Table 1. 1996 US prevalence rates and numbers for hay fever/allergic rhinitis without asthma by age, sex, race, and family income

Prevalence rates	Age 18-44 (unless otherwise noted)	Age 45-64	Total population
Per 1,000 persons	109.4	104.8	89.8
By sex	Male, under 45: 86.3 Female, under 45: 92.1	Male: 85.6 Female: 122.8	Not available (NA)
By race	White, under 45: 92.0 Black, under 45: 66.2	White: 111.0 Black: 64.6	NA
By family income	< $10,000, under 45: 82.7 $10,000-19,999, under 45: 69.1 $20,000-34,999, under 45: 75.1 $35,000 or more, under 45: 108.9	< $10,000: 106.9 $10,000-19,999: 111.8 $20,000-34,999: 105.0 $35,000 or more: 109.2	NA

Prevalence numbers, in thousands	Age 18-44 (unless otherwise noted)	Age 45-64	Total population
Number	11,809	5,572	23,721
By sex	Male, under 45: 7,751 Female, under 45: 8,248	Male: 2,198 Female: 3,374	NA
By race	White, under 45: 13,404 Black, under 45: 1,665	White: 5,077 Black: 350	NA
By family income	< $10,000, under 45: 1,128 $10,000-19,999, under 45: 1,673 $20,000-34,999, under 45: 2,797 $35,000 or more, under 45: 8,406	< $10,000: 290 $10,000-19,999: 621 $20,000-34,999: 983 $35,000 or more: 2,866	NA

Source: Centers for Disease Control and Prevention, National Center for Health Statistics. Current estimates from the National Health Interview Survey, 1996. Vital and Health Statistics, Series 10, No. 200. DHHS Publication No. (PHS) 99-1528. Hyattsville, MD: US Department of Health and Human Services. October 1999.

Table 2. 1996 US prevalence rates and numbers for hay fever/allergic rhinitis without asthma, by geographic location and place of residence

Geographic location	Prevalence rates per 1,000 persons	Prevalence numbers, in thousands
US	89.8	23,721
Northeast	78.3	4,220
Midwest	85.5	5,424
South	94.9	8,593
West	97.3	5,484

Place of residence	Prevalence rates per 1,000 persons	Prevalence numbers, in thousands
All Metropolitan Statistical Areas (MSA)	90.6	18,887
Central city	86.3	6,742
Not central city	93.3	12,145
Not MSA	86.5	4,834

Source: Centers for Disease Control and Prevention, National Center for Health Statistics. Current estimates from the National Health Interview Survey, 1996. Vital and Health Statistics, Series 10, No. 200. DHHS Publication No. (PHS) 99-1528. Hyattsville, MD: US Department of Health and Human Services. October 1999.

Table 3. Search strategy – preliminary general search, MEDLINE, 1966 through September 2001

Set	Search term	Results
1	exp rhinitis/	12649
2	pollinosis.tw.	842
3	hay fever.tw.	1215
4	rhinitis.tw.	8000
5	or/1-4	15475
6	desensitization, immunologic/	4765
7	immunotherapy.tw.	15633
8	desensitization.tw.	11430
9	or/6-8	29720
10	and/5,9	1679
11	limit 10 to human	1647
12	limit 11 to english language	1128
13	limit 12 to randomized controlled trial	159
14	exp filtration/	21390
15	air conditioning/	1546
16	air pollution, indoor/	2810
17	dust/	11250
18	“bedding and linens”/	2461
19	mites/	5942
20	environmental control.tw.	696
21	mite$.tw.	6141
22	or/14-21	45324
23	5 and 22	1312
24	limit 23 to human	1280
25	limit 24 to english language	930
26	limit 25 to randomized controlled trial	66
27	drug therapy, combination/	65666
28	5 and 27	142
29	limit 28 to human	138
30	limit 29 to english language	104
31	limit 30 to randomized controlled trial	54
32	exp psychology, industrial/	36848
33	exp “costs and cost analysis”/	110582
34	burden of illness.tw	188
35	or/32-34	144427
36	5 and 35	72
37	limit 36 to human	71
38	limit 37 to english language	68
39	leukotriene antagonists/tu	241
40	interleukin-4/tu	141
41	antibodies, anti-idiotypic/	9499
42	or/39-41	9879
43	5 and 42	106
44	limit 43 to human	103
45	limit 44 to english language	92
46	limit 45 to randomized controlled trial	17
47	quality of life/	28524
48	health status/	17994
49	karnofsky performance status/	404
50	activities of daily living/	21523
51	or/47-50	62587
52	5 and 51	117
53	limit 52 to human	117
54	limit 53 to english language	107
55	limit 54 to abstracts	94
56	exp anti-inflammatory agents, steroidal/tu	45608
57	5 and 56	619

(continued on next page)

Set	Search term	Results
58	limit 57 to human	614
59	limit 58 to english language	505
60	limit 59 to randomized controlled trial	190
61	cetirizine/tu	194
62	fexofenadine/tu	0
63	loratadine/tu	145
64	terfenadine/tu	168
65	or/61-64	441
66	exp histamine h1 antagonists/tu	7227
67	66 not 65	6786
68	5 and 65	225
69	limit 68 to human	223
70	limit 69 to english language	198
71	limit 70 to randomized controlled trial	127
72	limit 67 to human	6094
73	limit 72 to english language	4250
74	limit 73 to randomized controlled trial	787
75	71 or 74	914

Table 4. Search strategy – clinician specialty differences, MEDLINE, 1966 to October Week 3 2001

Set	Search term	Results
1	physicians,family/	8358
2	exp physician's practice patterns/	11285
3	family practice/	38292
4	internal medicine/	9345
5	"referral and consultation"/	29576
6	specialties, medical/	11701
7	specialties, surgical/	935
8	surgery/	17749
9	exp attitude of health personnel/	55556
10	exp "outcome and process assessment (health	151936
11	"allergy and immunology"/	2635
12	or/1-11	310954
13	exp rhinitis/	12676
14	pollinosis.tw.	843
15	hay fever.tw.	1217
16	rhinitis.tw.	8034
17	or/13-16	15518
18	and/12,17	450
19	from 18 keep 28,43-44,50,52,63,66,108,110,1	18
20	limit 18 to yr=1966-1998	289
21	limit 20 to yr=1966-1997	217
22	from 21 keep 30,33,40,43,88,99,107,156,205,	10

