Evidence Table 1. Randomized controlled studies evaluating treatment of nonallergic rhinitis
Part I.

Author Year UI	Intervention	Duration	Demographics	Inclusion criteria	Exclusion criteria
Balle 1977 78016773	Disodium cromoglycate 21 mg daily vs. placebo double-blind crossover	4 weeks	Location: Denmark Mean age: ND Age range: 16 –53 % Male ND Race: ND Enrolled: 25 Evaluated: 24 Number of sites: 1	2 year history of vasomotor rhinitis requiring treatment	Asthma requiring treatment active sinusitis nasal polyposis
Renvall 1979 79214155	Oral PPA 100 mg vs. oral PPA 50mg vs. placebo RCT-Parallel	1 week	Location: Sweden Mean age: 42 Age range: 15-78 % Male: 32/70= 45.7% Race: ND Enrolled: 70 Evaluated: 70 Number of sites: 1	Rhinitis symptoms for a "long time / many years"	Usage of decongestant drugs History suggestive of allergy
Broms 1982 83046227	PPA 100mg vs. PPA 50mg vs. antihistamine	10 days	Location: Sweden Mean age: ND Age range: 18-65 % Male: ND Race: ND Enrolled: 20 Evaluated: 20 Number of sites: 1	Symptomatic nonallergic rhinitis	ND

Evidence Table 1. Randomized controlled studies evaluating treatment of nonallergic rhinitis
Part I. (continued)

Author Year UI	Intervention	Duration	Demographics	Inclusion criteria	Exclusion criteria
Nelson 1982 82240276	Cromolyn sodium 4% solution (6 sprays/d) vs. placebo RCT- Parallel	8 weeks	Location: US Mean age: 41 Age range: 18-60 % Male: 8/23 Race: ND Enrolled: 23 Evaluated: 23 - 12 (cromolyn) and 11 (placebo) Number of sites: 1	Negative skin prick test or ID skin test	ND
Jokinen 1983 84120896	Ipratropium 40μg vs. placebo Double blind cross-over	8 weeks	Location: Finland Mean age: 30 Age range: 14-66 % Male: ND Race: ND Enrolled: 30 Evaluated: 30 Number of sites: 1	Symptoms of vasomotor rhinitis requiring treatment for at least 1 year Normal sinus X-ray Negative skin test No anatomic nasal abnormality	NR
Malmberg 1983 84082739	Ipratropium 320 μg/d vs. placebo RCT-crossover	6 weeks	Location: Finland Mean age: 69.6 Age range: 48-87 % Male: 13/34 = 38.2% Race: ND Enrolled: 34 Evaluated: 34 (later changed to 33 when 1 patient stopped drug) Number of sites: 1	Elderly History of dripping (watery) vasomotor rhinitis	ND

Evidence Table 1. Randomized controlled studies evaluating treatment of nonallergic rhinitis
Part I. (continued)

Author Year UI	Intervention	Duration	Demographics	Inclusion criteria	Exclusion criteria
Bende 1985 86093211	Ipratropium vs. budesonide 100 μg bid x iod Open comparison crossver	40 days	Location: Sweden Mean age: 48 Age range: 22-70 % Male: 10/14 Race: ND Enrolled: 14 Evaluated: 14 Number of sites: 1	Symptoms of excessive nasal secretion for many years Negative routine skin prick test Previous treatment with decongestant and antihistamines ineffective	ND
Kirkegaard 1987 87167181	Ipratropium 80 μg vs ipratropium 400 μg qid vs placebo RCT- Parallel	10 weeks: 2wk- run-in 6wk- two 3wk treatment periods 2wk- open assessment of high-dose therapy	Location: Scandinavia Mean age: 51 Age range: 19-84 % Male: 50% Race: ND Enrolled: 39 Evaluated: 36 Number of sites: 1	Consecutively referred patients Predominant symptoms of working rhinorrhea Non-seasonal symptoms for at least 1 year Negative skin test	Nasal septal deviation Nasal polyposis Pregnant Other medications
Kirkegaard 1988 89074206	Ipratropium 80 μg qid vs. placebo double-blind crossover	3 weeks	Location: Sweden Mean age: ND Age range: ND % Male ND Race: ND Enrolled: 38 Evaluated: 38 Number of sites: 1	Perennial symptoms Negative skin test	ND

Evidence Table 1. Randomized controlled studies evaluating treatment of nonallergic rhinitis
Part I. (continued)

Author Year UI	Intervention	Duration	Demographics	Inclusion criteria	Exclusion criteria
Sjogren 1988 89086030	Ipratropium 200 μg vs ipratropium 100 μg vs Ipratropium 40 μg vs placebo Dosing study, non randomized	1 day	Location: Sweden Mean age: 38.8 (women) and 55.6 (men) Age range: 21-77 % Male: 11/24= 45.8% Race: ND Enrolled: 24 Evaluated: 24 Number of sites: 1	Rhinorrhea Negative skin test	Asthma Sinusitis Nasal polyposis “airway infection” Pregnancy Anticholinergics, antihistamines, antidepressants, and neuroleptics and steroids
Jessen 1990 90350004	Ipratropium 160 μg vs. beclomethasone 400 μg Double-dummy double-blinded randomized crossover trial	7 weeks	Location: Sweden Mean age: 49 Age range: (20-77) % Male: 10/24 Race: ND Enrolled: 31 Evaluated: 24 Number of sites: 1	Negative skin prick test	Nasal polyps Chronic asthma Pregnancy
Wight 1992 92405460	Budesonide 400 μg vs budesonide 800 μg Placebo-controlled, double-blinded crossover RCT	12 weeks 2 3-week active treatment periods	Location: UK Mean age: 31 Age range: 16-62 % Male: 30/59 Race: 53 Caucasian, 3 Black, 3 Others Enrolled: 59 Evaluated: 59 Number of sites: 1	12 months of perennial rhinitis	Seasonal allergic rhinitis Recurrent chronic rhinosinusitis Nasal polyps Nasal structural abnormality

Evidence Table 1. Randomized controlled studies evaluating treatment of nonallergic rhinitis
Part I. (continued)

Author Year UI	Intervention	Duration	Demographics	Inclusion criteria	Exclusion criteria
Graf 1999	Oxymetazoline 0.5mg/mL + Benzalkonium 0.1mg/mL vs oxymetazoline (3 sprays/d) RCT-Parallel	10 days	Location: Sweden Mean age: 38 Age range: 15-69 % Male: 9/35 = 25.7% Race: ND Enrolled: 35 Evaluated: 35 Total: 18 (oxymetazoline w/ benzalkonium) and 17 (oxymetazoline w/o benzalkonium Number of sites: 1	Vasomotor rhinitis	No medications for nasal symptoms within 30 days Negative skin test for allergy

Evidence Table 1. Randomized controlled studies evaluating treatment of nonallergic rhinitis
Part II.

Author Year UI	**Treatment outcomes studied**	**Symptom scale**	**Outcomes-efficacy**
Balle 1977 78016773	Sneezing score Rhinorrhea score Nasal congestion score Rescue antihistamine usage	Diary cards: scale 0-3	Mean monthly diary scores for sneezing significantly reduced in active treatment group (20 vs. 28 p<0.05) Mean monthly diary scores for nasal congestion significantly reduced in active treatment group (24.7 vs. 27.4 p<0.05)
Renvall 1979 79214155	Mean Total Symptom Score: Nasal obstruction Nasal secretion	Symptom Scale: Patient symptom questionnaire with scoring system -interviewed by doctors on day 1 and day 4 symptom scale(1-4)	For nasal obstruction, significant (p< 0.05) differences between 100 mg PPA and placebo and between high dose and low dose (p< 0.05) For nasal secretion, significant difference (P<0.05) between high dose and low dose. No other significant differences found Minimal data presented
Broms 1982 83046227	Mean Total Symptom Score Nasal airway resistance Nasal secretion Sneezing	Symptom scale: Diary card (2/d) Symptom intensity - 4 point scale 0-3 Sneezing- similar scale, but recording number of sneeze attacks	Unable to extract data from graphs “symptoms of nasal secretion and sneezing were reduced by PPA” “PPA is not an ideal nose decongestant” “DHE in dose lower than those giving adrenoceptor blockage seemed to be suitable drug”

Evidence Table 1. Randomized controlled studies evaluating treatment of nonallergic rhinitis
Part II. (continued)

Author Year UI	**Treatment outcomes studied**	**Symptom scale**	**Outcomes-efficacy**
Nelson 1982 82240276	Total Mean Symptom Score Rhinorrhea Nasal congestion Sneezing Itchy nose Itchy eyes Itchy throat Post-nasal drip Mouth breathing Nose-blowing	Symptom scale Patients completed questionnaire 2x/ day Symptom severity- 0-5 scale 0=none to 5= extreme Sneezing or nose blowing- by # of sneezes/ nose blows	For specific symptom scores, drug was statistically significant for itchy nose, itchy eyes (both P<0.01), and amount of nose blowings (P<0.02), but NS w/respect to runny nose, stuffy nose, itchy throat, mouth breathing, postnasal drip, sneezing episodes.
Jokinen 1983 84120896	Total Mean symptom score Rhinorrhea Sneezing Itchy nose Nasal blockage	Symptom scale: Diary cards- 0-3 scale. Number of handkerchiefs, nasal smears, McNemar test	Ipratropium had marked effects on nasal discharge; p< 0.001; also in amount of handkerchiefs used. Tx had no effects on nasal blockage, sneezing and tickling: changes all NS.
Malmberg 1983 84082739	Total mean symptom score Rhinorrhea Nasal congestion Sneezing Itchy eyes Nose blowing	Symptom scale Patient diary: 0-3 scale with 0= no symptoms, to 3= severe symptoms Nasal blowing- by counting handkerchiefs (1:1)	For nose-blowing frequency: smaller frequency of nose blowing during treatment with ipratropium P < 0.001 For rhinorrhea: Symptom score of 1.21 with ipratropium vs score of 1.52 with placebo; P < 0.001 For nasal congestion and Itchy eyes P = NS for both

Evidence Table 1. Randomized controlled studies evaluating treatment of nonallergic rhinitis
Part II. (continued)

Author Year UI	**Treatment outcomes studied**	**Symptom scale**	**Outcomes-efficacy**
Bende 1985 86093211	Nasal symptom scores: Secretion Blockage Sneezing Itching Stinging Drying Bleeding	VAS	Budesonide had a significant effect on nasal secretion and sneezes ($p<0.01$) No numerical data provided. Results presented as a graph. 12/14 patients wanted to continue budesonide. 2/14 found neither drug of value.
Kirkegaard 1987 87167181	Total Mean Symptom Score Rhinorrhea Nasal Congestion Sneezing	Symptom Scale: Diary card- For nasal blockage- 0-3 (free/easy breathing-3= completely abolished) For other nasal symptoms -recorded number of sneezes and nose blowings	Number of nose blowings were 47% lower during active lowdose tx compared to placebo ($P<0.01$), other slight reduction w/high dose compared to placebo ($P<0.05$). Active tx, hi or low, had no effect on number of sneezes or nasal blockage index.
Kirkegaard 1988 89074206	Average daily nose-blowing episodes	Diary cards x2hrs self-assessed questionnaires bid	Mean daily number of nose-blowing episodes significantly reduced when compared with placebo (29 ± 7.3 vs 17.6 ± 4.2)
Sjogren 1988 89086030	Mean total symptom score: Rhinorrhea Sneezing Volume of nasal secretion	Symptom scale: Nasal secretion – measured vol. secretion after pre-tx w/different dosages of med. Other nasal symptoms- McNemar test	Doses of 40 and 100 tx reduced volume of secretion, greatest reduction was found w/200 mg when compared to placebo. Ipratropium reduced significantly hypersecretion induced by metacholine when compared to placebo. 15 sneezing episodes w/placebo compared to 7 w/tx, NS. No changes in other nasal symptoms (itching).

Evidence Table 1. Randomized controlled studies evaluating treatment of nonallergic rhinitis
Part II. (continued)

Author Year UI	**Treatment outcomes studied**	**Symptom scale**	**Outcomes-efficacy**
Jessen 1990 90350004	Nasal symptom scores: Secretion Sneezing Blockage	0-4 symptom scale	No significant difference between ipratropium and beclomethasone.
Wight 1992 92405460	Nasal resistance to airflow. Nasal secretic eosinophilic count. Patient subjective symptom score. Effect on local and stimulated plasma control.	0-3 subjective assessment scale.	Nasal obstruction was significantly improved with budesonide. There was no significant difference between doses.
Graf 1999	Total mean symptom score Nasal congestion	Symptom scale: Visual analog scale (0-100) Nasal mucosal swelling measured by rhinostereo-metry and acoustic rhinometry	Reduction in mucosal swelling after 10 days for O+B was statistically significant at all 3 histamine provocation levels (P<0.001); for O alone, NS Mean symptom score for nasal stuffiness For O+B, a score of 50 at baseline and 49 after treatment --for O alone, a score of 48 at baseline and 51 after treatment

Evidence Table 1. Randomized controlled studies evaluating treatment of nonallergic rhinitis
Part III.

Author Year UI	**Outcome-safety**	**Potential Bias**	**Funding**
Balle 1977 78016773	No adverse events noted	Pooled crossover data Analyzed 23 of 24 patients Reasons for withdrawals not given. Internal validity C	ND
Broms 1982 83046227	No major adverse effects: Minor adverse effects: Total adverse effects: reported by 17/19 patients -Headache- 10 patients- 7 patients in placebo group, 2 in PPA group and 1 in PPA + BDE group -Micturition difficulties- 2 patients taking PPA	Small sample No data on demographics No info on the missing person	Government
Nelson 1982 82240276	No major adverse effects: Minor adverse effects: Increased nasal symptoms for 4 cromolyn patients, 4 placebo patients Nasal symptoms include: lacrimation, eyelid puffiness, nasal stuffiness, nasal irritation, sneezing, headaches, sore throat, and sleepiness	Most patients continued to experience usual NARES syndrome symptoms throughout the rhinitis study No benefit of DSG in NARES 4 Non-drug related withdrawals during study 3 from placebo group, 1 from cromolyn group: 2 patients due to concurrent use of diuretic mediation, other 2 patients due to occupational duties (their data while enrolled was included)	ND

Evidence Table 1. Randomized controlled studies evaluating treatment of nonallergic rhinitis
Part III. (continued)

Author Year UI	**Outcome-safety**	**Potential Bias**	**Funding**
Jokinen 1983 84120896	No major adverse effects. Minor adverse effects: 3 ipratropium therapy interruptions- (1)nose bleeding, (2) headache, and (3) increase symptoms 2 placebo therapy interruptions- (1) increased symptoms, and (2) tour abroad Report of mild side-effects: 11 patients taking ipratropium treatment, 7 patients taking placebo treatment -Nasal irritation- 8 patients from ipratropium group and 5 patients from placebo group reported effect -Nasal dryness- 6 patients taking ipratropium and 3 patients taking placebo -Throat irritation- 2 patients taking ipratropium and 1 patient taking placebo		Pharmaceutical
Malmberg 1983 84082739	Major adverse effects: 3 withdrawals- 1 patient from placebo group (no reason given); 2 patients from ipratropium group due to drying of mucosa Minor adverse effects: -Nasal dryness- 15 from ipratropium group and 9 from placebo group -Nasal irritation- 18 from ipratropium group and 8 from placebo group		ND
Bende 1985 86093211	“no serious adverse effects were noted”	Non-randomized open label study	ND

Evidence Table 1. Randomized controlled studies evaluating treatment of nonallergic rhinitis
Part III. (continued)

Author Year UI	**Outcome-safety**	**Potential Bias**	**Funding**
Kirkegaard 1987 87167181	Minor adverse effects: -Nasal dryness- 61% patients on ipratropium 80m; 72% patients on ipratropium 400 36% patients taking placebo. -Mouth dryness 42% patients on ipratropium 80 78% patients on ipratropium 400; 28% patients taking placebo; -Dysuria (Urinolic difficulties) 11% patients on ipratropium 80 28% patients on ipratropium 400 6% patients taking placebo; -Blurred vision 8% patients on ipratropium 80 14% patients on ipratropium 400 8% patients taking placebo	Other reasons for withdrawal: -1 pt- failed to fill score card -1pt- lost score card -1pt- did not follow last treatment protocol	ND
Kirkegaard 1988 89074206	Only adverse event noted was nose dryness in both active & placebo groups; no numbers given	Small sample size No data on adverse effect numbers Category C	ND
Sjogren 1988 89086030	No major adverse effects Minor adverse effects: Sweating- 1 patients after treatment with 400 μg ipratropium		Pharmaceutical
Jessen 1990 90350004	“side effects of treatment were negligible”		ND

Evidence Table 1. Randomized controlled studies evaluating treatment of nonallergic rhinitis
Part III. (continued)

Author Year UI	**Outcome-safety**	**Potential Bias**	**Funding**
Wight 1992 92405460	No increase in adverse effects occurred with higher dosage.		Astra Pharmaceutical
Graf 1999	ND		Pharmaceutical

Evidence Table 2. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Non-sedating antihistamines versus nasal corticosteroids
Part I.

Author **Year** **UI**	**Intervention**	**Duration**	**Demographics**	**Inclusion criteria**	**Exclusion criteria**
Munch 1983 84050113	**Seasonal Allergic Rhinitis** Dexchlor-pheniramine vs Budesonide RCT-Parallel After treatment, used intranasal allergen for post-challenge	21 days	Location: Denmark Mean age: 29 Age range: 18-65 % Male: 50% Race: ND Enrolled: 61 - 30 (dexchlorpheniramine) and 31 (budesonide) Evaluated: 60 - 29 (dexchlorpheniramine) and 31 (budesonide) Number of sites: 4	At least 15 years old Rhino-conjunctivitis for last 2 seasons Positive skin prick test to timothy grass	Asthma Sinusitis Nasal septal deviation Nasal polyposis Childbearing potential PAR SAR in pollen season Treated with other drugs or gluticocorticoids for last 2 weeks
Backhouse 1986 86165329	**Seasonal Allergic Rhinitis** Terfenadine vs Flunisolide RCT-Parallel	11 weeks	Location: UK Mean age: 35 Age range: 18-65 % Male: 52/99 Race: ND Enrolled:99 - 50 (terfenadine) and 49 (terfenadine and flunisolide) Evaluated: 82 - 33 (terfenadine) and 49 (terfenadine + flunisolide) Number of sites: 1	Moderate to severe symptoms of SAR for at least 2 years	Sinusitis Nasal septal deviation Nasal polyposis Pregnant/lactating Other RTI (respiratory tract infection) Systemic steroid use within 3 months Any allergy therapy within 2 weeks

Evidence Table 2. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Non-sedating antihistamines versus nasal corticosteroids
Part I. (continued)

Author Year UI	Intervention	Duration	Demographics	Inclusion criteria	Exclusion criteria
Wood 1986 86245576	**Seasonal Allergic Rhinitis** Astemizole vs Beclomethasone RCT- Parallel	13 weeks	Location: UK Mean age: 27.9 Age range: > 12 % Male: 35/73 Race: ND Enrolled: 74 Evaluated: 73 - 39 (astemizole) and 34 (beclomethasone) Number of sites: 1	"sound clinical history of hay fever"	Nasal polyposis "severe chronic rhinitis (vasomotor or intrinsic rhinitis)" Received systemic corticosteroid within 4 weeks Pregnant or lactating or likely to become pregnant
Juniper 1989 89175902	**Seasonal Allergic Rhinitis** Astemizole vs Beclomethasone [also tested Astemizole + Beclomethasone treatment] RCT-Parallel	42 days	Location: Canada Mean age: 39.8 Age range: 18-70 % Male: 53.3% Race: ND Enrolled: 90 Evaluated: 90: 30 each group Number of sites: 1	Rhinoconjunctivitis requiring treatment during 2 seasons Skin prick test	Pregnant/nursing mothers Perennial rhinitis No trial drug use within 6 weeks
Robinson 1989 90002391	**Perennial Allergic Rhinitis** Terfenadine vs Beclomethasone dipropionate (BDP) RCT- cross-over (unextractable)	4 weeks	Location: UK Mean age: 30.9 Age range: 18-65 %Male: 7/20 Race: ND Enrolled: 20 (10 each group) Evaluated: 13 - 5 (Group B-received terfenadine 1st), 8 (Group A- received beclomethasone 1st) [**see outcomes-efficacy section for clarification**] Number of sites: 1	With normal sinus X-ray and free from "serious" illness	With sinusitis, nasal septal deviation, and nasal polyposis. Pregnant women and those receiving or would require medicine affecting perennial rhinitis, such as antihistamines

Evidence Table 2. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Non-sedating antihistamines versus nasal corticosteroids
Part I. (continued)

Author **Year** **UI**	**Intervention**	**Duration**	**Demographics**	**Inclusion criteria**	**Exclusion criteria**
Darnell 1994 95196117	**Seasonal Allergic Rhinitis** Terfenadine vs. fluticasone RCT-Parallel	6 weeks	Location: Europe Mean age: 28 Age range: > 12 %Male: Race: ND Enrolled:214 : Evaluated: 173 Number of sites: 15	Positive skin-prick test to grass pollen Symptoms of seasonal allergic rhinitis for past two seasons	Sinusitis Corticosteroids or cromoglycate within one month Antihistamines within 6 weeks Immunotherapy within one year Perennial rhinitis Pregnancy
Van Bavel 1994 95085365	**Seasonal Allergic Rhinitis** Terfenadine vs. fluticasone [placebo also tested] RCT-Parallel	14 days	Location: USA Mean age: 39.2 Age range: > 12 % Male: 49% Race: ND Enrolled: 232 Evaluated: 232 - 78 (fluticasone), 77(terfenadine), and 77 (placebo) Number of sites: 5?	Symptomatic at entry with symptom score of 200/400 on 4/ 7 days preceding treatment Moderate to severe seasonal allergic rhinitis diagnosed as below 1yr history Nasal mucosal appearance consistent with allergic rhinitis Positive skin test to mountain cedar w/in 12 months Normal HPA axis by morning cortisol	No oral antihistamines or cromolyn for at last 2 weeks prior to screening No astemizole or inhaled intranasal or systemic steroids for 1 month prior to screening

