

CHEST & HEART

NEWS LETTER

Now-a-days, tobacco stands out as the agent most responsible for avoidable illness and death. Millions of peoples consume this toxin on a daily basis. Its use brings premature death and contributes to profound disability and pain in many ways. In fact, tobacco use is the chief avoidable cause of illness and death, causing cancer, heart disease, stroke, complications of pregnancy, and chronic obstructive pulmonary disease. With 70 percent of smokers seeing a physician each year, more than 70 percent of them report wanting to quit.

Tobacco Use as a True Drug Dependence

All drug addictions warrant clinical intervention, including tobacco dependence. Tobacco dependence exhibits classic characteristics of drug dependence. For example, nicotine is psychoactive, tolerance producing, and causes physical dependence characterized by withdrawal symptoms. Many smokers typically cycle through multiple periods of relapse and remission and persist in tobacco use for many years.

Tobacco Dependence Shows Many Features of A Chronic Disease

Tobacco dependence shows many features of a chronic disease. Although a minority of tobacco users achieves permanent abstinence in an initial quit attempt, the majority persists in tobacco use for many years and typically cycle through multiple periods of relapse and remission.

By recognizing that tobacco dependence is a chronic condition, clinicians will better understand the relapsing nature of the ailment and the requirement for ongoing, rather than just acute care. This framework helps clinicians view relapse as a subsequent component of this chronic disease, rather than a lack of motivation or commitment on the patients' part or lack of ability on the clinicians' part. A failure to appreciate

the chronic nature of tobacco dependence may undercut clinicians' motivation to treat tobacco use consistently.

How to Treat Tobacco Smokers Who are Willing to Quit?

ASK

It is imperative that clinicians ask EVERY patient about tobacco use status at EVERY visit. This occurs most consistently when there are systems in place, such as a vital signs stamp or electronic prompt on electronic medical records that systematically result in universal tobacco use status documentation.

ADVISE

Once tobacco use status has been identified and documented, clinicians should advise all tobacco users to quit. Even brief advice to quit by a clinician results in greater quit rates. Smokers cite a clinician's advice to quit as an important motivator for attempting to stop smoking. Therefore, clinicians should urge all tobacco users to quit. This advice should be clear and strong. For example, "As your physician, I must tell you that the most important thing you can do to improve your health is to stop smoking."

The advice should be personalized to the individual's own situation (e.g. medical condition, family status, costs of tobacco).

ASSESS

After providing a clear, strong, and personalized message to quit smoking, the clinician must determine whether or not the patient is willing to quit at this time. One direct way to assess readiness to quit is to follow the ADVISE message with the simple question, "Are you willing to try to quit at this time?"

ASSIST

Assisting the patient in his or her quit attempt can be done using either a brief or an intensive intervention. Level of intensity of the intervention has a strong dose-response effect.

Treating Tobacco Use and Dependence



The 5 A's For Patients Willing To Quit

- ASK about tobacco use.
- ADVISE to quit.
- ASSESS willingness to make a quit attempt.
- ASSIST in quit attempt.
- ARRANGE for follow-up.



- **Brief intervention** - Even a minimal intervention, lasting less than 3 minutes, can significantly increase overall tobacco abstinence rates.

- **Intensive intervention** - The longer the session of person-to-person contact, and the more overall person-to-person contact, and the greater the number of visits, the more successful the treatment outcome.

In a 3- to 10-minute intervention, a clinician can provide a counseling session which can significantly impact a smoker's quit success.

Effective assistance can be provided by multiple providers, in multiple formats, including counseling and practice telephone support.

One way to systematically integrate tobacco cessation is by the use of the cessation tear sheet. This tear sheet can

allow clinicians to personalize intervention and can be given to patients as a take away.

Counseling

It is recommended that counseling include the following components:

- Provision of practical counseling (problem-solving/skills training) such as helping the patient identify events, internal states, or activities that increase the risk of smoking or relapse, identifying and practicing coping or problem-solving skills, and providing basic information about smoking and successful quitting.