Table 5. Search strategy – environmental measures (1), MEDLINE, 1966 to October Week 1 2001

Set	Search term	Results
1	exp rhinitis/	12654
2	air pollutants, Environmental/ip	49
3	Allergens/ip	972
4	MITES/	5946
5	1 or 2 or 3 or 4	18967
6	Rhinitis/pc	64
7	air pollution/pc	2146
8	respiratory hypersensitivity/pc	206
9	dust/pc	288
10	Micropore Filters/	1779
11	FILTRATION/	11554
12	INSECTICIDES/	7545
13	Insect Control/	3225
14	air-cleaning.tw.	48
15	(air adj filter).tw.	96
16	(air adj cleaner$).tw.	48
17	acaricide.tw.	343
18	acardust.tw.	3
19	hepa.tw.	582
20	(allergen adj avoidance).mp. [mp=title, abstract, registry number word, mesh subject heading]	216
21	(allergen adj control).mp. [mp=title, abstract, registry number word, mesh subject heading]	27
22	(environmental adj control$).mp. [mp=title, abstract, registry number word, mesh subject heading]	811
23	6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22	27516
24	5 and 23	543
25	randomized-controlled-trial (pt)	151353
26	meta-analysis (pt)	5987
27	controlled-clinical-trial (pt)	58987
28	clinical-trial (pt)	319348
29	random$.ti,ab,sh.	254436
30	(meta-anal$ or metaanaly$ or meta analy$).ti,ab,sh.	9346
31	((doubl$ or singl$) and blind$).ti,ab,sh.	67067
32	exp Clinical trials/	127044
33	crossover.ti,ab,sh.	18070
34	25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33	501236
35	24 and 34	89

Table 6. Search strategy – environmental measures (2), MEDLINE, 1966 to October Week 1 2001

Set	Search term	Results
1	exp rhinitis/	12654
2	air pollutants, Environmental/ip	49
3	Allergens/ip	972
4	MITES/	5946
5	1 or 2 or 3 or 4	18967
6	Rhinitis/pc	64
7	air pollution/pc	2146
8	respiratory hypersensitivity/pc	206
9	dust/pc	288
10	Micropore Filters/	1779
11	FILTRATION/	11554
12	INSECTICIDES/	7545
13	Insect Control/	3225
14	air-cleaning.tw.	48
15	(air adj filter).tw.	96
16	(air adj cleaner$).tw.	48
17	acaricide.tw.	343
18	acardust.tw.	3
19	hepa.tw.	582
20	6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19	26537
21	Randomized Controlled Trials/	20303
22	5 and 20	421
23	21 and 22	1
24	pollinosis.tw.	842
25	hay fever.tw.	1216
26	rhinitis.tw.	8011
27	mite$.tw.	6147
28	5 or 24 or 25 or 26 or 27	23563
29	exp filtration/	21404
30	air conditioning/	1548
31	air pollution, indoor/	2815
32	dust/	11255
33	“bedding and linens”/	2463
34	20 or 29 or 30 or 31 or 32 or 33	51223
35	randomized-controlled-trial (pt)	151353
36	meta-analysis (pt)	5987
37	controlled-clinical-trial (pt)	58987
38	clinical-trial (pt)	319348
39	random$.ti,ab,sh.	254436
40	(meta-anal$ or metaanaly$ or meta analy$).ti,ab,sh.	9346
41	((doubl$ or singl$) and blind$).ti,ab,sh.	67067
42	exp Clinical trials/	127044
43	crossover.ti,ab,sh.	18070
44	35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43	501236
45	28 and 34	2799
46	44 and 45	291
47	limit 46 to (human and english language)	224

Table 7. Included study designs, by key research question

Question	Topic	Included study designs
1 2	Costs and work performance Relationship between symptom outcomes or disease-specific quality of life and work performance	Any empirical study involving more than 20 patients with allergic rhinitis. Includes randomized controlled trials (RCTs), case series, cohort studies, non-randomized comparison studies, surveys, and secondary data analyses.
3a	Environmental measures	RCTs, non-randomized prospective cohort comparisons
3b 3c	Immunotherapy Combination drug therapy	RCTs, pseudo-randomized placebo-controlled trials
4 5	Clinician specialty differences Racial and ethnic variation	Any empirical study involving more than 20 patients with allergic rhinitis. Includes RCTs, case series, cohort studies, non-randomized comparison studies, surveys, and secondary data analyses.

Table 8. Abstract and full-text screening criteria

Key research questions:

1. How do currently clinically available treatments for allergic rhinitis affect costs and work performance?
2. What is the relationship between symptom outcomes or disease-specific quality-of-life measures and work performance among adults with allergic rhinitis? Can data on symptomatic outcome or quality of life be reliably translated into work performance measures?
3. How effective are (a) environmental measures, (b) immunotherapy, and (c) combined treatments, such as with antihistamines and nasal steroids or antihistamines and oral decongestants, for relief of symptoms in adults with allergic rhinitis?
4. How do different types of healthcare providers (generalists, allergy specialists, and otolaryngologists) treat adults with allergic rhinitis, and how do treatment outcomes vary by provider?
5. In adult patients with symptoms of allergic rhinitis, does the prevalence, treatment patterns or response to treatment vary according to a patient's race or ethnicity?

