Recommendation from the Danish Health Technology Council concerning

Domiciliary non-invasive ventilation for patients with chronic obstructive pulmonary disease

Recommendation from the Danish Health Technology Council:

The Danish Health Technology Council recommends treatment with domiciliary non-invasive ventilation as a supplement to standard care for patients with chronic obstructive pulmonary disease and one of the following indications:

- Persistent respiratory insufficiency ($paCO_2 \geq 7kPa$) and more than two weeks since last acute exacerbation
- ≥3 NIV-requiring acute exacerbations within the last year
- Patients who cannot be weaned off non-invasive ventilation after an acute exacerbation

About this recommendation:

The recommendation is based on the fact that treatment with domiciliary non-invasive ventilation (NIV) for patients with chronic obstructive pulmonary disease (COPD) and corresponding clinical indications yields positive clinical outcomes, such as increased survival, improved health-related quality of life, and an extended time to hospitalisation-requiring acute exacerbations. In addition, domiciliary NIV increases patients' treatment satisfaction, everyday coping abilities, and sense of security. Neither patients nor their relatives consider the use of domiciliary NIV as a significant burden in their daily lives.

The Council notes that individual patients' needs and conditions should be considered when offering domiciliary NIV and that the treatment constitutes a supplement to standard treatment of COPD. Additionally, those responsible for the treatment should ensure that patients is in sufficient standard treatment before domiciliary NIV is offered. In accordance with the guidelines (COPD – LT-NIV) from the Danish Respiratory Society, the Council emphasises that domiciliary NIV should only be offered to patients with COPD and a clinical indication for its use.

The Council draws attention to the fact that the budget impact analysis exclusively describes regional expenses for domiciliary NIV. The budget impact analysis indicates regional savings over a five-year period with a positive recommendation, but the Council emphasises that underlying expenses for the treatment of COPD at the regional and municipal level are not included.

The Council assesses that the quality of evidence is satisfactory within Clinical effectiveness and safety. However, it is acknowledged that the number of studies available is limited. Therefore, the Council recommends that the regions monitor the clinical effectiveness, safety, and the use of domiciliary NIV in Danish practice going forward. The other perspectives are primarily illuminated through newly acquired empirical data and targeted analyses. The Council considers the overall evidence base to be sufficient to support the Council's recommendation.

Overall, the Council concludes that treatment with domiciliary NIV for patients with COPD and a clinical indication for its use delivers value relative to its economic consequences.

About the technology	Domiciliary NIV is a patient-centered treatment that is anchored with the user, i.e., the patient, and not explicitly in the patient's home. The equipment for domiciliary NIV is used by the patient as a supplement to standard treatment of COPD and cannot replace ongoing standard care. The purpose of using domiciliary NIV is to enhance the patients' general quality of life and reduce the risk of acute exacerbation of COPD symptoms and death, partly by lowering the blood CO_2 levels. In accordance with the guidelines (COPD – LT-NIV) from the Danish Respiratory Society, the Council emphasizes that it is often relevant to have a conversation about the patient's wishes regarding the end of life phase as a part of standard treatment.
Patient population	The recommendation concerns adults (≥ 18 years) with chronic obstructive pulmonary disease and one of the following indications: • Persistent respiratory insufficiency (paCO2 >7kPa) and more than two weeks since last acute exacerbation • >3 NIV-requiring acute exacerbations within the last year • Patients who cannot be weaned off NIV after an acute exacerbation The recommendation is conditional on patients being motivated to use domiciliary NIV and being cognitively and physically able to remove the NIV mask themselves.
Scope of application	The recommendation applies to the public Danish hospitals.
Implementation	The analysis has not delved into the evidence for different ways of organising treatment with domiciliary NIV. Therefore, there is no basis for pointing to a specific model. The Council encourages adapting the implementation to local conditions, with the goal of ensuring easy and equal access to treatment across the country.
Procurement procedure	The Council emphasizes that, going forward, national tenders for the area could advantageously be conducted to achieve lower and more uniform prices, which currently vary between regions. In future procurements, priority should be given to NIV machines that support digital monitoring of treatment.