Evidence Table 2. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Non-sedating antihistamines versus nasal corticosteroids
Part I. (continued)

Author **Year** **UI**	**Intervention**	**Duration**	**Demographics**	**Inclusion criteria**	**Exclusion criteria**
Hilberg 1995 96098156	**Seasonal Allergic Rhinitis** Terfenadine vs Budesonide [Placebo also tested] RCT- cross-over (extractable)	42 days- 14 days for each of 3 treatments	Location: Denmark Mean age: 25.4 Age range: 23-33 % Male: 14/17= 82% Race: Caucasian Enrolled: 18 Evaluated: 17 Number of sites: 1	Non-smoking volunteers “typical hay fever symptoms in the season” Positive prick test RAST against timothy of at least class 3	Asthma Prior nasal surgery “gross nasal pathology” Smoking
Schoenwetter 1995 96070357	**Seasonal Allergic Rhinitis** Loratidine vs Triamcinolone RCT-Parallel	28 days	Location: US Mean age: 31.2 Age range: 12-70 % Male: 43% Race: ND Enrolled: 298 - 149 each group Evaluated: 274 - 140 for loratadine, and 134 for triamcinolone Number of sites: ND	2 seasons of SAR symptoms	Sinusitis Nasal septal deviation Nasal polyposis Decongestants/antihistamine use within 42 days Oral/ nasal steroid use in 3 months Pregnant/lactating
Bernstein 1996 96213647	**Seasonal Allergic Rhinitis** astemizole vs. Triamcinolone RCT parallel	4 weeks	Location: US Mean age: 35.7 Age range: ND % Male: 46% Race: ND Enrolled: 239 - 120 (Triamcinolone) and 119 (Astemizole) Evaluated: 209 - 104 (Triamcinolone), and 105 (Astemizole) Number of sites:9	2 year history of symptoms Positive skin test Qualifying symptom score	Recent steroid use Recent cromolyn Recent immunotherapy Sinusitis Nasal polyposis Septal deviation Rhinitis Medicamentosa

Evidence Table 2. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Non-sedating antihistamines versus nasal corticosteroids
Part I. (continued)

Author **Year** **UI**	**Intervention**	**Duration**	**Demographics**	**Inclusion criteria**	**Exclusion criteria**
Bronsky 1996 UI	**Seasonal Allergic Rhinitis** Terfenadine vs. fluticasone RCT Parallel	4 weeks	Location: US Mean age: 35.7 Age range: ND % Male Race: ND Enrolled: 239 Evaluated: 209 Number of sites:9	>12years old Positive skin test Nasal mucosal appearance consistent with SAR 1 year history of symptoms	Antihistamines within 2 weeks Cromolyn sodium within 2 weeks Steroids (all Types) within 4 weeks Astemizole within 4 weeks
Bronsky 1996 96194242	**Seasonal Allergic Rhinitis** Terfenadine vs. fluticasone [Placebo also tested] RCT-Parallel	28 days	Location: US Mean age: 30 Age range: > 12 % Male: 58% Race: ND Enrolled: 348 - 117 (fluticasone), 116 (terfenadine) and 115 (placebo) Evaluated: 319 - 111 (fluticasone), 103 (terfenadine) and 105 (placebo) Number of sites: 10	Moderate to severe seasonal allergic rhinitis diagnosed by 1)positive skin test to at least one spring allergen 2)nasal mucosa appearance consistent with diagnosis of SAR 3)at least 1 year history of symptoms 4)moderate-severe symptoms by diary 5)morning plasma cortisol ≥ 7μg/dL 6)nasal symptom score ≥ 200/400 on 4/7 days immediately preceding enrollment	Oral antihistamine or cromolyn sodium within 2 weeks Astemizole or inhaled/systemic corticosteroids within 1 month

Evidence Table 2. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Non-sedating antihistamines versus nasal corticosteroids
Part I. (continued)

Author **Year** **UI**	**Intervention**	**Duration**	**Demographics**	**Inclusion criteria**	**Exclusion criteria**
Jordana 1996 96191239	**Seasonal Allergic Rhinitis** Loratadine vs. fluticasone RCT Parallel	4 weeks	Location: US Mean age: 12±17 Age range: ND % Male Race: ND Enrolled: 242 Evaluated: 240 - 121 (Fluticasone) and 119 (Loratadine) Number of sites: 5	Moderate to severe allergic rhinitis symptoms	Viral rhinitis Perennial rhinitis Steroids within 1 month Cromoglycate within 1 month Loratidine within 1 week Sinusitis Nasal surgery Structural nasal abnormalities
Gehanno 1997 97332767	**Seasonal Allergic Rhinitis** Loratidine vs. fluticasone RCT- Parallel	4 weeks	Location: France Mean age: 37.0 (fluticasone), and 41 (loratadine) Age range: > 12 % Male: 47% (fluticasone) and 42% (loratadine) Race: ND Enrolled: 114 Evaluated: 114 - 57 each group Number of sites: “multi-center”	Positive skin test to seasonal allergens	Women of childbearing potential Patient received oral, inhaled or intranasal corticosteroids within 1 month Intranasal cromolyn within 15 days prior to study
Juniper 1997 UI	**Seasonal Allergic Rhinitis** Terfenadine vs. Fluticasone RCT	6 weeks	Location: US Mean age: 41 Age range: ND % Male Race: ND Enrolled: 240 Evaluated: 240 Number of sites: 5	Diagnosis of SAR Symptomatic in previous season Positive ragweed skin test	Sinusitis Nasal polyposis Perennial rhinitis Immunotherapy within 12 months Antihistamine therapy All steroid therapy

Evidence Table 2. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Non-sedating antihistamines versus nasal corticosteroids
Part I. (continued)

Author **Year** **UI**	**Intervention**	**Duration**	**Demographics**	**Inclusion criteria**	**Exclusion criteria**
Juniper 1997 97286890	**Seasonal Allergic Rhinitis** Terfenadine vs. fluticasone RCT Parallel	6 weeks	Location: Canada Mean age: ND Age range: 17-66 % Male: 48% (fluticasone) and 53% (terfenadine) Race: ND Enrolled: 61 Evaluated: 60 Number of sites: 1	Diagnosis seasonal allergic rhinoconjunctivitis Nasal symptoms requiring treatment during previous ragweed season Positive skin test for ragweed	Sinusitis Nasal polyposis Perennial rhinoconjunctivitis Chronic nasal obstruction, polyposis or sinusitis Allergen injection of treatment within past 12 months Pregnant/nursing mothers Other diseases requiring antihistamine or oral steroid
D'Ambrosio 1998 99133169	**Seasonal Allergic Rhinitis** Cetirizine vs fluticasone [also one group treated with both cetirizine and fluticasone] RCT-Parallel	60 days	Location: Italy Mean age: 28.1 Age range: > 14 % Male: 9/18 Race: ND Enrolled: 60 Evaluated: 54 18(cetirizine), 19 (fluticasone), and 17 (cetirizine and fluticasone) Number of sites: 1	Clinical history of SAR Positive skin test	Use of drugs that may interfere with results of study

Evidence Table 2. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Non-sedating antihistamines versus nasal corticosteroids
Part I. (continued)

Author **Year** **UI**	**Intervention**	**Duration**	**Demographics**	**Inclusion criteria**	**Exclusion criteria**
Ratner 1998 98390023	**Seasonal Allergic Rhinitis** Loratadine vs. fluticasone [also studies combination of Loratadine + Fluticasone; placebo also tested] RCT- Parallel	14 days	Location: US Mean age: 40.1 Age range: >12 % Male: 46% Race: ND Enrolled:600 Evaluated: 569 142 (Loratadine), 142 (Fluticasone), 145 (Loratadine +Fluticasone), and 140 (Placebo) Number of sites: 5	Positive Skin prick to allergen	Nasal septal deviation Nasal polyposis Any treatment with trial drugs within 6 weeks Decongestants or steroids within 4 weeks “Candidal infection” Pregnant or lactating
Ortolani 1999 20068053	**Seasonal Allergic Rhinitis** Levocabastine vs fluticasone vs. placebo RCT-Parallel	6 weeks	Location: Italy Mean age: 29 Age range: 13-64 % Male: 169/288 Race: ND Enrolled:288 Evaluated: 288 Number of sites: 16	Clinical history of SAR for at least 2 years Positive skin prick test to seasonal pollens	Sinusitis Nasal septal deviation Nasal polyposis Long-acting Antihistamines Nasal systemic steroids(x 4 weeks) Pregnant/lactating PAR Paranasal sinuses/ respiratory tract infection Nasal surgery within past year

Evidence Table 2. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Non-sedating antihistamines versus nasal corticosteroids
Part I. (continued)

Author **Year** **UI**	**Intervention**	**Duration**	**Demographics**	**Inclusion criteria**	**Exclusion criteria**
Condemi 2000 20289854	**Seasonal Allergic Rhinitis** Loratidine vs. Triamcinolone RCT-Parallel	28 days	Location: US Mean age: 32 Age range: 12 - 69 % Male: 45% Race: 90% Caucasian Enrolled: 351 - 175 (triamcinolone) and 176 (loratadine) Evaluated: 317 - 160 (triamcinolone) and 157 (loratadine) Number of sites: 11	2 year consecutive history Positive skin prick test to grass pollen Combined symptom score of at least 24 on 4 of 5 baseline days (4 point scale, max 60)	Sinusitis Nasal septal deviation Rhinitis medicamentosa Nasal candidiasis Pregnant, lactating, childbearing women Recent use of treatment: corticosteroids, intranasal cromolyn, topical decongestants, systemic steroids, long-acting antihistamines

Evidence Table 2. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Non-sedating antihistamines versus nasal corticosteroids
Part II.

Author Year UI	**Treatment outcomes studied**	**Symptom scale**	**Outcomes-efficacy**
Munch 1983 84050113	Mean total symptom score Rhinorrhoea Nasal congestion Sneezing Itchy eyes Itchy throat	Sneezing (morning and evening): 0= no symptoms, 1= slight, 2= moderate, 3= severe Rhinorrhea and Blockage- rating scale Total Nasal symptom score- combination of sneezing, rhinorrhoea, and blockage scores	Global patient assessment: score of 82 for budesonide and 62 for dexchlorpheniramine P= 0.06 Total Nasal Symptom score: More improvement of symptoms for patients taking budesonide compared dexchlorpheniramine with p< 0.05 for budesonide vs dexchlorpheniramine Sneezing + Nose blowings: Dexchlorpheniramine group- not much diurnal variation during therapy Budesonide- symptom reduction for morning and evening symptoms Nasal blockage More improvement for morning and evening symptoms in patients taking budesonide compared to dexchlorpheniramine with p< 0.05 for budesonide vs dexchlorpheniramine Nasal itching No significant differences between groups, but trend for favoring budesonide over dexchlorpheniramine

Evidence Table 2. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Non-sedating antihistamines versus nasal corticosteroids
Part II. (continued)

Author Year UI	**Treatment outcomes studied**	**Symptom scale**	**Outcomes-efficacy**
Backhouse 1986 86165329	Total mean symptom score Rhinorrhoea Nasal congestion Sneezing Nose blowing Eye symptoms	Symptom scale Sneezing/nose-blowing 1= never/seldom 2= infrequent 3=frequent 4=very frequent Runny nose, stuffy nose, and ocular symptoms 1=none 2=mild 3=moderate 4=severe overall assessment (done at end of every visit) – excellent, good, poor, none or worse symptoms	All values taken from Week 7- when pollen level was highest Global Physician Assessment: Good/excellent response achieved by 62% of subjects in terfenadine group and 96% in terfenadine+flunisolide group, with p< 0.001 for terfenadine + flunisolide group vs terfenadine group Sneezing Symptom score of 1.9 with terfenadine, vs 1.4 with terfenadine+flunisolide, with p = 0.02 Nasal Blowing Symptom score of 2.3 with terfenadine vs 1.5 with terfenadine+flunisolide with p= 0.001 Nasal Congestion Symptom score of 2.2 with terfenadine vs 1.5 with terfenadine+flunisolide with p=0.008
Wood 1986 86245576	Total Mean Symptom Score Sneezing Rhinorrhoea Blocked nose Itchy eyes	Symptom scale Diary card that included five 10 cm visual analogue scale	Results presented as graphs mostly “No statistically significant difference between the scores for the astemizole and the beclomethasone from using an ANOVA for overall severity of symptom or for blocked nose, sneezing or runny nose Both medications decrease the VAS (0-100 scale) symptom scores at baseline to around 10-20 for individual symptoms of sneezing, rhinitis and rhinorrhoea

Evidence Table 2. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Non-sedating antihistamines versus nasal corticosteroids
Part II. (continued)

Author Year UI	**Treatment outcomes studied**	**Symptom scale**	**Outcomes-efficacy**
Juniper 1989 89175902	Total mean symptom score Nasal Congestion Sneezing Watery eyes Asthma	Symptom scale: Diary entries: Symptom severity: 0-3 scale: 0= absent 1=mild 2=moderate 3=severe Symptom duration: 0-3 scale: 0=absent 1=few short episodes 2= many episodes 3= continuous symptoms also evaluated after wk1,3,and 6 by clinician	Overall efficacy evaluation (from mean daily scores) Beclomethasone showed better improvement than astemizole for sneezing, stuffy nose, and runny nose Beclomethasone + Astemizole showed better improvement than astemizole for nasal symptoms, but little difference compared to beclomethasone Sneezing: Mean daily score of 0.395 for astemizole, score of 0.193 for beclomethasone, and score of 0.155 for astemizole + beclomethasone Rhinorrhoea: Mean daily score of 0.406 for astemizole, score of 0.152 for beclomethasone, and score of 0.192 for astemizole + beclomethasone Nasal Congestion: Mean daily score of 0.594 for astemizole, score of 0.319 for beclomethasone, and score of 0.322 for astemizole + beclomethasone

Evidence Table 2. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Non-sedating antihistamines versus nasal corticosteroids
Part II. (continued)

Author Year UI	**Treatment outcomes studied**	**Symptom scale**	**Outcomes-efficacy**
Robinson 1989	Mean total symptom score Rhinorrhoea Sneezing Nasal Congestion Watery Eyes Itchy Nose Itchy eyes Post nasal drip (PND) Nasal irritation	Symptom scale for patients with daily record card- 5 pt scale 0= no symptoms 1= mild 2= moderate 3= severe 4= very severe	**Treatment groups: Group A – Sequence #1 : Beclomethasone 1st period, then Terfenadine 2nd period Group B – Sequence #2 : Terfenadine 1st period, then Beclomethasone 2nd period Patient Preference: 9 preferred Beclomethasone, 2 preferred Terfenadine, and 2 had no preference Sneezing For group A, symptom score of 1.0 with terfenadine vs symptom score of 0.48 with beclomethasone; P = 0.04 for symptom category in general For group B, symptom score of 0.49 with terfenadine vs symptom sore of 0.25 with beclomethasone Rhinorrhoea For group A, symptom score of 1.29 with terfenadine vs symptom score of 0.69 with beclomethasone; P= 0.0006 for symptom category in general For group B, symptom score of 0.94 with terfenadine vs symptom score of 0.08 with beclomethasone Nasal Congestion For group A, symptom score of 0.92 with terfenadine vs symptom score of 0. 76 with beclomethasone; P= N/S for symptom For group B, symptom score of 0.85 with terfenadine vs symptom score of 0.84 with beclomethasone Nasal Itch For group A, symptom score of 0.62 with terfenadine vs symptom score of 0.39 with beclomethasone; P= N/S for symptom For group B, symptom score of 0.36 with terfenadine vs symptom score of 0.1 with beclomethasone

Evidence Table 2. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Non-sedating antihistamines versus nasal corticosteroids
Part II. (continued)

Author **Year** **UI**	**Treatment outcomes studied**	**Symptom scale**	**Outcomes-efficacy**
Darnell 1994 95196117	Mean total Symptom Score Sneezing Nasal Congestion Rhinorrhoea Itchy nose	**Overall assessment**- vertical line made by patients on 10 cm visual analogue scale Left=no symptoms, Right= worst symptoms **Individual Symptom** scale- 4 pt scale for each symptom [0-3, 0=best,3=worst] **Blockage-** 0= breathing freely easily, 1= slightly difficult, 2= moderately difficult, 3= difficult-impossible **Sneezing** 0=absent, 1= occasionally present, 2= troublesome episodes, 3= frequent troublesome episodes **nasal itching/rhinorrhoea** 0=absent,1=mostly unaware, 2= not a persistent distraction, 3= persistent distraction **drowsiness** 0=absent, 1= mild, 2= moderate, 3= severe	Nasal blockage P= 0.009 for fluticasone vs terfenadine, and p= 0.02 for fluticasone vs terfenadine Sneezing Days free of symptoms: 25 days with terfenadine, 40 days with fluticasone, and 20 days with placebo; P<0.001 for fluticasone vs placebo, and p= 0.057 for fluticasone vs terfenadine Rhinorrhoea Days free of symptoms: 45 days with terfenadine, 55 days with fluticasone, and 35 days with placebo; p<0.001 for fluticasone vs placebo, and p= 0.021 for fluticasone vs terfenadine Nasal congestion Days free symptoms on waking: 5 days with terfenadine, 35 days with fluticasone, and 6 days with placebo; p<0.017 for fluticasone vs placebo, and p<0.012 for fluticasone vs terfenadine Days free of symptoms during the day: 15 days with terfenadine, 45 days with fluticasone, and 10 days with placebo; p < 0.028 for fluticasone vs placebo, and p<0.01 for fluticasone vs terfenadine

Evidence Table 2. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Non-sedating antihistamines versus nasal corticosteroids
Part II. (continued)

Author Year UI	**Treatment outcomes studied**	**Symptom scale**	**Outcomes-efficacy**

Van Bavel
1994
95085365
	Total Mean Symptom Score
	Rhinorrhoea
	Nasal Congestion
	Sneezing
	Itchy nose
	Nasal eosinophils
		Symptom Scale
		Diary cards- visual analog scale ranging from 0 (absent) to 100 (severe)
		- all symptoms evaluated in evening except nasal obstruction, which was also evaluated on awakening
		Rhinoprobe measurements (days 1and 15)- rated # inflammatory cells w/ 5 pt scale:
		0= none, 1= few, scattered; 2= moderate number, small clumps; 3= large clumps, not covering entire field; and 4= clumps covering entire field
		Overall physician assessment: following categories: significant improvement, mild improvement, no change, mildly worse, moderately worse, or significantly worse
			Overall clinician assessment:
			Significant/ Moderate Improvement: 64% in fluticasone group with p < 0.01 for drug vs placebo; 49% in terfenadine group with p< 0.01 for fluticasone vs terfenadine; and 44% in placebo group
			Mild Improvement: No change, or Mildly Worse: 33% in fluticasone group, 49% in terfenadine group, and 52% in placebo group
			Moderately or significantly worse: 2% in fluticasone group, 1% in terfenadine group, and 4% in placebo group
			
			Sneezing:
			Fluticasone did significantly better than placebo or terfenadine with p< 0.05. Terfenadine did significantly worse than fluticasone with p< 0.05
			
			Rhinorrhoea:
			Fluticasone did significantly better than placebo and terfenadine with p< 0.05. Terfenadine did significantly worse than fluticasone with p < 0.05
			
			Congestion:
			Fluticasone did significantly better than placebo or terfenadine with p< 0.05. Terfenadine did significantly worse than fluticasone with p < 0.05
			
			No mean symptom scores given for individual symptoms or magnitude of change- better work at 14 days only.

Evidence Table 2. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Non-sedating antihistamines versus nasal corticosteroids
Part II. (continued)

Author Year UI	**Treatment outcomes studied**	**Symptom scale**	**Outcomes-efficacy**
Hilberg 1995 96098156	Total Mean Symptom Score Nasal Congestion Nasal Itch Sneezing Nasal secretion	Symptom Scale Questionnaire- Visual 100 mm Linear Analog Scale- no symptoms to intolerable symptoms	Overall effect Minimum cross-sectional area (cm^2) (*Minimum cross-sectional area was tested to evaluate correlation with olfactory function) Area of 1.03 with terfenadine with $p < 0.01$ for terfenadine vs placebo; area of 1.11 with budesonide with $p < 0.005$ for budesonide vs placebo; area of 0.99 with placebo Nasal Volume (cm^3) Volume of 16.45 with terfenadine with $p< 0.1$= NS for terfenadine vs placebo; volume of 16.98 with budesonide with $p < 0.01$ for budesonide vs placebo; volume of 15.74 with placebo Budesonide also significantly improved nasal congestion Olfactory threshold- no results Surrogate end- points of uncertain clinical value
Schoenwetter 1995 96070357	Total Mean symptom score Rhinorrhoea Nasal congestion Sneezing Itchy Eyes Itchy nose Postnasal drip (PND)	Symptom Scale 4-pt scale: 0= no symptoms 1= mild symptoms 2= moderate symptoms 3=severe symptoms	Overall assessment: % symptom change of 31% with loratadine and 51% with triamcinolone with $p \leq 0.001$ for triamcinolone vs loratadine Sneezing % symptom change of 35% with loratadine and 58% with triamcinolone with $p\leq 0.001$ for triamcinolone vs loratadine Nasal Congestion % symptom change of 21% with loratadine and 42% with triamcinolone with $p\leq 0.001$ for triamcinolone vs loratadine Nasal Itch % Symptom change of 39% with loratadine and 55% with triamcinolone with $p\leq 0.001$ for triamcinolone vs loratadine

Evidence Table 2. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Non-sedating antihistamines versus nasal corticosteroids
Part II. (continued)

Author Year UI	**Treatment outcomes studied**	**Symptom scale**	**Outcomes-efficacy**
Bernstein 1996 96213647	Mean total nasal symptom score Nasal itch Nasal congestion Postnasal drip Rhinorrhoea Sneezing Ocular symptoms	SYMPTOM SCALE: Diary cards: 0-3 scale was used during run-in period to evaluate patient symptom severity	Triamcinolone produced moderate to complete relief in 77% of patients vs. 63% of placebo patients. P<0.01 Total nasal score reduced by 50% with triamcinolone vs. 37% with astemizole. p<0.01 Nasal itch reduced by 54% with triamcinolone vs. 42% with astemizole p<0.05 Nasal congestion reduced by 43% with triamcinolone vs. 27% with astemizole p<0.05 Sneezing reduced by 56% with triamcinolone vs. 42% with astemizole p<0.05
Bronksy 1996	Global assessment-MD Global assessment patient Sneezing Rhinorrhoea Nasal congestion on awakening Nasal itch Nasal outflow Nasal cytology score	SYMPTOM SCALE: Diary cards: 0-3 scale	

Evidence Table 2. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Non-sedating antihistamines versus nasal corticosteroids
Part II. (continued)

Author Year UI	**Treatment outcomes studied**	**Symptom scale**	**Outcomes-efficacy**
Bronsky 1996 96194242	Total Mean Symptom Scale Rhinorrhoea Nasal Congestion Sneezing Itchy nose	Symptom scale- Visual Analogue scale From 0(absent) to 100 (severe)	**Global patient assessment:** Total nasal symptom score of 113 with fluticasone with p< 0.05 for fluticasone vs placebo; score of 171 with terfenadine with p< 0.05 for fluticasone vs terfenadine (no p value for terfenadine vs placebo); score of 191 with placebo **Overall nasal symptom percent change from baseline** : Change of -57% with fluticasone with p< 0.001 for fluticasone vs placebo; percent change of –38% with terfenadine and p< 0.001 for fluticasone vs terfenadine; percent change of –32% with placebo **Global clinician assessment:** Total nasal symptom score of 115 with fluticasone and p< 0.05 for fluticasone vs placebo; score of 163 with terfenadine and p < 0.05 for fluticasone vs terfenadine; score of 174 with placebo Percent change from baseline of –52% with fluticasone and p< 0.001 for fluticasone vs placebo; percent change of –33% with terfenadine and p< 0.001 for fluticasone vs terfenadine; score of –22% with placebo **Sneezing** Clinician assessment: score of 21 with fluticasone and p< 0.05 for fluticasone vs placebo; score of 33 with terfenadine and no p-value for fluticasone vs terfenadine; score of 36 with placebo Patient Assessment: Score of 23 with fluticasone and p< 0.05 for fluticasone vs placebo; score of 39 with terfenadine and p< 0.05 for fluticasone vs terfenadine; score of 45 with placebo **Rhinorrhoea** Clinician assessment: score of 31 with fluticasone and p< 0.05 for fluticasone vs placebo; score of 40 with terfenadine and p< 0.05 for fluticasone vs terfenadine; score of 43 with placebo Patient assessment: score of 29 with fluticasone and p< 0.05 for fluticasone vs placebo; score of 42 with terfenadine and p< 0.05 for fluticasone vs terfenadine; score of 47 with placebo **Nasal obstruction during day** Clinician assessment: score of 39 with fluticasone and p< 0.05 for fluticasone vs placebo; score of 54 for terfenadine and p < 0.05 for fluticasone vs terfenadine; score of 53 with placebo.

