related to previously observed values of the same items. Poisson regression models will be used to analyze healthcare utilization. The dataset will not be made publicly available or shared due to the General Data Protection Regulation (GDPR), which the study complies with. The outcomes will be investigated both combined and separately across the two subgroups (the municipalities).

We anticipate missing patient- and caregiver-reported data resulting from participant attrition but expect these losses to occur similarly in both the intervention and control groups.

The qualitative evaluation will include semi-structured interviews with all relevant stakeholders such as clinical nurses, doctors, and daily managers, purposively sampled from multiple organizational levels. It

will consist of a minimum of 15 informants with recruitment continuing until sufficient information power is reached (37) or when no more informants are available. The data will be audio-recorded, transcribed verbatim, and analyzed using thematic analysis (38) and will be coded using NVivo software. The MRC process evaluation's core domains (20) will serve as guidance for the interview guide.

## 2.10. Study dissemination

The research team has developed a plan to disseminate the relevant results of the GRACE intervention to internal and external policy makers, such as hospital management and national politicians, trial participants, and other relevant or interested stakeholders. The results of the study will be documented and communicated in scientific, peer-reviewed, international, and national journals irrespective of the outcome.

## 2.11. Ethics & Registration

The GRACE pilot RCT is carried out in accordance with the Helsinki Declaration and has been approved by the Regional Committee on Health Research Ethics (H-25009646). All study participants will provide written, informed consent for their participation. The study was registered at ClinicalTrials.gov before recruitment commencement (NCT06967324). The patients will not be offered any remuneration for their participation.

During the trial, we expect hospitalizations, worsening of illness, and deaths. These are not adverse effects of the trial but are to be expected in both the control and intervention groups due to the natural progression of the patient's illness. This will lead to a higher dropout rate and more missing data in the follow-up of patient-reported outcomes.

# 3. Discussion

This study will provide an indication of the effectiveness, feasibility, and mechanisms of the GRACE intervention and decide if the intervention should progress to a full RCT. The included municipalities differ significantly in terms of population composition, organizational structure, and available resources, which may affect the outcomes of the intervention, its fidelity, and the feasibility measures. When analyzing outcomes, this will be accounted for to the extent possible, and the included sample will also be stratified by municipality to ensure data are available for both. However, the municipalities' differences will also give us valuable feasibility data for two different-sized municipalities. The rest of the municipalities in Denmark fall between the two sizes and can therefore use the feasibility data that is more applicable to their own municipality, should they be interested in the model.

The chosen outcomes include analyses of healthcare costs. The intervention may incur additional costs during the intervention period due to the quarterly needs assessments. However, the healthcare cost analysis can result in a range of possible scenarios. For example, overall costs in municipalities may increase as patients stay in their own homes for more extended periods. It is also possible that the opposite occurs, with patients being hospitalized more often due to closer contact with a health

professional in their own home. It is also possible that municipalities incur higher initial costs but lower costs over the next few years as patient trajectories are more proactive. Our co-production process revealed that municipalities often enter late in these patients' healthcare trajectory without a proper plan in place or any knowledge of the patient, resulting in highly acute, reactive, costly, and time-consuming trajectories. Currently, the analysis does not include a follow-up beyond 12 months; however, a follow-up at 5 years post-intervention could provide valuable insights into the long-term cost-effectiveness of the intervention.

The GRACE intervention uses the Danish version of the ICECAP-SCM as a central part of the intervention in the form as suggested by Coast et al. (2016) (23), which omits the examples "having your funeral planned" and "saying goodbye to family and friends" from the seventh item. Coast and colleagues argue that this omission may be advantageous when respondents are not necessarily aware of their prognosis (23). This argument resonated with participants in the co-production intervention development group who are experienced COPD clinicians, and it informed the decision. Although the measure has undergone forward and backward translation, it has not yet undergone a complete psychometric evaluation prior to the initiation of the trial, which may impact the trial's results. A bias in face validity may be introduced, and the measure may not capture the intended meaning, thereby biasing our results. However, as the translation is conducted thoroughly, it is unlikely that the meaning will be distorted to this extent.

The GRACE intervention utilizes ICECAP-SCM as an element of the intervention, where nurses use it to guide the needs assessments with the patients, while the responses are also being collected by the researchers as an outcome measurement. Using the same instrument as both an intervention tool and an outcome measure introduces the risk of measurement bias that could ultimately affect the reliability of the results (39). However, in the GRACE intervention, the ICECAP-SCM will be used as a conversational tool every 3 months and will not serve as a gatekeeper for further treatment or care. The participants are asked to rank their most important needs themselves, thereby accounting for personal values and goals and acknowledging the potential discrepancy between problem intensity and felt need (38). The nurses will then work based on their rankings instead of their score. This means that the patient does not have to give a negative response on the ICECAP-SCM to receive further treatment or care, which may counter possible coaching effects. Finally, a 3-month time interval may help reduce the potential recall effect.

A range of caregiver-related outcomes are included despite the absence of systematic targeting of caregivers within the intervention content. We aim to improve the quality of life for people with COPD by ensuring they have appropriate, holistic, cross-sectoral support and community assistance. Given that caregiver burden is a well-recognized phenomenon among individuals caring for patients with severe COPD (40), the intervention may affect the caregiver's quality of life and caregiver burden, too, deeming the inclusion of these potential outcomes warranted.

