Welcome to this June issue of Respiratory Research Review on the topic of COPD.

Research continues to inform us how to provide the best care for our patients. For example, by assisting us to identify COPD patients in the first place, to choose treatments and by exploring future therapies. COPD is, in principle, a preventable disease affecting at least 200,000 adults in NZ, around 14% of the population. With such a large number of the population affected, it is unsurprising that COPD costs the country about NZ$5.6 billion with a direct health expenditure cost of almost $500 million. The NZ government is proposing legalisation of the sale and supply of nicotine containing e-cigarettes and e-liquid, on the premise that vaping is less harmful than smoking. Still, ‘the Ministry of Health does not have enough evidence to recommend e-cigarettes confidently as a smoking-cessation tool. Smokers should use approved smoking-cessation medicines, such as nicotine-replacement therapy, to support them to stop smoking and seek behavioural support from stop-smoking services’ (Ministry of Health). In that aspect, it echoes the recommendations from the COPD GOLD 2017 guidelines. At a population level it has been observed that high school students who use e-cigarettes are more likely to start smoking tobacco (Ref. Control).

The GOLD 2017 – Global Strategy for the Diagnosis, Management and Prevention of COPD is comprehensive; however, it is not a quick read with 139 pages. The executive summary report is condensate to 15 pages of text and a well-written reminder of the guiding principles. One change is the different role of spirometry. Spirometry is still the key test to confirm the diagnosis and to assess airflow limitation. The assessment of risk of exacerbation and essentially pharmaceutical treatment is guided by the patient symptoms as assessed by the COPD Assessment Test (CAT score) and the history of exacerbation over the last year. The assessment of exacerbation risk then defines the starting medication, the direction of escalation or for the first time the reduction of therapy.

Medical lung volume reduction using bronchoscopically delivered vapors, coils, sclerosing agents or bronchial valves continues to increase in its evidence base. It appears not too dissimilar to surgical techniques, in that careful patient selection is crucial to the success of this treatment. Pallav Shah and colleagues have published an insightful review on a state of the art technique of lung volume reduction for emphysema. The elephant in the room for COPD care is our challenge to integrate care for COPD and cardiac disease. Sara Roveris and colleagues from the COPD GOLD committee have published a very practical review with simple flow diagrams on how to manage patients with COPD who have heart failure, ischaemic heart disease, arrhythmias and most notably atrial fibrillation. It is fun to read.

The Thoracic Society of Australia and New Zealand has published their new rehabilitation guidelines. With input of the consumer groups, they structured the information into nine simple questions. If you can answer them all, you don’t need to read the guidelines, otherwise, click here.

1. Is pulmonary rehabilitation effective compared with usual care in patients with COPD?
2. Does pulmonary rehabilitation affect healthcare utilisation?
3. Is home- or community-based pulmonary rehabilitation as effective as a hospital-based programme?
4. In patients with mild disease severity, is pulmonary rehabilitation more effective than usual care?
5. Are programmes with longer duration more effective than the standard 3-week programmes?
6. Does ongoing supervised exercise at lower frequency than the initial programme maintain exercise capacity and QOL at 12 months in patients with COPD?
7. Does a structured education programme enhance the benefits of pulmonary rehabilitation?
8. Do patients who experience oxygen desaturations have greater improvements if oxygen supplementation is provided during training?
9. Is pulmonary rehabilitation effective in chronic respiratory diseases other than COPD?

My answers are: 1) yes, 2) yes, 3) yes, 4) yes, 5) no, 6) no, 7) no, 8) maybe, and 9) yes. Hopefully the authors won’t take offense to my interpretation and I am certainly willing to engage in discussions once you have checked the answers yourself.

Kind regards,
Professor Lutz Beckert
lutzbeckert@researchreview.co.nz

Abbreviations used in this issue
6MWD = 6-minute walk distance
COPD = chronic obstructive pulmonary disease
FEV1 = forced expiratory volume
HR = hazard ratio
PEF = peak expiratory flow
QOL = quality of life

---

GSK’s Ellipta portfolio of COPD and Asthma treatments is here.

