

ADVANCES IN AMBULATORY OXYGEN WORKSHOP AND LONG-TERM OXYGEN THERAPY IN REAL-LIFE PRACTICE

The practical workshop took place on Sunday 27th September 2015 and the symposium took place on Monday 28th September 2015, as part of the European Respiratory Society (ERS) International Congress 2015 in Amsterdam, Netherlands

PRACTICAL WORKSHOP

Chairperson

Enrico Clini¹

Speakers

Enrico Clini,¹ Daniel Veale,² Joao Carlos Winck³

MINI SYMPOSIUM

Chairperson

Jean-François Muir⁴

Speakers

Mike Kampelmacher,⁵ Isabelle Vivodtzev,⁶ Stuart Little⁷

1. University of Modena, Reggio Emilia, Italy

2. Dieulefit Santé, Dieulefit, France

3. Porto University, Porto, Portugal

4. Rouen University Hospital, Rouen, France

5. University Medical Center Utrecht, Utrecht, Netherlands

6. Grenoble University Hospital, Grenoble, France

7. NHS Dumfries and Galloway, Dumfries, UK

Disclosure: Enrico Clini, Daniel Veale, Isabelle Vivodtzev, and Joao Carlos Winck have no relevant conflicts of interest to disclose. Jean-François Muir, Mike Kampelmacher, and Stuart Little received support from Invacare to attend the ERS conference and symposium.

Acknowledgements: Writing assistance was provided by Dr Lucy Smithers, ApotheCom.

Support: The publication of this article was funded by Invacare. The views and opinions expressed are those of the authors and not necessarily of Invacare.

Citation: EMJ Respir. 2015;3(2):63-70.

MEETING SUMMARY

The practical workshop presented recent advances in the field of ambulatory oxygen (AO), with experts discussing identification of patients who would benefit from AO, as well as current trials to measure specific benefits of AO in chronic patients. In particular, AO prescription in clinical practice and developments in pulsed-dose delivery of AO as a more efficient method of oxygen delivery were extensively discussed. After audience questions, the attendees had the opportunity to handle the AO systems on display in order to gain greater insight into their functionality and wearability, which should assist them in providing the most appropriate device for each patient.

The symposium addressed considerations required when prescribing long-term oxygen therapy (LTOT). Dr Kampelmacher reviewed current indications for LTOT, emphasising the importance of accurate assessment of patients for LTOT, optimisation of oxygen dose, and patient education. Dr Vivodtzev discussed the evidence for LTOT in patients with exercise-induced desaturation, the role of portable oxygen concentrators, and the optimisation necessary to benefit from their use. The symposium concluded with a health economic study presented by Dr Little, demonstrating the cost benefits of a reform of the Scottish healthcare oxygen supply service.

Advances in Ambulatory Oxygen

Professor Enrico Clini

Prof Clini opened the workshop by reviewing which patients should be given AO. The most recent guidelines recommend that AO should not be routinely prescribed for all patients needing stationary oxygen supplementation, but should be offered to improve walking and exercise within a pulmonary rehabilitation course, with muscle training encouraged in patients with reduced lung function.¹

Patient selection is an important unresolved issue. Lung function measurements have some predictive value for low ($FEV_1 < 50\%$) and high ($FEV_1 \geq 80\%$) scores,² but do not address those with intermediate scores, and there is variation in oxygen saturation between patients who have the same lung function. A scoring system for identifying patients at risk of walking-induced desaturation has recently been developed, which takes both resting oxygen saturation and lung function into account.³ However, the type of exercise used to test for exertional desaturation is also a contributory factor.⁴

The efficacy of LTOT for chronic obstructive pulmonary disease (COPD) patients who are normoxic at rest but who desaturate during physical activity was identified as an important issue for future research.⁵ In clinical practice, AO is often prescribed to patients outside of the guideline recommendations in order to enable them to carry out activities of daily living. While these patients report improved quality of life, such as reduced breathlessness and tiredness, AO does not appear to fully improve ability to exercise nor to increase survival.⁶ The functional limitations of the oxygen delivery system (e.g. portability of oxygen cylinders) may contribute to this, but providing AO to patients who will not benefit has cost implications both for patients and for the healthcare system. Current research includes the Long-term Oxygen Treatment Trial (LOTT, NCT00692198) study of the survival and quality-of-life benefits of LTOT versus no LTOT in COPD patients who are normoxic at rest but who desaturate during exercise; results are yet to be reported. Results are also awaited from the OM-COPD trial (NCT01722370) investigating the physiological benefits of AO therapy in this COPD patient population.