Pharmacotherapy

The PHS Guideline has identified 5 first-line pharmacotherapies for smoking cessation and recommends that smokers attempting to quit be urged and/or prescribed a medication. These five first-

Pharmacotherapy	Precautions/contradictions	Side Effects	Dosage
Bupropion SR	- History of seizure - History of eating disorders	- Insomnia - Dry mouth	- 150 mg every morning for 3 days, then 150 mg twice daily (Begin treatment 1-2 weeks before quit)
Varenicline	- Significant renal impairment - Patient undergoing dialysis	- Nausea - Insomnia - Abnormal dreams - Dry mouth	- Days 1 to 3: 0.5 mg tablet every morning - Days 4 to 7: 0.5 mg tablet twice daily - Days 8 to end of treatment: 1 mg tablet twice daily (Begin treatment 1 week before quit date)
Nicotine Gum		- Mouth soreness - Dyspepsia	- 1-24 cigs/day-2mg gum (up to 24 pieces/day) - 25+ cigs/day-4mg gum (up to 24 pieces/day)
Nicotine Lozenge		- Nausea - Insomnia	- Patients smokes 1st cigarette more than 30 min. after waking-2mg - Patient smokes 1st cigarette less than 30 min. after waking-4mg
Nicotine Inhaler		- Local irritation of mouth and throat	6-16 cartridges/day
Nicotine Nasal Spray		- Nasal irritation	- 8-40 doses/day
Nicotine Patch		- Local skin reaction - Insomnia	- 21 mg/24 hours - 14 mg/24 hours - 7 mg/24 hours - 15 mg/16 hours
Pharmacotherapy	Duration	Availability	Avg. Cost/day
Bupropion SR	- 7-12 weeks maintenance up to 6 months	Prescription only - Zyban - Wellbutrin SR - generic SR	1 box of 60 tablets, 150 mg: - Zyban: \$185.99 - Wellbutrin SR: \$167.99 - generic SR: \$101.99
Varenicline	- 3 to 6 months	Prescription only - Chantix	Cost varies. Approximately \$115 per month
Nicotine Gum	- Up to 12 weeks	OTC only - Nicorette - Nicorette Mint - Nicorette Orange - generic	2mg-1 box of 50 Pieces: -Nicorette: \$29.99 -Generic: \$22.994mg 4mg-1 box of 50 Pieces: -Nicorette: \$32.99
Nicotine Lozenge	- Up to 12 weeks	OTC only - Commit lozenge - generic (Nicabate)	2mg-48 lozenges: -Commit: \$29.99 4mg-48 lozenges: -Commit: \$29.99 -generic: \$24.99
Nicotine Inhaler	Up to 6 months	Prescription only - Nicotrol Inhaler	1 box of 168 cartridges: \$166.99
Nicotine Nasal Spray	- 3-6 months	Prescription only -Nicotrol NS	1 metered dose dispenser, 40 mls: \$190.99
Nicotine Patch	- 4 weeks then 2 weeks then 2 weeks -8 weeks	OTC only - Nicoderm CQ - Nicotrol - generic Prescription only -generic (Legend)	21 mg, box of 7: -Nicoderm: \$29.00 -generic: \$21.99 14 mg, box of 7: -Nicoderm: \$29.00 -generic: \$21.99

line therapies are: bupropion SR, nicotine gum, nicotine inhaler, nicotine nasal spray, nicotine patch. In addition, since the publication of the 2000 Guideline, the FDA has now approved 2 other medications: the nicotine lozenge and varenicline.

Suggestions for the Clinical Use of Pharmacotherapies for Smoking Cessation

See table-1

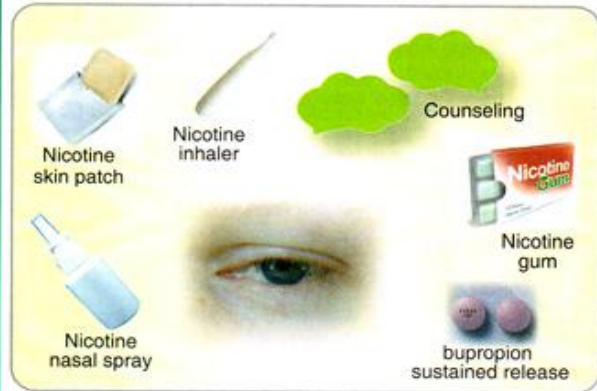


Figure - These medications have all been approved by the FDA for smoking cessation and have been shown to significantly improve abstinence rates.