The Expert Committee's summary of the analysis report

About the analysis

The Danish Health Technology Council's recommendation is based on the analysis report regarding domiciliary non-invasive ventilation (NIV) for patients with chronic obstructive pulmonary disease. The analysis aims to answer the following research question:

Should domiciliary non-invasive ventilation be used as a treatment for adult patients with chronic obstructive pulmonary disease and one of the following indications:

- Persistent respiratory insufficiency (paCO2 >7kPa) and more than two weeks since last acute exacerbation
- >3 NIV-requiring acute exacerbations within the last year
- Patients who cannot be weaned off NIV after an acute exacerbation

Clinical effectiveness and safety

The analysis of clinical effectiveness and safety is based on four *randomized controlled trials* (RCT studies). The evidence includes comparative data on all outcome measures except 'Complications'.

The results, based on the Expert Committee's clinical assessment, apply to adults with chronic obstructive pulmonary disease who have persistent respiratory insufficiency ($PaCO_2 \geq 7kPa$) and more than two weeks since the last acute exacerbation (referred to as 'Stable population') or who have ≥3 NIV-requiring acute exacerbations in the past year (referred to as 'Unstable population'). Thus, the results do not cover patients who cannot be weaned off NIV after an acute exacerbation (referred to as 'Acute population'). Due to the life-threatening aspect for the 'Acute population', it is not ethically possible to investigate clinical effectiveness and safety for this indication group in RCT studies.

The analysis of clinical effectiveness and safety identifies a statistically significant and clinical relevant difference in effects between domiciliary NIV and standard treatment for:

- Median time to death
- Proportion of patients who have died after one year
- Median time to hospitalization-requiring acute exacerbation
- Health-related quality of life measured with the *Saint Georg's Respiratory Questionnaire* (SGRQ)

Thus, the evidence supports that domiciliary NIV prolongs time to death and time to hospitalization-requiring acute exacerbation, while also reducing the proportion of patients who have died after one year and improving health-related quality of life. The assessment of evidence quality with the *Grading of Recommendations, Assessment, Development and Evaluation* (GRADE) varies for the respective outcome measures. While confidence in the meta-analysis results for 'Median time to death' and 'Median time to hospitalization-requiring acute exacerbation' is 'Moderate', confidence is rated as 'Low' for 'Proportion of patients who have died after one year' and 'Very low' for 'Health-related quality of life measured with SGRQ'. The Expert Committee assesses that the results for the respective outcome measures are consistent with their experiential knowledge from the use of domiciliary NIV in clinical practice.

For the remaining outcome measures, including 'Median number of hospitalization-requiring acute exacerbations', 'Health-related quality of life

	measured with *Severe Respiratory Insufficiency Questionnaire*', and 'Average number of hospitalisations', no significant difference in effect has been detected between domiciliary NIV and standard treatment. The assessment of evidence quality with GRADE is 'Very low' for the respective outcome measures, indicating low confidence in the results, and the true effect is likely to be significantly different from what the analysis suggest. The Expert Committee notes that 'Median number of hospitalisation-requiring acute exacerbations' and 'Average number of hospitalisations' are informed by one study where the sample size is not calculated to detect a difference in effect for these outcome measures, posing a risk of type-2 error. From the evidence base, no serious complications, including collapsed lung, aspiration, and lung infection, have been observed with the use of domiciliary NIV.
Organisational implications	The analysis of Organisational implications is based on clinical treatment guidelines, care processes, as well as interviews with clinical healthcare providers and nurses responsible for treatment and care from all regions, and also with care-responsible municipal nurses. Analysis of the submitted clinical treatment guidelines and process descriptions reveals an inter- and intraregional variation in how treatment with domiciliary NIV is organised and structured in the regions. Differences emerge at various stages of the overall treatment process, as confirmed through interviews with responsible treatment informants and municipal informants. The treatment guidelines and interviews indicate that variation in treatment processes is partly due to differences in how treatment with domiciliary NIV is locally organised and partly reflects a desire to accommodate the individual patient's needs, preferences, and personal circumstances. The Expert Committee assesses that some variation in the organisation of treatment can be expected, given the diversity of local conditions, but it should be attempted to standardize treatment offerings as much as possible so that patients across regions have equal opportunities for treatment with domiciliary NIV. Based on this, the Expert Committee concludes that the approach to treatment with domiciliary NIV should be standardized more consistently nationwide. In this context, the Expert Committee maintains that the responsibility for domiciliary NIV lies within the pulmonary medicine specialty, where a specialist in pulmonary medicine, possibly with a subspecialty in COPD, holds the treatment responsibility. For nurses responsible for treatment in pulmonary ambulatory clinics, it is a crucial requirement that they possess a fundamental pulmonary medical experience, knowledge of respiratory physiology, NIV treatment, and equipment, as well as familiarity and experience in dealing with patients with severe COPD. The Expert Committee assesses that these competencies are also relevant for municipal nurses. Additionally, for municipal nurses, an essential prerequisite is that they have experience and understanding of the everyday life of citizens with severe COPD and how domiciliary NIV serves as a supportive measure to standard treatment. The Expert Committee assesses that treatment with domiciliary NIV will not result in a significant shift of tasks from the region to the municipality, as it involves home treatment primarily managed by the patient and their relatives for the majority of all treatment courses. However, as COPD progresses, there may be increased complexity of care and needs for the individual, including the handling of practical tasks, medical treatment, and also treatment with domiciliary NIV. In such cases, there will be a shift of tasks from the *individual* to the municipality.