Inclusion/exclusion criteria:

1 Not original research or relevant review
2 Not allergic rhinitis or allergic rhinitis not applicable to research questions
3 Case report
4 Small case series (≤ 20 patients, no controls)
5 Large case series (> 20 patients, no controls)
6 Non-randomized assignment to treatment (comparison group, but not randomly assigned)
7 Randomized controlled trial
8 Relevant review
9 Original research on other aspects (for use as background or in model, e.g., prevalence, natural history, diagnostic testing)
10 Basic science
11 Survey and secondary data

Inclusion rules:

Question 1:	codes 5-9,11:	Evidence tables for codes 5, 6 7, 11
Question 2:	codes 5-9,11:	Evidence tables for codes 5, 6, 7, 11
Question 3a:	codes 6-9,11:	Evidence tables for codes 6, 7
Question 3b:	codes 7-9,11:	Evidence tables for code 7
Question 3c:	codes 7-9,11:	Evidence tables for code 7
Question 4:	codes 5-9,11:	Evidence tables for codes 5, 6, 7, 11
Question 5:	codes 5-9,11:	Evidence tables for codes 5 ,6, 7,11

Table 9. Summary of results of abstract and full-text screening

Articles identified	1593
Abstracts:	
Included	546
Excluded	1089
Full-text articles:	
Included	258
Excluded	288

Table 10: Full-text screening results, by key research question and by inclusion/exclusion criteria

INCLUDED ARTICLES (ET = included in evidence tables)	
Question 1 (Note: one article screened for this question reported results of both an RCT and a large case series)	**54**
5-large case series (> 20 patients, no controls): ET	14
6-non-randomized controlled trials: ET	0
7-randomized controlled trial: ET	7
8-relevant review	11
9-original research on other aspects for use in background or model	13
11-survey or secondary data: ET	11
Question 2 (screened with Question 1 articles)	**6**
5-large case series (> 20 patients, no controls): ET	0
6-non-randomized controlled trials: ET	0
7-randomized controlled trial: ET	3
8-relevant review	2
9-original research on other aspects for use in background or model	0
11-survey or secondary data: ET	1
Question 3a (environmental measures)	**40**
6-non-randomized controlled trials: ET	1
7-randomized controlled trial: ET	26
8-relevant review	9
9-original research on other aspects for use in background or model	0
11-survey or secondary data	4
Question 3b (immunotherapy)	**80**
7-randomized controlled trial: ET	62
8-relevant review	11
9-original research on other aspects for use in background or model	4
11-survey or secondary data	3
Question 3c (combination treatments)	**32**
7-randomized controlled trial: ET	31
8-relevant review	0
9-original research on other aspects for use in background or model	1
Question 4	**26**
5-large case series (> 20 patients, no controls): ET	4
6-non-randomized controlled trials: ET	0
7-randomized controlled trial: ET	0
8-relevant review	12
9-original research on other aspects for use in background or model	6
11-survey or secondary data: ET	1
Question 5	**8**
5-large case series (> 20 patients, no controls)	1
6-non-randomized controlled trials	0
7-randomized controlled trial	0
8-relevant review	3
9-original research on other aspects for use in background or model	0
11-survey or secondary data	4

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EXCLUDED ARTICLES

Question 1	**82**
1-not original research or relevant review	24
2-not allergic rhinitis or not applicable to study questions	48
3-case report	0
4-small case series (≤ 20 patients, no controls)	1
10-basic science	0
Excluded during data abstraction (e.g., no relevant data reported)	9
Question 2 (screened with Question 1 articles)	**15**
1-not original research or relevant review	6
2-not allergic rhinitis or not applicable to study questions	5
3-case report	0
4-small case series (≤ 20 patients, no controls)	0
5-large case series (> 20 patients, no controls)	0
10-basic science	1
Excluded during data abstraction (no relevant data)	3
Question 3a (environmental measures)	**41**
1-not original research or relevant review	10
2-not allergic rhinitis or not applicable to study questions	10
3-case report	0
4-small case series (≤ 20 patients, no controls)	0
5-large case series (> 20 patients, no controls)	3
6-non-randomized controlled trials	0
10-basic science	11
Excluded during data abstraction (e.g., no relevant data, insufficient data, no symptom outcomes or other relevant outcomes, only atopic dermatitis)	7
Question 3b (immunotherapy):	**87**
1-not original research or relevant review	5
2-not allergic rhinitis or not applicable to study questions	71
3-case report	0
4-small case series (≤ 20 patients, no controls)	0
5-large case series (> 20 patients, no controls)	1
6-non-randomized controlled trials	4
10-basic science	2
Excluded during data abstraction (e.g., no separate results for allergic rhinitis, asthma data only, no symptom outcomes)	4
Question 3c (combination treatments)	**25**
1-not original research or relevant review	5
2-not allergic rhinitis or not applicable to study questions	14
3-case report	0
4-small case series (≤ 20 patients, no controls)	0
10-basic science	0
Excluded during data abstraction (no relevant data)	6
Question 4	**30**
1-not original research or relevant review	6
2-not allergic rhinitis or not applicable to study questions	9
3-case report	0
4-small case series (≤ 20 patients, no controls)	1

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10-basic science	1
Excluded during data abstraction (e.g., no relevant allergic rhinitis data; no data on provider differences)	13
Question 5	**21**
1-not original research	2
2-not allergic rhinitis or not applicable to study questions	18
3-case report	0
4-small case series (≤ 20 patients, no controls)	0
10-basic science	0
Excluded during data abstraction (e.g., no relevant data)	1

Table 11. Partial data abstraction – sample

Study	Design and Interventions	Patient Population	Outcomes Reported	Results	Quality Score/Notes
Andri, Senna, Betteli, et al., 1992 **#210**	Design: RCT, parallel-group, method of randomization not described Interventions: 1) Terfenadine 60 mg bid + nimesulide 100 mg bid (n = 15) 2) Terfenadine 60 mg bid + placebo (n = 15) Duration of study treatment: 30 days No other drugs "likely to affect hay fever" permitted No pre-trial washout period described Dates: **Location:** **Setting:** **Type(s) of providers:**	No. of subjects at start: 30 Dropouts/withdrawals: No. of subjects at end: Inclusion criteria: Exclusion criteria: Age: Sex: Race: [IF RESULTS ARE BROKEN DOWN BY RACE/ETHNICITY, PLEASE MAKE THIS CLEAR IN "RESULTS" COLUMN] Other:	1) Investigator-assessed symptom severity 2) Patient-assessed symptom severity: nasal itching, nasal obstruction, sneezing, running nose, eye irritation, and eye watering graded daily by patients scale of 0 (none) to 3 (severe) 3) Patient global assessment of efficacy: recorded once at end of trial – categorical scale keyed to perceived degree of improvement in symptoms (< 50%, 50-80%, > 80%) 4) Adverse events: Not clear how reported/ recorded	1) Investigator-assessed symptom severity: DO NOT ABSTRACT 2) Patient-assessed symptom severity: 3) Patient global assessment of efficacy: 4) Adverse events:	[IF ARTICLE SHOULD BE EXCLUDED, PLEASE EXPLAIN WHY HERE] Quality Scoring: Notes: Local pollen counts conducted daily during trial.