Clinical guidelines for prescribing pharmacotherapy for smoking cessation

See table-2

ARRANGE

Arranging follow-up contact is the final step in treating tobacco use and dependence.

The clinician should schedule a follow-up contact soon after the quit date, preferably within the first week. This early follow-up is recommended because the majority of smokers trying to quit who subsequently relapse return to smoking within the first 2 weeks.

If the patient has used tobacco, discuss the circumstances surrounding the relapse and attempt to elicit a recommitment to quitting. Remind the patient that a relapse should be viewed as a learning experience. It may take the tobacco user multiple attempts to successfully quit smoking. Each time the patient relapses he or she learns more about what will help and what will be harmful for the next quit attempt. Also, relapse is consistent with the chronic nature of tobacco dependence; it is not a sign of personal failure of the tobacco user or the clinician.

[References available on request]

Who should receive pharmacotherapy for smoking cessation?	All smokers trying to quit except in the presence of special circumstances. Special consideration should be given before using pharmacotherapy with selected populations: those with medical contraindications, those smoking less than 10 cigarettes/day, pregnant and adolescent smokers.
What are the first-line pharmacotherapies recommended in this Guideline?	All seven of the FDA-approved pharmacotherapies for smoking cessation are recommended including bupropion SR, Varenicline, nicotine gum, nicotine inhaler, nicotine nasal spray, nicotine lozenge, and the nicotine patch.
What factors should a clinician consider when choosing among the seven first-line pharmacotherapies?	Because of the lack of sufficient data to rank-order these seven medications, choice of a specific first-line pharmacotherapy must be guided by factors such as clinician familiarity with the medications, contraindications for selected patients, patient preference, previous patient experience with a specific pharmacotherapy (positive or negative), and patient characteristics (e.g., history of depression, concerns about weight gain).
Are pharmacotherapeutic treatments appropriate for lighter smokers (e.g., 10-15 cigarettes/day)?	If pharmacotherapy is used with lighter smokers, clinicians should consider reducing the dose of first-line pharmacotherapies.
When should second-line agents be used for treating tobacco dependence?	Consider prescribing second-line agents for patients unable to use first-line medications because of contraindications or for patients for whom first-line medications are not helpful. Monitor patients for the known side effects of second-line agents.
Which pharmacotherapies should be considered with patients particularly concerned about weight gain?	Bupropion SR and nicotine replacement therapies, in particular nicotine gum, have been shown to delay, but not prevent, weight gain.
Which pharmacotherapies should be considered with patients with a history of depression?	Bupropion SR appears to be effective with this population.
Should nicotine replacement therapies be avoided in patients with a history of cardiovascular disease?	No. Nicotine replacement therapies are safe and have not been shown to cause adverse cardiovascular effects. However, the safety of these products has not been established for the immediate post-MI period or in patients with severe or unstable angina.
May tobacco dependence pharmacotherapies be used long-term (e.g., 6 months or more)?	Yes. This approach may be helpful with smokers who report persistent withdrawal symptoms during the course of pharmacotherapy or who desire long-term therapy. A minority of individuals who successfully quit smoking use ad libitum NRT medications (gum, nasal spray, inhaler) long-term. The use of these medications long-term does not present a known health risk. Additionally, the FDA has approved the use of bupropion SR for long-term maintenance indication.
May nicotine replacement pharmacotherapies ever be combined?	Yes. There is evidence that combining the nicotine patch with either nicotine gum or nicotine nasal spray increases long-term abstinence rates over those produced by a single form of NRT.



Cesarean Delivery May Increase Risk of Developing Asthma

J Pediatr. 2008;153:112-116.

Infants delivered by cesarean delivery had a moderately higher risk for the development of asthma vs those not delivered by cesarean delivery, according to the results of a population-based cohort study.