Evidence Table 2. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Non-sedating antihistamines versus nasal corticosteroids
Part II. (continued)

Author Year UI	**Treatment outcomes studied**	**Symptom scale**	**Outcomes-efficacy**
Bronsky 1996 96194242 (cont.)			Patient assessment: score of 35 with fluticasone and p< 0.05 for fluticasone vs placebo; score of 50 with terfenadine and p < 0.05 for fluticasone vs terfenadine; score of 51 with placebo. **Nasal obstruction on awakening** Patient assessment: score of 41 with fluticasone and p< 0.05 for fluticasone vs placebo; score of 57 with terfenadine and p< 0.05 for fluticasone vs terfenadine; score of 56 with placebo **Nasal Itch** Clinician assessment: score of 25 with fluticasone and p< 0.05 for fluticasone vs placebo; score of 37 with terfenadine and p< 0.05 for terfenadine vs placebo; score of 42 with placebo Patient assessment: score of 26 with fluticasone and p< 0.05 for fluticasone vs placebo; score of 40 with terfenadine, and p < 0.05 for fluticasone vs terfenadine; score of 48 with placebo
Jordana 1996 96191239	Nasal congestion (day) Nasal congestion (night) Sneezing Nasal itching Rhinorrhoea Ocular irritation Peak inspiratory nasal flow	Symptom scale: 4 point scale: 0-3	Day and night nasal congestion significantly reduced by fluticasone p<0.0001 Sneezing reduced by fluticasone p<0.001 Nasal itching reduced by fluticasone p<0.003 Measurement included symptom-free days: fluticasone group had statistically significantly lower median symptom scores than loratadine for nasal blockage during the day Nasal blockage: (p= 0.0006) Sneezing: (p= 0.0054) Runny nose: (p < 0.0001) Nasal Itch: (p= 0.029)

Evidence Table 2. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Non-sedating antihistamines versus nasal corticosteroids
Part II. (continued)

Author Year UI	**Treatment outcomes studied**	**Symptom scale**	**Outcomes-efficacy**
Gehanno 1997 97332767	Total Mean Symptom Score Rhinorrhoea Nasal Congestion Sneezing Itchy nose Night/daytime obstruction-	Symptom scale: Severity nasal symptoms -4 pt scale: with 0= no symptoms to 3= very frequent symptoms Overall symptom severity- visual analog scale from 0 (no symptoms) to 100 (severe symptoms)	Global symptom assessment: Nasal symptom score: On day 14, 61% patient improvement in fluticasone group vs 43% patient improvement in loratadine group, p = 0.02 for fluticasone vs loratadine On day 28, 72% patient improvement in fluticasone group vs 49% patient improvement in loratadine group, p= 0.009 for fluticasone vs loratadine Overall symptom score: On day 28, 80% success rate in fluticasone group vs 70% success rate in loratadine group. Values interpolated from figure. Success defined as “very effective” or “effective” out of 4 point scale Global clinician assessment: Nasal symptom score: On day 14, 62% patient improvement in fluticasone group vs 48% patient improvement in loratadine group, p= 0.008 for fluticasone vs loratadine On day 28, 73% patient improvement in fluticasone group vs 56% patient improvement in loratadine group, p= 0.002 for fluticasone vs loratadine Overall symptom score: On day 28, 80% success rate in fluticasone group vs 63% success rate in loratadine group. Values interpolated from figure. Success defined as “very effective” or “effective” out of 4 point scale
Juniper 1997	Rhinoconjunctivitis HRQL score Rescue terfenadine usage		Health-related quality of life score higher in fluticasone group p<0.052

Evidence Table 2. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Non-sedating antihistamines versus nasal corticosteroids
Part II. (continued)

Author Year UI	**Treatment outcomes studied**	**Symptom scale**	**Outcomes-efficacy**
Juniper 1997 97286890	Total Mean symptom score Nasal symptoms Eye-symptoms Non-nasal symptoms Sleep impairment Practical problems Activity limitations Emotional function	Symptom scale At each visit, patients required to complete Rhinoconjunctivitis Quality of Life Questionnaire Symptom severity score: 7 point scale with 0= no bothered, to 6= extremely bothered	⊕ symptom score difference indicates Fluticasone better than Terfenadine-differences based on HRQL scores Overall global assessment: At height of ragweed season: symptom score difference of 0.11 between fluticasone and terfenadine. P= 0.052 At end of season, score difference of 0.14 between drugs Sneezing At height of ragweed season, symptom score difference of 0.21 between fluticasone and terfenadine At end of season, score difference of 0.31 between drugs P=0.005
D'Ambrosio 1998 99133169	Total Mean Symptom Score Rhinorrhoea Nasal Congestion Sneezing Itchy eyes	Symptom Scale 0= no symptoms 1=slight symptoms not interfering with the patient's daily activity and/or sleep 2= moderate symptoms, occasionally interfering with daily activity and sleep 3=grave symptoms, seriously interfering with activity and sleep	Overall Clinician assessment: Symptom score of 2.9 with cetirizine with p< 0.05 for initial vs final; score of 4.8 with fluticasone with p < 0.05 for initial vs final; and score of 2.2 with treatment of cetirizine and fluticasone, with p< 0.05 for initial vs final P< 0.05 for cetirizine vs fluticasone; p< 0.05 for fluticasone vs treatment of both cetirizine and fluticasone; and p= NS (> 0.05) for cetirizine vs treatment of both cetirizine of fluticasone Nasal Sneezing Symptom score of 0.4 with cetirizine, score of 1.8 with fluticasone, and score of 0.6 with both cetirizine and fluticasone Rhinorrhoea Symptom score of 0.6 with cetirizine, score of 1.3 with fluticasone, and score of 0.4 with both cetirizine and fluticasone Nasal Congestion Symptom score of 1.5 with cetirizine; score of 0.4 with fluticasone, and score of 0.7 with both cetirizine and fluticasone Nasal Itch Symptom score of 0.4 with cetirizine, score of 1.3 with fluticasone, and score of 0.5 with both cetirizine and fluticasone

Evidence Table 2. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Non-sedating antihistamines versus nasal corticosteroids
Part II. (continued)

Author Year UI	**Treatment outcomes studied**	**Symptom scale**	**Outcomes-efficacy**
Ratner 1998 98390023	Total Mean Symptom Score Rhinorrhoea Nasal Congestion Sneezing Itchy nose Nasal mucosa consistent with rhinitis	Symptom scale Diary Cards: Visual analog scale 0- 100 with 0= absent, and 100= severe -symptoms evaluated in evening	**Global patient evaluation:** Overall treatment: 62/142 patients indicated symptom *improvement with Loratadine and p< 0.001 for drug vs placebo; 90/142 patients indicated improvement with Fluticasone and p < 0.001 for drug vs placebo; 96/145 indicated improvement with Loratadine + Fluticasone with p < 0.001 for drug combination vs placebo and p< 0.001 for drug combo vs loratadine; and 61/140 indicated improvement with placebo (*improvement= significant, moderate + mild improvement) Total Nasal Symptoms Score: Score of 220 with Loratadine with p< 0.001 for loratadine vs placebo; score of 140 with fluticasone with p< 0.001 for fluticasone vs placebo and p< 0.001 for fluticasone vs loratadine; score of 110 with Loratadine +Fluticasone with p< 0.05 for drug combo vs fluticasone for mean change from baseline, p < 0.001 for drug combo vs loratadine, plus p < 0.001 for drug combo vs placebo; and score of 230 with placebo **Global clinician evaluation:** Total Symptoms: Score of –102.0 for Loratadine; score of –187.0 for fluticasone with p < 0.05 for fluticasone vs placebo, and p < 0.05 for fluticasone vs loratadine; score of 186.0 for Loratadine + Fluticasone with p < 0.05 for drug combo vs placebo, and p < 0.05 for drug combo vs loratadine; score of –102.0 for placebo Total Nasal Symptom Score: Score of 210 with Loratadine with p < 0.001 for loratadine vs placebo; score of 110 with fluticasone with p < 0.001 for fluticasone vs placebo and p < 0.001 for fluticasone vs loratadine; score of 110 with Loratadine + Fluticasone with p < 0.001 for drug combo vs placebo and p < 0.001 for drug combo vs loratadine; and score of 220 with placebo Following scores are from evaluations after 2 weeks **Sneezing:** Score of –26.3 for Loratadine; score of –48.4 for fluticasone with p < 0.05 for fluticasone vs placebo, and p < 0.05 for fluticasone vs loratadine; score of – 45.7 for Loratadine + Fluticasone with p < 0.05 for drug combo vs placebo, and p < 0.05 for drug combo vs loratadine; score of –26.6 for placebo loratadine; score of –27.1 for placebo

Evidence Table 2. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Non-sedating antihistamines versus nasal corticosteroids
Part II. (continued)

Author Year UI	**Treatment outcomes studied**	**Symptom scale**	**Outcomes-efficacy**
Ratner 1998 98390023 (cont.)			**Rhinorrhoea:** Score of –26.9 for Loratadine; score of –46.3 for fluticasone with p < 0.05 for fluticasone vs placebo, and p < 0.05 for fluticasone vs loratadine; score of –49.6 for Loratadine + Fluticasone with p < 0.05 for drug combo vs placebo, and p < 0.05 for drug combo vs **Nasal Congestion:** Score of –20.0 for Loratadine; score of –42.5 for fluticasone with p < 0.05 for fluticasone vs placebo, and p < 0.05 for fluticasone vs loratadine; score of –42.6 for Loratadine + Fluticasone with p < 0.05 for drug combo vs placebo, and p < 0.05 for drug combo vs loratadine; score of –20.0 for placebo **Nasal Itch:** Score of –29.3 for Loratadine; score of –50.0 for fluticasone with p < 0.05 for fluticasone vs placebo, and p < 0.05 for fluticasone vs loratadine; score of –48.2 for Loratadine + Fluticasone with p < 0.05 for drug combo vs placebo, and p < 0.05 for drug combo vs loratadine; score of –28.4 for placebo
Ortolani 1999 20068053	Total Mean Symptom Score Rhinorrhoea Nasal congestion Sneezing Watery eyes Itchy nose Itchy eyes	Patients- record symptoms on diary card (nasal and ocular symptoms) Nasal obstruction symptom scale 0= not present 1= slightly difficult to breathe through nose 2= moderately difficult 3= very difficult/ impossible All other symptom scales 0= none 1= mild (occasionally present) 2= moderate (rather frequent) 3= severe (persistent)	Higher % symptom-free days in patients in fluticasone group compared to those given placebo for symptoms of obstruction, rhinorrhea, sneezing, and itching Higher % of symptom-free days without obstruction and rhinorrhea and better frequency distribution of nasal scores for each symptom for patients in fluticasone group compared to those in levocabastine group *****Data: Median number of symptom-free days and Frequency distribution of median score given! *****No actual numerical data. All info in bar graphs.

Evidence Table 2. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Non-sedating antihistamines versus nasal corticosteroids
Part II. (continued)

Author Year UI	**Treatment outcomes studied**	**Symptom scale**	**Outcomes-efficacy**
Condemi 2000 20289854	Total Mean Symptom Score Rhinorrhoea Sneezing Nasal Congestion Watery eyes Itchy nose Itchy eyes Itchy throat	Symptom scale: Patient diary cards- 4 pt scale 0= none; symptoms absent 1= mild, symptoms present, but not annoying 2= moderate, symptoms present and annoying 3= severe, symptoms interfere with daily activities or sleep Daily pollen counts, clinical laboratory tests, and physical examinations were also done Patients also completed RQLQ at visits 2,3, and 4	Global patient assessment: (at 4 weeks) Rhinoconjunctivitis Quality of Life Questionnaire: overall score of 1.48 with triamcinolone vs score of 1.82 with loratadine; p < 0.05 Global physician assessment: Improvement with triamcinolone: total 136 patients (78%) showed improvement 54 patients (31%) showed moderate improvement 64 patients (37%) showed marked improvement 18 patients (10%) showed complete improvement p= NS Improvement with loratadine: total 116 patients (67%) showed improvement 51 patients (29%) showed moderate improvement 60 patients (35%) showed marked improvement 5 patients (3%) showed complete improvement p= NS Following scores taken at 4 weeks • Total Nasal score Mean weekly score of 3.8 with triamcinolone vs score of 5.0 with loratadine P < 0.5 • Sneezing Mean weekly score of 1.0 with triamcinolone vs score of 1.3 with loratadine P< 0.05 • Rhinorrhoea Mean weekly score of 1.25 with triamcinolone vs score of 1.5 with loratadine P < 0.05 • Nasal Congestion Mean weekly score of 1.3 with triamcinolone vs score of 1.5 with loratadine P < 0.5

Evidence Table 2. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Non-sedating antihistamines versus nasal corticosteroids
Part II. (continued)

Author Year UI	**Treatment outcomes studied**	**Symptom scale**	**Outcomes-efficacy**
Condemi 2000 20289854 (continued)			• Nasal Itch Mean weekly score of 1.1 with triamcinolone vs score of 1.4 with lortadine P= NS, but statistically significant at week 2 and week 3 Overall percent improvement from 48% to 58% in triamcinolone group Overall percent improvement from 36% to 46% in loratadine group

Evidence Table 2. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Non-sedating antihistamines versus nasal corticosteroids
Part III.

Author **Year** **UI**	**Outcome-safety**	**Potential Bias**	**Funding**
Munch 1983 84050113	No major adverse effects. Minor adverse effects: 1 withdrawal in dexchlorpheniramine group due to sedation effects Sedation during the day in 1st week- $p < 0.01$ for dexchlorpheniramine vs budesonide Sedation in the morning in 1st week- $p < 0.01$ for dexchlorpheniramine vs budesonide		ND

Evidence Table 2. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Non-sedating antihistamines versus nasal corticosteroids
Part III. (continued)

Author Year UI	**Outcome-safety**	**Potential Bias**	**Funding**
Backhouse 1986 86165329	No major adverse effects. Minor adverse effects: 17 withdrawals from terfenadine group- 12 due to medical reasons (10pts- poor symptom control, 1pt- headache, and 1pt- glandular fever) 5 withdrawals from terfenadine and flunisolide group- 2 due to medical reasons (2pts- poor symptom control) p< 0.005 between group withdrawals Total # reports of side effects: 28 from terfenadine group and 35 from terfenadine +flunisolide group -Nasal Irritation- 8 reports form terfenadine group and 10 reports from terfenadine +flunisolide group -Drowsiness- 9 reports from terfenadine group and 6 reports from terfenadine+ flunisolide group -Nausea- 5 reports from terfenadine group and 1 report from terfenadine + flunisolide group	Other reasons for withdrawal: 1pt-pregnant, , 2 patients- lack of symptoms, 3pt- personal reasons, 1 pt- lost to followup, and 1pt- leaving country	ND

Evidence Table 2. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Non-sedating antihistamines versus nasal corticosteroids
Part III. (continued)

Author **Year** **UI**	**Outcome-safety**	**Potential Bias**	**Funding**
Wood 1986 86245576	No major adverse effects. Minor adverse effects: “adverse effect did not appear to be a problem with either group” -Tiredness, drowsiness, sleepiness- 4 from astemizole group and 2 from beclomethasone group -stomach pains- 4 from beclomethasone group, none from astemizole group	Author is the investigator, care giver, and outcome assessor It is difficult to figure out how he could have ensure concealed randomization and double blinding, etc Mostly graph results	Pharmaceutical

Evidence Table 2. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Non-sedating antihistamines versus nasal corticosteroids
Part III. (continued)

Author **Year** **UI**	**Outcome-safety**	**Potential Bias**	**Funding**
Juniper 1989 89175902	No major adverse effects Minor adverse effects: -Drowsiness- 9 patients taking astemizole, 4 patients taking beclomethasone, and 4 patients taking astemizole + beclomethasone -Hunger- 3 patients taking astemizole, 3 patients taking beclomethasone, and 4 patients taking astemizole+beclomethasone -Dry nose/ lips etc.- 0 patients taking astemizole, 2 patients taking beclomethasone, and 3 patients taking astemizole + beclomethasone -Nasal bleeding- 0 patients taking astemizole, 2 patients taking beclomethasone, and 3 patients taking astemizole+ beclomethasone -Headache- 1 patient taking astemizole, 1 patient taking beclomethasone, and 3 patients taking astemizole+beclomethasone -Thirst- 0 patients taking astemizole, 2 patients taking beclomethasone, and 1 patient taking astemizole+beclomethasone -Skin rash- 0 patients taking astemizole, 2 patients taking beclomethasone, and 1 patient taking astemizole +beclomethasone -Nausea- 0 patients taking astemizole, 0 patients taking beclomthasone, and 2 patients taking astemizole+beclomethasone	Allowance of standardized concomitant medication prevented dropouts Other reasons for withdrawal: 1 patient- forgot to take medication	Pharmaceutical

Evidence Table 2. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Non-sedating antihistamines versus nasal corticosteroids
Part III. (continued)

Author Year UI	**Outcome-safety**	**Potential Bias**	**Funding**
Robinson 1989	No major adverse effects. Minor adverse effects 5 withdrawals- (2 after terfenadine treatment, 3 after beclomethasone treatment) -Drug-related adverse effect- 2 patients taking terfenadine causing nose-bleed, and frequent falling asleep; and 1 patient taking beclomethasone causing upset stomach/pain, are drug-related -Adverse effects- 2 patients taking terfenadine, and 5 patients taking beclomethasone reported adverse effects	Poorly described Small population	Pharmaceutical
Darnell 1994 95196117	No major adverse effects. Minor adverse effects 11 patients withdrew due to adverse effects: 5 from terfenadine group(1 pt- fatigue, 1pt-nasal itching+epistaxis,1pt-oral burning sensation,1pt-asthma, 1- acute asthma attack) 1 from fluticasone group(headache and breathlessness), 5 from placebo (1pt-nasal burning sensation, 1pt-developed erythematous rash,1pt-became pregnant, 1pt-developed Hepatitis A, 1pt-developed asthma) -Headache- 30 patients reported effect -Exacerbations of SAR- 18 patients Overall report of adverse effects- 56% from terfenadine group, 57% from fluticasone group, and 61% from placebo group	Poor enumeration of results Numeric data not given- data extracted by estimation of bar graph Other reasons for withdrawal: Non-compliance with protocol- 34 patients Usage of dis-allowed drugs- 11 patients	Pharmaceutical

Evidence Table 2. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Non-sedating antihistamines versus nasal corticosteroids
Part III. (continued)

Author Year UI	**Outcome-safety**	**Potential Bias**	**Funding**
Van Bavel 1994 95085365	No major adverse effects. Minor adverse effects: 15 withdrawals: 4 patients withdrew due to adverse effects: 1 from fluticasone group due to asthma (drug unrelated);1 due to secondary effects of allergic asthma and bronchitis (drug unrelated); 1 from fluticasone due to headache (drug related); and 1 from terfenadine group due to trauma (drug unrelated) 7 patients due to lack of efficacy Asthma- 2 patients in fluticasone group Headache- 4 patients in fluticasone group, 7 patients in terfenadine group, and 3 patients in placebo group Overall adverse effects: 24 patients in fluticasone group, 23 patients in terfenadine group, and 15 patients in placebo group reported adverse effects	Didn't provide mean baseline and mean p values for treatment symptoms scores Other reasons for withdrawal: 3 patients due to protocol violations (1 from each group) 1 patient did not return for followup visit	ND
Hilberg 1995 96098156	No side effects listed	Tiny study Challenge Mode Surrogate endpoint of uncertain clinical value Budesonide superior to terfenadine in treatment of nasal congestion in hay fever, especially in postchallenge reaction Other reasons for withdrawal: One patient left study for personal reasons (17/18 completed study)	Pharmaceutical

Evidence Table 2. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Non-sedating antihistamines versus nasal corticosteroids
Part III. (continued)

Author Year UI	**Outcome-safety**	**Potential Bias**	**Funding**
Schoenwetter 1995 96070357	No major adverse effects. Minor adverse effects 2 withdrawals form triamcinolone group (possible reason- patient 1- paresthesia, dizziness, nausea, and dyspepsia; patient 2- headache and myalgia(10 withdrawals form loratadine group due to adverse effects (1pt- epistaxis possibly due to drug, reasons for other 9 withdrawals not known) -Headache- 35% of patients from loratadine group and 43% of patients form triamcinolone group -Rhinitis- 10% from loratadine group and 4% from triamcinolone group	Triamcinolone significantly better for all endpoints than loratadine	Pharmaceutical
Bernstein 1996 96213647	No major adverse effects in either group. Minor adverse effects 4 withdrawals in each group for URI AE Pharyngitis NS Headache NS Weight gain 11% of astemizole group vs. 2% of triamcinolone group, $p<0.05$	No placebo group Analysis not intention to treat for efficacy data	Pharmaceutical
Bronsky 1996	No major adverse effects. No statistically significant incidence between groups Most common minor adverse event was headache.		

