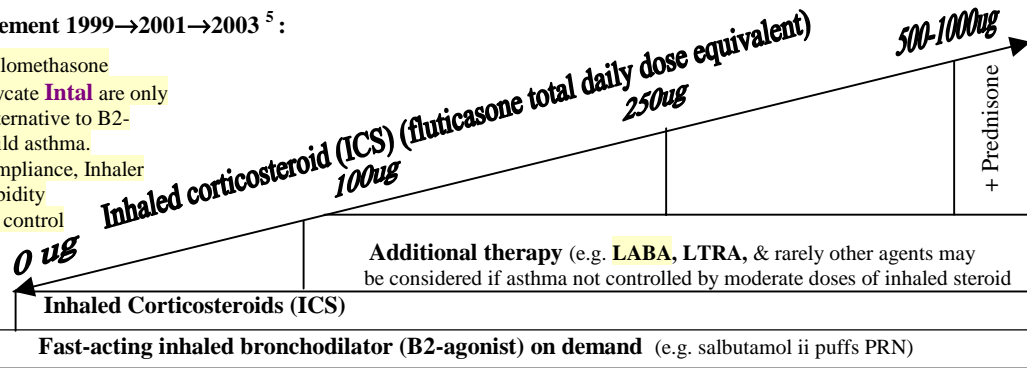
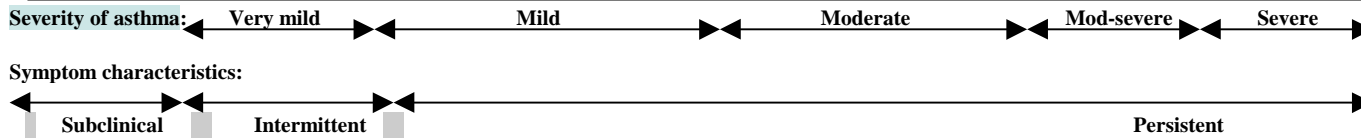


ASTHMA continuum of management 1999→2001→2003⁵:

- fluticasone **Flovent** ~2X potency of beclomethasone
- mast cell stabilizers eg. sodium cromoglycate **Intal** are only modestly effective but may be 2nd line alternative to B2-agonists in EIB, or to low-dose ICS in mild asthma.
- Regulary assess**: Control, Triggers, Compliance, Inhaler Technique & Co-morbidity
- modify maintenance therapy to maintain control



Environmental control, Education, Written action plan & Follow-up (reduce/avoid exposure to allergens & respiratory irritants e.g. dust, pets, smoke)



5. Summary of recommendations from the Canadian asthma consensus reports 1999,2001,2003 - Original adapted from, by permission of the publisher, CMAJ, 1999; 161(11 Suppl), pp.S1-15, 1999 Canadian Medical

Clinical difference: Asthma COPD

Age of onset	Usually <40yr	usually >40yr
Smoking history	not causal	usually >10pk yrs
Sputum production	infrequent	often
Allergies	often	infrequent
Disease course	stable (with exacerbations)	progressive (with exacerbations)
Spirometry	often normalizes	never normalizes
Clinical symptoms	intermittent & variable	persistent

COPD CANADIAN continuum of management 2003→2004¹⁹:

(Other recent guidelines: Global 2003¹, American Thoracic 2004² & Nice 2004³ Guidelines)

Increasing Dyspnea & Disability

Tiotropium + LABA/ICS +/- theophylline + SABA prn
 Consider long term OXYGEN or SURGICAL treatment if chronic respiratory failure. Control DYSPNEA symptoms (eg. morphine, lorazepam, diazepam, midazolam, chlorpromazine), COUGH (eg. codeine, morphine, bupivacaine) & SECRETIONS (eg. scopolamine patch, atropine, N-acetylcysteine) at end of life.