Ambulatory Oxygen Prescription in Practice

Doctor Daniel Veale

As with any therapy, AO should be appropriately prescribed for each patient with precision, specifying the dose, frequency, and timing. There are many questions that need to be answered in order to define these parameters for AO. Reliability in the measurement of blood gas is needed, as well as a standard definition of the level of desaturation at which a patient should be given AO (currently there is variation between clinicians regarding which level should be considered significant).⁷ The oxygen dose may also be important given the potential for oxygen toxicity.

The cost of AO to the healthcare system (in the USA, for example, one million Americans are on LTOT at a cost of over \$2 billion per year)⁸ necessitates that AO is only prescribed to patients who will benefit, and that oxygen is used efficiently. The key recommendations in prescribing effective and efficient oxygen therapy have been identified by the LTOT Consensus as: education of all stakeholders, technical optimisation of LTOT delivery systems, evaluation of optimal oxygen delivery in individual patients, and patient compliance with the therapy.

Patient compliance with LTOT can be influenced by disease severity, being prescribed oxygen for >15 hours, acceptance of treatment, availability of an ambulatory device, and patient education.⁹ The prescriber can address these factors by ensuring that the indication for the therapy is correct, that the patient is educated, and that there is good medical and technical follow-up in the use of their device. Negotiation with the patient to modify their lifestyle is also part of good prescribing practice.

Ideally, portable oxygen devices would be small, silent, easy to handle, validated, and tested. Trials comparing the XPO₂ and SOLO₂ pulsed-delivery systems with continuous-flow oxygen in patients with COPD showed no significant difference in the overall improvement in exercise ability (6-minute walk test [6MWT]), but there was significant variability in effectiveness between individual patients (Figure 1).^{10,11} Each prescription should thus be individualised and validated by an ambulatory walk test to determine the effective setting. While the XPO₂ and SOLO₂ portable concentrators were similar in clinical performance to continuous liquid oxygen, they gave patients more freedom of movement to continue physical and social activities.

Figure 1 removed due to copyright expiration.

Figure 1: Oxygen saturation during 6-minute walk test (6MWT) with XPO₂ pulsed-dose oxygen delivery (A) or SOLO₂ pulsed-dose oxygen delivery (B) versus C100 continuous-flow oxygen delivery.

Note the individual variation in results indicated by the error bars.

Reprint permission requested from Elsevier (Couillard A et al. *Rev Mal Respir.* 2010;27:1030-8).

The Use of Pulsed Dose in Ambulatory Oxygen

Professor Joao Carlos Winck

Pulsed-dose oxygen delivery is an 'on-demand' delivery system for low-concentration oxygen therapy¹² that can provide the same oxygen saturation to patients at a much lower volume per minute than continuous-flow oxygen. Pulsed-dose systems aim to increase the oxygen tank duration and battery life of the concentrator and allow adjustable oxygen delivery, as well as smaller, more wearable machines. Delivering the oxygen

bolus early in inspiration provides patients with the same oxygen concentration as continuous-flow oxygen.¹³ In models of lung function, the fraction of inspired oxygen (FiO₂) is affected by the interaction of the patient's inspiratory flow pattern and flow from the oxygen source.¹³ With a constant flow of oxygen, it is estimated that the final third of inspired volume remains in 'dead space' and does not reach the alveolar region of the lungs to participate in gaseous exchange. With pulsed-dose delivery, triggered by the patient's inspiratory effort, no anatomical reservoir is established and the FiO₂ is not reduced.¹³

Pulsed-dose devices have varying characteristics, such as the minute volume delivered at different pulse frequencies or their oxygen delivery performance in normal and COPD-affected lung models,¹⁴ and their performance in clinical practice should be evaluated. Previous studies have shown that pulsed-dose oxygen during exercise can provide similar oxygen saturation to continuous flow,¹⁵ although a comparison of four different demand oxygen delivery systems found significant differences in performance, with better performance shown by the devices that delivered a bolus of oxygen at the onset of inspiration.¹⁶

Several trials comparing pulsed-dose oxygen with continuous-flow oxygen have found comparable clinical efficacy, although patients preferred the portable devices.^{10,17,18} During exercise, a 3-fold increase in oxygen flow compared with resting levels is recommended.¹⁷ Clinical evaluation of different oxygen concentrators for preventing desaturation during the 6MWT in patients with COPD found differences in performance,¹⁹ which reinforces the recommendation for evaluating efficacy of the individual patient's prescription.