Evidence Table 2. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Non-sedating antihistamines versus nasal corticosteroids
Part III. (continued)

Author Year UI	**Outcome-safety**	**Potential Bias**	**Funding**
Bronsky 1996 96194242	No major adverse effects. Minor adverse effects: 6 patients withdrew due to adverse events : 1 patient from fluticasone group ("potentially related to study medication"), 2 from terfenadine group (1pt potentially from medication, 2nd patient from treatment), and 3 patients from placebo group (perhaps from secondary effects of treatment) 6 patients withdrew due to lack of efficacy: 3 from terfenadine and 3 from placebo groups Headaches: 3 from fluticasone group reported effect, 3 from terfenadine group, and 5 from placebo group [unclear if resulted from drug treatment]	Drop-out rate lower for fluticasone group Highly selected sample consistent with typical patients seen in office Other reasons for withdrawal 17 patients: 5 from fluticasone group, 8 from terfenadine group, and 4 from placebo group due to noncompliance, protocol violation, or withdrew consent not clear if drop-outs excluded from analysis or if included until time of drop-out	Pharmaceutical (Glaxo)
Jordana 1996 96191239	Commonest adverse events were headache and pharyngitis Significant increase in headache in fluticasone group		ND

Evidence Table 2. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Non-sedating antihistamines versus nasal corticosteroids
Part III. (continued)

Author Year UI	**Outcome-safety**	**Potential Bias**	**Funding**
Gehanno 1997 97332767	Major adverse effects: -1 withdrawal in loratadine group for adverse effects: 1 patient had history of epilepsy and developed convulsions requiring hospitalization. Minor adverse effects: ~2 withdrawals in fluticasone group due to lack of efficacy ~5 withdrawals in loratadine group due to: -4 withdrawals for lack of efficacy -1 patient had severe dizziness, sweating and weakness -Nausea- 1 patient in fluticasone group -Asthma attack- 1 patient in fluticasone group -Respiratory disorder- 1 patient in loratadine group and 1 patient in fluticasone group -Convulsions, dizziness, sweating, and weakness- each adverse effect reported by 1 patient in loratadine group	Other reasons for withdrawals (from 9 withdrawals in loratadine group: 2 patients failed to return, and 1 patient due to noncompliance	Pharmaceutical
Juniper 1997	No information on safety	No placebo group	No data on funding
Juniper 1997 97286890	No major adverse effects. Minor adverse effects 1 withdrawal from fluticasone group due to nausea (asked to be transferred to beclomethasone, but failed to keep last appointment)	Designed to replicate “real life” by allowing cross-over and PRNs Open (unblinded)	Pharmaceutical (Glaxo)

Evidence Table 2. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Non-sedating antihistamines versus nasal corticosteroids
Part III. (continued)

Author Year UI	**Outcome-safety**	**Potential Bias**	**Funding**
D'Ambrosio 1998 99133169	No major adverse effects. Minor adverse effects: Burning throat/ nose: 2 patients in fluticasone group and 3 patients in cetirizine+fluticasone group Dizziness- 4 patients in cetirizine group and 3 patients from cetirizine+fluticasone group Gastric disorders- 1 patient in cetirizine group Visual trouble- 1 patient in cetirizine group	Other reasons for withdrawal- 6 patients left for personal reasons	ND
Ratner 1998 98390023	No Major adverse effects: Minor adverse effects: -Blood in nasal mucous- 5-10 patients in active treatment group and 5 patients in placebo -Epitaxis- less than 6 patients for all treatments -Xerostomia- less than 12 patients for all treatments	Other reasons for withdrawal: 8 withdrawals due to allergic rhinitis 13 withdrawals due to lack of efficacy 7 withdrawals due to other reasons	Pharmaceutical

Evidence Table 2. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Non-sedating antihistamines versus nasal corticosteroids
Part III. (continued)

Author Year UI	**Outcome-safety**	**Potential Bias**	**Funding**
Ortolani 1999 20068053	No major adverse events. Minor adverse effects: 32 patients withdrew: 11 patients in levocabastine group, 9 patients in fluticasone group, and 12 patients in placebo group -Respiratory symptoms- 5 patients from levocabastine group, 5 from fluticasone group, and 8 patients from the placebo group -Exacerbations of nasal symptoms- 2 patients from levocabastine group, 0 patients from fluticasone group, and 1 from placebo group Adverse effects: 0 patients in levocabastine group, 3 in fluticasone group, and 1 in placebo group Lack efficacy: 5 patients in levocabastine group, 1 patient in fluticasone group, and 4 patients in placebo group	Good study Other reasons for withdrawal: 16 patients excluded (insufficient data): 6 from levocabastine group, 4 from fluticasone group, and 6 from placebo group	Pharmaceutical
Condemi 2000 20289854	Major adverse effects: 4 dropouts from the triamcinolone group due to headache, rhinitis , and chest pain 3 dropouts due to loratadine Headache: 25 patients total from triamcinolone group and 27 patients from loratadine group reported effect Minor adverse effects: None indicated	Other reasons for withdrawal: 15 patients due to protocol deviation 9 patients due to treatment failure 3 patients due to lost to followup	Pharmaceutical

Evidence Table 3. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Sedating versus nonsedating antihistamines
Part I.

Author Year UI	Intervention	Duration	Demographics	Inclusion criteria	Exclusion criteria
Brostoff 1982 83014720	**Perennial Allergic Rhinitis** Chlorpheniramine vs. terfenadine vs. placebo RCT- Parallel	2 weeks	Location: UK Mean age: none Age range: 18-65 %Male: ND Race: ND Enrolled: 60 Evaluated: 60 Number of sites: 1	Moderate to severe perennial allergic rhinitis symptoms.	ND
Gastpar 1982 83100633	**Seasonal Allergic Rhinitis** Clemastine vs. terfenadine RCT –Parallel	12 weeks	Location: Germany Mean age: ND Age range: 16-37 % Male: 50% Race: ND Enrolled:20 Evaluated: 20 Number of sites: 1	History of seasonal allergic rhinitis Positive skin test	Asthma Cromoglycate within 24 hours Corticosteroids within 1 week Depot corticosteroids within 8 weeks Malignant/chronic disease Pregnancy/lactation Drug abuse/ alcoholism
Malmberg 1983 83253693	**Seasonal Allergic Rhinitis** Chlorpheniramine vs. astemizole vs. placebo RCT-Parallel	36 days	Location: Finland Mean age ND Age range: 16-53 % Male: 43.1% Race: ND Enrolled: 51 Evaluated: 51 Number of sites: 1	Seasonal birch pollen symptoms for 8 years Positive birch pollen skin test or birch RAST Positive nasal provocation with birch pollen	Other nasal disease

Evidence Table 3. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Sedating versus nonsedating antihistamines
Part I. (continued)

Author Year UI	Intervention	Duration	Demographics	Inclusion criteria	Exclusion criteria
Gutkowski 1985 86030956	**Seasonal Allergic Rhinitis** Dexchlorpheniramine vs. terfenadine RCT- Parallel	14 days	Location: Canada Mean age: ND Age range: 12-60 % Male: ND Race: ND Enrolled: 177 Evaluated: 174 Number of sites: 4	Positive skin test for ragweed History of ragweed allergy	Corticosteroid within 2 weeks Pregnant/ lactating
Hugonot 1986 86248368	**Seasonal Allergic Rhinitis** Mequitazine vs. terfenadine RCT- Parallel	1 week	Location: France Mean age: 29.7 Age range: 18-65 % Male: 49.6% Race: ND Enrolled: 147 Evaluated: 141 Number of sites: 1	Seasonal allergic rhinitis symptoms	None listed
Backhouse 1987 89062246	**Seasonal Allergic Rhinitis** Chlorpheniramine vs terfenadine RCT-Parallel	6 days	Location: UK Mean age: ND Age range: 18-65 % Male: 47% Race: ND Enrolled: 138 Evaluated: 121 Number of sites: 1	Positive skin test and documented allergy to grass pollen within past two years.	Pregnancy or lactation, any "major systemic illness", antihistamines within 4 weeks
Johansen 1987 87205847	**Seasonal Allergic Rhinitis** Dexchlorpheniramine vs. terfenadine RCT-Parallel	3 weeks	Location: Denmark Mean age: 31 Age range: 18-63 % Male: ND Race: ND Enrolled:42 Evaluated: 38 Number of sites: 1	Symptoms of seasonal allergic rhinitis for at least 2 years Positive skin prick test	Antihistamines within 3 days, cromoglycate within 3 days, oral corticosteroid use within 2 weeks, depot corticosteroid use within 8 weeks, hyposensitization therapy during previous 12 months, pregnant/lactating

Evidence Table 3. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Sedating versus nonsedating antihistamines
Part I. (continued)

Author Year UI	Intervention	Duration	Demographics	Inclusion criteria	Exclusion criteria
Pastorello 1987 88016480	**Seasonal Allergic Rhinitis** Dexchlorpheniramine vs. terfenadine RCT- Parallel	7 days	Location: Italy Mean age: ND Age range: 13-63 % Male: ND Race: ND Enrolled: 65 Evaluated: 62 Number of sites: 2	History of seasonal allergic rhinitis Diagnosis by history, RAST, positive skin test	Oral steroids within 1 week, nasal decongestants within 1 week, other antihistamines, sedatives or tranquilizers within 3 days
Buckley 1988 88131974	**Seasonal Allergic Rhinitis** Chlorpheniramine vs. terfenadine vs. placebo RCT-Parallel	7 days	Location: US Mean age: ND Age range: 12-66 % Male: 53% Race: ND Enrolled:244 Evaluated: 215 Number of sites: 6	Reversible seasonal hay fever symptoms >12 years old Late summer or fall allergic rhinitis and conjunctivitis Positive skin test	Asthma, sinusitis, nasal polyposis, pregnant/lactating, upper respiratory infection, history of steroid use during past 2 years, antibiotics or cromoglycate within 7 days,antihistamine or decongestant within 2 years
Druce 1998 98250349	**Perennial Allergic Rhinitis** Brompheniramine vs loratadine vs. placebo RCT- Parallel	7 days	Location: US Mean age: 33 Age range: 18-56 %Male: 46.4% Race: ND Enrolled: 338 Evaluated: 297 Number of sites: 5	History of allergic rhinitis Active symptoms Evidence of nasal mucosal changes with antigen exposure	Astemizole within 30 days Cold/allergy medication within 72 hours; Antihistamine within 24 hours Pregnancy/lactation
Thoden 1998 98413360	**Seasonal Allergic Rhinitis** Brompheniramine vs. terfenadine vs. placebo RCT- Parallel	14 days	Location: US Mean age: ND Age range: 15- 92 % Male: ND Race: ND Enrolled:370 Evaluated: 343 Number of sites: 3	Symptoms of allergic rhinitis	Astemizole within 30 days, other allergy medication within 72 days, pregnancy or lactating, contra-indication to antihistamine usage

Evidence Table 3. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Sedating versus nonsedating antihistamines
Part I. (continued)

Author **Year** **UI**	**Intervention**	**Duration**	**Demographics**	**Inclusion criteria**	**Exclusion criteria**
Weiler 2000 20143057	**Seasonal Allergic Rhinitis** Diphenhydramine vs fexofenadine	5 weeks	Location: US Mean age: 31 Age range: 25-44 % Male: 37.5% Race: ND Enrolled:41 Evaluated: 40 Number of sites: 1	History of alcohol use Seasonal allergic rhinitis symptoms Previous successful use of antihistamine Licensed driver	Pregnancy, excessive alcohol use, tobacco use in past year, excessive caffeine intake

Evidence Table 3. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Sedating versus nonsedating antihistamines
Part II.

Author Year UI	**Treatment outcomes studied**	**Symptom scale**	**Outcomes-efficacy**
Brostoff 1982	Mean total symptom score- Rhinorrhoea Sneezing Itchy eyes Nasal Congestion Watery Eyes Itchy throat Itchy nose	0-3 symptom scale, and (9 symptoms scored) 3-severe; 2- moderate; 1- mild; 0- absent	Mean score improvement from 7.6 to 5.1 with terfenadine Mean score improvement from 8.0 to 4.6 with chlorpheniramine Mean score improvement from 7.8 to 5.8 with placebo
Gastpar 1982 83100633	Total Mean symptom score Not indicated	Symptom Scale Not indicated But lab tests (blood chemistry, hematology, and urinalysis) plus IgE antibodies and ophthalmological examinations were conducted	No clinical data reported 15 patients treated with terfenadine showed significant decrease in IgE values (p< 0.001) vs 5 patients in clemastine group who showed only slight reduction Terfenadine tablets did not cause abnormal changes in laboratory values (blood chem, hematology, and urinalysis) and did not alter physiological body functions(heart rate, respiratory rate, body temp and blood pressure) after oral administration of (120mg/day)
Malmberg 1983 83253693	Total Mean Symptom Score Running nose Nasal blockage Sneezing Itchy nose Itchy eyes Red eyes Eye Swelling	Symptom scale: 4 pt scale (0-3) recorded on diary cards	Overall patient assessment: both antihistamines were better than placebo Overall physician assessment: both antihistamines were better than placebo

Evidence Table 3. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Sedating versus nonsedating antihistamines
Part II. (continued)

Author Year UI	**Treatment outcomes studied**	**Symptom scale**	**Outcomes-efficacy**
Gutkowski 1985 86030956	Total Mean symptom score Rhinorrhoea Nasal Congestion Sneezing Watery eyes Itchy nose Itchy eyes	Symptom Scale Symptom severity- 0-3 scale, with 0= none to 3= severe Overall treatment response assessment scale: 1= excellent- 75% improvement or more 2= good-between 75% and 50% improvement 3= fair-between 50% and 25% improvement 4= poor-less than 25% improvement 5= treatment failure	Global patient assessment: Mean score of 2.5 with dexchlorpheniramine and score of 3.2 with terfenadine. P < 0.001 Global physician assessment Mean score of 2.4 with dexchlorpheniramine and score of 3.2 with terfenadine. P< 0.001 64% of dexchlorpheniramine group had good/excellent response vs 40% of terfenadine group had good/excellent response Total signs and symptoms: Mean symptoms score of 5.9 with dexchlorpheniramine, and score of 8.8 with terfenadine. P< 0.001 Total Nasal Symptoms: Mean symptom score of 3.9 with dexchlorpheniramine and score of 5.9 with terfenadine. P< 0.001

Evidence Table 3. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Sedating versus nonsedating antihistamines
Part II. (continued)

Author Year UI	**Treatment outcomes studied**	**Symptom scale**	**Outcomes-efficacy**
Hugonot 1986 86248368	Total Mean Symptom Score Rhinorrhoea Nasal congestion Sneezing Itchy nose Itchy eyes	Symptom scale Patient diary card- with 0 to 3 scale for nasal itching, sneezing, runny nose, blocked nose, irritated eyes, and presence and intensity of somnolence On day 0 and day 7, patient judged degree of discomfort on visual analogue scale Physician assessment: on days 0 and 7, physician evaluated associated symptoms (lacrimation, irritated throat, and cough) and judged efficacy on day 7	Global patient assessment: Daily symptom score- no difference between treatment groups Global physician assessment: Not much difference in global efficacy between treatment groups All p values= N/S
Backhouse 1987 89062246	Total Mean Symptom Score Sneezing itchy or watery eyes Running or blocked nose	Symptom Scale 4 point scale 0= absent 1= slight 2= moderate 3= severe	Sneezing Overall symptoms core of 83 with chlorpheniramine and score of 78 with terfenadine Rhinorrhoea Overall score of 82 with chlorpheniramine and score of 79 with terfenadine Nasal Congestion Overall symptom score of 85 with chlorpheniramine and score of 81 with terfenadine All scores compiled from patient diary scores. No p values given

Evidence Table 3. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Sedating versus nonsedating antihistamines
Part II. (continued)

Author Year UI	**Treatment outcomes studied**	**Symptom scale**	**Outcomes-efficacy**
Johansen 1987 87205847	Total mean symptom score Sneezing Nasal congestion Runny nose Itchy nose Eye symptoms Tiredness	Symptom scale 4-point scale 0= no symptoms 1= mild symptoms 2= moderate symptoms 3= severe symptoms	Sneezing Symptom score of 0.58 with dexchlorpheniramine vs score of 0.65 with terfenadine Nasal Congestion Symptom score of 0.55 with dexchlorpheniramine vs score of 0.63 with terfenadine Nasal itch Symptom score of 0.37 with dexchlorpheniramine vs score of 0.53 with terfenadine Dexchlorpheniramine revealed significant ($p<0.05$) improvement in symptoms for nasal itching and tiredness (improved on treatment) Compared to dexchlorpheniramine, terfenadine did poorly

Evidence Table 3. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Sedating versus nonsedating antihistamines
Part II. (continued)

Author Year UI	**Treatment outcomes studied**	**Symptom scale**	**Outcomes-efficacy**
Pastorello 1987 88016480	Total Mean Symptom Score Rhinorrhoea Nasal Congestion Sneezing Watery eyes Itchy nose Itchy throat Itchy eyes Red Eyes	Symptom Scale Symptom severity- 5 point scale: 0= absent 1= poor 2= mild 3= severe 4= very severe Physician evaluation – based on skin test (+ to ++++), rhinomanometry and symptom evaluation done on "every entry" and after 7 days	Global patient assessment: 25/32 patients in terfenadine group rated treatment good/excellent; 7/32 patients in terfenadine group rated treatment poor/nil 22/30 patients in dexchlorpheniramine group rated treatment good/excellent; 8/ 30 patients in dexchlorpheniramine group rated treatment poor/nil Difference between drug effects not significant (p> 0.05) Global physician assessment: Rhinomanometric data: reduction in total nasal resistance after treatment, but not significant from baseline, and no significant difference between two groups p> 0.05 between 2 groups [no absolute data] Nasal Sneezing: Mean pre-score of 2.2 and post-score of 0.93 with terfenadine; mean pre-score of 2.1 and post-score of 0.82 with dexchlorpheniramine; p > 0.05 between two groups Rhinorrhoea Mean pre-score of 1.93 and post-score of 0.93 with terfenadine; mean pre-score of 1.85 and post-score of 1.15 with dexchlorpheniramine. P> 0.05 between two groups Nasal Congestion: Mean pre-score of 1.57 and post-score of 1.37 with terfenadine; mean pre-score of 1.64 and post score 1.28 with dexchlorpheniramine. P> 0.05 between two groups Both drug significantly reduce all symptoms except nasal obstruction for both groups, and cough/itchy throat for terfenadine group No significant difference between groups

Evidence Table 3. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Sedating versus nonsedating antihistamines
Part II. (continued)

Author Year UI	**Treatment outcomes studied**	**Symptom scale**	**Outcomes-efficacy**
Buckley 1988 88131974	Total Mean Symptom score Rhinorrhoea Nasal Congestion Sneezing Watery eyes Itchy nose Itchy eyes Itchy throat	Symptom scale Sneezing, rhinorrhea, nasal itch, ocular symptoms: 5 point scale (0= absent to 4= very severe) effectiveness of patient treatment (at final visit): 6-point scale (0= worse to 5= complete relief)	Global patient assessment: % patients would use treatment again: 60% in terfenadine group with p= 0.04 for terfenadine vs placebo; 66% in chlorpheniramine group with p= 0.006, and 45% in placebo group p= 0.006 for chlorpheniramine vs placebo and p= 0.01 for terfenadine vs placebo Global Physician assessment: P< 0.001 for chlorpheniramine vs placebo and p= 0.001 for terfenadine vs placebo Sneezing P< 0.05 for chlorpheniramine vs placebo and p< 0.05 for terfenadine vs placebo Rhinorrhoea P< 0.05 for chlorpheniramine vs placebo and p< 0.05 for terfenadine vs placebo Only p values stated, no raw data

Evidence Table 3. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Sedating versus nonsedating antihistamines
Part II. (continued)