Table 12. Oxford Centre for Evidence-based Medicine levels of evidence (May 2001)[1]

Level	Therapy/prevention, aetiology/harm	Prognosis	Diagnosis	Differential diagnosis/symptom prevalence study	Economic and decision analyses
1a	Systematic review (SR) (with homogeneity*) of RCTs	SR (with homogeneity*) of inception cohort studies; CDR† validated in different populations	SR (with homogeneity*) of Level 1 diagnostic studies; CDR† with 1b studies from different clinical centres	SR (with homogeneity*) of prospective cohort studies	SR (with homogeneity*) of Level 1 economic studies
1b	Individual RCT (with narrow Confidence Interval‡)	Individual inception cohort study with ≥ 80% follow-up; CDR† validated in a single population	Validating** cohort study with good††† reference standards; or CDR† tested within one clinical centre	Prospective cohort study with good follow-up****	Analysis based on clinically sensible costs or alternatives; systematic review(s) of the evidence; and including multi-way sensitivity analyses
1c	All or none§	All or none case-series	Absolute SpPins and SnNouts††	All or none case-series	Absolute better-value or worse-value analyses ††††
2a	SR (with homogeneity*) of cohort studies	SR (with homogeneity*) of either retrospective cohort studies or untreated control groups in RCTs	SR (with homogeneity*) of Level >2 diagnostic studies	SR (with homogeneity*) of 2b and better studies	SR (with homogeneity*) of Level >2 economic studies
2b	Individual cohort study (including low quality RCT; e.g., <80% follow-up)	Retrospective cohort study or follow-up of untreated control patients in an RCT; Derivation of CDR† or validated on split-sample§§§ only	Exploratory** cohort study with good†††reference standards; CDR† after derivation, or validated only on split-sample§§§ or databases	Retrospective cohort study, or poor follow-up	Analysis based on clinically sensible costs or alternatives; limited review(s) of the evidence, or single studies; and including multi-way sensitivity analyses
2c	"Outcomes" Research; Ecological studies	"Outcomes" Research		Ecological studies	Audit or outcomes research
3a	SR (with homogeneity*) of case-control studies		SR (with homogeneity*) of 3b and better studies	SR (with homogeneity*) of 3b and better studies	SR (with homogeneity*) of 3b and better studies
3b	Individual Case-Control Study		Non-consecutive study; or without consistently applied reference standards	Non-consecutive cohort study, or very limited population	Analysis based on limited alternatives or costs, poor quality estimates of data, but including sensitivity analyses incorporating clinically sensible variations.
4	Case-series (and poor quality cohort and case-control studies§§)	Case-series (and poor quality prognostic cohort studies***)	Case-control study, poor or non-independent reference standard	Case-series or superseded reference standards	Analysis with no sensitivity analysis
5	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"	Expert opinion without explicit critical appraisal, or based on economic theory or "first principles"

[1] Produced by Bob Phillips, Chris Ball, Dave Sackett, Doug Badenoch, Sharon Straus, Brian Haynes, Martin Dawes since November 1998. Available at: http://163.1.96.10/docs/levels .html#levels. Accessed May 30, 2002.

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Users can add a minus-sign "-" to denote the level of that fails to provide a conclusive answer because of:
· EITHER a single result with a wide Confidence Interval (such that, for example, an ARR in an RCT is not statistically significant but whose confidence intervals fail to exclude clinically important benefit or harm)
· OR a Systematic Review with troublesome (and statistically significant) heterogeneity.
· Such evidence is inconclusive, and therefore can only generate Grade D recommendations.

*	By homogeneity we mean a systematic review that is free of worrisome variations (heterogeneity) in the directions and degrees of results between individual studies. Not all systematic reviews with statistically significant heterogeneity need be worrisome, and not all worrisome heterogeneity need be statistically significant. As noted above, studies displaying worrisome heterogeneity should be tagged with a "-" at the end of their designated level.
†	Clinical Decision Rule. (These are algorithms or scoring systems which lead to a prognostic estimation or a diagnostic category.)
‡	See note #2 for advice on how to understand, rate and use trials or other studies with wide confidence intervals.
§	Met when all patients died before the Rx became available, but some now survive on it; or when some patients died before the Rx became available, but none now die on it.
§§	By poor quality cohort study we mean one that failed to clearly define comparison groups and/or failed to measure exposures and outcomes in the same (preferably blinded), objective way in both exposed and non-exposed individuals and/or failed to identify or appropriately control known confounders and/or failed to carry out a sufficiently long and complete follow-up of patients. By poor quality case-control study we mean one that failed to clearly define comparison groups and/or failed to measure exposures and outcomes in the same (preferably blinded), objective way in both cases and controls and/or failed to identify or appropriately control known confounders.
§§§	Split-sample validation is achieved by collecting all the information in a single tranche, then artificially dividing this into "derivation" and "validation" samples.
††	An "Absolute SpPin" is a diagnostic finding whose Specificity is so high that a Positive result rules-in the diagnosis. An "Absolute SnNout" is a diagnostic finding whose Sensitivity is so high that a Negative result rules-out the diagnosis.
‡‡	Good, better, bad and worse refer to the comparisons between treatments in terms of their clinical risks and benefits.
†††	Good reference standards are independent of the test, and applied blindly or objectively to applied to all patients. Poor reference standards are haphazardly applied, but still independent of the test. Use of a non-independent reference standard (where the 'test' is included in the 'reference', or where the 'testing' affects the 'reference') implies a level 4 study.
††††	Better-value treatments are clearly as good but cheaper, or better at the same or reduced cost. Worse-value treatments are as good and more expensive, or worse and the equally or more expensive.
**	Validating studies test the quality of a specific diagnostic test, based on prior evidence. An exploratory study collects information and trawls the data (e.g. using a regression analysis) to find which factors are 'significant'.
***	By poor quality prognostic cohort study we mean one in which sampling was biased in favour of patients who already had the target outcome, or the measurement of outcomes was accomplished in <80% of study patients, or outcomes were determined in an unblinded, non-objective way, or there was no correction for confounding factors.
****	Good follow-up in a differential diagnosis study is >80%, with adequate time for alternative diagnoses to emerge (eg 1-6 months acute, 1-5 years chronic)