Tiotropium + LABA + SABA prn






































Tiotropium + LABA [+ long acting theophylline (watch blood levels, DIs & SEs)] + SABA prn
 Consider pulmonary rehabilitation (exercise & education)






SABA prn (or regular ipratropium or Combivent)

(Tiotropium or LABA) + SABA prn

Pharmacotherapy	None but avoid risk factors; Consider annual influenza VACCINATION ; pneumococcal vaccine at least once in their lives & perhaps repeating every 5-10yrs. Stop smoking & educate about COPD. Targeted spirometry in those at risk of COPD. Treat acute exacerbations -AECOPD (antibiotics for purulent/severe exacerbations).			
Spirometry	Normal spirometry (post bronchodilator FEV ₁ /FVC ≥ 0.7 +/- FEV ₁ ≥ 80% predicted)	FEV ₁ 60-79% predicted FEV ₁ /FVC < 0.7	FEV ₁ 40-59% predicted FEV ₁ /FVC < 0.7	FEV ₁ <40% predicted FEV ₁ /FVC < 0.7
Symptoms	Asymptomatic smoker, ex-smoker or chronic cough/sputum	Shortness of breath from COPD when hurrying on the level or walking up a slight hill (MRC 2)	Shortness of breath from COPD causing the pt to stop walking after ~100m (or after a few mins) on the level (MRC 3-4)	Shortness of breath from COPD resulting in the patient too breathless to leave house, breathlessness after undressing (MRC 5) or the presence of chronic respiratory failure or clinical signs of right heart failure
COPD Stage	O: At risk	I: Mild	II: Moderate	III: Severe

#: tiotropium reduced the number of exacerbations vs ipratropium at the dose used; however **no significant** differences in the number of **hospitalizations**. Vincken W, et al. Tiotropium Study Group (1 yr trial). Eur Respir J. 2002 Feb;19(2):209-16.
 FEV₁=forced expiratory volume in 1 second FVC=forced vital capacity LABA/ICS = LABA combination with an inhaled corticosteroid (eg. Advair, Symbicort) LABA=long acting beta₂ agonist (ie. formoterol or salmeterol) MRC= Medical Research Council dyspnea scale SABA= short acting beta₂ agonist (eg. salbutamol) SABD= short acting bronchodilator (eg. beta₂ agonist like salbutamol or anticholinergics like ipratropium)
 19. Can Respir J. 2003 May-Jun; Suppl A. Canadian Thoracic Society COPD Guidelines: 2003.