Finally, the intervention has many elements that constitute it as a complex intervention (41). Therefore, elucidating the mechanisms of the intervention will be challenging. We have designed the evaluation

with a process evaluation (42) to clarify these mechanisms to the extent possible, so that the pilot results can be used to develop a full-scale randomized controlled trial of the GRACE intervention.

# Declarations

*4.1. Ethics approval and consent to participate*

The GRACE pilot randomized controlled trial is carried out in accordance with the Declaration of Helsinki and has been approved by the Regional Committee on Health Research Ethics (H-25009646). All study participants will provide written, informed consent prior to enrollment.

*4.2. Consent for publication*

Not applicable.

*4.3. Availability of data and materials*

No datasets have yet been generated. Data will be made available upon reasonable request once the study has been completed.

*4.4. Competing interests*

The authors declare no competing interests.

*4.5. Funding*

The study is sponsored by the Novo Nordisk Foundation (Grant number: NNF23OC0083795). The funding source had no role in the study design, data collection, data analysis, interpretation of data, writing of the manuscript, or the decision to submit the article for publication.

*4.6. Authors' contributions*

**ID:** Methodology; Project Administration; Resources; Software; Visualization; Writing – Original Draft; Writing – Review & Editing.
**KB:** Conceptualization; Funding Acquisition; Investigation; Methodology; Resources; Supervision; Writing – Review & Editing.
**MS:** Conceptualization; Supervision; Writing – Review & Editing.
**MR:** Conceptualization; Supervision; Writing – Review & Editing.
All authors have read and approved the final manuscript.

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*4.8. Trial registration*

ClinicalTrials.gov, NCT06967324.

*4.9. Protocol version*

*Protocol version **1**, dated **27th of March 2026**.*

*4.10. Declaration of generative AI and AI-assisted technologies in the manuscript preparation process*

During the preparation of this work the author(s) used Grammarly and ChatGPT in order to refine the language used in the manuscript. After using this tool/service, the author(s) reviewed and edited the content as needed and take(s) full responsibility for the content of the published article.

*4.11. Trial status*

Recruitment for the GRACE pilot randomized controlled trial began in November 2025 and is currently ongoing. We anticipate completing participant recruitment by mid-April 2026, with final data collection and study completion expected in April 2027. This protocol corresponds to version 1 (27$^{th}$ of March 2026), finalized prior to completion of recruitment.

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# Figures

| Component | Usual care | The GRACE Intervention |
|---|---|---|
| **Identification of target group of palliative care** | Ad hoc | Systematic screening<br>Formal inclusion criteria (See Table 1) |
| **Palliative care needs assessment** | Ad hoc | Systematic and ongoing needs assessments using ICECAP-SCM |
| **Cross-sectoral communication methods** | Reactive<br>Written one-way communication | Proactive<br>Systematic virtual cross-sectoral conference between community nurses and the respiratory palliative team (two-way) |
| **Setting goals with the patient** | Ad hoc | A tool designed to go from values and needs to well-defined goals<br>Goals shared across sectors |
| **Competence development** | Driven by personal interest | 1-day session<br>Virtual cross-sectoral conferences with insights and small teaching session |

**Figure 1**

*Components of the GRACE intervention vs usual care*

| | Enrollment | | | Post-Randomization | | | Close-out |
|---|---|---|---|---|---|---|---|
| TIMEPOINT | *1 year follow back* | $-t_i$ to 0 | 0 | *$T_1$ - 3 months* | *$T_2$ - 6 months* | *$T_3$ - 9 months* | *$T_4$ – 12 months* |
| Eligibility screen | | X | | | | | |
| Informed consent | | X | | | | | |
| Screening log | | X | | | | | |
| Randomization | | | X | | | | |
| INTERVENTION/COMPARATOR | | | | | | | |
| *GRACE* | | | X → | → | → | → | X |
| *USUAL CARE* | | | X → | → | → | → | X |
| ASSESSMENTS - PATIENT | | | | | | | |
| *Demographics* | | X | | | | | |
| *Hospital Anxiety and Depression scale (HADS)* | | X | | X | X | X | X |
| *Indications of palliative needs (ICECAP-SCM)* | | X | | X | X | X | X |
| *Impact of health on everyday life (SF-12)* | | X | | X | X | X | X |
| *General Self Efficacy (GSE)* | | X | | X | X | X | X |
| *Healthcare providers involved* | X | | | | | | X |
| *Healthcare use (Municipality, Hospital, Community Nursing and General Practice)* | X | | | | | | X |
| *Survival* | | | | | | | X |
| *Feasibility as indicated by qualitative interviews of healthcare professionals, patients, and caregivers* | | | | | | | X |
| ASSESSMENTS - CAREGIVERS | | | | | | | |
| *General Well-Being (WHO-5)* | | X | | X | X | X | X |
| *Hospital Anxiety and Depression scale (HADS)* | | X | | X | X | X | X |
| *Zarit Burden Interview (Caregiver burden - ZBI-22-SF)* | | X | | X | X | X | X |

**Figure 2**

*Participant timeline: Schedule of enrollment, interventions, and assessments*

Marked in **bold** is the primary outcome.

# Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- SPIRIT2025ChecklistGRACEFULL.pdf
- Supplementarymaterial.docx