Grades of Recommendation

A	consistent level 1 studies
B	consistent level 2 or 3 studies ***or*** extrapolations from level 1 studies
C	level 4 studies ***or*** extrapolations from level 2 or 3 studies
D	level 5 evidence ***or*** troublingly inconsistent or inconclusive studies of any level

"Extrapolations" are where data is used in a situation which has potentially clinically important differences than the original study situation.
"Extrapolations" are where data is used in a situation which has potentially clinically important differences than the original study situation.

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2. Sackett DL. Rules of evidence and clinical recommendations on use of antithrombotic agents. Chest 1986 Feb; 89 (2 suppl.):2S-3S.
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4. Yusuf S, Cairns JA, Camm AJ, Fallen EL, Gersh BJ. Evidence-Based Cardiology. London: BMJ Publishing Group, 1998.

Table 13. Summary of types of data reported in studies abstracted in Evidence Table 1

Study	Data source	Per-patient burden of illness for selected populations	Total burden-of-illness estimates for US population	Cost-effectiveness	Work performance	Symptoms	Health-related quality of life
Blanc, Trupin, Eisner, et al., 2001	Telephone survey	X[1]			X	X	X
Burton, Conti, Chen, et al., 2001	Survey, work productivity data				X		
Cockburn, Bailit, Berndt, et al., 1999a; Cockburn, Bailit, Berndt, et al., 1999b	Prescription claims data, work productivity data				X		
Crystal-Peters, Crown, Goetzel, et al., 2000	1995 National Health Interview Survey and Bureau of Labor Statistics		X[2]				
Cuffel, Wamboldt, Borish, et al., 1999	Health care claims						
Donahue, Greineder, Connor-Lacke, et al., 1999	Health care claims	X					
Fell, Mabry, and Mabry, 1997	Survey	X[1]			X	X	
Gilmore, Alexander, Mueller, et al., 1996	Health care claims						
Keith, Haddon, and Birch, 2000	Randomized controlled trial	X		X[3]			
Kessler, Almeida, Berglund, et al., 2001	Survey	X			X		
Kozma, Schulz, Sclar, et al., 1996	Randomized controlled trial			X		X	
Lee, Cummins, and Okamoto, 2001	Health care claims	X					
Leickly, Sears-Ewald, and Ownby, 1989	Randomized controlled trial					X	
Liao, Leahy, and Cummins, 2001	Health care claims	X					
Malone, Lawson, Smith, et al., 1997	1987 National Medical Expenditure Survey		X				

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Study	Data source	Per-patient burden of illness for selected populations	Total burden-of-illness estimates for US population	Cost-effectiveness	Work performance	Symptoms	Health-related quality of life
Manor, Matthews, and Power, 2001	Survey					X	
McMenamin, 1994	Multiple national surveys, government statistics		X				
Meltzer, Casale, Nathan, et al., 1999	Randomized controlled trial				X		X
Ray, Baraniuk, Thamer, et al., 1999	Multiple national surveys, expert opinion		X				
Reilly, Tanner, and Meltzer, 1996	Randomized controlled trial				X	X	X
Revicki, Leidy, Brennan-Diemer, et al., 1998	Survey				X	X	X
Ross, 1996	Multple national surveys, government statistics				X		
Santilli, Nathan, Glassheim, et al., 2001	Survey	X[1]				X	
Santos, Cifaldi, Gregory, et al., 1999 (Study 1)	Health care claims	X					
Santos, Cifaldi, Gregory, et al., 1999 (Study 2)	Randomized controlled trials	X			X	X	X
Schädlich and Brecht, 2000	Multiple published estimates			X			
Stahl, van Rompay, Wang, et al., 2000	Randomized controlled trials			X			
Storms, Meltzer, Nathan, et al., 1997	Survey		X		X		
Sussman, Mason, Compton, et al., 1999	Randomized controlled trials				X	X	
Tanner, Reilly, Meltzer, et al., 1999	Randomized controlled trials				X		X

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Study	Data source	Per-patient burden of illness for selected populations	Total burden-of-illness estimates for US population	Cost-effectiveness	Work performance	Symptoms	Health-related quality of life
Trotter, 2000	Prescription claims	X					
Yawn, Yunginger, Wollan, et al., 1999	Patient registry	X					

[1] Costs not assigned, but estimates of resource utilization reported.
[2] Indirect costs only.
[3] Cost-benefit analysis in which benefits were measured with a willingness-to-pay survey.

Table 14. Placebo-controlled randomized controlled trials of injection immunotherapy (IT) for seasonal allergic rhinitis, by type of allergen

Allergen	Number of trials	Number of subjects	Number of trials favoring IT	Number of trials with negative or equivocal results
Ragweed	18	990	14	4
Grass (any)	13	604	12	1
Tree (any)	7	168	7	0
Parietaria	4	170	4	0

Table 15. Data abstracted for meta-analysis of placebo-controlled trials of immunotherapy (IT) for seasonal allergic rhinitis