Author Year UI	**Treatment outcomes studied**	**Symptom scale**	**Outcomes-efficacy**
Druce 1998 98250349	Mean total symptom score Rhinorrhoea Nasal Congestion Sneezing Watery Eyes Itchy Nose Itchy eyes Itchy throat Ocular Redness	0 – 4 scale for symptom severity 0= none 1= mild 2= moderate 3= severe 4= very severe 11pt scale for global evaluation 0= poor to 10= excellent	**Global Patient Assessment:** At day 3 (visit #2)- Symptom score of 5.8 with brompheniramine, p < .001 for brompheniramine compared to placebo; vs Symptom score of 4.1 with loratadine ,p< 0.001 for brompheniramine vs loratadine; Symptom score of 3.4 with placebo At day 7(visit#3)- Symptom score of 7.3 with brompheniramine, p< .05 for brompheniramine compared to placebo; vs symptom score of 9.7 with loratadine, p<.05 for brompheniramine vs loratadine; symptom score of 11.6 with placebo **Global Physician Assessment:** At day 3 (visit #2)- Symptom score of 5.9 with brompheniramine, p<0.001 for brompheniramine compared to placebo; vs symptom score of 4.6 with loratadine, p<0.001 for brompheniramine vs loratadine; symptom score of 4.0 with placebo At day 7(visit #3)- Symptom score of 6.7 with brompheniramine, p<0.05 for brompheniramine compared to placebo; vs symptom score of 8.7 with loratadine, p<0.05 for brompheniramine vs loratadine; symptom score of 10.8 with placebo When data from visit #2 and visit #3 were summarized: Loratadine > P, P < 0.05 Summed cluster symptoms (Rhinorrhoea, Sneezing, and Congestion) **Global Patient Assessment:** At day 3 (visit #2)- Symptom score of 3.5 with brompheniramine, p< 0.01 for brompheniramine vs placebo; Symptom score of 4.1 with loratadine, p<0.05 for loratadine vs placebo; P < 0.01 for brompheniramine vs loratadine; symptom score of 5.3 with placebo At day 7(visit #3)- Symptom score of 3.2 with brompheniramine, p<0.01 for brompheniramine vs placebo; symptom score of 4.3 with loratadine, p- NS for loratadine vs placebo; P< 0.01 for brompheniramine vs loratadine; symptom score of 4.8 with placebo **Global Physician Assessment:** At day 3 (visit #2)- Symptom score of 3.4 with brompheniramine, p<0.01 for brompheniramine vs placebo; symptom score of 4.3 with loratadine, p <0.05 for loratadine vs placebo; P<0.01 for brompheniramine vs loratadine;

Evidence Table 3. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Sedating versus nonsedating antihistamines
Part II. (continued)

Author Year UI	**Treatment outcomes studied**	**Symptom scale**	**Outcomes-efficacy**
Druce 1998 98250349 (continued)			symptom score of 5.0 with placebo At day 7(visit #3)- Symptom score of 3.0 with brompheniramine, p<0.01 for brompheniramine vs placebo; symptom score of 4.4 with loratadine, p<0.05 for loratadine vs placebo; P<0.01 for brompheniramine vs loratadine; symptom score of 4.8 with placebo
Thoden 1998 98413360	Mean total Symptom Score Rhinorrhoea Nasal congestion Sneezing Watery eyes Itchy nose Itchy eyes Itchy throat	Physician assessment- 5 pt symptom scale (0= none to 4= very severe) Patient/physician global overall effectiveness- 10 pt scale (0= poor to 10= excellent) [done 3 times- day3, d7 &d14)	Overall, brompheniramine did better than placebo and terfenadine in relieving symptoms Summed symptom score 1)"Severity rating": 10.1 for 12mg brompheniramine, 11.9 for terfenadine, and 12.9 for placebo; p < 0.05 for 12 mg brompheniramine vs placebo 2) "Total nasal symptom: 4.3 for 12mg brompheniramine, 5.1 for terfenadine, and 5.5 for placebo; p<0.05 for 12mg brompheniramine vs placebo Improvement in nasal symptoms, including nasal sneezing, congestion, and itching greater in 12mg brompheniramine than terfenadine (p≤0.05) Sneezing: p<0.05 for 8mg brompheniramine vs placebo, and p<0.05 for 12mg brompheniramine vs placebo Nasal congestion: p<0.05 for 12mg brompheniramine vs placebo; p<0.05 for 12mg brompheniramine vs terfenadine; and p<0.05 for 8mg bromphenriamine vs placebo in chart Nasal itching: p<0.05 for 8mg bromphenriamine vs terfenadine; p= 0.05 for 12mg brompheniramine vs terfenadine; p= 0.05 for 8mg brompheniramine vs placebo; and p= 0.05 for 12mh brompheniramine vs placebo

Evidence Table 3. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Sedating versus nonsedating antihistamines
Part II. (continued)

Author Year UI	**Treatment outcomes studied**	**Symptom scale**	**Outcomes-efficacy**
Weiler 2000 20143057	Driving skills	Symptom score – none Data analyzed with SAS software, versions 6.12 and 7.0	Overall assessment: Mean coherence value of 0.88 with diphenhydramine, value of 0.915 with fexofenadine, value of 0.92 with alcohol, and value of 0.9 with placebo Minimum following distance of 16.3m with diphenhydramine, distance of 17.1m with fexofenadine, distance of 15.1m with alcohol, and distance of 17.4m with placebo Steering instability of 0.527 with diphenhydramine, instability of 0.492 with fexofenadine, instability of 0.512 with alcohol, and instability of 0.495 with placebo Left-lane excursions of 3.15 with diphenhydramine, excursions of 1.17 with fexofenadine, excursions of 2.12 with alcohol, and excursions of 1.32 with placebo (based on distance crossed over center line when during left turns)

Evidence Table 3. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Sedating versus nonsedating antihistamines
Part III.

Author Year UI	**Outcome-safety**	**Potential Bias**	**Funding**
Brostoff 1982	No major adverse effects. Minor adverse effects: -Stomach Upset – 1 patient taking chlorpheniramine -Headache/Fatigue- 2 patients taking terfenadine 12 withdrawals- 5 due to placebo, 3 due to chlorpheniramine, and 4 due to terfenadine Minor adverse effects: -3 patients (20%) from placebo, 9 (53%(from chlorpheniramine, and 6(38%) from terfenadine -sedation	No utility of antihistamines in PAR (contrast to usual observations in SAR)	ND
Gastpar 1982 83100633	No major adverse effects Minor adverse effects -Sedation- 2 patients from clemastine group and 0 patients from terfenadine group reported effects -attacking allergic rhinitis and conjunctivitis- 2 patients from clemastine group and 1 patient from terfenadine group reported effect	Purpose of study was to evaluate tolerance of terfenadine	ND

Evidence Table 3. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Sedating versus nonsedating antihistamines
Part III. (continued)

Author **Year** **UI**	**Outcome-safety**	**Potential Bias**	**Funding**
Malmberg 1983 83253693	No major adverse effects. Minor adverse effects: 4 withdrawals- 3 patients from placebo group due to headaches or fatigue, and 1 patient from pheniramine group (unlisted reason) Tiredness- 8 patients in pheniramine group, 5 patients in astemizole group, and 5 patients in placebo group Palpitations- 1 patient in pheniramine group , and 1 patient in placebo group Headache- 6 patients in pheniramine group, 4 patients in astemizole group, and 3 patients in placebo group GI- symptoms- 1 patient in pheniramine group	Not possible to extract meaningful data	Government

Evidence Table 3. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Sedating versus nonsedating antihistamines
Part III. (continued)

Author Year UI	**Outcome-safety**	**Potential Bias**	**Funding**
Gutkowski 1985 86030956	No major adverse effects. Minor adverse effects: 45 withdrawals: 22 from dexchlorpheniramine and 23 from terfenadine 34 treatment failures: 14 from dexchlorpheniramine and 20 from terfenadine 5 discontinued due to adverse effects (4 from dexchlorpheniramine group and 1 patient from terfenadine) Any adverse effect- 49 patients in dexchlorpheniramine group, and 35 patients in terfenadine group; p< 0.05 Dizziness- 4 patients in dexchlorpheniramine group and 6 patients in terfenadine group Somnolence- 38 (43%) patients in dexchlorpheniramine group and 18 (21%) in terfenadine group. p< 0.002 Headaches- 3 in dexchlorpheniramine group and 4 in terfenadine group Dry-mouth- 4 in dexchlorpheniramine group and 6 in terfenadine group	Poor patient characterization Other reasons for withdrawal- 6 patients for miscellaneous reasons	ND
Hugonot 1986 86248368	No major adverse effects. Minor adverse effects: 4 patients withdrew from mequitazine treatment: 2 patients from lack of efficacy, 1 patient from severe headache, and 1 patient from blurred vision 2 patients withdrew from terfenadine treatment- 1 for inefficacy, and 1 for somnolence, dizziness, and nausea (most likely drug-unrelated because was taking terfenadine before study and when resumed again after reported effect, were no side-effects)	Other reasons for withdrawal: 4 patients excluded because of unallowed concomitant treatment 2 additional patient excluded due to procedural technicality (assigned 2 patients 1 number so unable to distinguish between their treatments)	Pharmaceutical funding

Evidence Table 3. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Sedating versus nonsedating antihistamines
Part III. (continued)

Author Year UI	**Outcome-safety**	**Potential Bias**	**Funding**
Backhouse 1987 89062246	No major adverse effects. Minor adverse effects: Withdrawal due to drowsiness: 4 patients from the chlorpheniramine group and 2 patients from the terfenadine group; p< 0.05 Withdrawal due to lack of efficacy: 2 patients from chlorpheniramine group and 1 patient from terfenadine group Overall adverse effects: 51% from, chlorpheniramine and 37 % from terfenadine. P= 0.03	Poorly defined study population Other withdrawals: 8 withdrawals due to failure to attend, or protocol deviation	Unfunded
Johansen 1987 87205847	No major adverse effects. Minor adverse effects: Severe tiredness- 6 from dexchlorpheniramine group (2 withdrew) ; 2 from terfenadine group	Small study Other reasons for withdrawal: 2 patients, one from each group, did not complete protocol	ND
Pastorello 1987 88016480	No major adverse effects. Minor adverse effects 3/33 in terfenadine group and 16/32 in dexchlorpheniramine group reported adverse effects Significantly greater number of side effects in dexchlorpheniramine group	No baseline characteristics given	ND

Evidence Table 3. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Sedating versus nonsedating antihistamines
Part III. (continued)

Author Year UI	**Outcome-safety**	**Potential Bias**	**Funding**
Buckley 1988 88131974	Major adverse effects No indicated withdrawals due to adverse effects Minor adverse effects -Headache- 3.8% of patients from chlorpheniramine group, 11.1% from terfenadine group, and 9.5% from placebo group reported headaches Sedation- 7.6% from chlorpheniramine, 2.5% from terfenadine and 2,4% from placebo group reported drowsiness Nausea- 3.7% from terfenadine group, 0% from chlorpheniramine group, and 1.2% from placebo group Dryness of mouth, nose, throat- 1.2% from terfenadine group, 1.3% from chlorpheniramine group, and 2.4% from placebo group	Only p values stated, no raw data -Study well-done but most data reported graphically -did not look at change in scores, only new scores -Did not directly compare p values between chlorpheniramine vs terfenadine Reasons for patient exclusion from efficacy analysis: Inter-current infection, non-compliant use of study medication, incomplete data, or use of interfering concomitant medication	ND

Evidence Table 3. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Sedating versus nonsedating antihistamines
Part III. (continued)

Author Year UI	**Outcome-safety**	**Potential Bias**	**Funding**
Druce 1998 98250349	No major adverse effects. Minor adverse effects: 10 withdrawals due to adverse effects: 2 in placebo group due to “cold” and “flu”, 7 in brompheniramine due to somnolence, 1 in brompheniramine due to hypertension Overall, 25 experienced adverse effects with brompheniramine, 14 with loratadine, 22 with placebo Any side effect: At visit 2: 53% taking brompheniramine, 33% taking loratadine, and 36% taking placebo reported adverse effects At visit 3: 34% taking brompheniramine, 20% taking loratadine, and 29% taking placebo reported adverse effects Somnolence At visit 2: 28% taking brompheniramine, 6%taking loratadine, and 9% taking placebo reported somnolence. P<0.001 At visit 3: 10% taking brompheniramine, 2%taking loratadine, and 3% taking placebo reported somnolence. P<0.01 Dizziness At visit 2: 6.3% taking brompheniramine, 2%taking loratadine, and 0%taking placebo experienced dizziness	Poorly defined population But well designed study	Pharmaceutical

Evidence Table 3. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Sedating versus nonsedating antihistamines
Part III. (continued)

Author Year UI	**Outcome-safety**	**Potential Bias**	**Funding**
Thoden 1998 98413360	No major adverse effects. Minor adverse effects: 12 subjects withdrew due to adverse effects (6 from, 12 mg brompheniramine 2 from 8mg brompheniramine, 3 from terfenadine, and 1 from placebo) -Somnolence- 37 patients(34.9%) taking 12mg brompheniramine, 25 patients (23.8%) taking 8mg brompheniramine, 12 patients (11.3%) taking terfenadine, and 6 (11.3%) patients taking placebo p<0.001 for 12mg brompheniramine vs 8mg brompheniramine, terfenadine and placebo; p<0.05 for one vs each other p< 0.05 for 8mg brompheniramine vs terfenadine and placebo p<0.05 for one vs each other -Adverse experiences- 155 (41.9%) total: 61 patients(57.5%) taking 12mg brompheniramine (with p< 0.05 for brompheniramine vs placebo), 40 patients(38.1%) taking 8mg brompheniramine, 33 patients(31%) taking terfenadine, and 21 patients(39.6%) taking placebo	Other reasons for withdrawal: 27 subjects did not adhere to protocol	Pharmaceutical
Weiler 2000 20143057	No major adverse effects 1 withdrawal (no reason given) No minor adverse effects	Unusual end points, but otherwise valid	Pharmaceutical (Hoechst Marion Roussel, Inc)

Evidence Table 4. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Cromoglycate or cromolyn versus placebo
Part I.

Author **Year** **UI**	**Intervention**	**Duration**	**Demographics**	**Inclusion criteria**	**Exclusion criteria**
Coffman 1971 72025239	**Seasonal Allergic Rhinitis** Disodium cromoglycate vs placebo RCT- parallel	14 days	Location: UK Mean age: ND Age range: 9-61 % Male: 20/33 Race: British and West Indian Enrolled: 35 - 16 (cromoglycate) and 17 (placebo) Evaluated: 33 - 16 (cromoglycate) and 15 (placebo) Number of sites: 1	Positive prick test to grass pollen History of seasonal allergic rhinitis for at least 2 years	None indicated
Engstrom 1971 72012845	**Seasonal Allergic Rhinitis** Cromoglycate 20mg capsules insufflated qid. vs. placebo	6 weeks	Location: Denmark Mean age: ND Age range: 7-17 % Male 79 Race: ND Enrolled: 39 Evaluated: 38 Number of sites:2	2 year history of allergic rhinitis symptoms during birch pollen season. Positive skin test to birch. Positive nasal provocation test to birch	None noted

Evidence Table 4. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Cromoglycate or cromolyn versus placebo
Part I. (continued)

Author Year UI	Intervention	Duration	Demographics	Inclusion criteria	Exclusion criteria
Holopainen 1971 71066421	**Seasonal Allergic Rhinitis** Cromoglycate vs Placebo RCT Parallel	28 days	Location: Sweden Mean age: ND Age range: 5- 43 % Male: ND Race: ND Enrolled: 29 Evaluated: 27 - 13 (cromoglycate) and 14 (placebo) Number of sites: 1	Known history of allergic rhinitis due to pollen Positive skin test Positive nasal provocation test	None indicated
Anderson 1972 73004602	**Seasonal Allergic Rhinitis** Disodium cromoglycate 10mg qid vs. placebo RCT parallel	2 weeks	Location: UK Mean age: 32 Age range: 10-63 % Male ND Race: ND Enrolled:18 Evaluated: 18 Number of sites:1	History of hay fever symptoms requiring repeat prescriptions At least two year history of hay fever	None
Hopper 1972 73166771	**Perennial Allergic Rhinitis** Cromoglycate versus Placebo RCT- Cross-over (extractable)	28 days	Location: UK Mean age: ND Age range: not given %Male: ND Race: ND Enrolled: ≥ 38 Evaluated: 38 (19 each group) Number of sites: 1	6 month history of perennial rhinitis symptoms Allergic appearance of nasal mucosa Eosinophilia ≥ 6% Positive skin test	None noted
Shore 1972 72159215	**Seasonal Allergic Rhinitis** Disodium cromoglycate 5mg qid vs. placebo RCT crossover	8 weeks	Location: S. Africa Mean age: ND Age range: <18 % Male ND Race: ND Enrolled:41 Evaluated: 41 Number of sites:1	Symptomatic seasonal allergic rhinitis	Adenoidal obstruction

Evidence Table 4. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Cromoglycate or cromolyn versus placebo
Part I. (continued)

Author Year UI	Intervention	Duration	Demographics	Inclusion criteria	Exclusion criteria
Thorne 1972 73089706	**Perennial Allergic Rhinitis** Cromoglycate vs Placebo RCT-cross-over (extractable)	8 weeks	Location: UK Mean age: N/A Age range: 10-65 %Male: ND Race: ND Enrolled: 40 Evaluated: 35 Number of sites: 1	With perennial rhinitis symptoms for at least 2 years With severe symptoms not responding to antihistamines Constant symptoms-perennial 10 years and younger	Those with viral rhinitis or nasal polyposis Those with seasonal symptoms of oral/ systemic steroids within 3 months Pregnant women
Blair 1973 74098976	**Seasonal Allergic Rhinitis** Sodium Cromoglycate versus Placebo RCT- Parallel	6 weeks	Location: UK Mean age: 29 Age range: 10-49 % Male: 17/40 Race: ND Enrolled: 40 Evaluated: 40 - 20 people each group Number of sites: 1	History of Seasonal allergic rhinitis Positive skin test	Viral rhinitis Nasal polyposis Those patients who had responded adequately to antihistamines Pregnant
Hetherington 1973 73166772	**Seasonal Allergic Rhinitis** Disodium cromoglycate 5mg capsule qid vs placebo RCT parallel	14 days	Location: Australia Mean age: ND Age range: ND Adult % Male ND Race: ND Enrolled:40 Evaluated: 35 Number of sites:1	Hay fever for past two seasons requiring treatment	Asthma Immunotherapy Nasal disease
Illum 1973 74133656	**Seasonal Allergic Rhinitis** Disodium cromoglycate vs. placebo RCT parallel	3 weeks	Location: Denmark Mean age: ND Age range: >18 % Male ND Race: ND Enrolled:37 Evaluated: 37 Number of sites: 1	2 year history of seasonal allergic rhinitis with grass pollen Positive skin test to grass pollen Positive nasal provocation test to grass pollen	Asthma Total nasal obstruction Pregnancy

Evidence Table 4. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Cromoglycate or cromolyn versus placebo
Part I. (continued)

Author Year UI	Intervention	Duration	Demographics	Inclusion criteria	Exclusion criteria
Jenssen 1973 74098975	**Seasonal Allergic Rhinitis** Sodium cromoglycate vs. placebo	N/A	Location: Norway Mean age: ND Adult Age range: >18 % Male ND Race: ND Enrolled:10 Evaluated: 10 Number of sites: 1	Seasonal allergic Rhinitis symptoms during grass pollen season	None noted
Manners 1973 74098980	**Seasonal Allergic Rhinitis** Sodium cromoglycate versus Placebo RCT- Parallel	28 days	Location: UK Mean age: 26 (cromoglycate) and 29 (placebo) Age range: 12-64 % Male: ND Race: ND Enrolled: 50 Evaluated: 46 - 23 People each group Number of sites: 1	At least 2 years of sneezing and nasal discharge during hay fever season Positive skin prick test to grass pollen Use of antihistamines for previous 2 summers	Immunotherapy Usage of “antispasmodics” or steroids
Sunderman 1973 73237443	**Perennial Allergic Rhinitis** Cromoglycate vs Placebo RCT- cross-over (extractable)	28 days	Location: Australia Mean age: 35 Age range: not given %Male: ND Race: ND Enrolled: 74 Evaluated: 68 Number of sites: 1	3 year history of chronic perennial rhinitis	Patients with nasal polyposis Patients responding to antihistamine Those with steroid therapy within 3 months Patients with nasal polyps or those with seasonal exacerbations

Evidence Table 4. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Cromoglycate or cromolyn versus placebo
Part I. (continued)

Author Year UI	Intervention	Duration	Demographics	Inclusion criteria	Exclusion criteria
Brain 1974 76192641	**Perennial Allergic Rhinitis** Cromoglycate Vs Placebo RCT-cross-over (extractable)	28 days	Location: UK Mean age: 26.5 Age range: 18-65 %Male: 15/29= 51.7% Race: ND Enrolled: 34 Evaluated: 29 Number of sites: 1	1 year history of perennial rhinitis not responding to antihistamines/ decongestants Capable of cooperation /completing diary card	Those with nasal polyposis, or steroid use within 3 months
Blair 1975 75185857	**Perennial Allergic Rhinitis** Cromoglycate Vs. Placebo RCT- cross-over(extractable)	8 weeks	Location: UK Mean age: none Age range: 7-54 %Male: 11/19 = 57.9% Race: ND Enrolled: 20 Evaluated: 19 Number of sites: 1	Perennial rhinitis	With viral rhinitis or nasal polyposis Patients with local nasal sepsis or previous immunotherapy within 2 years
Fagerberg 1975 75221540	**Perennial Allergic Rhinitis** Cromoglycate vs Placebo RCT- cross-over (extractable)	28 days	Location: Sweden Mean age: 30.6 Age range: 17-54 %Male: 12/23 Race: ND Enrolled: 23 Evaluated: 23 - 12 (Active-Placebo) and 11 (Placebo-Active) Number of sites: 1	1 year history of perennial rhinitis requiring treatment	With nasal polyposis
Girard 1975 76042257	**Perennial Allergic Rhinitis** Cromoglycate versus Placebo RCT- Parallel	4 weeks	Location: Switzerland Mean age: 30.4 Age range: 14-57 %Male: 16/30 Race: ND Enrolled: 30 Evaluated: 30 (15 for each group) Number of sites: 1	2 year history of perennial rhinitis Symptoms sufficiently severe as to require treatment	None listed

Evidence Table 4. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Cromoglycate or cromolyn versus placebo
Part I. (continued)