"Whether CS [cesarean section] is associated with asthma has been widely debated in recent years, and the issue remains far from resolved," write Mette C. Tollånes, MD, from the University of Bergen in Bergen, Norway, and colleagues. "Several studies have reported a moderately increased risk of asthma in children delivered by CS, whereas others have found no such association. "With few exceptions, these studies were characterized by rather small study populations and short follow-up periods."

The goal of this study was to evaluate the relationship between cesarean delivery and later development of asthma with use of a population-based cohort of 1,756,700 singletons reported to the Medical Birth Registry of Norway between 1967 and 1998. The primary outcome was asthma registered in the National Insurance Scheme, which provides cash benefits to families of children with severe chronic illnesses, during follow-up to age 18 years or the year 2002. Multivariate Cox proportional hazard models were used to determine associations between exposure (spontaneous vaginal delivery, instrumental vaginal delivery, or cesarean delivery, with planned and emergency cesarean delivery analyzed separately from 1988 onward) and outcome.

During follow-up, the cumulative incidence of asthma was 4.0 per 1000. Compared with children delivered by spontaneous vaginal delivery, those delivered by cesarean delivery had a 52% increased risk for asthma (adjusted hazard ratio [HR], 1.52; 95% confidence interval [CI], 1.42 - 1.62). Between 1988 and 1998, planned cesarean delivery was associated with a 42% increased risk for asthma (HR, 1.42; 95% CI, 1.25 - 1.61), and emergency cesarean delivery was associated with a 59% increased risk for asthma (HR, 1.59; 95% CI, 1.44 - 1.75). "We found a moderately increased risk of asthma in the children delivered by CS," the study authors write.

Reducing Daily Cigarette Smoking May Not Lower Risk for Premature Death

Tob Control. 2006;15:472-480.

Reducing daily cigarette smoking by 50% in heavy smokers did not significantly lower risk for premature death from specified smoking-related diseases and from any cause, according to the results of a prospective cohort study.

"Numerous population studies have given ample evidence that quitting smoking entirely results in a marked reduction in the ill effects of smoking," write Aage Tverdal, MD, and Kjell Bjartveit, MD, of the Norwegian Institute of Public Health in Oslo. "Up to now, however, only one large prospective study has explored the long-term effects of unassisted reduced smoking."

In 3 counties in Norway, 24,959 men and 26,251 women, aged 20 to 49 years, were screened for cardiovascular risk factors in the mid-1970s and again after 3 to 13 years, and they were followed up through 2003. The main endpoints were absolute and adjusted relative risks of all-cause mortality and mortality from cardiovascular disease, ischemic heart disease, all smoking-related cancer and lung cancer.

Compared with sustained heavy smokers, smokers who reduced their daily consumption by 50% (reducers) had the following adjusted relative risks for mortality: all-cause, 1.02 (95% confidence interval [CI], 0.84 - 1.22); cardiovascular disease, 1.02 (95% CI, 0.75 - 1.39); ischemic heart disease, 0.96 (95% CI, 0.65 - 1.41); smoking-related cancer, 0.86 (95% CI, 0.57 - 1.29); and lung cancer, 0.66 (95% CI, 0.36 - 1.21).

The difference in cigarette consumption between 2 examinations did not significantly predict mortality from any of the above causes. Furthermore, sustained reducers who continued smoking at reduced rates at both the second and third follow-up examinations did not have a lower risk than those who were heavy smokers at all 3 examinations.

"Long-term follow-up provides no evidence that heavy smokers who cut down their daily cigarette consumption by 50% reduce their risk of premature death significantly," the authors write. "In health education and patient counselling, it may give people false expectations to advise that reduction in consumption is associated with reduction in harm."

"Undoubtedly, reduction in consumption may have a place as a temporary measure in systematic smoking cessation," the authors conclude. "Nevertheless, the results of this study, and those of the Copenhagen Study, make it imperative to reassess this recommendation as a permanent solution, and raise the question whether it offers people false expectations. The study proves quite clearly the only safe way out of the risk caused by smoking: people who quit smoking have achieved a risk level that is remarkably lower than in those who continued to smoke."