Study	Allergen	Symptom measure-ment period	Outcome	IT mean	IT SD	IT n	Placebo mean	Placebo SD	Placebo n	Statistical test	P-value	IPD?
Ariano, Kroon, Augeri, et al., 1999	Tree	7 mo	Combined Sx/Rx	550 (median)	NR	11	1250 (median)	NR	11	Non-parametric	p = 0.02	No
Arvidsson, Löwhagen, and Rak, 2002	Tree	6 wk	Sx severity	1.3 (median)	0-5.2 (range)	22	2.1 (median)	0.6-5.6 (range)	24	Non-parametric	p = 0.05	No
Arvidsson, Löwhagen, and Rak, 2002	Tree	6 wk	Rx use	NR	NR	22	NR	NR	24	Non-parametric	p = 0.004	No
Bernstein, Tennenbaum, Georgakis, et al., 1976	Ragweed	4 wk	Sx severity	1.097 (mean daily score)	NR	58 (est.)	1.378 (mean daily score)	NR	54 (est.)	Not specified	p < 0.05	No
Bernstein, Tennenbaum, Georgakis, et al., 1976	Ragweed	4 wk	Rx use	0.411 (measured score)	NR	58 (est.)	0.584 (measured score)	NR	54 (est.)	Not specified	p < 0.01	No
Bødtger, Poulsen, Jacobi, et al., 2002	Tree	2 wk	Rx use	32.5 (median)	6.0-71.0 (range)	17	51.0 (median)	14.0-76.0 (range)	17	Non-parametric	p < 0.04	No
Bødtger, Poulsen, Jacobi, et al., 2002	Tree	2 wk	Rx use	52.0 (median)	2.0-114.0 (range)	17	102.0 (median)	2.0-186.0 (range)	17	Non-parametric	p < 0.02	No
Bousquet, Frank, Soussana, et al., 1987	Grass	6 wk	Sx severity	61.0	35.0	35	109	33	16	Non-parametric	p < 0.01	No
Bousquet, Hejjaoui, Skassa-Brociek, et al., 1987	Grass	4 wk	Sx severity	9.5 (median)	10.0	15	20.5 (median)	7	11	Non-parametric	p < 0.005	Graph

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Study	Allergen	Symptom measure-ment period	Outcome	IT mean	IT SD	IT n	Placebo mean	Placebo SD	Placebo n	Statistical test	P-value	IPD?
Bousquet, Hejjaoui, Skassa-Brociek, et al., 1987	Grass	4 wk	Rx use	0.84	2.25	15	2.67	1.54	11	Non-parametric	p < 0.01	Graph
Bousquet, Hejjaoui, Soussana, et al., 1990	Grass	6 wk	Sx severity	63.6	32.5	20	108.6	33.2	15	Non-parametric	p < 0.005	Graph
Bousquet, Hejjaoui, Soussana, et al., 1990	Grass	6 wk	Rx use	38.6	37.6	20	66.4	51.7	15	Non-parametric	p < 0.05	No
Bousquet, Hejjaoui, Soussana, et al., 1990	Grass	6 wk	Sx days	22.9	11.4	20	40.2	7.1	15	Non-parametric	p < 0.01	No
Bousquet, Maasch, Hejjaoui, et al., 1989	Grass	4 wk	Sx severity	14.8	22.9	18	63.5	54.6	14	Non-parametric	p < 0.001	No
Bousquet, Maasch, Hejjaoui, et al., 1989	Grass	4 wk	Rx use	22.9	39.1	18	53.7	54.1	14	Non-parametric	p < 0.001	No
Bousquet, Maasch, Hejjaoui, et al., 1989	Grass	4 wk	Sx days	9.0	10.7	18	26.5	8.6	14	Non-parametric	p < 0.01	Graph
Brunet, Bedard, Lavoie, et al., 1992	Ragweed	4 wk	Sx severity	4.7	0.7 (SEM)	13	7.5	1.2 (SEM)	14	Non-parametric	p < 0.05	Graph
Brunet, Bedard, Lavoie, et al., 1992	Ragweed	4 wk	Rx use	0.9	0.2 (SEM)	13	0.7	0.2 (SEM)	14	Non-parametric	p < 0.6	No

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Study	Allergen	Symptom measure-ment period	Outcome	IT mean	IT SD	IT n	Placebo mean	Placebo SD	Placebo n	Statistical test	P-value	IPD?
Cockcroft, Cuff, Tarlo, et al., 1977	Ragweed	Not specified	Sx severity	4.95	NR	21	5.75	NR	21	Parametric	p = NS (0.05 < p < 0.10)	No
Cockcroft, Cuff, Tarlo, et al., 1977	Ragweed	Not specified	Sx severity	2.29	NR	21	4.37	NR	21	Parametric	p < 0.05	No
Creticos, Reed, Norman, et al., 1996	Ragweed	4 mo pre-trial observa-tion; year-1 data	Sx severity	3.5 (year 1)	0.5	29	4.3 (year 1)	0.5	24	Parametric	p < 0.1	No
Grammer, Shaughnessy, Bernhard, et al., 1987	Ragweed	5 wk	Combined Sx/Rx	7.76	NR	30	17.4	NR	30	Parametric	p = 0.02	No
Grammer, Shaughnessy, Suszko, et al., 1983	Grass	9 wk	Combined Sx/Rx	210	75 (SEM)	10	500	115 (SEM)	13	Non-parametric	p = 0.02	No
Grammer, Zeiss, Suszko, et al., 1982	Ragweed	7 wk	Combined Sx/Rx	332.	64 (SEM)	21	530	83 (SEM)	19	Parametric	p = 0.022	No
Hirsch, Kalbfleisch, and Cohen, 1982	Ragweed	6 wk	Sx severity	24.8	15.1	20	45.9	18.6	14	Parametric	p < 0.004	No
Hirsch, Kalbfleisch, and Cohen, 1982	Ragweed	6 wk	Rx use	4.0	7.4	20	8.3	2.3	14	Parametric	p < 0.025	No
Iliopoulos, Proud, Adkinson, et al., 1991	Ragweed	Not specified	Combined Sx/Rx	NR	NR	21	NR	NR	20	Non-parametric	p < 0.04	No