Fewer studies have been performed on the efficacy of nocturnal pulsed-dose oxygen delivery in patients with COPD and nocturnal hypoxaemia. An early comparison found on-demand oxygen delivery was comparable to continuous-flow oxygen in the majority of patients,²⁰ which was confirmed by a more recent study using a portable concentrator.²¹ A Spanish study comparing the use of a single portable pulsed-dose device with combined use of stationary and portable oxygen delivery in patients with COPD found that patients preferred using the single pulsed-dose device, but also found that hypoxaemia was

more frequent with a single device, especially at night.²² Individual patient titration of settings, using an oximeter to evaluate oxygen saturation, would be recommended for nocturnal use, although there are not sufficient data at present to make recommendations for calibration of night-time oxygen delivery with pulsed-dose devices.

In a study simulating air travel, comparison of the performance of several pulsed-dose oxygen delivery devices found that patients needed to use the maximum settings in order to maintain oxygen saturation, which rapidly drained the batteries.²³ While the portability of pulsed-dose oxygen delivery can make travel easier for people with COPD, these findings are useful to take into account when considering air travel (Figure 2).

Q&A session

Could the panel comment on progress with oximeter-controlled pulsed-dose oxygen flow system devices?

Prof Winck answered that there is only one system commercially available at present, but that the technology would be developed more widely as oximeter control made good sense. For clinicians, it made evaluation of efficacy and trialling the device's performance in patients much easier.

Is it important for the patient to be in a stable state before starting LTOT? Or can it be started while the patient is still in an exacerbated state, before they leave hospital?

Prof Veale answered that the recommendation for patients to start LTOT when stable is due to the original trials of LTOT, which were carried out in patients who were stable. He felt that it was worth giving LTOT to patients during exacerbations and in hospital.



Figure 2: Following the audience questions, attendees were invited to a hands-on demonstration of ambulatory oxygen delivery devices.

Long-Term Oxygen Therapy in Real-Life Practice: Introduction

Professor Jean-François Muir

LTOT has entered a new era as a result of technological developments such as portable oxygen concentrators, concentrator-compressors, and, in the future, concentrator-liquefiers. The smaller size of these oxygen delivery systems can improve patients' mobility and quality of life. Recent recommendations by the French government specified the type of equipment that should be prescribed for a patient's particular oxygen needs,²⁴ which have resulted in increased use of portable oxygen concentrators and decreased use of liquid oxygen tanks, with reduced costs to the healthcare system.

Current Indications of Long-Term Oxygen Therapy

Doctor Mike Kampelmacher

Dr Kampelmacher discussed current guidelines for prescribing LTOT¹ to identify which patients will benefit from which type of oxygen therapy. Oxygen therapy is prescribed for hypoxaemia, defined as resting daytime PaO₂ ≤7.3 kPa,¹ and not for breathlessness alone, as there is no evidence that oxygen improves breathlessness. Hypoxaemia can be measured most easily by pulse oximeters, but more accurately by arterial blood gas (ABG) measurements; pulse oximetry alone should not be used to assess patients for LTOT prescription.¹

When prescribing oxygen, clinicians should be aware of, and educate patients about, the risks of fire (especially among patients who smoke), explosion, and freezing with gaseous and liquid oxygen, as well as the possibility of toxicity, if FiO₂ is greater than 0.4, and hypercapnia.^{25,26} However, hypercapnia should not prevent the treatment of hypoxaemia.