Snaps

Healthcare Providers Should Offer Smoking-Cessation Advice More Often

MMWR Morb Mortal Wkly Rep. 2007;56(28):708-712.

Healthcare providers should offer smoking-cessation advice more often, according to the results of a Canadian survey. Only half of persons in that survey who visited healthcare providers in the preceding 12 months reported receiving smoking-cessation advice, suggesting that healthcare professionals may be missing valuable opportunities to educate their patients about how to quit smoking.

"Tobacco use is the most preventable cause of premature death and disease in Canada," write J. Stevenson, from the Tobacco Control Programme, Health Canada, and colleagues. "One of the objectives of the Canadian Federal Tobacco Control Strategy (FTCS) 2001-2011 is to reduce smoking prevalence in Canada from 25% to 20%. Although evidence indicates that an effective and efficient way of providing smoking-cessation information to smokers is through contact with health-care providers little data in Canada exist regarding smoking-cessation advice from this group."

Canadian Tobacco Use Monitoring Survey collected data from approximately 20,800 respondents. The survey contained questions about provision of smoking-cessation advice by healthcare professionals, including physicians, dentists or dental hygienists, and pharmacists, in the 12 months before the survey.

Of the current smokers who had visited a physician in the preceding 12 months, 51% reported that they were advised at that visit to reduce or to stop smoking. Only 38% of the youngest smokers (aged 15-19 years) received smoking-cessation advice, but this rate increased with increasing age. In the 20- to 24-year age group, 33% of males and 50% of females were advised by a physician to reduce or quit smoking.

For healthcare professionals other than physicians, about 36% of survey respondents were advised to reduce or stop smoking by dentists or dental hygienists, and about 16% received this advice from pharmacists.

"Although 88% of current smokers in Canada reported visiting a health-care provider in the preceding 12 months, only half of these smokers reported being advised to reduce or quit smoking," an accompanying editorial note points out. "Health-care providers are in a unique position to offer smoking-cessation advice and provide information on smoking-cessation aids to their patients; however, the results of this analysis indicate that many of these opportunities are being missed."

"A smoker's chance of quitting increases after receiving smoking-cessation information and support from various health-care providers in different disciplines," the editorial concludes. "Although certain health-care providers have included smoking-cessation activities in their practices, the results indicate that either many health professionals are missing this opportunity to provide smoking-cessation advice or that smokers are not seeking this advice from their health-care providers. Practice guidelines to identify smokers and encourage cessation could help increase the number of smokers who receive smoking-cessation counseling from their health-care providers."



Synbiotics May Increase a Child's Resistance to Respiratory Tract Infections

Pediatrics. 2008;122:8-12. Published online July 1, 2008.

The use of probiotics and prebiotics may increase a child's resistance to respiratory tract infections, according to the results of a double-blind randomized trial.

"Live probiotic bacteria and dietary prebiotic oligosaccharides (together termed synbiotics) increasingly are being used in infancy, but evidence of long-term safety is lacking," write Kaarina Kukkonen, MD, from University of Helsinki in Helsinki, Finland, and colleagues. "Probiotics and prebiotics are known to modulate immune responses."

Pregnant mothers carrying infants at high risk for allergy were randomized to receive a mixture of 4 probiotic species (*Lactobacillus rhamnosus* GG and LC705, *Bifidobacterium breve* Bb99, and *Propionibacterium freudenreichii* ssp *shermanii*) or a placebo for 4 weeks before delivery. For 6 months after birth, infants received the same probiotics with 0.8 g of galactooligosaccharides or a placebo daily.

Follow-up visits at ages 3, 6, and 24 months included clinical examinations and interviews for collection of safety and growth data. Questionnaires administered at ages 3, 6, 12, and 24 months also assessed these outcomes. Two-year follow-up assessment was completed for 925 of 1018 eligible infants.

In both groups, infants grew normally, with no apparent between-group differences in neonatal morbidity, infantile colic or other feeding-related behaviors, or serious adverse events. Antibiotics were prescribed less often in the synbiotic vs the placebo group (23% vs 28%) during the 6-month intervention. During follow-up, respiratory tract infections were less frequent in the synbiotic vs the placebo group (mean, 3.7 vs 4.2 infections).