	The Expert Committee notes that municipal nurses desire a closer collaboration with the responsible outpatient clinics for consultation and advice regarding treatment courses and equipment, despite managing a smaller portion of treatment courses with domiciliary NIV. However, the Expert Committee also observes that cases requiring municipal assistance typically involve significant care complexity, thereby increasing the need for close cooperation between the hospital and municipality. Additionally, there is a desire for greater uniformity in written treatment guidelines, course descriptions, and procedural documents to ensure consistency in knowledge about cleaning and equipment, making it easier to delegate tasks to other healthcare professionals. The Expert Committee highlights that the lack of close collaboration between the hospital and municipality can have implications for patient safety and impact the healthcare professional's relationship with the patient. The Expert Committee supports the assessment that a good relationship and trust between the healthcare professional and patients with severe COPD are essential for the success with domiciliary NIV. Furthermore, the Expert Committee believes that relatives who may assist with practical help and provide support for the treatment can also facilitate the process. It's emphasized that treatment with domiciliary NIV does not require specific healthcare skills for the patient or their potential relatives. However, the patient must be motivated and adherent to treatment, and for safety reasons, be physically and cognitively able to remove the mask themselves. Overall, the Expert Committee assesses that there is support and awareness in professional circles for the use of domiciliary NIV. However, they also note that the organisational aspects for further dissemination could be improved, including standardizing the implementation of domiciliary NIV across the country and enhancing tools to facilitate collaboration between responsible ambulatory clinics and home nursing services. In this context, the Expert Committee draws attention to the fact that there may be different organisational possibilities for treatment with domiciliary NIV, and in the regions, there are examples of involving other professional groups in the treatment, such as ‘the extended arm’ of the pulmonary ambulatory clinic. The Expert Committee observes that, through interviews with responsible treatment personnel, there is a consistent perception that awareness of chronic hypercapnia and domiciliary NIV as a treatment is increasing among colleagues, but there is room for improvement. With broader awareness, it becomes possible to identify patients with chronic hypercapnia earlier and consequently initiate treatment with domiciliary NIV earlier, provided that the clinical indications, according to the DLS’ guidelines, are met.
Patient perspective	The analysis of the Patient perspective is based on an interview study involving patients using domiciliary NIV or those who have opted out of the treatment, as well as their family members. The findings from the primary data collection are supported by two primary studies derived from a systematic literature search. The analysis of the patient material indicates that the clinical benefits (e.g. improved sleep) of domiciliary NIV outweigh the negative aspects (e.g. mask discomfort) associated with the treatment. The majority of patients describe domiciliary NIV as life-changing, because everyday life went from being characterized by acute exacerbations requiring hospitalization, worry and fatigue, to one of hope and increased energy for various activities. Domiciliary NIV is not a burden in everyday life once patients have become familiar with the device. In general, patients feel sufficiently equipped to manage domiciliary NIV after hospital training, but the initial period is fraught with frustration. If the negative aspects of domiciliary NIV are not addressed within a short period of time, patients may opt out of