The prescription of LTOT is indicated to improve oxygenation in patients who have been given short-term oxygen therapy to treat hypoxaemia, or electively in patients with persistent low oxygenation.¹ The assessment for LTOT is by ABG measurement in the absence of supplemental oxygen in patients who have been clinically stable for around 8 weeks since their last

exacerbation. Patients should be reassessed and informed that their LTOT may be discontinued if blood gas assessments show clinical improvement.¹ In some cases, LTOT is also indicated in patients with exercise-induced hypoxaemia or nocturnal hypoxaemia.

The Nocturnal Oxygen Therapy Trial (NOTT) and Medical Research Council trials in patients with COPD or chronic bronchitis and emphysema, respectively, showed significantly increased survival in the LTOT arms.^{27,28} The hypoxaemia indications for prescribing LTOT are based on these trials, with subsequent studies confirming the survival benefit of LTOT given for at least 15 hours per day.²⁹ The evidence for other benefits, such as reduced pulmonary vascular resistance, reduced haematocrit, reduced hospital admissions, improved quality of life, improved exercise tolerance, and improved neurophysiological functioning, is not as robust due to being based on smaller studies.

When prescribing LTOT, clear instructions should be given to patients regarding the aims and effects of the treatment and the potential complications and dangers, and a follow-up visit by a specialist nurse should be carried out within 4 weeks of initiating therapy. The oxygen flow rate should aim to give patients PaO₂ levels of 8.0–9.3 kPa or SaO₂ levels >90%, achieved by pulse oximetry titration. Ambulatory and nocturnal oximetry may be performed to allow more accurate flow rates to be prescribed for exercise and sleep, respectively,²⁹ as some patients who are adequately oxygenated during the day may become desaturated during sleep.³⁰ Home oxygen therapy can be withdrawn from patients who smoke if the risks are considered to be too high.²⁷ Furthermore, there is evidence that patients who continue to smoke while on LTOT may have worse survival.³¹

Prescription of LTOT for moderate hypoxaemia is not indicated in the British Thoracic Society guidelines, as there is no evidence for a survival benefit. A recent study, the National Emphysema Treatment Trial, suggested that LTOT may be associated with worse survival in patients with moderate hypoxaemia.³² The LOTT study aims to determine the effect on mortality and hospitalisation in patients with COPD and moderate resting hypoxaemia, or normoxia and exercise-induced desaturation, with results expected during 2015.³³

Long-Term Oxygen Therapy During Exercise

Doctor Isabelle Vivodtzev

Providing AO to those with chronic respiratory failure allows patients to exercise without becoming hypoxaemic, and exercise is a key part of pulmonary rehabilitation in patients with COPD. Currently, there is some debate as to whether normoxic patients who only desaturate during exercise should be given LTOT.^{1,34}

It has been shown that AO improves quality of life in patients with COPD.³⁵ Initial portable oxygen delivery devices (liquid or gaseous oxygen) had drawbacks to their use, in particular the dependence on a delivery service.³⁶ Pulsed-dose delivery devices were developed in order to reduce oxygen requirements and improve portability, and demonstrated similar performance to continuous-flow in patients at rest.³⁷ However, the clinical efficiency of pulsed-dose oxygen delivery devices versus continuous-flow oxygen during exercise is controversial.³⁸ The portable oxygen concentrator is an alternative technological development, which has potential advantages for AO in that it is free of the constraints of a delivered oxygen supply, has fewer safety risks, costs less, and could offer the patient more autonomy during travel. However, a study comparing devices found that the efficacy appeared to vary depending on the disease pathology (COPD or interstitial lung disease), ventilatory patterns were different between pulsed-dose and continuous-flow, and there were technological and technical differences in performance between devices. Crucially, the bolus of oxygen delivered was often chosen arbitrarily and not adjusted during exercise.³⁹

Initial portable oxygen concentrators have undergone recent improvements to give more efficient and robust devices. Larger concentrators for autonomous home-based filling now provide further choice to patients. Tests of new oxygen concentrators show equivalent clinical efficacy between pulsed-dose delivery of liquid oxygen and pulsed-dose delivery from an oxygen concentrator in exercise tests. However, the wide variation seen between individual patients necessitates titration of the dose,¹⁰ and clinical studies are needed to identify more precise methods of titration with pulsed-dose delivery.