"Feeding synbiotics to newborn infants was safe and seemed to increase resistance to respiratory infections during the first 2 years of life," the study authors write.



Long-acting Beta-agonists in stable COPD: A Review

Treatment guidelines indicate that inhaled bronchodilators are the standard of care in COPD patients. Short-acting inhaled bronchodilators (short-acting β_2 -agonists [SABAs] and anticholinergics) are recommended for the relief of symptoms on an as-needed basis, whereas long-acting inhaled bronchodilators (long-acting β_2 -agonists [LABAs] or tiotropium) in a regularly scheduled regimen or short-acting agents are recommended as first-line therapy in symptomatic patients with moderate-to-severe COPD. Although the consensus with regard to the central role of inhaled bronchodilators as first-line therapy is unanimous worldwide with the highest scientific level of evidence, several questions remain concerning different aspects of management. Of particular concern is the evidence that LABA use could lead to an increased risk for adverse events and respiratory deaths in patients with asthma and COPD. However, previous reviews presented very restrictive inclusion criteria and several shortcomings that affect the validity of their conclusions. Thus, these reviews studied only cardiovascular effects from patients with asthma and COPD that compare SABAs and LABAs, included only poorly reversible COPD patients, and did not assess outcomes such as COPD exacerbations requiring withdrawal and respiratory mortality. Additionally, one review performed its analysis on redundant data. Consequently, to clarify these issues, we performed a systematic review to assess the safety, as the primary end point outcome, and secondarily the efficacy of the use of LABAs in patients with COPD compared with placebo and anticholinergics.

A total of 27 randomized controlled trials met inclusion criteria and were selected for analysis. Two studies were excluded from analysis because they included results for patients enrolled in previous trials. Thus, Brusasco et al. presented combined results of Donohue et al. and a similar unpublished trial, and van Noord et al. reported the same data from the study of Rutten van Molken et al. All trials were of good quality (Jadad score > 2). Data for 20,527 patients (72% male) with 26,389 patient-years of follow-up were available for metaanalysis (mean age, 63.3 \pm 10.3 years). All studies enrolled patients with stable COPD that met moderate-to-severe GOLD criteria (stages 2 and 3) [average baseline FEV₁, 43% of predicted]. Eighteen studies allowed the concomitant use of ICS (percentage of patient's range, 12 to 88%).

Fourteen studies comparing LABA with placebo evaluated the incidence of severe COPD exacerbations. The overall cumulative incidence was 7.5% in the LABA group and 10.8% in the placebo group, with a significant exacerbation rate reduction of 3.3% (95% CI, 1.9 to 4.8). The RR reduction was similar with a fixed model (RR, 0.78; 95% CI, 0.67 to 0.91) or a random model (RR, 0.80; 95% CI, 0.69 to 0.92). The NNT was 30 (95% CI, 20 to 52). The fail-safe N test, which is the number of unpublished studies with null results needed to negate the current finding, was 23. When examining trials in which patients showed >15% reversibility to salbutamol, there were no significant differences in the effects of formoterol vs salmeterol on exacerbations. When examining trials using salmeterol, there were no significant differences in effects between studies enrolling patients with

poorly reversible and reversible obstruction. Also, we did not find a significant difference between patients treated with LABAs vs placebo with the two arms exposed or not exposed to ICS. Because many studies allowed the concomitant use of ICS, we performed an additional analysis including only trials that truly examine monotherapy without ICS (2,447 patients). Thus, like the previous analysis, there was no significant difference between the LABA-without-ICS group compared with the same intervention with concomitant ICS group.