Author **Year** **UI**	**Intervention**	**Duration**	**Demographics**	**Inclusion criteria**	**Exclusion criteria**
Holopainen 1975 76084510	**Perennial Allergic Rhinitis** Cromoglycate versus Placebo RCT- cross-over (extractable)	28 days	Location: Finland Mean age: 35 Age range: 6-69 %Male: 15/40 Race: ND Enrolled: 49 Evaluated: 40 - 19 (active-placebo) and 21 (placebo- active) Number of sites: 1	2 year history of perennial rhinitis Sufficiently severe to require treatment Symptoms present year-round	Viral rhinitis Nasal polyposis Previous immunotherapy and were no longer symptomatic
Leiferman 1975	**Seasonal Allergic Rhinitis** Cromolyn sodium powder vs Placebo RCT-Parallel	49 days	Location: US Mean age: 34 Age range: 14-66 % Male: 65% Race: ND Enrolled:26 Evaluated: 24 (12 each group) Number of sites: 1	Symptoms of ragweed pollinosis for several years Positive ragweed skin test Elevated IgE to ragweed	Immunotherapy within 5 years
Wilson 1975 76101270	**Seasonal Allergic Rhinitis** Sodium cromoglycate vs placebo RCT-cross-over (extractable)	4 weeks	Location: NZ Mean age: 28 Age range: 6-76 % Male: 50% Race: ND Enrolled: 39 Evaluated: 38 Number of sites: 1	Severe and intractable chronic perennial rhinitis for at least 3 years	Responded to antihistamine Steroid treatment within 3 months Obstructive polyposis Seasonal exacerbations Pregnancy

Evidence Table 4. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Cromoglycate or cromolyn versus placebo
Part I. (continued)

Author **Year** **UI**	**Intervention**	**Duration**	**Demographics**	**Inclusion criteria**	**Exclusion criteria**
Hasegawa 1976 77001950	**Seasonal Allergic Rhinitis** Cromoglycate 10mg vs placebo RCT crossover	1 time dose	Location: UK Mean age: ND Age range: ND % Male ND Race: ND Enrolled: 38 Evaluated: 29 Number of sites:1	History of seasonal allergic rhinitis confirmed by history, physical and skin testing. Nasal airway resistance > 1.5 Symptomatic at time of study.	None noted
Knight 1976 76238158	**Seasonal Allergic Rhinitis** Disodium cromoglycate vs placebo RCT- cross-over (extractable)	28 days	Location: Canada (Toronto and Hamilton) Mean age: ND Age range: 10-59 % Male: 29/77 Race: ND Enrolled: 77 Evaluated: 77 - 36 (cromoglycate) and 41 (placebo) Number of sites: 2	Allergic to ragweed pollen by history and positive skin prick test	Large nasal polyps Chronic nasal/ sinus infection
Backman 1977 78120309	**Perennial Allergic Rhinitis** Cromoglycate vs Placebo RCT- cross-over (extractable)	28 days	Location: Sweden Mean age: none Age range: ND %Male: ND Race: ND Enrolled: 91 Evaluated: 91 - 51 (Cromoglycate powder) and 40 (Cromoglycate solution) Number of sites: 1	Perennial rhinitis or with history, clinical, nasal cytology	None noted

Evidence Table 4. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Cromoglycate or cromolyn versus placebo
Part I. (continued)

Author **Year** **UI**	**Intervention**	**Duration**	**Demographics**	**Inclusion criteria**	**Exclusion criteria**
Frostad 1977 78062986	**Seasonal Allergic Rhinitis** Cromoglycate vs Placebo RCT Parallel	3 months- May, June, and July	Location: Norway Mean age: 23.9 Age range: 15- 34 % Male: 21/44 Race: ND Enrolled: 44 Evaluated: 44 - 25 (cromoglycate) and 19 (placebo) Number of sites: 1	History of previous seasonal allergic rhinitis during grass pollen season Positive test to grass pollen Positive nasal provocation test to grass pollen Symptoms of allergic rhinitis during pollen season Residing in area during grass pollen season	Asthma Perennial rhinitis symptoms
Handelman 1977 77119242	**Seasonal Allergic Rhinitis** Cromolyn sodium Vs. placebo	6 weeks	Location: US Mean age: ND Age range: 5-51 % Male Race: ND Enrolled: 104 Evaluated: 88 Number of sites: 2	2 year history of ragweed allergy Positive skin test Ragweed IgE titer > 60mg/ml Reside within 25 miles	Asthma Perennial rhinitis Corticosteroids Cromolyn Bronchodilators Recent change in immunotherapy Regimen/new immunotherapy regimen
Lofkvist 1977 77131029	**Perennial Allergic Rhinitis** Intranasal Cromolyn Sodium Vs Placebo RCT- cross-over (extractable)	13 weeks	Location: Sweden Mean age: 34 Age range: 18-65 %Male: ND Race: ND Enrolled: 49 - 25 (placebo) and 24 (cromolyn sodium) Evaluated: 26 - 2 (placebo) and 24 (cromolyn sodium) Number of sites: 1	Included those with “vasomotor for many years”, and those with negative allergic skin tests	Those with asthma, nasal septal deviation, and nasal polyposis were not included

Evidence Table 4. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Cromoglycate or cromolyn versus placebo
Part I. (continued)

Author Year UI	Intervention	Duration	Demographics	Inclusion criteria	Exclusion criteria
McDowell 1977 77264819	**Seasonal Allergic Rhinitis** Cromolyn 2% aqueous nasal spray vs placebo RCT- cross-over (un-extractable)	4 weeks	Location: US Mean age: ND Age range: 17-71 % Male: ND Race: ND Enrolled: 17 Evaluated: 13 Number of sites: 1	At least 3 years of perennial allergic rhinitis by history or physical examination Immediate symptoms requiring medication Positive skin test to dust or mold Otherwise good health	Asthma Nasal polyposis Chronic nasal disease (other than PAR) Cromolyn or systemic or topical steroids within 3 months
Posey 1977 78063003	**Seasonal Allergic Rhinitis** 4% cromolyn sodium vs placebo nasal spray [also compares use of drug administered before and during weed pollen season] RCT-Parallel	8 weeks	Location: US Mean age: 30 Age range: 12-54 % Male: 52.9% Race: ND Enrolled: 34 Evaluated: 34 Preseasonal Study-17 each group Coseasonal Study- 9 (cromolyn) and 13 (placebo) Number of sites: 1	Late summer allergic rhinitis symptoms 2-yr history of SAR positive skin test to ragweed, sage mix positive nasal allergen challenge	Sinusitis Nasal septal deviation Nasal polyposis Perennial rhinitis Topical steroids within 1 month
Van der Bijl 1977 78033928	**Seasonal Allergic Rhinitis** Cromoglycate Vs Placebo RCT-Parallel	4 weeks	Location: Netherlands Mean age: 28.4 Age range: 7-60 % Male: 19/32 Race: ND Enrolled:40 (20 each group) Evaluated: 32 18(cromoglycate) and 14 (placebo) Number of sites: 1	Diagnosis of seasonal allergic rhinitis, symptomatic	None noted

Evidence Table 4. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Cromoglycate or cromolyn versus placebo
Part I. (continued)

Author **Year** **UI**	**Intervention**	**Duration**	**Demographics**	**Inclusion criteria**	**Exclusion criteria**
Warland 1977 77262676	**Perennial Allergic Rhinitis** Cromoglycate versus Placebo RCT- cross-over (extractable)	28 days	Location: Norway Mean age: 25.4 Age range: 15-57 %Male: 9/17 Race: ND Enrolled: 17 Evaluated: 17 - 10 (active-placebo) and 7 (placebo-active) Number of sites: 1	History of perennial allergic rhinitis for at least 1 year	None noted
Sorri 1979 79205990	**Seasonal Allergic Rhinitis** Cromoglycate vs. placebo	4 weeks	Location: Finland Mean age: ND Age range: ND % Male ND Race: ND Enrolled: 38 Evaluated: 38 Number of sites: 1	1 year history of perennial rhinitis necessitating treatment	None noted
Sipila 1987 88110026	**Seasonal Allergic Rhinitis** Nedocromil sodium 1% 5.2mg daily vs. placebo RCT parallel	4 weeks	Location: Finland Mean age: ND Age range: >16 % Male ND Race: ND Enrolled:59 Evaluated: 54 Number of sites: 2	>16 years History of birch pollen rhinitis in previous 2 seasons Positive skin test to birch pollen	Viral rhinitis Nasal septal Deviation Steroid use Vasoconstrictor use Cromoglycate use Pregnancy

Evidence Table 4. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Cromoglycate or cromolyn versus placebo
Part II.

Author Year UI	**Treatment outcomes studied**	**Symptom scale**	**Outcomes-efficacy**
Coffman 1971 72025239	Total mean symptom score Sneezing Rhinorrhoea Nasal obstruction Nasal itch	Symptom score: Diary cards: 0-3 scale	Global clinician assessment: 9/16 successful patient response with cromoglycate vs 5/15 successful patient response with placebo
Engstrom 1971 72012845	Total nasal symptom score Total eye symptom score Global assessment by clinician Rescue antihistamine usage	Symptom scale used: Range 0-3 0=none 1=occasional 2=intermittent 3=constant	Global assessment by clinician as follows: 5 of 18 successes with placebo and 14 of 20 successes in active treatment group (p<0.01) Significantly improved total nasal score for weeks 3 and 5 and peak pollen season period only with active treatment.
Holopainen 1971 71066421	Mean sneezing score Mean rhinorrhoea score Mean nasal congestion score Mean nasal itch score	Symptom scale used: Range 0-3 0=absent 1=mild 2=moderat e 3=severe	Mean diary sneezing symptom score: 30.8 in placebo group, 23.5 in active treatment group p>0.05 Mean diary rhinorrhoea score: 59.5 in placebo group vs. 34.3 in active treatment group p<0.025 Mean diary nasal congestion score: 52.3 in placebo group vs. 12 in active treatment group p<0.05 Mean diary nasal itch score: 21.6 in placebo group vs. 13.5 in active treatment group p<0.05
Anderson 1972 73004602	Total Mean Symptom Score Rhinorrhoea Sneezing Sore, itching eyes	No symptom scale Diary cards and clinician assessment	8/9 successes and 1/9 failures with cromoglycate 1/9 successes and 8/9 failures with placebo

Evidence Table 4. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Cromoglycate or cromolyn versus placebo
Part II. (continued)

Author Year UI	**Treatment outcomes studied**	**Symptom scale**	**Outcomes-efficacy**
Hopper 1972 73166771	Mean total symptom score Rhinorrhoea Sneezing Nasal congestion	Symptom scale: 0= no symptoms 1= occasional symptoms 2= intermittent symptoms 3= constant symptoms	Global patient assessment: 16 success + 3 failures with cromoglycate vs 9 successes, 9 failures + 1 unsure with placebo; p< 0.05 for drug vs placebo Global clinician assessment: 14 successes + 5 failures with cromoglycate vs 8 successes + 11 failures with placebo; p< 0.05 for drug vs placebo Sneezing (% of scores that fell in 2-3 range on scale): 1% with cromoglycate vs 11% with placebo; p < 0.01 for drug vs placebo Rhinorrhoea (% of scores that fell in 2-3 range on scale): 12% with cromoglycate vs 32% with placebo; p< 0.01 for drug vs placebo Nasal Congestion (% of scores that fell in 2-3 range on scale): 14% with cromoglycate vs 30% with placebo; p < 0.01 for drug vs placebo Nasal itch NA
Shore 1972 72159215	Global assessment by patient Global assessment by clinician	No symptom scale specified.	Global assessment by patient 15 of 21 rated placebo success 16 of 20 rated active treatment successful p>0.05 Global assessment by clinician: In 7 of 21 rated placebo successful In 12 of 20 rated active treatment successful p<0.057

Evidence Table 4. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Cromoglycate or cromolyn versus placebo
Part II. (continued)

Author Year UI	**Treatment outcomes studied**	**Symptom scale**	**Outcomes-efficacy**
Thorne 1972	Mean Total Symptom Score Rhinorrhoea Nasal Congestion Sneezing	0-3 symptom scale 0= no symptoms 1= occasional symptoms 2= intermittent symptoms 3= constant symptoms	Global assessment done by patient in diary: Total symptom score of 2608 with cromoglycate vs score of 3053 with placebo, p= ND Patient Evaluation based on diary score Sneezing- Symptom score of 18.5 +/-13.7 with cromoglycate vs score of 24.5 +/- 14.1 with placebo; p<0.0005 for cromoglycate vs placebo Rhinorrhoea- Symptom score of 26.7 +/- 15.9 with cromoglycate vs score of 32.3 +/- 18.7 with placebo; p< 0.002 for cromoglycate vs placebo Nasal Congestion- Symptom score of 35.7 +/- 24.7 with cromoglycate vs score of 38.5 +/- 24.7 with placebo; p = NS In those patients receiving placebo, find all symptoms significantly lower (blockage, discharge, sneezing). In patients receiving cromoglycate, find only sneezing and discharge (rhinorrhoea) significantly reduced
Blair 1973 74098976	Global assessment by patient and clinician of total symptom score (rhinorrhoea, congestion, itching and sneezing) Patient wish to continue with treatment Whether symptoms improved over last season (patient rated)	N/A	Global assessment by patient 3 of 15 placebo successes vs 13/20 active treatment successes p<0.025 Global assessment by clinician 2 of 16 placebo rated successful; 11 of 20 on active treatment rated successful p<0.025 Symptoms improved over last year in 4 of 15 of placebo group and 8 of 19 of active treatment group NS

Evidence Table 4. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Cromoglycate or cromolyn versus placebo
Part II. (continued)

Author Year UI	**Treatment outcomes studied**	**Symptom scale**	**Outcomes-efficacy**
Hetherington 1973 73166772	Rhinorrhoea symptom score Nasal congestion symptom score Overall symptom severity as rated by patient.	Symptom scale: Severity of nose-running and nose-blocking: range= 0-6 General condition assessment: 3-point scale	• Rhinorrhoea symptom severity No significant difference between groups • Nasal congestion symptom severity No significant difference between groups • Overall symptom severity rating by patient Good to fair in 10 of 16 of placebo group, 19 of 19 of active treatment group p<0.05
Jenssen 1973 74098975	Total Mean Symptom Score Nasal resistance following nasal allergen challenge	N/A	Nasal resistance following allergen challenge Nasal resistance improved in 7 of 8 patients on active treatment
Illum 1973 74133656	Total Mean Symptom Score Sneezing score Rhinorrhoea score Nasal congestion score Nasal itch score	Symptom scale Range 0-3 0=no symptoms 3=severe symptoms	Global assessment by patient: No significant differences between groups. No significant difference between groups in sneezing, rhinorrhoea, nasal congestion sneezing and eye symptom scores.
Manners 1973 74098980	Global assessment by patient Global assessment by clinician Sneezing score Rhinorrhoea score Nasal congestion score Nasal itch score Eye symptoms Rescue antihistamine usage Nasal eosinophils on nasal smear	Symptom scale used Range 0-3 0=absent 1=mild 2=moderat e 3=severe	Global assessment by patient: In placebo group 13 of 23 rated successful vs. 15 if 23 if active treatment group p>0.05 Global assessment by clinician: 7 of 23 rated successes in placebo group vs. 10 of 23 in active treatment group p>0.05 Mean sneezing score week 2 and 3: 19.7 in placebo group vs. 19.2 in active treatment group p>0.8 Mean rhinorrhoea score weeks 2 and 3: 20.3 in placebo group vs. 14.7 in active treatment group p>0.05 Mean nasal congestion score weeks 3 and 4: 12.7 in placebo group vs. 12.4 in active treatment group p>0.9 Mean nasal itch score weeks 3 and 4: 15.3 in placebo group vs. 12.7 in active treatment group p>0.4

Evidence Table 4. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Cromoglycate or cromolyn versus placebo
Part II. (continued)

Author Year UI	**Treatment outcomes studied**	**Symptom scale**	**Outcomes-efficacy**
Sunderman 1973	Mean total symptom score Rhinorrhoea Nasal Congestion Sneezing	Symptom scale No scale given	Out of 68 patients, 53 patients preferred cromoglycate, 0 preferred placebo, and 15 had no preference; p < 0.05 for cromoglycate vs placebo Report stated that symptoms of rhinorrhoea, obstruction, and sneezing in cromoglycate group significantly improved p< 0.05 (absolute data not given)
Brain 1974 76192641	Mean total nasal symptom score Nasal sneezing Rhinorrhoea Nasal congestion Nasal itch	No symptom scale Mild/Moderate-Severe (0-3)	Global patient assessment: 20 preferred cromoglycate, 6 preferred placebo, and 3 indicated no preference P<.01 Nasal sneezing symptom score of 32.5 with placebo vs. 22.6 with cromoglycate, p<.025 Rhinorrhoea symptom score of 34 with placebo vs. 23.5 with cromoglycate, p<.02 Nasal congestion symptom score of 37.3 with placebo vs 26.2 with cromoglycate, p< .05 Nasal Itch symptom score of 24.8 with placebo vs 16.1 with cromoglycate, p< .012

Evidence Table 4. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Cromoglycate or cromolyn versus placebo
Part II. (continued)

Author Year UI	**Treatment outcomes studied**	**Symptom scale**	**Outcomes-efficacy**
Blair 1975	Mean total symptom score Nasal Sneezing Rhinorrhoea Nasal congestion Nasal Itch	Symptom severity score based on 0-3 scale	Overall patient assessment: 14 preferred cromoglycate, and 3 preferred placebo, 1 patient indicated no preference (out of 18 because one patient symptoms classified as intrinsic or nonallergic) Nasal sneezing symptom score (out of 15 people) of 20.5 with cromoglycate vs score of 28.2 with placebo; p> 0.1 for drug vs placebo [~change in score of -0.7 with cromoglycate vs +0.1 change in score with placebo; p< 0.01 for drug vs placebo] (*note* out of 15 people, instead of 19, because some failed to adequately record daily symptoms) Rhinorrhoea symptom score of 27.1 with cromoglycate vs 40.3 with placebo; p< 0.05 for drug vs placebo [~change in score of -0.7 with cromoglycate vs +0.1 change in score with placebo; p< 0.1 for drug vs placebo] Nasal congestion symptom score of 29.7 with cromoglycate vs 49.1 with placebo; p< 0.1 for drug vs placebo [~change in score of -0.1 with cromoglycate vs –0.1 change in score with placebo; p< 0.02 for drug vs placebo] Nasal Itch symptom score of 19.4 with cromoglycate vs 23.2 reduction with placebo; p> 0.1 for drug vs placebo [~change in score of -1.2 with cromoglycate; vs +0.2 change in score with placebo; p< 0.01 for drug vs placebo]

Evidence Table 4. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Cromoglycate or cromolyn versus placebo
Part II. (continued)

Author Year UI	**Treatment outcomes studied**	**Symptom scale**	**Outcomes-efficacy**
Fagerberg 1975	Mean Total Symptom Score Rhinorrhoea Nasal congestion Sneezing Itchy nose	Symptom scale 0-3: Mild-Moderate-Severe	Sneezing (n=23) In clinician evaluation, mean difference of –0.7 with cromoglycate vs difference of –0.3 with placebo; p> 0.1 for cromoglycate vs placebo In patient evaluation recorded in diary card, mean symptom score of 19.5 with cromoglycate vs mean score of 30.2 with placebo; p < 0.01 for cromoglycate vs placebo Rhinorrhoea (n=23) In clinician evaluation, mean difference of –0.8 with cromoglycate vs difference of –0.1 with placebo; p< 0.01 for cromoglycate vs placebo In patient evaluation recorded in diary card, mean symptom score of 37.9 with cromoglycate vs mean score of 47.2 with placebo; p < 0.05 for cromoglycate vs placebo Nasal congestion (n=23) In clinician evaluation, mean difference of –0.8 with cromoglycate vs difference of –0.3 with placebo; p< 0.02 for cromoglycate vs placebo In patient evaluation recorded in diary card, mean symptom score of 29.3 with cromoglycate vs score of 35.2 with placebo; p< 0.1 for cromoglycate vs placebo Nasal Itch (n= 21 included data- 2 cases of inconclusive data) In clinician evaluation, mean difference of –0.2 with cromoglycate vs difference of +0.1 with placebo; p>0.10 for cromoglycate vs placebo In patient evaluation recorded in diary card, mean symptom score of 8.7 with cromoglycate vs score of 15.5 with placebo; p> 0.05 for cromoglycate vs placebo

Evidence Table 4. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Cromoglycate or cromolyn versus placebo
Part II. (continued)

Author Year UI	**Treatment outcomes studied**	**Symptom scale**	**Outcomes-efficacy**
Girard 1975 76042257	Mean total symptom score Rhinorrhoea Sneezing Nasal congestion Nasal itch Eosinophilia Nasal outflow resistance	Symptom scale: Daily record cards- 0- 3 scale with 0= no symptoms to 3= severe symptoms	Global patient assessment: 12/15 patients rated cromoglycate successful in symptom treatment vs 6/15 in placebo group. P < 0.03 for drug vs placebo Global clinician assessment: 13/15 successful cases vs 5/15 successful cases. P< 0.008 for drug vs placebo Sneezing Mean difference of –0.6 with cromoglycate and difference of 0 with placebo; p < 0.02 for drug vs placebo Rhinorrhoea Mean difference of –0.1 with cromoglycate vs difference of –0.6 with placebo; p> 0.05 for drug vs placebo Nasal congestion Mean difference of –1.4 with cromoglycate vs difference of –0.3 with placebo; p< 0.02 for drug vs placebo Nasal itch Mean difference of –0.7 with cromoglycate vs difference of –0.2 with placebo; p< 0.05 for drug vs placebo

Evidence Table 4. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Cromoglycate or cromolyn versus placebo
Part II. (continued)

Author Year UI	**Treatment outcomes studied**	**Symptom scale**	**Outcomes-efficacy**
Holopainen 1975 76084510	Mean total symptom scale Rhinorrhoea Nasal congestion Sneezing Nasal Itch	Symptom scale Nasal Symptoms 0-3 scale: none, mild, moderate, and severe Nasal patency 0-2 scale: open, partially blocked, and completely blocked Overall examination of nose: 0-4 scale	Sneezing Clinician mean score: score of 0.7 for cromoglycate vs score of 1.0 for placebo; p> 0.10 for drug vs placebo Patient mean diary score: score of 17.4 for cromoglycate vs score of 22.5 for placebo; p<0. 05 for drug vs placebo Rhinorrhoea Clinician mean score: score of 1.1 for cromoglycate vs score of 1.4 for placebo; p>0.10 for drug vs placebo Patient mean diary score: score of 30.9 for cromoglycate vs score of 37.8 for placebo; p< 0.01 for drug vs placebo Nasal Congestion Clinician mean score: score of 1.2 for cromoglycate vs score of 1.7 for placebo; p < 0.01 for drug vs placebo Patient mean diary score: score of 32.1 for cromoglycate vs score of 39.1 for placebo; p< 0.01 for drug vs placebo Nasal itch Clinician mean score: score of 0.4 for cromoglycate vs score of 0.8 for placebo; p< 0.05 Patient mean diary score: score of 12.2 for cromoglycate vs score of 16.5 for placebo; p< 0.05 for drug vs placebo. Study combined groups from each arm of cross-over..