Generic /Pregnancy code	Dosage Form & Strength	TRADE	Dose Range / day	Usual Adult Asthma Dose	\$/30d 	Comments
Corticosteroids -Inhaled*first line to prevent asthma (not for acute asthma); use regularly at the lowest effective dose to prevent asthma ♦caution pts on long-term high dose & osteoporosis ¹²						
Beclomethasone diprop. (BDP) 	MDI 50ug, 100ug BDP products from GlaxoSmithKline (e.g. <i>Becloforte, Beclodisk, Beclovent Rotacaps</i>)	QVAR -shaking not required	100-600 ug	i-ii puffs BID (~200ug/d)	\$ 48	♦SE: oral thrush, dysphonia; to ↓SE's, use spacer & rinse mouth ♦QVAR = ↑potency due to ↑lung deposition; ↓oral & systemic SEs ♦Fluticasone: 2X as potent as BDP & less systemic absorption ♦if ↑dose required, ? add LABA or LTRA ♦DI: itraconazole & ritonavir ↑risk of Cushing's ^{13,14}
Budesonide 	Turbuhaler 100,200,400ug *Neb. 0.25, 0.5, 1 mg/2ml	PULMICORT PULMICORT NEBUAMP	400-2400 ug 0.5 - 4mg	400ug puffs BID 1mg per neb BID	\$ 46 \$ 125	
Fluticasone propionate 	MDI 50,125,250ug Diskus 50, 100, 250, 500ug	FLOVENT HFA -CFC free FLOVENT Diskus -contains lactose	100-1000 ug	ii 125ug puffs BID 250ug inhaled BID	\$ 52 \$ 52	
SABA -Inhaled Short-Acting B2 Agonist ♦effective for treating acute asthma; if using >3X/week add inhaled corticosteroid; frequent use suggests poor control; ✓ prevent exercise-induced bronchospasm						
Salbutamol 	MDI 100ug <i>CFC free</i> (also avail. as 2 ⁵ ,4 ⁵ mg tab; 0.4mg/ml oral liquid)	VENTOLIN, APO-,RATIO-Airomir/Ratio Salbutamol HFA <i>CFC free</i> VENTODISK -contains lactose VENTOLIN INHAL'N SOLN VENTOLIN NEBULES P.F.	prn - 1200ug prn - 1600ug prn - 15mg prn - 15mg	i-ii puffs PRN i-ii puffs PRN 200ug inhaled PRN 2.5mg per neb PRN 2.5mg per neb PRN	\$ 15 \$ 15 \$ 56 \$ 49 \$ 75	♦EIB: ii puffs 15min pre-exercise ♦SE: tremor, nervousness, ↑HR, headache, ↓K ⁺ , ↑insulin secretion, hyperglycemia esp. in diabetics ♦oral agents available but have slower onset and cause more SE's
Terbutaline 	Turbuhaler 500ug	BRICANYL	prn - 4000ug	500ug inhaled PRN	\$ 18	
Fenoterol 	MDI 100ug(*nebs ^{0.025 & 0.0625%})	BEROTEC	prn - 1600ug	i-ii puffs PRN	\$ 20	♦PF = "preservative free" nebs
LABA -Inhaled Long-Acting B2 Agonist ♦add-on agent in pts requiring higher-dose corticosteroids (steroid sparing effect?); ✓ nocturnal asthma & EIB; not for acute asthma but formoterol approved for PRN use						
Formoterol 	Capsules for inhal'n 12ug Turbuhaler 6ug, 12ug	FORADIL CAPS for inhal'n OXEZE -contains lactose	24-48ug (max 72ug/24hr)	12ug inhaled BID 12ug puff BID	\$ 57  \$ 59 	♦full B2 agonist (∴ caution SE: tremor/↑HR in elderly); fast ONSET
Budesonide+Formoterol 	Turbuhaler 100ug/6ug, 200ug/6ug	SYMBICORT 100,200 -contains lactose	400-2400 ug/ 24-48ug	100ug/6ug 2 puff BID 200ug/6ug 2 puff BID	\$ 79  \$ 100 	♦combo convenient but less flexible dose; may be ↓\$, COPD mod-severe dx 15,16
Salmeterol Xinafoate 	MDI 25ug Diskus 50ug	SEREVENT SEREVENT Diskus -contains lactose	100ug	ii puffs BID 50ug inhaled BID	\$ 69  \$ 69 	♦partial B2 agonist ♦slower onset ♦↑asthma deaths esp. African American -SMART trial 17