For more information, please go to www.medsafe.govt.nz
Association of long-term, low-intensity smoking with all-cause and cause-specific mortality in the National Institutes of Health

Authors: Inoue-Choi M et al.

Summary: The AARP Diet and Health Study sought to clarify the effects of long-term, low-intensity smoking on mortality from all causes and for specific causes, using data from 290,215 adults (mean age 71 years) aged 59–82 years at the start of the study. The participants were asked about smoking behaviours during nine periods across their lives. Among current smokers, 159 reported smoking <1 cigarette per day consistently throughout the years that they smoked and 1493 reported consistently smoking 1–10 cigarettes per day. In each of these groups, the all-cause mortality risk was substantially higher than for never-smokers (respective HRs 1.64 [95% CI 1.07, 2.51] and 1.67 [1.64, 2.13]). Associations were similar between genders for all-cause mortality and were observed across a range of smoking-related causes of death, with a particularly strong association for lung cancer mortality (respective HRs 9.12 [95% CI 2.92, 28.47] and 11.61 [8.25, 16.35] for <1 and 1–10 cigarettes per day). Former smokers of <1 and 1–10 cigarettes per day who quit at age ≥50 years had higher all-cause mortality risks than those who quit at a younger age (respective HRs 1.44 [95% CI 1.12, 1.85] and 1.42 [1.27, 1.59]).

Comment: Patients frequently report that they have cut their smoking down to 10 cigarettes or less, rather than transitioning to complete smoking cessation, and many maintain this level of smoking for many years. Internationally about a quarter of people smoke <10 a day and a further quarter smoke not every day and only at social engagements. The perception is that this is a ‘safe’ level of smoking. This epidemiological study based on more than 100,000 people gives a clear answer. Bottom line: compared with never-smokers, even occasionally smoking is associated with an increased risk of mortality, especially lung cancer. There is no risk-free tobacco smoking.

Reference: JAMA Intern Med 2017;177(1):87–95

Abstract

Longitudinal study of e-cigarette use and onset of cigarette smoking among high school students in Hawaii

Authors: Wills TA et al.

Summary: The impact of e-cigarette use during adolescence on subsequent smoking behaviour was explored in this longitudinal school-based survey of 2338 students from Hawaii. Among never-smokers at baseline, students who used e-cigarettes at baseline were more likely to have started smoking cigarettes at 1-year follow-up (adjusted odds ratio 2.87 [95% CI 2.03, 4.05]); baseline e-cigarette use did not significantly affect smoking frequency at 1 year among ever-smokers at baseline. Uptake of e-cigarette use among never-users of cigarettes and e-cigarettes at baseline was predicted by age, ethnicity, lower parental education/support, a greater degree of rebelliousness and the belief that e-cigarettes are healthier.

Comment: The Ministry of Health is proposing to legalise nicotine-containing e-cigarettes with the intention of facilitating smoking cessation to make Aotearoa smoke-free by 2025. Ministry of Health. We need to be watchful that the public health benefit of assisting smoking cessation is not being undermined by the emerging health issue of e-cigarette use in adolescents, which may contribute to renormalising smoking. In this study, the authors report on a longitudinal observation of teenagers over 1 year and noted that e-cigarette use was associated with increased tobacco smoking. Bottom line: e-cigarette use in teenagers appears to be a marker of tobacco smoking uptake.


Abstract

Prognosis of asymptomatic and symptomatic, undiagnosed COPD in the general population in Denmark

Authors: Čikš Y et al.

Summary: To examine the prognosis of asymptomatic and symptomatic, undiagnosed COPD, these researchers analysed prospective data from a cohort of 95,288 members of the Danish general population, of whom 32,518 were regarded as being at high risk for COPD. Among those at high risk for COPD, 11% met the COPD criteria and 78% were undiagnosed, with 71% of undiagnosed cases being asymptomatic. There were 800 COPD exacerbations, 2038 cases of pneumonia and 2769 deaths (152 due to respiratory disease) among the high-risk cohort during median follow-up of 6.1 years. Compared with individuals without COPD, those with undiagnosed, asymptomatic COPD and those with undiagnosed, symptomatic COPD had elevated risks of exacerbations (respective adjusted HRs 5.0 [95% CI 2.8, 8.9] and 15.5 [11.0, 21.8]), pneumonia (1.7 [1.3, 2.2] and 2.8 [2.4, 3.3]) and death from any cause 1.3 [1.1, 1.6] and 2.0 [1.8, 2.3]; those with undiagnosed, symptomatic COPD were also significantly at increased risk of death from respiratory causes (4.3 [2.8, 6.7]).