treatment before the clinical benefits are realized. The practical work involved in managing domiciliary NIV is perceived as limited for patients with treatment success, and the majority express that they would be able to manage the treatment independently. However, the environment, including relatives as well as regional and municipal measures, play a supportive role in different ways. While relatives have a practical role in relation to everyday tasks, which is primarily attributed to COPD, offers such as telemonitoring and contact person arrangements in hospitals help to create a sense of security around domiciliary NIV. In general, domiciliary NIV is considered life-giving due to the progression of the disease, and patients report a high level of satisfaction and support for the treatment.

Based on the results anchored in the patient material, factors that can be facilitating and/or constitute barriers to the initiation and use of domiciliary NIV have been deduced:

Facilitating factors

- Individualized training
- Caring staff with expertise in the treatment with domiciliary NIV
- Information material
- Quick consultation after start-up
- Contact person arrangement
- Telemonitoring
- Rapidly experienced effect of domiciliary NIV
- Relatives
- Home care

Barriers

- Side effects (e.g. headaches)
- Challenges (e.g. mask leakage)
- Advanced disease progression
- The use of domiciliary NIV during the daytime
- Cleaning of the device
- Co-existing conditions (e.g. back problems)

The identified factors align with what the Expert Committee experiences in clinical practice, although the list is not expected to be exhaustive. In addition, the Expert Committee notes that disease progression, comorbidity, and limited understanding of the disease can be barriers for patients to accept domiciliary NIV and adhere to the recommended treatment. For this reason, it is crucial that healthcare professionals take into account the individual patient's capabilities in addressing any potential aspect of inequality. In this regard, the Expert Committee observes the need for collaboration between hospitals and municipalities, as local measures can enable more patients to succeed with the treatment.

The analysis of the relatives' material indicates that relatives have a limited practical role in the treatment with domiciliary NIV. It is primarily the individual patient who handles and cleans the equipment. In return, the diagnosis of COPD and the progression of the disease has been life-changing, because relatives have taken on the responsibility for everyday practical tasks while, together with their partner/parent, having to rethink their future dreams. The findings align with what the Expert Committee experiences in clinical practice, although there is awareness that the sample of relatives is limited. In addition, the Expert Committee notes that they encounter relatives in clinical practice who take a significant role in the treatment, partly because they handle correspondence with the healthcare system and are on 'alert' due to the progression of the disease. During acute exacerbations, relatives can support the patient with domiciliary NIV or initiate medical treatment to prevent hospitalization, possibly with backup from the responsible healthcare providers. However, the Expert Committee observes that relatives experience fewer hospitalizations due to domiciliary NIV, contributing to more calmness in everyday life.