Salmeterol+Fluticasone 	Diskus 50ug/100ug, 50ug/250ug, 50ug/500ug MDI 25ug/125ug, 25ug/250ug	ADVAIR Diskus 100,250,500 -contains lactose ADVAIR 125,250 MDI	2 inhalations 2-4 inhalations	ADVAIR 100-250 DISKUS 1 inh BID ADVAIR 125-250 MDI 2 inh BID	93-109  99-152 	♦combo convenient but less flexible dosing; maybe ↓\$, COPD mod-severe dx15
Mast cell stabilizers ♦efficacy highly variable from pt to pt; not for acute attacks; may taper to BID over several weeks after effect achieved; role in pediatric, cold air induced asthma & EIB						
Sodium Cromoglycate (Cromolyn nebs 20mg/2ml) 	MDI 1mg/puff 20mg Spincap for inhal'n	INTAL Inhaler INTAL Spincaps	2-8mg ? 40-160mg	ii puff QID (Up to 16puffs/day) 1 cap for inhal'n QID	\$ 64 \$ 73	♦~4week trial needed to evaluate effect; safe in children
Nedocromil 	MDI 2mg/puff	TILADE	4-16mg	ii puffs QID	\$ 73	♦taste may limit compliance
Anticholinergics ♦possible alternative/"add on" to SABAs in asthma (delayed onset; longer duration); role in COPD?; ♦SE: dry mouth, taste disturbance; (Avoid eye contact: mydriasis/glaucoma)						
Ipratropium bromide 	MDI 20 ug  ; *Neb. 250ug/2ml;500ug/2ml Inhalation soln (must be diluted)	ATROVENT, ATROVENT HFA	80-320ug 375-2000ug	ii puffs TID-QID (Max 3-4 qid) 250ug per nebule TID 250ug inhalation soln TID	\$ 26-32 \$ 88 \$ 66	♦ > effect in elderly than SABA's ♦caution: glaucoma, urine retent. ♦useful in COPD ¹⁸
Ipratropium bromide + Salbutamol -Combo 	MDI 20ug/100ug  ; *Neb. 500ug+2.5mg / 2ml	COMBIVENT	6-12 puffs	ii puffs TID 1 neb TID	\$ 32 \$ 117	♦use only if combo indicated ♦PRN use in asthma
Tiotropium 	18ug cap for inhalation	SPIRIVA	1 inhaled cap	1 cap inhaled OD	\$ 82  	♦dose od,slower onset,↑\$ for COPD ^{19,20}
LTRA -Leukotriene Receptor Antagonists ♦not 1 st line ²¹ ; not for acute asthma; steroid sparing effect?; ↑ effect of SABAs; oral tx advantage?; ✓ EIB & ASA sensitive pts						
Montelukast (4 [®] mg oral granule) 	4 & 5mg chew-tab; 10mg tab	SINGULAIR (age 1-5⇒4mg; 6-14⇒ 5mg)	10mg	10mg po HS (or AM if for EIB)	\$ 84  	♦rare eosinophilic vasculitis rx's?
Zafirlukast 	20mg tab	ACCOLATE (only for age ≥12yrs)	40mg	20mg po BID on empty stomach	\$ 59  	♦Zafirlukast: DI ^{warf/theoph} , & ↑LFT's
Theophylline Preparations (Oral) ♦3 rd line therapy due to systemic toxicity and mild bronchodilator activity; useful as 'add on' agent in some pts requiring high dose corticosteroids						
Aminophylline =80%theoph. 	225 ⁵ , 350 ⁵ mg SR tab	PHYLLCONTIN	450-1250mg	350mg po BID	\$ 26	♦SE: N&V, abdom. cramps, HA, nervousness, tremor, insomnia, ↑HR ♦DI: ↓theo level: carbamazepine, phenytoin, rifampin ↑theo level: cimetidine, ciprofloxacin, erythromycin, fluvoxamine & verapamil
Oxtriphylline =66%theoph. 	100,200,300mg tab	CHOLEDYL (also 50 & 100mg/5ml elixir)	600-1600mg	200mg po QID	\$ 17	
Theophylline ²² (many products avail. such as SR bid agents) 	5.33mg/ml elixir; SR tab (q12h) 400 ⁵ , 600 ⁵ mg SR tab (q24h)	Apo-Theo-LA, Novo-Theophyl SR UNIPHYL (SR products can be halved)	300-1000mg (Toxic ^{cp} >110 umol/l)	300mg po BID 400-600mg po HS	\$ 17 \$ 25-27	