AO provision needs to be tailored to patients' needs, including their level of activity.⁴⁰ Recent French

recommendations are for liquid oxygen only in active patients needing more than 3 L/min oxygen, whereas portable or transportable oxygen concentrators are recommended for less active patients who need less than this amount. The range of portable oxygen concentrators now available makes it possible to suit the device to the patient's needs for autonomy, their level of activity, and their level of hypoxaemia.

Health Economic Aspects of Long-Term Oxygen Therapy

Doctor Stuart Little

Dr Little presented preliminary findings from a health economic study of the HomeFill oxygen concentrator system in the Scottish health service. The region studied, Dumfries and Galloway, was a largely rural, sparsely populated area where patients were often remote from healthcare resources. Originally, the system for oxygen provision was a mixture of hospitals with a national oxygen provision service, and primary care and community pharmacies with private provision of oxygen delivery devices. In primary care, inappropriate oxygen prescription (e.g. for breathlessness only) was an issue.

An exploratory study (n=22) of oxygen-conserving, pulsed-dose delivery devices in the Dumfries and Galloway region showed a clear increase (40%) in time spent outside the home and a 50% reduction in oxygen cylinders used, thus providing quality-of-life benefits and financial savings. Another small study (n=20) of the HomeFill oxygen concentrator system in the same region found it to be very popular with patients, who reported increased freedom and confidence and decreased concern about supply. The cost reduction to the healthcare system, including reduction in transport and fuel costs, was estimated at 77%.⁴¹

In 2013, the National Oxygen Project was established in Scotland to provide a nationally coordinated service with a contracted service provider, instead of the previous pharmacy-led, regionally organised system, offering both pre-filled oxygen cylinders and home refillable cylinders (the HomeFill system). This was a more robust system, developed to be more cost-effective, and involved clinicians to ensure a patient-centred service. The reform included development of a single, consistent care pathway. The National Oxygen Project aimed

to benefit patients by providing an accurate diagnosis, ensuring prescription of the most appropriate mode of treatment, offering equal access to treatment for all, focussing treatment on the patient's needs with planned follow-up, and improving quality of life. The system also benefitted the clinician, being consistent and simplified, and offering electronic prescribing and a range of modalities, as well as cost benefits.

A survey of HomeFill users following implementation of the new system gave similar results to the earlier exploratory study. All patients (100% of 450 respondents) found it easy to use and rated the quality of service as 'as good as or better than the previous oxygen service'. In patients who left the home more than four times per week, there was a 50% increase in time spent away from home, and 92% of patients reported an increase in quality of life. The cost reduction compared with the previous system was estimated at 77%.⁴² These findings led to a full health economic analysis of the HomeFill system compared with use of DD-size oxygen cylinders. The model extrapolation for Scotland estimated savings of €2 million per year, although this was thought to be an underestimation and a sensitivity analysis suggested savings of €6 million per year.

Q&A session

How many of the audience titrate oxygen therapy at night systematically?

Most clinicians do not titrate oxygen use at night, but prescribe a set amount of oxygen. Those who do are likely to be those for whom home oximeter

use is reimbursed, and the use of an oximeter in the home setting is an ideal opportunity for data collection.

How would the panel treat a patient with mild hypoxaemia and exercise dyspnoea?

The NOTT study showed poorer survival in patients with breathlessness using LTOT, but this could be because the breathlessness was linked to other comorbidities that caused increased mortality.

Dr Vivodtzev added that the patient's lifestyle and oxygen needs are important, and there is financial pressure to reduce liquid oxygen consumption. It is worth considering what other sources of oxygen the patient could use, and trialling different ones in the patient with exercise tests. Since different exercise tests have differing oxygen requirements, the patient's oxygen needs should ideally be evaluated in the home or during daily living activities.

Will the Scottish system spread due to its marked economic benefits?

In setting up the Scottish standardised oxygen assessment service, the service providers and the organising team for the national service worked together to develop an efficient, effective service, and consequently the patient response has been good. While one could hope it would set a model for the UK, NHS England works somewhat differently. It is worth noting that the private care and primary pharmacies were resistant to the national reform of oxygen services in Scotland, as they stood to lose revenue from the prescribing of oxygen.