	Overall, the Expert Committee assesses that patients with involved relatives in the treatment have better adherence to domiciliary NIV and consequently, better treatment outcomes. Overall, the Expert Committee assesses that there is broad support for the treatment in encounters with patients and relatives in clinical practice.
Health economics	The analysis of Health Economics relies on studies conducted with the purpose of elucidating the health economic consequences of treating indicated patients with domiciliary NIV, including a *cost-utility* analysis, a cost-effectiveness analysis, and a budget impact analysis. Based on the health economic analyses, the Expert Committee assesses that domiciliary NIV creates significant value for patients in terms of the accumulation of quality-adjusted life years (QALYs) through higher survival and by avoiding hospitalization-requiring acute exacerbations relative to standard treatment (1.29 vs. 0.64 QALYs), albeit at higher costs (DKK 457,438 vs. DKK 305,789). This results in an incremental cost-effectiveness ratio of DKK 234,248/QALY. The Expert Committee notes that the positive effect of home NIV experienced in patients' everyday lives is not included in the cost-utility analysis, and therefore, the positive impact of domiciliary NIV in the cost-utility analysis may be underestimated. The estimated longer survival for patients undergoing treatment with domiciliary NIV means that these patients may experience more hospitalization-requiring acute exacerbations in their lifetime (6.07 vs. 5.09 hospitalization-requiring acute exacerbations). The higher costs associated with domiciliary NIV are largely driven by higher costs for more hospitalization-requiring acute exacerbations over the total lifetime and the valued resource burden on patients and their relatives in terms of cleaning the NIV equipment. The Expert Committee notes that the resource burden on patients and relatives does not constitute a real transfer. If the cost-utility analysis is calculated solely with the inclusion of regional costs, the incremental cost-effectiveness ratio is DKK 142,705/QALY. If costs for the treatment and care of COPD are included, the incremental cost-effectiveness ratio increases to DKK 878,175/QALY, due to the estimated higher survival in the patient group undergoing treatment with domiciliary NIV. The budget impact analysis estimates that a positive recommendation for domiciliary NIV for indicated patients with COPD would result in a five-year budget impact of approximately -DKK 37 million. The Expert Committee notes that the investment required for the purchase of NIV equipment and resource allocation to staff responsible for initiating domiciliary NIV programs within the five-year time frame of the budget impact analysis is largely offset by the hospitalization-requiring acute exacerbations avoided through the use of home-NIV. In connection with this, the Expert Committee notes that the cost of hospitalization-requiring acute exacerbations is valued low in the base case analysis (DKK 60,203 per hospitalization-requiring acute exacerbation). The Expert Committee draws attention to the fact that if the cost is increased to DKK 120,406 per hospitalization-requiring acute exacerbation (sensitivity analysis 4), the budget impact is estimated at -DKK 120 million. The Expert Committee assesses that the actual savings in terms of avoided hospitalization-requiring acute exacerbations due to the use of home-NIV may be higher than estimated in the base case analysis. The budget impact analysis does not include any potential implementation costs that may occur with the desire for increased adoption of home

NIV for indicated patients with COPD. The Expert Committee emphasizes that if regional expenses for COPD treatment are included, the five-year budget impact will be approximately DKK 30 million. The Expert Committee also points out that municipal expenses for COPD are expected to increase due to the expected higher survival among patients undergoing home-NIV treatment. Additionally, the Expert Committee notes that the budgetary consequences of a potential positive recommendation for home-NIV are not stabilized at the end of the analysis, and further budgetary impact can be expected beyond the projected five years in the budget impact analysis.

The health economic analyses and budget impact analysis are subject to uncertainty, partly due to methodological choices in the analyses and the valuation of NIV equipment and hospitalization-requiring acute exacerbations. However, the Expert Committee assesses that the results are relatively robust overall.

The Expert Committee notes that the health economic results are contingent on the conditions described for the analysis, including the organisation of home-NIV treatment and the valuation of cost components. In this context, the Expert Committee evaluates that clinically optimal and efficient treatment with home-NIV is best offered under conditions that enable an adequate level of competence among the treating staff and where the initiation of home-NIV treatment is carried out in an outpatient setting. The Expert Committee also observes that, in the event of a positive recommendation for home-NIV, resources should be allocated for NIV equipment, as well as personnel resources to manage the treatment, as this is essential for the success of the treatment.

Overall, the Expert Committee assesses that treatment with home-NIV for indicated patients with COPD creates significant value in terms of quality-adjusted life years relative to the economic consequences of its use.

About the recommendation from the Danish Health Technology Council

The Danish Health Technology Council's recommendation is intended as an aid for regions when deciding on the use of a given health technology. The recommendation is based on the Expert Committee's analysis report. Depending on the health technology under examination, this report includes a review of one or more of the following perspectives: 1) Clinical effectiveness and safety, 2) Patient perspective, 3) Organisational implications, and 4) Health economics.

This recommendation is based on the Danish Health Technology Council's analysis report regarding the use non-invasive ventilation in treating patients with chronic obstructive pulmonary disease, which was prepared collaboratively by the Expert Committee and the secretariat. The analysis report was prepared with outset in the Danish Health Technology Council's process guide and methodological guidelines. The Expert Committee's terms of reference are available on the Danish Health Technology Council's website.

Information about this document		
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