Comment: COPD GOLD doesn’t recommend screening for COPD. These Danish researchers analysed data from the 100,000 people of the Copenhagen General Population Study. The authors identified an at-risk population for COPD based on age over 40 years. 10 pack-year history of smoking and no known history of asthma. This at-risk population of about 30,000 was invited for spirometry, and about 3000 had undiagnosed COPD. Compared with people with COPD, people with undiagnosed, symptomatic COPD had increased risks of exacerbations, pneumonia and death. Bottom line: people with undiagnosed COPD carry an increased risk and we need better strategies to identify COPD.


Abstract

Independent commentary by Professor Lutz Beckert.

Professor Lutz Beckert is the Head of Department of Medicine of the University of Otago, Christchurch. He is also a Respiratory Physician at Canterbury District Health Board with particular clinical interests in interstitial lung disease, pulmonary vascular disease, respiratory physiology and COPD (chronic obstructive pulmonary disease). Lutz is happy to be contacted to discuss research ideas either as a sounding board or considering future collaborations.

Reference:

Upgrade your COPD patients to SPIOLTO® RESPIMAT®

www.turnopenpress.co.nz

www.medsafe.govt.nz

For more information, please go to www.medsafe.govt.nz

www.researchreview.co.nz
A new approach for identifying patients with undiagnosed chronic obstructive pulmonary disease

**Authors:** Martinez FJ et al., on behalf of the High-Risk-COPD Screening Study Group

**Summary:** These US researchers set out to develop a way to identify undiagnosed COPD requiring treatment using a cross-sectional, case-control study of patients recruited from primary-care settings. Case patients had COPD with ≥1 exacerbation in the past year or FEV₁ <60% of predicted without exacerbation in the past year, and controls had no COPD or had mild COPD (FEV₁ >60% predicted and no exacerbation in the past year); PEF and spirometry readings were obtained for 186 cases and 160 controls. Cases had a lower mean FEV₁, percentage of predicted than controls (42.5% vs. 62.5%). The respective sensitivity and specificity values for differentiating cases from all controls were 95.7% and 44.4% for CAPTURE (a 5-item questionnaire), 88.0% and 77.5% for PEF, and 89.7% and 78.1% for CAPTURE and PEF combined; the respective values for differentiating cases from non-COPD controls were 95.7% and 67.8% for CAPTURE, 88.0% and 90.8% for PEF and 89.7% and 93.1% for CAPTURE and PEF combined.

**Comment:** Spirometry is the standard method of diagnosing COPD; however, access to quality spirometry and skilful interpretation is not always optimal. These American authors report a simple 5-item screening questionnaire to identify COPD patients who would most likely benefit from therapy. The five questions explore exposure, symptoms of breathlessnes, tiring easily and acute respiratory illness. Maybe this will assist us ‘Finding the missing millions: can a new questionnaire help to detect undiagnosed chronic obstructive pulmonary disease?’, as the insightful accompanying editorial suggests. **Bottom line:** although promising, trials should be conducted in primary care before adding it to the workload in general practice.

Reference: Am J Respir Crit Care Med 2017;195(6):748–56

### Home-based rehabilitation for COPD using minimal resources

**Authors:** Holland AE et al.

**Summary:** In this study assessing whether home-based pulmonary rehabilitation has equivalent outcomes to centre-based pulmonary rehabilitation, 166 patients with stable COPD were randomised to receive 8 weeks of pulmonary rehabilitation by either the standard outpatient centre-based model or a new home-based model including one home visit and seven once-weekly telephone calls from a physiotherapist. The primary outcome was change in 6MWD at 12 months. The home-based pulmonary rehabilitation model produced short-term clinical outcomes that were equivalent to centre-based pulmonary rehabilitation, but neither model maintained postrehabilitation gains at 12 months.