Evidence Table 4. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Cromoglycate or cromolyn versus placebo
Part II. (continued)

Author Year UI	**Treatment outcomes studied**	**Symptom scale**	**Outcomes-efficacy**
Leiferman 1975	Total mean symptom score Sneezing Coughing Stuffy, or runny nose Red, itchy eyes asthma	Symptom score (0-3) [score 2 times/day-midnight-noon, and noon-midnight]	Global patient assessment: All patients(12 pair of patients)- overall score of 9.5 with cromolyn vs score of 10.5 with placebo; p> 0.10 for drug vs placebo Group 1 (7pair patients– patients with pre-seasonal Radio-allergosorbent test(RAST) readings > 5%)- overall score of 7.5 with cromolyn vs score of 12 with placebo; p< 0.03 for drug vs placebo Group 2 (5 pair patients- those with RAST<5%)- overall score of 11 with cromolyn vs score of 8 with placebo; p> 0.10 for drug vs placebo [scores approximated from graph] End-study questionnaire on efficacy of treatment (10 subjects from each group): 40% of cromolyn group vs 10% of placebo group found treatment extremely beneficial 30% in both groups found treatment moderately beneficial 10% in both groups found treatment slightly beneficial 20% of cromolyn group vs 50% of placebo group found treatment not beneficial 80% of cromolyn group vs 50% of placebo group indicated would use treatment next year

Evidence Table 4. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Cromoglycate or cromolyn versus placebo
Part II. (continued)

Author Year UI	**Treatment outcomes studied**	**Symptom scale**	**Outcomes-efficacy**
Wilson 1975 76101270	Mean total symptom score Nasal blockage Nasal Discharge Nasal Sneezing	Symptom scale Daily diary cards No scale given	Global patient assessment: Patient preference: 20/38 preferred cromoglycate, and 8/38 preferred placebo Sneezing: Physician assessment: From baseline, change in score of – 0.5 with cromoglycate, and change of –0.4 with placebo; data missing on significance, but clearly NS Patient assessment (n= 37): total symptom score of 19.0 with cromoglycate and score of 20.2 with placebo, p= NS Rhinorrhoea (nasal “discharge”) Physician assessment: From baseline, change in score of –0.6 with cromoglycate and change of –0.6 with placebo; p= NS Patient assessment (n= 37): total symptom score of 32.3 with cromoglycate and score of 31.7 with placebo; p= NS Nasal Congestion Physician assessment: From baseline, change in score of –0.9 with cromoglycate and change of –0.6 with placebo; p= NS Patient assessment (n= 37): total symptom score of 33.7 with cromoglycate and score of 37.8 with placebo; p= NS No meaningful difference between those groups with placebo or cromolyn administered first
Hasegawa 1976 77001950	Total nasal symptom score comprising sneezing, rhinorrhoea, congestion and itchy nose. Nasal airways resistance		Total nasal symptom score improved in 1 of 16 in placebo group and 10 of 16 on active treatment. $p<0.05$ Nasal airway resistance improved to greater than 1.5 in 0 placebo patients and 11 active treatment patients $p<0.05$

Evidence Table 4. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Cromoglycate or cromolyn versus placebo
Part II. (continued)

Author Year UI	**Treatment outcomes studied**	**Symptom scale**	**Outcomes-efficacy**
Knight 1976 76238158	Total Mean symptom score Sneezing Nasal obstruction Rhinorrhoea Itchy eyes Itchy nose Sinus pain	Symptom scale: Personal/ telephone interviews: Degree- very good, good, or poor responders Anti-ragweed IgE antibody level (RAST level) ; scale 0-4 0= negative 1= borderline 2=clearly positive 3= strongly positive 4=highly positive	Overall patient evaluation: 25/34 successful patient responses with cromoglycate, and 12/41 successful responses with placebo Inconclusive results- there is a Toronto group of patients + Toronto group which are analyzed separately, never together
Backman 1977	Mean total Symptom Score N/A	Symptom Scale N/A	Patient Global Assessment: Cromoglycate 2% solution Vs placebo - Out of 40 patients 23 patients preferred cromoglycate vs 10 patients preferred placebo (significant p value not given Cromoglycate powder- 10mg/nostril, 4x daily Vs Placebo- Out of 51 patients 31 patients preferred SCG powder, 3 preferred placebo, 17 patients with no preference indicated Outcomes only reported for 33/ 40 patients. Information for 7 patients missing. Also, MD outcomes only given for 2 studies, so un- interpretable for this group

Evidence Table 4. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Cromoglycate or cromolyn versus placebo
Part II. (continued)

Author Year UI	**Treatment outcomes studied**	**Symptom scale**	**Outcomes-efficacy**
Frostad 1977 78062986	Patient global rating Clinician global rating 28-day sneezing score 28-day rhinorrhoea score 28 day nasal congestion score Total nasal symptom score	Diary card- Symptom scale: 0-3 scale Each patient also asked to record number of antihistamine tablets/ day	Global assessment by patient: 5 of 19 of placebo group rated treatment successful vs. 25 of 25 of active treatment group p<0.01 Global assessment by clinician: Rated 3 of 19 of placebo patients successfully treated vs. 25 of 25 of active treatment. No p value provided. 28-day sneezing score 45.6 in placebo group vs. 25.3 in active treatment group p<0.01 28-day rhinorrhoea score 39.9 in placebo group vs. 22.5 in active treatment group p<0.05 Nasal congestion 28-day score 38.1 in placebo group and 23.8 in active treatment group p<0.01 Total nasal symptom score 123.5 in placebo group vs. 71.6 in active treatment group p<0.01
Handelman 1977 77119242	Sneezing Rhinorrhoea Ocular irritation Nose-blowing episodes Chlorpheniramine usage IgE titer	0-3	Sneezing significantly reduced by cromolyn sodium vs. placebo p<0.013 Rhinorrhoea significantly reduced by cromolyn sodium p<0.001
Lofkvist 1977	Mean total symptom score Blocking Running Sneezing Itching	No symptom scale supplied	Shows an effect with DSCG No significance for symptom free condition, patient preference, or diary card scores. Saw “dramatic improvement in symptoms in some patients after treatment with SCG” (42) No significant difference detected between SCG and placebo treatment (42)

Evidence Table 4. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Cromoglycate or cromolyn versus placebo
Part II. (continued)

Author Year UI	**Treatment outcomes studied**	**Symptom scale**	**Outcomes-efficacy**
McDowell 1977 77264819	Total Mean Symptom Score Itchy nose Runny nose Stuffy nose Mouth breathing Postnasal drip Itchy eyes Itchy throat	Symptom Scale Symptom severity: 6 point scale- 0= no occurrence, 1= mild, and 5= extreme and causing considerable interference with sleep and/or life	Following values are averaged symptom scores for 4 weeks Sneezing: From baseline of 4.0, score of 3.0 with cromoglycate and score of 3.4 with placebo; p = ND Rhinorrhoea: From baseline 2.5, score of 1.9 with cromoglycate and score of 2.2 with placebo; p = ND
Posey 1977 78063003	Total Mean Symptom Score Rhinorrhoea Nasal Congestion Sneezing Itchy nose Itchy throat Mouth breathing Eye-irritation Post-nasal drip Nose-blowing	Symptom scale 5 point scale (0-4) with 0= no symptoms to 4= incapacitating symptoms	Pre-seasonal study: Overall patient assessment: 11/17 reported good/very good relief with cromoglycate; 7/15 patient reported good/very good relief with placebo $\chi 2$ (chi-squared) analysis indicates no significant difference between groups Overall physician assessment: found no significant differences between groups P< 0.025 Co-seasonal study Overall patient assessment- 4/9 patients treated with cromoglycate rated it good/very good; 8/ 13 patients treated with placebo rated it good/ very good $\chi 2$ analysis- revealed no significant difference between two groups; only 1 patient from placebo group reported very good relief p< 0.025 No raw data- all in graph form

Evidence Table 4. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Cromoglycate or cromolyn versus placebo
Part II. (continued)

Author Year UI	**Treatment outcomes studied**	**Symptom scale**	**Outcomes-efficacy**
Van der Bijl 1977 78033928	Total Mean Symptom score Rhinorrhoea Nasal Congestion Sneezing Itchy nose Itchy eyes	Symptom severity scale: 4 degrees- none, mild, moderate, severe	Global patient assessment: Overall success/ failure uncertain Sneezing: Clinician assessment: mean change of –0.7 with cromoglycate, and change of 0 with placebo. P< 0.5 for drug vs placebo Patient assessment: Mean diary card score of 28.8 with cromoglycate, and score of 35.9 with placebo. P> 0.05 for drug vs placebo Rhinorrhoea: Clinician assessment: Mean change of –1.0 with cromoglycate, and change of 0 with placebo. P< 0.1 for drug vs placebo Patient assessment:: Mean diary card score of 26.7 with cromoglycate and score of 35.4 with placebo. P> 0.05 for drug vs placebo Nasal Congestion: Clinician assessment: mean score of –0.5 with cromoglycate and score of –0.1 with placebo. P>0.05 for drug vs placebo Patient assessment: Mean diary card score of 28.1 with cromoglycate, and score of 26.5 with placebo. P> 0.05 Nasal Itch Clinician assessment: Mean change of –0.8 with cromoglycate and score of –0.1 with placebo. P< 0.05 for drug vs placebo Patient assessment: Men diary score of 23.6 with cromoglycate and score of 23.0 with placebo. P> 0.5 for drug vs placebo

Evidence Table 4. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Cromoglycate or cromolyn versus placebo
Part II. (continued)

Author Year UI	**Treatment outcomes studied**	**Symptom scale**	**Outcomes-efficacy**
Warland 1977 77262676	Mean total symptom score Rhinorrhoea Nasal congestion Sneezing Nasal itch	Symptom scale: Clinician and patient daily diary card scores : 0- 3 scale 0= no symptoms to 3= considerable symptoms	Patient overall preference (n= 17): 6 patients preferred cromoglycate vs 2 patients preferred placebo. 9 patients had no preference Sneezing Patient assessment (n= 14): Mean monthly score of 17.9 for cromoglycate vs score of 18.1 for placebo; p> 0.10 for drug vs placebo Clinician assessment (n= 16): Mean monthly score of 0.8 for cromoglycate vs score of 0.9 for placebo; p> 0.1 for drug vs placebo Rhinorrhoea Patient assessment (n= 14): Mean monthly score of 23.6 for cromoglycate vs score of 26.2 for placebo; p> 0.1 for drug vs placebo Clinician assessment (n= 17): Mean monthly score of 0.8 for cromoglycate vs score of 1.4 for placebo; p> 0.10 for drug vs placebo Nasal congestion Patient assessment: Mean monthly score of 27.4 for cromoglycate vs score of 28.4 for placebo; p > 0.1 for drug vs placebo- NS Clinician assessment: Mean monthly score of 1.11 for cromoglycate vs score of 1.3 for placebo; p > 0.1 for drug vs placebo; p> 0.1- NS Nasal Itch Clinician assessment- Mean monthly score of 0.5 for cromoglycate vs score of 0.8 for placebo; p> 0.1 for drug vs placebo
Sorri 1979 79205990	Patient preference Sneezing Rhinorrhoea Nasal itch Nasal congestion Antihistamine usage	0-3	Patient preference 22 preferred active treatment; 11 preferred placebo; 5 had no preference No comment on significance MD symptom assessment Significant improvement in rhinorrhoea only with active drug. No significant difference in sneezing, nasal congestion nasal itch or nasal patency

Evidence Table 4. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Cromoglycate or cromolyn versus placebo
Part II. (continued)

Author Year UI	**Treatment outcomes studied**	**Symptom scale**	**Outcomes-efficacy**
Sipila 1987 88110026	Sneezing score Rhinorrhoea score Nasal congestion score Nasal itch score Total symptom score Clinician overall rating Rescue antihistamine use Patient preference Nasal peak inspiratory flow	Symptom scale Range 0 – 4	Mean daily sneezing score 1.4 in placebo group vs. 1.17 with active treatment p=0.31 Mean daily rhinorrhoea score 1.4 in placebo group vs. 1.17 in active treatment group p=0.86 Mean daily nasal congestion score 1.34 in placebo group vs. 1.38 in active treatment group p=0.82 Mean daily nasal itch score 1.31 in placebo group vs. 0.91 in placebo group p<0.04 Total mean nasal symptom score 5.39 in placebo group vs. 4.7 in active treatment group p=0.34 Patient preference: 8 of 27 preferred placebo; 17 of 27 preferred active treatment p<0.03 Clinician rating: Rated 14 of 27 successes in active treatment group vs. 7 of 27 successes in placebo group P<0.05

Evidence Table 4. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Cromoglycate or cromolyn versus placebo
Part III.

Author Year UI	**Outcome-safety**	**Potential Bias**	**Funding**
Coffman 1971 UI 72025239	No major adverse effects. Minor adverse effects: “minimal” side effects- specifics not listed	No inclusion/exclusion criteria given Outcome measurement ambiguous Other reasons for withdrawal: 2 (from original group 35) withdrawals due to failure to comply to protocol, incomplete diaries or failure to report back to review	Pharmaceutical
Engstrom 1971 72012845	No safety data provided.	One patient omitted from analysis. No safety data. Applicability/Internal validity II/B	Pharmaceutical.
Holopainen 1971 71066421	No major adverse effects. 1 patient in placebo group experienced itching of throat. No minor adverse effects in active treatment group.	No baseline characteristics reported. 2 patients omitted from final analysis. Applicability II Internal validity B	ND
Anderson 1972 73004602	No major adverse effects. Minor adverse effects: Nasal irritation Nasal congestion Nausea Headache No significant difference between groups.	No baseline characteristics for Treatment groups. Applicability II Internal validity B	Pharmaceutical
Hopper 1972 73166771	No safety data provided	Generalizability- II / Internal Validity- C Reasons for patient exclusion: -2 due to existing colds -3 due to existing symptoms other than obstruction, rhinorrhoea, or sneezing -4 due to incomplete diaries	Pharmaceutical

Evidence Table 4. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Cromoglycate or cromolyn versus placebo
Part III. (continued)

Author Year UI	**Outcome-safety**	**Potential Bias**	**Funding**
Shore 1972 72159215	No major adverse effects. Minor adverse effects: Nausea, sneezing, cough, rash. No information on difference between active and placebo adverse effects.	No baseline characteristics provided. No information on difference in adverse effects between treatments. Applicability III Internal validity C	Government
Thorne 1972	No major adverse effects. Minor adverse effects -DSCG Insufflation followed by sneeze- 2 patients taking placebo and 1 patient taking cromoglycate reported effect -Soreness of nose- 1 patient taking placebo and 1 patient taking cromoglycate reported effect	Data combined from crossover areas Evaluated 35/40 Only 32 patients had complete diary data	Pharmaceutical
Blair 1973 74098976	No major adverse effects. Minor adverse effects: nasal irritation, sore throat in both groups; in addition, headache and unpleasant taste in active treatment group and itching of face in placebo group. No information on statistical significance of difference between groups.	Four patients omitted from final analysis as responded to rescue antihistamines – all in placebo group. No information on rescue antihistamine usage by group. Applicability II Internal validity B	ND
Hetherington 1973 73166772	No major adverse effects. Nasal irritation occurred in 1 patient in placebo group and 7 patients in cromoglycate group.	No baseline characteristics of groups. 35 of 40 patients evaluated Applicability II Internal validity B	Pharmaceutical
Illum 1973 74133656	No major adverse effects.	Global assessment by patient: No significant differences between groups. No significant difference between groups in sneezing, rhinorrhoea, nasal congestion sneezing and eye symptom scores.	

Evidence Table 4. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Cromoglycate or cromolyn versus placebo
Part III. (continued)

Author Year UI	**Outcome-safety**	**Potential Bias**	**Funding**
Jenssen 1973 74098975	Nasal resistance following allergen challenge Nasal resistance improved in 7 of 8 patients on active treatment No safety data	Small sample size Omitted 2 patients from analysis. No baseline characteristics of group provided. Applicability III Internal validity C	
Manners 1973 74098980	No safety data	Only analyzed individual symptom scores for weeks 3 and 4 of trial. Omitted 4 patients from final analysis as non-compliant with medication and diary keeping regimen.	ND
Sunderman 1973	No major adverse effects. 6 patients withdrew- no information Minor adverse effects -Sneezing- 1 patient taking placebo, and 0 patients taking cromoglycate reported effect	Pooled cross-over data No baseline characteristics Reasons for withdrawal not given	Pharmaceutical
Brain 1974 76192641	No major adverse effects in either group. 5 withdrawals –(1 due to severe nasopharyngitis, 1 due to severe nasal irritation development, 2 didn't complete visits, and 1 patient immunotherapy during study) Minor adverse effects- Headache Dry throat Sore throat Dizziness Nasal irritation	No baseline characteristics Analyzed 29/32 patients Cross-over trial pooled data No period 1 data	Pharmaceutical
Blair 1975	No major adverse effects. Minor adverse effects: No withdrawals for adverse effects (but one female patient after trials withdrew, finding the treatment "unpleasant and distasteful") -Nasal irritation and Sore throat (4 from placebo, and 3 from cromoglycate)	Pooled data from cross-over answers No baseline- find period data given Small sample size Analyzed 19/20	Pharmaceutical

Evidence Table 4. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Cromoglycate or cromolyn versus placebo
Part III. (continued)

Author Year UI	**Outcome-safety**	**Potential Bias**	**Funding**
Fagerberg 1975	No major adverse effects. Minor adverse effects -Itching/ nasal irritation- 3 patients taking placebo, and 4 patients taking cromoglycate -Sneezing- 3 patients taking placebo and 0 patients taking cromoglycate -Headache- 1 patient taking placebo, and 0 patients taking cromoglycate -"other" – 6 patients taking placebo, and 3 patients taking cromoglycate	Crossover pooled data	ND
Girard 1975 76042257	No major adverse effects. Minor adverse effects: Nasal irritation- 5 patients in cromoglycate group and 3 patients in placebo group Headache- 0 patients in cromoglycate group and 1 patients in placebo group	Small sample size No outcome data on rescue antihistamine use Analysis was intention to treat Randomization method / site not specified Generalizability- II/ Internal validity- B Other reasons for withdrawals: 3 withdrawals from active group- 2 due to treatment failure, and 1 due to partial success 8 withdrawals from placebo group- 6 due to no treatment benefit, and 2 due to induced nasal obstruction	Pharmaceutical
Holopainen 1975 76084510	No major adverse effects. Minor adverse effects: Nasal irritation- 8 reports due to cromoglycate and 9 reports due to placebo Headache- 1 report due to cromoglycate and 1 report due to placebo Eczema- 1 report due to cromoglycate, and no reports of effect due to placebo Tiredness- 1 report due to cromoglycate, and no reports of effect due to placebo	Analyzed 40/49 Mixed allergic and nonallergic perennial rhinitis Generalizability: II / Internal Validity: C Reasons for withdrawal: (9 total) 2 due to change in environment 2 were on another therapy 2 did not return after admission 2 did not return after treatment 1	Pharmaceutical

Evidence Table 4. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Cromoglycate or cromolyn versus placebo
Part III. (continued)

Author **Year** **UI**	**Outcome-safety**	**Potential Bias**	**Funding**
Leiferman 1975	Minor adverse effects 1 patient from placebo group withdrew due to nasal irritation (later also withdrew his treatment pair)	Unclear of what specific inclusion criteria Gave graph results of total score over whole time period only after saying that data from peak pollen period probably of greater value Did not give breakdown of scores by symptom Minimal data on SE 1-tailed p-values small N	Government and private foundation
Wilson 1975 76101270	No major adverse effects. Minor adverse effects: -Nausea: 1 patient from cromoglycate group -Headache: 1 patient from cromoglycate group -Sneezing- 3 patients from cromoglycate group and 1 patient from placebo group -Nasal dryness and Irritation- 1 patient from cromoglycate group and 6 patients from placebo group Epistaxis- 1 patient from cromoglycate group and 1 patient from placebo group Other adverse effects- 3 patients from cromoglycate group and 4 patients from placebo group (other effects include sore throat, itchy eyes, tiredness, aggravated symptoms, mucosa flakiness, dry mouth at night, and stinging	Small cross-over study, washout, unclear what scores mean	Pharmaceutical

Evidence Table 4. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Cromoglycate or cromolyn versus placebo
Part III. (continued)

Author **Year** **UI**	**Outcome-safety**	**Potential Bias**	**Funding**
Hasegawa 1976 77001950	No safety data	No baseline characteristics Pooled crossover data NO absolute values for individual or total nasal symptom scores. Applicability II Internal validity C	ND
Knight 1976 76238158	Sneezing, Coughing, and Headache- occurring in a few patients, but no numbers given -sneezing + coughing- seemed more prevalent in placebo group headaches- seemed more prevalent in the cromoglycate group	Inconclusive data Useless data Indeterminate number of subjects	Pharmaceutical
Backman 1977	No major adverse effects No withdrawals for adverse effects Minor adverse effects -Nasal Irritation- 9 taking placebo and 8 taking SCG reported effect -Headache- 1 taking placebo and 1 taking SCG reported -Eczema- 1 taking placebo and 0 taking SCG reported effect -Tiredness- 1 taking placebo, and 0 taking SCG reported effect	No withdrawals for adverse effects noted No data on 7 out of 40 patients- possible withdrawals, but not indicated as such No information given on possible withdrawals	ND
Frostad 1977 78062986	No major adverse effects noted Minor adverse effects as follows: Nasal irritation, no significant difference between groups. No withdrawals for adverse events.	Applicability II Internal validity B	ND

Evidence Table 4. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Cromoglycate or cromolyn versus placebo
Part III. (continued)

Author Year UI	**Outcome-safety**	**Potential Bias**	**Funding**
Handelman 1977 77119242	No data on withdrawals No major adverse events Minor adverse events: Nasal irritation Sneezing No significant difference between groups in incidence of these.	Only analyzed week 2-5 data of 6 weeks Analysis did not include all enrolled participants No information on reasons for study dropouts	ND
Lofkvist 1977	No major adverse effects. Minor adverse effects -Dryness and irritation in nose and throat (5 patients with SCG, and 4 patients with placebo)	Adequate duration study Shows an effect with DSCG	Pharmaceutical
McDowell 1977 77264819	No major adverse effects. Minor adverse effects: Transient burning and stinging- 10/17patient reports with cromoglycate and 13/17 patient reports with placebo Mild rash/pruritis- 2 patients in cromoglycate group and 3 patients in placebo group Nausea and dizziness- 1 patient in cromoglycate group and 1 patient in placebo group Nosebleed- 3 patients in cromoglycate group and 6 patients in placebo group Headache- 8 patients in cromoglycate group and 5 patients in placebo group Treatments had no effect on blood pressure, heart rate, respiratory rate, hematologic profiles, urinalysis or blood chemical parameters	Cross-over, washout period All data merged Nothing on order of drugs Reasons for withdrawals: 4 total: 3- poor compliance or incomplete data 1- severe nasal congestion, but not significant rhinorrhoea or sneezing	Pharmaceutical

Evidence Table 4. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Cromoglycate or cromolyn versus placebo
Part III. (continued)

Author **Year** **UI**	**Outcome-safety**	**Potential Bias**	**Funding**
Posey 1977 78063003	No major adverse effects. Minor adverse effects: 2 withdrawals: 1 patient due to severe symptoms not controlled by antihistamines; 1 patient from placebo group due to development of severe chemical rhinitis after 1 week Nasal irritation, rhinorrhea, and sneezing (no data given)	No raw data- all in graph form	ND
Van der Bijl 1977 78033928	No major adverse effects. Minor adverse effects: Nasal Irritation: 1 patient in placebo group Dizziness and Sneezing- 1 patient in cromoglycate group	Omitted 8 patients from final analysis (did not follow treatment protocol)	ND
Warland 1977 77262676	No major adverse effects. Minor adverse effects: Nasal irritation- 1 complaint due to cromoglycate and 3 complaints due to placebo Headache- 4 complaints due to cromoglycate and 2 complaints due to placebo Nausea- 1 complaint due to cromoglycate and 0 complaints due to placebo Other- 4 complaints due to cromoglycate and 3 complaints due to placebo	Combined data from cross-over trial Small sample size Not all patients enrolled were analyzed Generalizability- II / Internal Validity- C Other reasons for withdrawal 4 drop-outs total: 1 due to steroid use 3 due to lack of cooperation	ND
Sorri 1979 79205990			

Evidence Table 4. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Cromoglycate or cromolyn versus placebo
Part III. (continued)

Author **Year** **UI**	**Outcome-safety**	**Potential Bias**	**Funding**
Sipila 1987 88110026	No major adverse effects Minor side effects as follows: Sneezing 5 in active treatment Group Unpleasant taste 2 in placebo group Nasal irritation 2 in placebo group 2 in active treatment group Throat irritation 2 in active treatment group Dizziness 1 in placebo group	Considered data from peak pollen season only 5 patients omitted from analysis	ND

Evidence Table 5. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Sympathomimetic treatments
Part I.