Cost:markup & dispensing fee  prior approval for NIHB  Non Formulary in Sask =EDS B2=beta-2 DI=drug interaction EIB=exercise-induced bronchospasm HA=headache HR=heart rate MDI=metered dose inhaler SE=side effect
Spacer (e.g. **AEROCHAMBER**) will optimize MDIs delivery, ↑ efficiency, ↓ pharyngeal & systemic SE; *MDI+Spacer or "dry powder systems" generally preferable to nebs.  Avoid → soybean & peanut allergy  =scored tab
 Systemic glucocorticoids-indicated in & following acute asthma exacerbations e.g. **Prednisone**: Adult 30-60mg/d x7-10d; Children 1-2mg/kg OD x3-5d (max 50mg/d); Prednisolone **PEDIAFRED** 1mg/ml oral liquid avail.
 Due to environmental concerns, many CFC propellants are being changed to hydrofluoroalkanes (**HFA**); these have smaller particle size, deliver more drug to the lower airway & the spray is often softer & warmer than CFC inhalers.

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- ¹ Fabbri LM, Hurd SS; GOLD Scientific Committee. Global Strategy for the Diagnosis, Management and Prevention of COPD: 2003 update. Eur Respir J. 2003 Jul;22(1):1-2. <http://www.goldcopd.com>
- ² American Thoracic Society Guidelines 2004 <http://www.thoracic.org/copd>
- ³ Nice Guidelines 2004 http://www.nice.org.uk/pdf/CG012_niceguideline.pdf
- ⁴ Micromedex 2004
- ⁵ Boulet LP et al. Canadian **Asthma Consensus Report 1999**. CMAJ 1999; 161 (11 Suppl) & Boulet LP, et al.. What is new since the last (1999) Canadian Asthma Consensus Guidelines? Can Respir J. **2001** Mar-Apr;8 Suppl A:5A-27A & Lemiere C, Bai T, Balter M, et al. **Adult Asthma Consensus Guidelines Update 2003**. Can Respir J. 2004 May-Jun;11(Suppl A):9A-18A.
- ⁶ Anon. Drugs for Asthma. The Medical Letter. March 6, 2000: Vol. 42: issue 1073.
- ⁷ Walters EH, Walters J. Inhaled short acting beta2-agonist use in chronic asthma: regular versus as needed treatment (Cochrane Review). Cochrane Database Syst Rev. 2003;(2):CD001285.
- ⁸ Simon RA. Clinical implications of combination therapy on the future of asthma management. Allergy Asthma Proc. 2003 Mar-Apr;24(2):91-3.
- ⁹ Williams SG, Schmidt DK, Redd SC, Storms W; National Asthma Education and Prevention Program. Key clinical activities for quality asthma care. Recommendations of the National Asthma Education and Prevention Program. MMWR Recomm Rep. 2003 Mar 28;52(RR-6):1-8.
- ¹⁰ **Treatment Guidelines: Drugs for Asthma. The Medical Letter:** October, **2002**; (2) pp. 7-12.
- ¹¹ Sin DD, Man J, Sharpe H, Gan WQ, Man SF. Pharmacological management to reduce exacerbations in adults with asthma: a systematic review and meta-analysis. JAMA. 2004 Jul 21;292(3):367-76.
- ¹² Wong CA, Walsh LJ, Smith CJ, et al. Inhaled corticosteroid use and bone-mineral density in patients with asthma. Lancet. 2000 Apr 22;355(9213):1399-403.
- ¹³ Health Canada Endorsed Important Safety Information on FLUTICASONE PROPIONATE (FLONASE/ FLOVENT/ ADVAIR) and RITONAVIR (NORVIR/KALETRA) Jan 22, 2004
- ¹⁴ Bolland MJ, Bagg W, Thomas MG, Lucas JA, et al. Cushing's syndrome due to interaction between inhaled corticosteroids (budesonide) and itraconazole. Ann Pharmacother. 2004 Jan;38(1):46-9.
- ¹⁵ Sin DD, McAlister FA, Man SF, Anthonisen NR. Contemporary management of chronic obstructive pulmonary disease: scientific review. JAMA. 2003 Nov 5;290(17):2301-12.
- ¹⁶ Calverley PM, Boonsawat W, Cseke Z, Zhong N, et al. Maintenance therapy with budesonide and formoterol in chronic obstructive pulmonary disease. Eur Respir J. 2003 Dec;22(6):912-9.
- ¹⁷ <http://www.fda.gov/bbs/topics/ANSWERS/2003/ANS01248.html> FDA Warning Letter Aug 2003.
- ¹⁸ Calverley PM, Walker P. Chronic obstructive pulmonary disease. Lancet. 2003 Sep 27;362(9389):1053-61.
- ¹⁹ O'Donnell DE., Aaron S., Bourbeau J. et al. **Canadian Thoracic Society** recommendations for management of chronic obstructive pulmonary disease - **2003**. Can Respir J. May/June 2003;10 (Suppl A): 11A-33A. & State of the Art Compendium: Canadian Thoracic Society recommendations for the management of chronic obstructive pulmonary disease. Can Respir July/August **2004**; 11(Suppl B):7B-59B.
- ²⁰ Sutherland ER, Cherniack RM. **Management** of chronic obstructive pulmonary disease. N Engl J Med. **2004** Jun 24;350(26):2689-97.
- ²¹ Ducharme FM. Inhaled glucocorticoids versus leukotriene receptor antagonists as single agent asthma treatment: systematic review of current evidence. BMJ. 2003 Mar 22;326(7390):621.
- ²² Barr RG, Rowe BH, Camargo CA Jr. Methylxanthines for exacerbations of chronic obstructive pulmonary disease: meta-analysis of randomised trials. BMJ. 2003 Sep 20;327(7416):643.