**Comment:** This Australian paper, published in Thorax, has been voted as the most influential paper in the US. Our colleagues report on their randomised controlled trial comparing outpatient to home-based pulmonary rehabilitation. In the home-based arm, a physiotherapist spent 30 minutes at the patients’ homes to establish goals, set a programme and supervise the first session followed by seven structured telephone calls. While neither treatment had an effect after 12 months, the home-based therapy was at least as effective as outpatient rehabilitation in achieving a 6MWD gain, improvement of dyspnoea and hospital admission. **Bottom line:** home-based rehabilitation is at least as effective as standard courses at a hospital.


### Telehealthcare for patients suffering from chronic obstructive pulmonary disease: effects on health-related quality of life

**Authors:** Lilholt PH et al.

**Summary:** The Danish TeleCare North trial randomised 1225 patients with COPD by district to standard care with or without telehealthcare. There was no significant difference between the intervention and control arms for the adjusted mean 12-month changes for the physical and mental component summary scores of the Short Form 36-Item Health Survey, Version 2 (0.1 [95% CI –1.4, 1.7] and 0.4 [–1.7, 2.4]).

**Comment:** Telehealth has the potential to engage and empower patients in their care and so to improve their coping abilities and physical and mental well-being. In 2012 the Danish Government launched a plan to disseminate telemedicine nationally. The authors of this study report on a randomised trial, where more than 1000 patients were assigned to standard care or standard care plus telehealthcare. People in the telehealthcare arm who had an iPad or similar device, blood pressure monitor, pulse oximeter and scales at home showed some improvement in their mental health; however, **bottom line:** overall the addition of telehealth care to standard care did not improve health-related QOL.


### Duolin Freedom to breathe

**Duolin Inhaler** is used by over **36,000 PATIENTS**

- Salbutamol 100 mcg and Ipratropium bromide 20 mcg
- Indicated for COPD, bronchitis, emphysema
- Duolin Inhaler is fully funded with no special authority

**Duolin Inhaler**, PRESCRIPTION MEDICINE. Duolin Inhaler is indicated for the treatment of reversible bronchodilatation associated with obstructive airflow diseases in patients who require more than a single bronchodilator. Before prescribing Duolin Inhaler, please review the information on dosage, contraindications, precautions, interactions, and adverse effects. The datasheet is available at [www.medsafe.govt.nz](http://www.medsafe.govt.nz). Distributed by REX Medical Ltd, Auckland, New Zealand. TAPS NA 8904.

[CLICK HERE](http://www.medsafe.govt.nz)
Benefits of long-term pulmonary rehabilitation maintenance program in patients with severe chronic obstructive pulmonary disease

Authors: Gidli M-R et al.

Summary: Outcomes were reported for a prospective trial that randomised 143 patients with moderate-to-severe COPD to 3 years of pulmonary rehabilitation maintenance after an 8-week outpatient pulmonary rehabilitation programme or a control group. The 8-week programme, which was completed by 96.5% of participants, resulted in significant improvements in BODE (body mass index, airflow obstruction, dyspnoea and exercise) index scores, 6MWD and health-related QOL (p<0.001). The magnitude of change in 6MWD differed significantly between the intervention and control arms over the 3-year follow-up, with a slight initial increase in the intervention arm during the first year and lesser decline thereafter. BODE index changes differed significantly between baseline and 24 months. The 3-year adherence rate was significantly greater in the intervention arm than in the control arm (66% vs. 17% [p<0.001]).

Comment: The Holy Grail of pulmonary rehabilitation is maintenance of exercise performance following the initial intensive treatment, as defined by Carolyn Rochester and Martin Spruit in their accompanying editorial. These Spanish authors supplied exercycles and offered weekly supervised sessions following the rehabilitation course. Their pulmonary rehabilitation reached good improvement, in keeping with other studies. The benefit was maintained in the intervention group for 2 years; however, not to a greater degree than in other studies with simpler interventions, and bottom line: maintenance intervention was not associated with increased QOL and the physical aspects did not last the full 3 years.