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Study	Allergen	Symptom measure-ment period	Outcome	IT mean	IT SD	IT n	Placebo mean	Placebo SD	Placebo n	Statistical test	P-value	IPD?
Leynadier, Banoun, Dollois, et al., 2001	Grass	12 wk	Sx severity	49.5	NR	16	56	NR	13	Non-parametric	p = NS	No
Leynadier, Banoun, Dollois, et al., 2001	Grass	12 wk	Rx use	11.1	NR	16	40.8	NR	13	Non-parametric	p = 0.005	No
Lichtenstein, Norman, and Winken-werder, 1971	Ragweed	8 wk	Sx severity	7.25	NR	18	11.125	NR	21	Non-parametric	p < 0.01	Graph
McAllen, 1969	Grass	7 wk	Sx severity	54	NR	40	72	NR	20	Non-parametric	p = 0.074	No
McAllen, 1969	Grass	7 wk	Sx days	35	NR	40	28.5	NR	20	Non-parametric	p = 0.087	No
Norman, Lichtenstein, Kagy-Sobotka, et al., 1982	Ragweed	NR	Combined Sx/Rx	5.3	NR	16	8.8	NR	17	Non-parametric	p < 0.01	Graph
Ortolani, Pastorello, Incorvaia, et al., 1994	Tree	4 wk	Combined Sx/Rx	NR	NR	17	NR	NR	14	Non-parametric	p < 0.05	No
Parker, Whisman, Apaliski, et al., 1989	Tree	10 days	Combined Sx/Rx	57.0	NR	26	129.9	NR	25	Non-parametric	p = 0.0001	Yes
Pastorello, Pravettoni, Incorvaia, et al., 1992	Grass	4 wk	Combined Sx/Rx	NR	NR	10	NR	NR	9	Non-parametric	p < 0.01	No
Pence, Mitchell, Greely, et al., 1976	Tree	12 wk	Combined Sx/Rx	5.46	3.22	17	8.83	3.15	15	Parametric	p < 0.01	Yes

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Study	Allergen	Symptom measure-ment period	Outcome	IT mean	IT SD	IT n	Placebo mean	Placebo SD	Placebo n	Statistical test	P-value	IPD?
Van Metre, Adkinson, Amodio, et al., 1980	Ragweed	8 wk	Combined Sx/Rx	3.0	NR	15	5.0	NR	14	Non-parametric	p < 0.01	Graph
Van Metre, Adkinson, Amodio, et al., 1982	Ragweed	8 wk	Combined Sx/Rx	3.79	NR	15	11.14	NR	11	Non-parametric	p < 0.01	Graph
Varney, Gaga, Frew, et al., 1991	Grass	11 wk	Sx severity	360	NR	21	928	NR	16	Non-parametric	p = 0.001	No
Varney, Gaga, Frew, et al., 1991	Grass	11 wk	Rx use	129	NR	21	627	NR	16	Non-parametric	p = 0.002	No
Walker, Pajno, Limo, et al., 2001	Grass	11 wk (2 seasons: 1996 & 1998)	Grass	Difference between IT and placebo = 1186.5	241.5 to 1928.6	22	See IT mean	See IT SD	22	Non-parametric	p = 0.01	No
Walker, Pajno, Limo, et al., 2001	Grass	11 wk (2 seasons: 1996 & 1998)	Grass	Difference between IT and placebo = 1043.0	332.0 to 2667.1	22	See IT mean	See IT SD	22	Non-parametric	p = 0.007	No
Weyer, Donat, L'Heritier, et al., 1981	Grass	6 wk	Sx severity	16	10	17	24	8	16	Non-parametric	p < 0.09	No
Weyer, Donat, L'Heritier, et al., 1981	Grass	6 wk	Rx use	3	5	17	11	13	16	Non-parametric	p < 0.07	No
Weyer, Donat, L'Heritier, et al., 1981	Grass	6 wk	Combined Sx/Rx	10	7	17	18	15	16	Non-parametric	p < 0.03	No
Zenner, Baumgarten, Rasp, et al., 1997	Grass	10 wk	Sx severity	82.2	10.1	45	116	13.2	41	Non-parametric	p < 0.025	Graph
Zenner, Baumgarten, Rasp, et al., 1997	Grass	10 wk	Rx use	26% of 70 days	NR	45	33% of 70 days	NR	41	Non-parametric	p < 0.296	No

Abbreviations: IPD = individual patient data; IT = immunotherapy; mo = month(s); n = number of patients; NR = not reported; NS = not significant; Rx = medication; SD = standard deviation; SEM = standard error of the mean; Sx = symptom; wk = weeks

Table 16. Placebo-controlled randomized controlled trials of injection immunotherapy (IT) for perennial allergic rhinitis, by type of allergen

Allergen	Number of trials	Number of subjects	Number of trials favoring IT	Number of trials with negative or equivocal results
Dust mite	7	357	5	2
Dust mite and pollen	1	10	0	1
Cat	1	28	1	0
Mold (*Alternaria*)	1	22	1	0
Latex	1	14	1	0
Multiple antigens	1	36	1	0

Table 17. Randomized controlled trials comparing combination pharmacotherapy to monotherapy for allergic rhinitis

Treatment 1	Treatment 2	No. of comparisons	Results
Antihistamine + oral decongestant	Antihistamine	13	7 combination superior, 3 no significant difference, 3 no difference, no statistical test reported
Antihistamine + oral decongestant	Decongestant	10	8 combination superior, 2 possibly superior
Antihistamine + oral decongestant	Nasal glucocorticoid	1	No significant difference
Antihistamine + nasal glucocorticoid	Nasal glucocorticoid	7	3 combination superior, 4 no significant difference
Antihistamine + nasal glucocorticoid	Antihistamine	7	5 combination superior, 2 possibly superior
Antihistamine + mast cell stabilizer	Antihistamine	1	Combination superior
Antihistamine + NSAID	Antihistamine	2	Combination superior (1 study)
Antihistamine + ophthalmic antihistamine	Antihistamine	1	Combination reduced eye itching
Antihistamine + ipratropium	Antihistamine	1	Combination reduced rhinorrhea
Ipratropium + nasal glucocorticoid	Nasal glucocorticoid	1	Combination reduced rhinorrhea
Ipratropium + nasal glucocorticoid	Ipratropium	1	Combination reduced rhinorrhea
Nasal glucocorticoid + 3 days nasal decongestant	Nasal glucocorticoid	1	No significant difference
Nasal glucocorticoid + 3 days nasal decongestant	Antihistamine	1	Combination superior
Nasal antihistamine + nasal decongestant	Nasal antihistamine	1	No significant difference
Nasal antihistamine + nasal decongestant	Nasal decongestant	1	Combination superior