Author **Year** **UI**	**Intervention**	**Duration**	**Demographics**	**Inclusion criteria**	**Exclusion criteria**
Green 1966 67044478	**Perennial Allergic Rhinitis** (1)oxymetazoline HCl vs (2) Phenylephrine HCl	1 day	Location: UK Mean age: 3-13 Age range: <18 %Male: 15/33=45.5% Race: ND Enrolled: 33 Evaluated:33 Number of sites:1	Children with allergic rhinitis	N/A
Svensson 1980 81129988	**Seasonal Allergic Rhinitis** KWD 2131 and Terbutaline Sulphate vs Placebo RCT- cross-over (extractable)	2 months in pollen-free season – January-March	Location: Sweden Mean age: 28 Age range: 17-38 % Male: 14/29 Race: ND Enrolled: 29 Evaluated: 29 - 16 (normal) and 13 (SAR patients) Number of sites:2	Normal patients- normal IgE/serum readings SAR patients- positive skin and provocation tests Suffered form hay fever for at least 2 seasons All patients-asymptomatic	Normal patients- Symptoms of SAR, dermatitis, urticaria or bronchial asthma Asthma No heredity for above disease

Evidence Table 5. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Sympathomimetic treatments
Part I. (continued)

Author Year UI	Intervention	Duration	Demographics	Inclusion criteria	Exclusion criteria
Svensson 1981 82087563	**Seasonal Allergic Rhinitis** KWD 2131 (β-adrenoceptor stimulants) vs Placebo RCT- cross-over (extractable)	3 months	Location: Sweden Mean age: 24.5 Age range: 17-34 % Male: 13/22 Race: ND Enrolled: 22 Normal and seasonal allergic rhinitis volunteers Evaluated: 22 - 11 (normal) and 11(seasonal allergic rhinitis) Number of sites: ND	Normal patients- No symptoms of allergic rhinitis Normal IgE/serum Seasonal allergic rhinitis patients- Asymptomatic during trial Positive skin test for grass pollen Hay fever for at least last 2 years	None indicated
Svensson 1982 83040698	**Seasonal Allergic Rhinitis** KWD 2131 (β-adrenoceptor stimulants) vs placebo RCT- cross-over (extractable)	28 days	Location: Sweden Mean age: 27 Age range: 14-52 % Male: 23/27 Race: ND Enrolled: 27 Evaluated: 27 - 14 (KWD 2131-plac) and 13 (placebo- KWD 2131) Number of sites:1	Sensitive to grass pollen Positive skin or positive provocation test Suffered form hay fever for at least last two seasons Prior insufficient treatment with antihistamines, cromoglycate, beclomethasone, or hyposensitization	Currently undergoing hyposensitization therapy

Evidence Table 5. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Sympathomimetic treatments
Part I. (continued)

Author Year UI	Intervention	Duration	Demographics	Inclusion criteria	Exclusion criteria
Borum 1987 87239270	**Seasonal Allergic Rhinitis** Fenoterol (β-2-adrenostimulant) vs Placebo RCT- cross-over	5 weeks- 2.5 weeks for each treatment	Location: Denmark Mean age: 24.5 Age range: 18-65 % Male: 24/33 Race: ND Enrolled: 35 Evaluated: 33 - 17 (fenoterol- placebo) and 16 (placebo- fenoterol) Number of sites:1	Positive skin prick test to grass pollen SAR	Asthma Perennial Allergic rhinitis Patients receiving immunotherapy No topical steroid treatment for at least 1 month prior to study All other drug usage discontinued for at least 1 week prior to study
Shaikh 1995 96080200	**Perennial Allergic Rhinitis** Ephedrine saline wash (10% solution) vs Placebo RCT- cross-over (extractable)	4 weeks	Location: India Mean age: 25.69 Age range: 15-49 %Male: 68/118 = 57.6% Race: ethnically restricted Enrolled: 137 - 69 (placebo) and 68 (ephedrine) Evaluated: 118 -63 (placebo) and 55 (ephedrine) Number of sites:1	With PAR, normal spirometry values, and positive skin prick test	With asthma, and other atopic disease such as urticaria and eczema Also excluded patients who had SAR
Svensson 1995 96357837	**Seasonal Allergic Rhinitis** Terbutaline (β-2-receptor agonist) vs Placebo RCT- cross-over (extractable)	30 s each	Location: Sweden Mean age: 29 Age range: 21-49 % Male: 5/12= 58.3% Race: ND Enrolled: 12 Evaluated: 12 Number of sites:1	History of pollen-induced AR Positive skin prick test to birch or timothy	No other organic manifestation of their allergic disease No drugs permitted during 3-week period prior to study

Evidence Table 5. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Sympathomimetic treatments
Part I. (continued)

Author Year UI	Intervention	Duration	Demographics	Inclusion criteria	Exclusion criteria
Georgitis 1998 98372425	**Perennial Allergic Rhinitis** Atropine SO4 Spray (50 μg) Vs Atropine Spray (75 μg) [Nasal placebo also tested] RCT Parallel	2 weeks	Location: US Mean age: 31.6 Age range: 18-59 %Male: 60 Race: ND Enrolled: 45 Evaluated: 45 (15 each group) Number of sites:1	Normal Vital signs and Physical Examination w/o severe rhinorrhoea – runny nose or PN Drainage Rhinorrhoea severity score 3 or 4 and PND in 2-week baseline period [pre-inclusion: systemic steroids * 4wks; non-maintenance immunotherapy x 4wks; topical steroids x 2wks; antihistamine x 2 weeks; sympathomimetics x 2wks	Those with nasal septal deviation or nasal polyposis Grossly overweight or underweight Serious systemic disorders Local nasal obstruction (polyps, deviated septum, structural defect)

Evidence Table 5. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Sympathomimetic treatments
Part II.

Author Year UI	**Treatment outcomes studied**	**Symptom scale**	**Outcomes-efficacy**
Green 1966	Mean total symptom score Mucosal turgescence	1+ - 3+ scale with 3+ = turbinates so boggy and edematous that they touch nasal septum. Heavy serous or mucoid discharge; hyperemia or greyish membrane present to 1+ = hyperemia and serous secretion but no enlargement of the turbinates	Overall assessment: oxymetazoline proved significantly superior to phenylphedrine in inducing long-lasting nasal decongestion: Oxymetazoline- decongestion in 16/22 cases, and 9 cases decongestion period ≥ 5.5 hours Phenylephrine- decongestion in 11/22 cases, and 3 cases decongestion period ≥ 5.5 hours ~ at 0.5 hr:14/22 mucosal turgescence cases symptoms reduced with oxymetazoline vs reduction of 13/22 cases with phenylephrine ~at 1.0 hr: 14/22 mucosal turgescence cases symptoms reduced with oxymetazoline vs 7/22 reduction with phenylephrine ~at 2.0 hr: 14/22 mucosal turgescence cases symptoms reduced with oxymetazoline vs 7/22 reduction with phenylephrine ~at 5.0 hr: 12/22 mucosal turgescence cases symptoms reduced with oxymetazoline vs 4/22 reduction with phenylephrine ~at 6.0 hr: 12/22 mucosal turgescence cases symptoms reduced with oxymetazoline vs 4/22 reduction with phenylephrine (*note* out of 22 because 3 groups of 11 each tested with different solutions- 2 groups with 1 solutions A or B, and 1 group with both solutions (cross-over group))

Evidence Table 5. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Sympathomimetic treatments
Part II. (continued)

Author Year UI	**Treatment outcomes studied**	**Symptom scale**	**Outcomes-efficacy**
Svensson 1980 81129988	Total Mean Symptom Score Nasal Airway resistance Nasal symptoms Nasal secretions	Symptom Scale Nasal symptoms 0-3 scale Oedema and secretion- 0-3 scale (before and after drug administration) 0= no symptoms 1= mild 2= moderate 3= severe Hand tremor (before and after drug administration)- 0-3 scale Nasal air-flow-rhinomanometry readings	Terbutaline and placebo both induced minor increase in airway resistance to same degree; p= NS Terbutaline (0.5 mg) and KWD 2131 (1.25 mg) produced almost same nasal airway changes as compared to placebo Terbutaline (5 mg) and KWD 2131 (5 mg) both produced marked increase in nasal airway resistance - small change, but still significant with p< 0.05 for both stimulants No nasal changes in normal and SAR patients with all treatments
Svensson 1981 82087563	Total Mean symptom score Nasal Congestion Itchy Nose Nasal secretion Sneezing Nasal air resistance	Symptom Scale Nasal symptom scale- 0-3 scale Also used rhinomanometry to analyze nasal resistance	Nasal airway resistance (after histamine application)- values were statistically significant- mean value somewhat higher for SAR patients vs normal, but only occasional significant differences between groups Sneezing, Nasal stuffiness, and Nasal itch (after histamine application)- similar in both groups normal and SAR patients; occasional significant differences between groups P< 0.05 Nasal stuffiness, secretion, nasal itch, number of sneezes- occasional significance revealed P< 0.05

Evidence Table 5. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Sympathomimetic treatments
Part II. (continued)

Author Year UI	**Treatment outcomes studied**	**Symptom scale**	**Outcomes-efficacy**
Svensson 1982 83040698	Total mean symptom score Rhinorrhoea Nasal congestion Itchy nose Itchy eyes Itchy throat	Symptom scale Diary cards- Nasal blockage, running, itchy nose and ocular symptoms 0-3 scale: 0= no symptoms 1= mild symptoms 2= moderate symptoms 3= severe symptoms Sneezing attacks- 0-3 scale: 0= no attacks 1= 1-5 attacks 2= 6-15 attacks 3= more than 15 attacks/ 24 hrs oedema/ secretion – 0-3 scale physician evaluation-hematological and urine analysis also conducted	Global patient evaluation: P= NS: study did not reveal any significance between treatment groups Diary card scores- did not reveal any difference in symptom –relieving capacity between groups Overall evaluation: No significant differences documented between treatment with KWD 2131 and placebo No actual data- just graphs

Evidence Table 5. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Sympathomimetic treatments
Part II. (continued)

Author Year UI	**Treatment outcomes studied**	**Symptom scale**	**Outcomes-efficacy**
Borum 1987 87239270	Total Mean Symptom Score Sneezing Nose-blowings Secretion Blockage Ocular symptoms	Symptom Scale Nasal symptoms, secretion, and ocular symptoms (estimated during evenings)- 0-3 scale 0= no symptoms 1= slight symptoms 2= moderate symptoms 3= severe symptoms Nose –blowings - 1 tissue/blow Pollen counts also continuously monitored	Global patient evaluation: 21 patients preferred fenoterol, 5 patients preferred placebo, and 7 had no preference p< 0.01 Following scores out of n= 25 (8 withdrawals due to side effects) Sneezing After first treatment: (Group1- fenoterol/ Group2-placebo): Difference between run-in baseline score and 1st treatment, difference of 0.67 for G1 (fenoterol) vs score difference of 6.04 for G2 (placebo) P< 0.01 After second treatment: (Group1- placebo/Group 2- fenoterol) Difference between 1st and 2nd treatment score, difference of 3.04 for G1 (placebo) vs score difference of 4.48 for G2 (fenoterol) P< 0.01 Nasal Secretion After first treatment: (Group1- fenoterol/ Group2-placebo): Difference between run-in baseline score and 1st treatment, difference of 0.30 for G1 (fenoterol) vs score difference of 0.65 for G2 (placebo) P= NS After second treatment: (Group1- placebo/Group 2- fenoterol) Difference between 1st and 2nd treatment score, difference of 0.16 for G1 (placebo) vs score difference of 0.49 for G2 (fenoterol) P= NS Insignificant reduction for nose-blowings and blockage
Shaikh 1995	Mean total symptom score- Sneezing, Rhinorrhoea Nasal Blockage Postnasal drip	0-4 scale, with 0= worsening of symptoms or no improvement to 4= excellent improvement	Ephedrine treatment showed global score improvement with symptom score of 3.5 with ephedrine vs 0.8 symptom score with placebo; p < .001 for drug vs placebo Peak in spirometry, nasal flow rate – symptom score of 2-5 with placebo, and symptom score of 140??? With ephedrine; p< .01

Evidence Table 5. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Sympathomimetic treatments
Part II. (continued)

Author Year UI	**Treatment outcomes studied**	**Symptom scale**	**Outcomes-efficacy**
Svensson 1995 96357837	Total Mean Symptom Score Nasal Congestion Sneezing Itchy nose	Symptom Scale Nasal Symptoms: 0-3 scale 0= no symptoms 1= mild 2= moderate 3= severe symptoms Number of sneezes- 0-3 scale 0= none 1= 1-4 sneezes 2= 5-9 sneezes 3= 10+ sneezes -total symptom score- sum of nasal symptoms -pulse rate registration also done immediately after nasal lavage	Global physician assessment: Nasal blockage: $p < 0.05$ for terbutaline vs placebo Corporate nasal symptom: $p < 0.01$ for terbutaline vs placebo Terbutaline seemed to reduce all of the allergen challenge- induced nasal symptoms

Evidence Table 5. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Sympathomimetic treatments
Part II. (continued)

Author Year UI	**Treatment outcomes studied**	**Symptom scale**	**Outcomes-efficacy**
Georgitis 1998	Mean total symptom score Nasal Rhinorrhoea	Patients daily log of rhinitis symptoms - 5 pt scale Patients used scale 0-4 to rate severity of symptoms (“higher numerical value to short duration of control similar to use of higher scores for severity reflecting worse symptoms” p3) Global evaluation done by patients and physicians based on 6 pt-scale Global evaluation done also at weekly physician visits with 5pt scale (0- worse, 1- no control, and 5- complete control and relief of symptoms	Overall symptom score of 3.0 with atropine SO_4 spray(50μg), p<.05 compared to placebo; Overall symptom score of 3.0 with atropine sprain(75μg), p< .05 compared to placebo; Overall symptom score of 2.0 with placebo Post-natal drainage symptom score of 1.75 with atropine SO_4 spray(50μg) and p= .002 for drug1 compared to placebo vs symptom score of 1.6 with atropine sprain(75μg) and p= .002 drug2 compared to placebo; symptom score of 3.25 with placebo [~from baseline, -1.0 change in score with atropine SO_4 spray(50μg), p< .001 for drug 1 compared to placebo; vs –0.8 change in score with atropine sprain(75μg), p< .001 for drug 2 compared to placebo; -0.1 score change with placebo] Rhinorrhoea symptom score of 1.25 with atropine SO_4 spray(50μg), p= .002 for drug 1 compared to placebo; vs symptom score of 1.5 with atropine sprain(75μg), p= .002 for drug 2 compared to placebo; symptom score of 3.0 with placebo [~from baseline, -0.9 change in score with atropine SO_4 (50μg), p<.001 for drug 1 compared to placebo; vs -0.8 change in score with atropine sprain (75μg), p<.001 for drug 2 compared to placebo; -0.1 score change with placebo]

Evidence Table 5. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Sympathomimetic treatments
Part III.

Author Year UI	**Outcome-safety**	**Potential Bias**	**Funding**
Green 1966	No major adverse effects. Minor adverse effects- Local nasal burning problem (1/22 for patients taking oxymetazoline, and 2/22 patients taking phenylephrine)	Oxymetazoline produced longer-lasting nasal decongestion than phenylphedrine	ND
Svensson 1980 81129988	Major adverse effects: Tremor- induced in all patients after high dosage of terbutaline No minor adverse effects:		ND
Svensson 1981 82087563	No side effects indicated	Limitation in randomization process	ND
Svensson 1982 83040698	Minor adverse effects: 3 withdrawals- one potentially drug-related- 1 patient taking KWD 2131 experienced tremor	Other reasons for withdrawal (out of 3 withdrawals): 1 patient due to insufficient effect of treatment 1 patient due to intervening illness	ND

Evidence Table 5. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Sympathomimetic treatments
Part III. (continued)

Author Year UI	**Outcome-safety**	**Potential Bias**	**Funding**
Borum 1987 87239270	Major adverse effects: Minor adverse effects: 2 Withdrawals before study (out of n= 35) 1 patient due to headache after taking placebo 1 patient due to severe symptoms in pretreatment and after taking fenoterol 8 withdrawals during study (out of n= 33) due to tremor and/or restlessness [note- patients without side effects (n= 25)- 13 preferred fenoterol, 5 preferred placebo, 7 without preference p< 0.05] -Trembling/Restlessness-higher degree of trembling and restlessness during absorption of treatment -Nasal irritation- 30% complained of nasal irritation with both placebo and fenoterol		ND
Shaikh 1995	Major adverse effects- 19 total withdrawals- 2 patients complained of palpitations Minor adverse effects- -Heaviness of head (6 patients) -Burning sensation in nose for few min. after administration (5 patient) -Swallowing negligible amounts of fluid during ESNW administration (4 patients)	Not conventional Rx as in US/UK Other reasons for withdrawal: 4/ 19 dropped out due to inability to master technique of ephedrine nasal wash administration	ND

Evidence Table 5. Randomized controlled studies evaluating treatment of seasonal and perennial allergic rhinitis
Sympathomimetic treatments
Part III. (continued)

Author Year UI	**Outcome-safety**	**Potential Bias**	**Funding**
Svensson 1995 96357837	No major adverse effects indicated. Minor adverse effect- Tremor- 9 patients taking terbutaline experienced tremor, while 0 patients experienced effect with placebo Pulse rate- significant increasing increments recorded after 2 doses terbutaline, vs no increase with placebo High doses of topical terbutaline will produce antiallergic effects in human airways		ND
Georgitis 1998	No major adverse effects. Minor side effects: Pharyngitis, Taste perversion, Epistaxis, Dizziness, Dry Mouth, Chest Pain, Fever, Headache, Paresthesia, Pruritis, Dry Skin, Anxiety, Asthma, Bronchitis, Dyspepsia, Insomnia, Pain, Emotional Upset, and Tachycardia		Pharmaceutical

Evidence Table 6. Studies evaluating risk of asthma with allergic rhinitis

Part I.

Author **Year** **UI**	**Study Type**	**Duration**	**Demographics**	**Inclusion criteria**	**Exclusion criteria**
Settipane 1994	Prospective cohort	23 year followup	Location: US Mean age: 40 Age range: ND % Male ND Race: ND Enrolled: 1836 Evaluated: 738 Number of sites: 1	College student cohort	None
Anderson 1992	Prospective cohort study	23 year followup of 1958 birth cohort	Location: UK Mean age: 23 Age range: N/A % Male ND Race: ND Enrolled: 16833 Evaluated: 12521 Number of sites: N/A	1958 birth cohort	None

Part II.

Author **Year**	**Associations noted**	**Potential bias** **Funding**
Settipane 1994	Incidence of asthma in subjects with prior allergic rhinitis was 10.5% vs. 3.6% in those without. Greater than 3-fold risk of asthma in patients with prior allergic rhinitis.	No data on funding
Anderson 1992	Subjects with a history of allergic rhinitis had a 1.7-2.0 greater chance developing asthma symptoms during followup.	No data on funding