Reference: Am J Respir Crit Care Med 2017;196(5):622–9
Abstract

Sing Your Lungs Out – a community singing group for chronic obstructive pulmonary disease

Authors: McNaughton A et al.

Summary: This pilot feasibility study enrolled patients with COPD who had completed pulmonary rehabilitation in an exercise group into a community-based singing group that met each week for >1 year; 28 of 140 patients who had been approached entered the study, five withdrew in the first month, 21 completed 4-month assessments and 18 completed 1-year assessments. Mean attendance at the singing group was 85%. At 12 months, there was no significant change in total Hospital Anxiety and Depression Scale score (primary outcome; p=0.37), but the anxiety subscore had decreased by −0.9 points (p=0.038) and 6MWD had significantly increased by 65m (p<0.001).

Comment: Ongoing use of an exercise is not for everybody and neither is singing. Of the 140 patients approached, only 28 participated in a weekly singing group. The retention was great at 85%, although most had never considered singing in the past. The reduction in anxiety was not surprising, but even so it only just reached statistical significance. Surprising was the 65m gain in 6MWD. The reduction in residual and total lung capacity may need some further testing in a larger cohort. Bottom line: this pilot study should encourage further research into singing to improve lung function, walk distance and QOL.

Abstract

A systematic review of the effectiveness of discharge care bundles for patients with COPD

Authors: Ospina MB et al.

Summary: This was a systematic review of five clinical trials, seven uncontrolled trials and two interrupted time series evaluating discharge care bundles offered to patients with COPD. The care bundles included 26 distinct elements of care. Data pooled from four of the clinical trials that had moderate-to-high risk of bias revealed that discharge bundles for patients with COPD significantly reduced the likelihood of hospital readmission (risk ratio 0.80 [95% CI 0.65, 0.99]), but evidence that they reduce long-term mortality and improve QOL was insufficient.

Comment: Many DHBs arrange care bundles for patients with COPD after admission for an acute exacerbation. Care bundles may have an important role in providing consistent best practice; however, the evidence base for the bundles is thin and, as these Canadian authors point out, the individual components quite varied, containing up to twelve items. The authors consider the management of the following core items of a care bundle: smoking cessation, inhaler technique, disease management, pulmonary rehabilitation, outpatient follow-up and tailored care plans. Bottom line: discharge care bundles led to fewer readmissions; however, they didn’t reduce mortality nor did they improve QOL.

Abstract

Segmental volume reduction using thermal vapour ablation in patients with severe emphysema

Authors: Herth FJF et al.

Summary: Patients aged 45–75 years with severe, upper lobe-predominant emphysema, FEV1 20–45%, substantial hyperinflation and postrehabilitation 6MWD ≥140m were randomised to segmental vapour ablation (n=45) or standard medical management (n=24) in the 6-month, open-label STEP-UP trial. Compared with standard medical management, segmental vapour ablation was associated with mean relative improvements in FEV1 of 14.7% (p<0.0001) and St George’s Respiratory Questionnaire score of −9.7 points (p=0.0021). The most common serious adverse event was COPD exacerbation, affecting 24% of segmental vapour ablation recipients and 4% of standard medical management recipients. One of the deaths was judged to be possibly treatment-related. There were no pneumothoraces within 30 days of treatment.

Comment: We have alluded to the excellent review by Pallav Shah and colleagues on lung volume reduction for emphysema earlier. In this article, the European researchers report a randomised trial of 70 patients with severe COPD. In the intervention group diseased segments of the lung were ablated with vapour. At 6 months these patients had an improved FEV1, a reduced residual volume and improved QOL; however, they also had an increased rate of pneumonitis and exacerbations. Bottom line: vapour therapy can be applied in stages and in patients without an intact fissure; however, the long-term risk-benefit ratio is still uncertain.

Abstract

CLICK HERE to read previous issues of Respiratory Research Review