REFERENCES

1. Hardinge M et al. British Thoracic Society guidelines for home oxygen use in adults. *Thorax*. 2015;70(Suppl 1):i1-43.
2. van Gestel AJ et al. Prevalence and prediction of exercise-induced oxygen desaturation in patients with chronic obstructive pulmonary disease. *Respiration*. 2012;84(5):353-9.
3. Crisafulli E et al. Predicting walking-induced oxygen desaturations in COPD patients: a statistical model. *Respir Care*. 2013;58(9):1495-503.
4. Poulain M et al. 6-minute walk testing is more sensitive than maximal incremental cycle testing for detecting oxygen desaturation in patients with COPD. *Chest*. 2003;123(5):1401-07.
5. Croxton TL, Bailey WC. Long-term oxygen treatment in chronic obstructive pulmonary disease: recommendations for future research: an NHLBI workshop report. *Am J Respir Crit Care Med*. 2006;174(4):373-8.
6. Ameer F et al. Ambulatory oxygen for people with chronic obstructive pulmonary disease who are not hypoxaemic at rest. *Cochrane Database Syst Rev*. 2014;6:CD000238.
7. Lacasse Y et al. Nocturnal oxygen therapy in patients with chronic obstructive pulmonary disease: a survey of Canadian respirologists. *Can Respir J*. 2007;14(6):343-8.
8. Doherty DE et al. Recommendations of the 6th long-term oxygen therapy consensus conference. *Respir Care*. 2006;51(5):519-25.
9. Pepin JL et al. Long-term oxygen therapy at home. Compliance with medical prescription and effective use of therapy. ANTADIR Working Group on Oxygen Therapy. Association Nationale de Traitement à Domicile des Insuffisants Respiratoires. *Chest*. 1996;109(5):1144-50.
10. Couillard A et al. [Oxygen therapy by a portable concentrator with a demand valve: a randomised controlled study of its effectiveness in patients with COPD]. *Rev Mal Respir*. 2010;27(9):1030-8.
11. Melloni B et al. Commission Médico-Technique et Sociale (CMTS), Fédération Antadir. [Efficacité clinique du dispositif médical SOLO2™].