See the figure

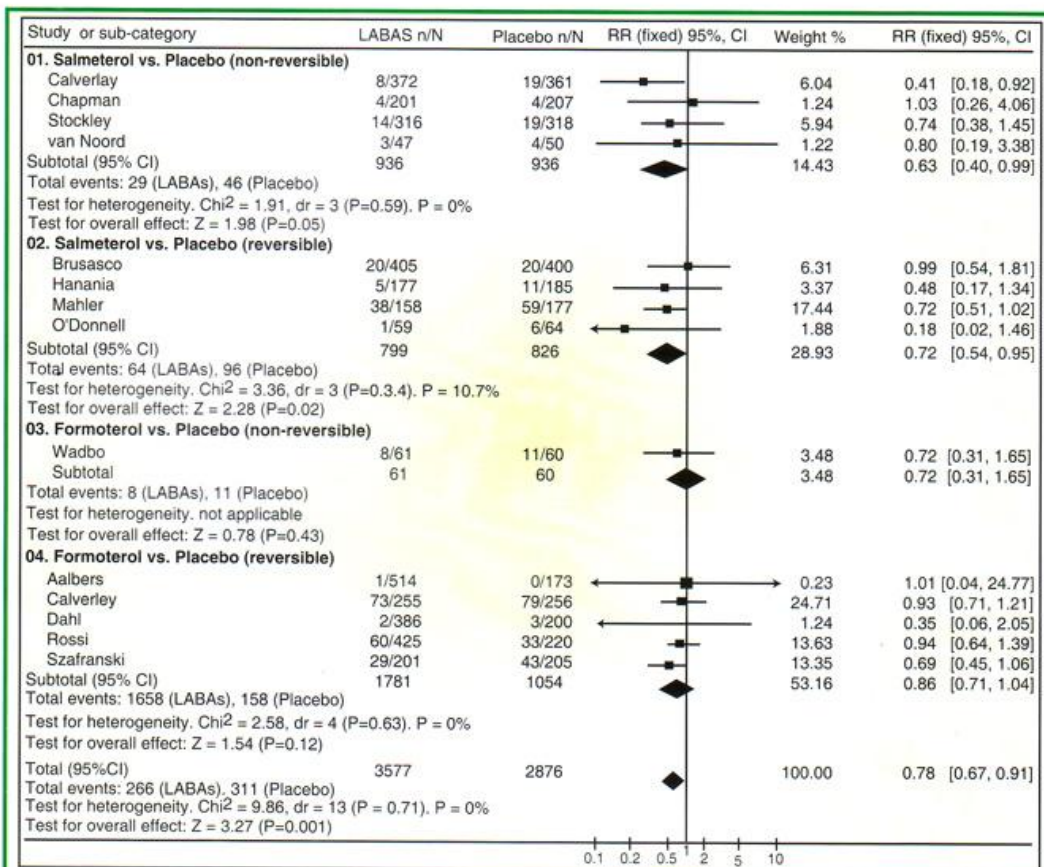
Pooled RR for COPD exacerbations requiring withdrawal or hospitalization (with 95% CI) of eligible studies comparing inhaled LABAs with placebo (n = number of exacerbations; N = number of patients). Trials are stratified by type of LABA (salmeterol or formoterol) and reversibility to SABA (poorly reversible or reversible).

This review found that compared with placebo, LABAs reduced severe exacerbations by 21% (NNT = 30). More important, LABAs patients did not differ in all-cause mortality rate, and contrary to a previous review they did not present differences in the rate of all and respiratory mortality, compared with placebo patients (98 reported respiratory deaths in 4,316 patients in the LABA-treated group and 88 deaths in 3,733 patients in the placebo group). The analysis including those studies without respiratory deaths showed a significant difference in the absolute risk reduction of all-cause mortality rate between both groups favoring LABAs (LABA mortality rate, 4.9%; placebo, 6.5%).

Although patients receiving LABAs showed statistically significant benefits in airflow limitation measures, quality of life, and use of rescue medication, the clinical relevance of these improvements remain elusive. Certainly, a FEV₁ increase of 112 mL and a reduction of four units in the SGRQ total score have been indicated as threshold changes for clinically significant improvements. However, the spirometric and quality-of-life benefits are limited by the presence of a high heterogeneity among studies. When we stratified studies by reversibility to SABAs, reversible COPD patients displayed a significant greater increase in mean change FEV₁ from baseline with salmeterol compared with poorly reversible patients.

With regard to the comparison with anticholinergics drugs, LABAs showed a nonsignificant trend toward fewer exacerbations compared with ipratropium. On the contrary, LABA treatment was associated with significantly more severe COPD exacerbations and a lesser increase in FEV₁ from baseline compared with tiotropium. Although based on a small number of trials, these results suggest the superiority of tiotropium over LABAs for the treatment of stable COPD patients, findings akin to previous data.