- Rapport d'évaluation]. 2011. Available at: http://www.invacare.fr/sites/fr/files/product_documents/c1cda1236659e-a76a4cf37543d3cdc18-70_so2-sales_and_images-fr_FR--1427707315-Rapport%20final%20-%20ANTADIR%20Eval%20Clin%20-%20Solo2.pdf. Last accessed: 4 November 2015.
12. Tiep BL et al. Low-concentration oxygen therapy via a demand oxygen delivery system. *Chest*. 1985;87(5):636-8.
 13. Zhou S, Chatburn RL. Effect of the anatomic reservoir on low-flow oxygen delivery via nasal cannula: constant flow versus pulse flow with portable oxygen concentrator. *Respir Care*. 2014;59(8):1199-209.
 14. Chatburn RL, Williams TJ. Performance comparison of 4 portable oxygen concentrators. *Respir Care*. 2010;55(4):433-42.
 15. Garrod R et al. Evaluation of pulsed dose oxygen delivery during exercise in patients with severe chronic obstructive pulmonary disease. *Thorax*. 1999;54(3):242-4.
 16. Fuhrman C et al. Comparison of four demand oxygen delivery systems at rest and during exercise for chronic obstructive pulmonary disease. *Respir Med*. 2004;98(10):938-44.
 17. Nasilowski J et al. Comparing supplementary oxygen benefits from a portable oxygen concentrator and a liquid oxygen portable device during a walk test in COPD patients on long-term oxygen therapy. *Respir Med*. 2008;102(7):1021-5.
 18. Strickland SL et al. A randomized multi-arm repeated-measures prospective study of several modalities of portable oxygen delivery during assessment of functional exercise capacity. *Respir Care*. 2009;54(3):344-9.
 19. Leblanc CJ et al. A comparative study of 3 portable oxygen concentrators during a 6-minute walk test in patients with chronic lung disease. *Respir Care*. 2013;58(10):1598-605.
 20. Cuvelier A et al. Nocturnal efficiency and tolerance of a demand oxygen delivery system in COPD patients with nocturnal hypoxemia. *Chest*. 1999;116(1):22-9.
 21. Chatburn RL et al. Nocturnal oxygenation using a pulsed-dose oxygen-conserving device compared to continuous flow. *Respir Care*. 2006;51(3):252-6.
 22. Yáñez AM et al. Oxygenation With a Single Portable Pulse-Dose Oxygen-Conserving Device and Combined Stationary and Portable Oxygen Delivery Devices in Subjects With COPD. *Respir Care*. 2015;60(3):382-7.
 23. Fischer R et al. Comparison of portable oxygen concentrators in a simulated airplane environment. *Respir Med*. 2013;107(1):147-9.
 24. Ministère des affaires sociales, de la Santé et des droits des femmes. Arrêté du 23 février 2015 portant modification des modalités de prise en charge de dispositifs médicaux et prestations associées pour l'oxygénothérapie. 2015. Available at: <http://www.legifrance.gouv.fr/eli/arrete/2015/2/23/AFSS1505233A/jo>. Last accessed: 4 November 2015.
 25. Aubier M et al. Effects of the administration of O₂ on ventilation and blood gases in patients with chronic obstructive pulmonary disease during acute respiratory failure. *Am Rev Respir Dis*. 1980;122(5):747-54.
 26. Aubier M et al. Central respiratory drive in acute respiratory failure of patients with chronic obstructive pulmonary disease. *Am Rev Respir Dis*. 1980;122(2):191-9.
 27. Nocturnal Oxygen Therapy Trial Group. Continuous or nocturnal oxygen therapy in hypoxemic chronic obstructive lung disease: a clinical trial. *Ann Intern Med*. 1980;93(3):391-8.
 28. Medical Research Council Working Party. Long term domiciliary oxygen therapy in chronic hypoxic cor pulmonale complicating chronic bronchitis and emphysema. Report of the Medical Research Council Working Party. *Lancet*. 1981;1(8222):681-6.
 29. Hardinge M et al. Guideline update: The British Thoracic Society Guidelines on home oxygen use in adults. *Thorax*. 2015;70(6):589-91.
 30. Plywaczewski R et al. Incidence of nocturnal desaturation while breathing oxygen in COPD patients undergoing long-term oxygen therapy. *Chest*. 2000;117(3):679-83.
 31. Strom K, Boe J. Quality assessment and predictors of survival in long-term domiciliary oxygen therapy. The Swedish Society of Chest Medicine. *Eur Respir J*. 1991;4(1):50-8.
 32. Drummond MB et al. Continuous oxygen use in nonhypoxemic emphysema patients identifies a high-risk subset of patients: retrospective analysis of the National Emphysema Treatment Trial. *Chest*. 2008;134(3):497-506.
 33. Stoller JK et al. Oxygen therapy for patients with COPD: current evidence and the long-term oxygen treatment trial. *Chest*. 2010;138(1):179-87.
 34. Soguel SN et al. Oxygen saturation during daily activities in chronic obstructive pulmonary disease. *Eur Respir J*. 1996;9(12):2584-9.
 35. Eaton T et al. Ambulatory oxygen improves quality of life of COPD patients: a randomised controlled study. *Eur Respir J*. 2002;20(2):306-12.
 36. Cuvelier A et al. Refillable oxygen cylinders may be an alternative for ambulatory oxygen therapy in COPD. *Chest*. 2002;122(2):451-6.
 37. Kerby GR et al. Clinical efficacy and cost benefit of pulse flow oxygen in hospitalized patients. *Chest*. 1990;97(2):369-72.
 38. Roberts CM et al. Comparison of the efficacy of a demand oxygen delivery system with continuous low flow oxygen in subjects with stable COPD and severe oxygen desaturation on walking. *Thorax*. 1996;51:831-4.
 39. Martí S et al. Are oxygen-conserving devices effective for correcting exercise hypoxemia? *Respir Care*. 2013;58(10):1606-13.
 40. Casaburi R et al. Influence of lightweight ambulatory oxygen on oxygen use and activity patterns of COPD patients receiving long-term oxygen therapy. *COPD*. 2012;9(1):3-11.
 41. Murphie P, Little S. Homefill: better for your patient, better for your pocket? *Prim Care Respir J*. 2011;20(2):223-4.
 42. Murphie P et al. National Homefill survey in Scotland. *Eur Respir J*. 2014;44(58):P3700.