In the last few years, several systematic reviews on the safety and efficacy of LABAs in COPD patients have been published. However, they offer incomplete information on



this topic. Thus, the four reviews did not assess outcomes such as severe COPD exacerbations and mortality.

Salpeter et al. evaluated the safety and efficacy of β -agonists (SABAs and LABAs) compared with placebo and anticholinergics in stable COPD (22 trials with a minimum of 3 months in duration). Of those, only 12 studies compared LABAs with placebo or anticholinergics (7,449 patients). They found that β -agonist (SABA and LABA) reduced the risk of severe COPD exacerbations but were associated with a significant increase in respiratory deaths (RR, 2.47; 95% CI, 1.12 to 5.45) compared with placebo.

Unlike this previous review, we restricted the analysis to studies that compared only LABAs with placebo or anticholinergics. Additionally, we extended the search to those trials with a minimum of 1 month in duration. As a result, 17 new randomized trials with a total of 13,845 patients have been added. Our analysis confirms some previous findings. Thus, LABAs decrease severe COPD exacerbations and showed benefits in terms of airflow limitation measures, quality of life, and use of rescue medication compared with placebo. The decrease in the incidence of severe COPD exacerbations and the increase in FEV₁ were greater with tiotropium than with LABAs. However, our findings did not identify any detrimental effect

of LABAs on respiratory mortality. This finding disagrees with those by Salpeter et al. In our analysis, we included five trials that reported respiratory deaths, three of which were included in the study of Salpeter et al. However, there were several differences between the study by Salpeter et al. and our current analysis: (1) we included two trials, a new large one trial, and respiratory deaths data from a second study obtained through a personal communication with its authors; (2) we excluded the study by Donohue et al. included in the review by Salpeter et al because the latter presented redundant data; (3) although Salpeter et al reported two respiratory deaths for the article by Boyd et al (one for each group), only the death that occurred in the placebo group had a respiratory cause (pneumonia). Also, the number of deaths by respiratory cause in the trial by Calverley et al was uncertain. In any case, whether or not this study is included the overall result was unchanged. When we added to the analysis seven additional studies that did not report any death, increasing the denominator, there was no difference in the absolute risk increase among both groups. However, the exclusion of the trial of Calverley et al resulted in a pooled analysis based only in four studies. On this case, there was a nonsignificant difference between LABAs and placebo groups.

References available on request

Association News

Continuing Medical Education program is one of the major activities of the association conducted by the Academic cell regularly. A scientific seminar "Suppurative Lung Disease" was held on 17th March 2008 at NAC Auditorium, NIDCH



2008 at NAC Auditorium. Keynote speaker was Dr. Md. Delwar Hossain, done under the sponsorship of Incepta Pharmaceuticals. Fourth Scientific Seminar was on "Management of Chest Infection and Chest Trauma" was held

under the sponsorship of UniMed UniHealth, Keynote speaker was Dr. Md. Shahedur Rahman Khan. World TB Day was observed on March 24, 2008 at BCPS Auditorium sponsored by SANDOZ Division of Novartis [BD] Ltd. An Award Ceremony was held on this day and AK Khan Memorial Gold Medal was given this year to National Professor Nurul Islam. Seven scientific papers were presented on this seminar. Another scientific seminar on "Diabetes Care in tuberculosis and standard of Medical Care in Diabetes" was held on 23rd April,

on 27 May 2008 at NAC Auditorium under the sponsorship of Sanofi Aventis. Keynote speaker was Dr. AKM Akramul Haque. A chest Diseases Refresher's Training 5 Course was held on NAC Auditorium from 27.07.08 to 31.07.2008. Total 25 chest disease specialist attended the program. The training program was sponsored by Sandoz Division. A concluding program was held at Aristocrat Hotel at Gulshan. All the scientific seminars were presided by Professor Mirza Mohammad Hiron and vote of thanks was given by Dr. Md. Zahirul Islam Shakil.

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