Table 18. Data abstracted for meta-analysis of combination treatment articles

Study	Combination	Mono-therapy	Outcome	Combo mean	Combo SD	Combo n	Mono mean	Mono SD	Mono n	Statistical test	P-value	Possible to calculate ES?
A. Antihistamine + decongestant combinations versus antihistamine alone, total symptom severity (see also Figure 3)												
Bronsky, Boggs, Findlay, et al., 1995	Loratadine+ pseudo-ephedrine	Loratadine	TSS	6.72	NR	212	5.6	NR	212	ANOVA	P < 0.05	Yes
Dockhorn, Williams, and Sanders, 1996	Acrivastine+ pseudo-ephedrine	Acrivastine	TSS	10.3	NR	176	12.3	NR	175	ANCOVA (1-sided)	P < 0.001	Yes
Falliers and Redding, 1980 (study 1)	Azatadine+ pseudo-ephedrine	Azatadine	TSS	70% reduc-tion	NR	30	52% reduc-tion	NR	30	ANOVA	NR	No
Falliers and Redding, 1980 (study 2)	Azatadine+ pseudo-ephedrine	Azatadine	TSS	82% reduc-tion	NR	10	58% reduc-tion	NR	10	ANOVA	NR	No
Grosclaude, Mees, Pinelli, et al., 1997	Cetirizine+ pseudo-ephedrine	Cetirizine	TSS	0.85	NR	230	1.03	NR	226	ANOVA	P < 0.001	Yes
Henauer, Seppey, Hugenot, et al., 1991	Terfenadine+ pseudo-ephedrine	Terfenadine	TSS	NR	NR	25	NR	NR	25	ANOVA	P = 0.69	Yes
Meran, Morse, and Gibbs, 1990	Acrivastine+ pseudo-ephedrine	Acrivastine	TSS	1.66	2.25	40	2.04	2.25	40	ANOVA (log-trans-formed scores)	P = 0.45	Yes
Sussman, Mason, Compton, et al., 1999	Fexofenadine + pseudo-ephedrine	Fexo-fenadine	TSS	2.32	NR	215	2.05	NR	218	ANCOVA	P ~ 0.16	Yes

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Study	Combination	Mono-therapy	Outcome	Combo mean	Combo SD	Combo n	Mono mean	Mono SD	Mono n	Statistical test	P-value	Possible to calculate ES?
Williams, Hull, McSorley, et al., 1996	Acrivastine+ pseudo-ephedrine	Acrivastine	TSS	8.5	NR	202	9.8	NR	202	ANCOVA	P < 0.001 (1-sided)	Yes
B. Antihistamine + decongestant versus antihistamine alone, nasal symptom severity (see also Figure 4)												
Bertrand, Jamart, Marchal, et al., 1996	Cetirizine+ pseudo-ephedrine	Cetirizine	Nasal obstruc-tion	Graph	NR	70	Graph	NR	70	CMH (categori-cal)	P = 0.005	No
Bronsky, Boggs, Findlay, et al., 1995	Loratadine+ pseudo-ephedrine	Loratadine	NSS	NR	NR	212	NR	NR	212	ANOVA	P < 0.01	Yes
Dockhorn, Williams, and Sanders, 1996	Acrivastine+ pseudo-ephedrine	Acrivastine	NSS	3.8	NR	176	4.7	NR	175	ANCOVA (1-sided)	P < 0.001	Yes
Falliers and Redding, 1980 (study 1)	Azatadine+ pseudo-ephedrine	Azatadine	NSS	68% reduc-tion	NR	30	35% reduc-tion	NR	30	ANOVA	P < 0.05	Yes
Falliers and Redding, 1980 (study 2)	Azatadine+ pseudo-ephedrine	Azatadine	NSS	73% reduc-tion	NR	10	27% reduc-tion	NR	10	ANOVA	P < 0.05	Yes
Grosclaude, Mees, Pinelli, et al., 1997	Cetirizine+ pseudo-ephedrine	Cetirizine	NSS	1.19	NR	230	1.43	NR	226	ANOVA	P < 0.001	Yes
Meran, Morse, and Gibbs, 1990	Acrivastine+ pseudo-ephedrine	Acrivastine	NSS	1.89	NR	40	2.41	NR	40	ANOVA (log-trans-formed scores)	P < 0.01	Yes

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Study	Combination	Mono-therapy	Outcome	Combo mean	Combo SD	Combo n	Mono mean	Mono SD	Mono n	Statistical test	P-value	Possible to calculate ES?
Sussman, Mason, Compton, et al., 1999	Fexofenadine + pseudo-ephedrine	Fexo-fenadine	NSS	0.56	NR	215	0.36	NR	218	ANCOVA	P < 0.0005	Yes
Williams, Hull, McSorley, et al., 1996	Acrivastine+ pseudo-ephedrine	Acrivastine	NSS	2.3	NR	202	2.7	NR	202	ANCOVA	P < 0.001 (1-sided)	Yes
C. Antihistamine + decongestant combination versus decongestant alone, total symptom severity (see also Figure 5)												
Bronsky, Boggs, Findlay, et al., 1995	Loratadine+ pseudo-ephedrine	Pseudo-ephedrine	TSS	6.72	NR	212	5.32	NR	212	ANOVA	P < 0.05	Yes
Dockhorn, Williams, and Sanders, 1996	Acrivastine+ pseudo-ephedrine	Pseudo-ephedrine	TSS	10.3	NR	176	11.8	NR	177	ANCOVA (1-sided)	P = 0.002	Yes
Falliers and Redding, 1980 (study 1)	Azatadine+ pseudo-ephedrine	Pseudo-ephedrine	TSS	70% reduc-tion	NR	30	43% reduc-tion	NR	30	ANOVA	NR	No
Falliers and Redding, 1980 (study 2)	Azatadine+ pseudo-ephedrine	Pseudo-ephedrine	TSS	82% reduc-tion	NR	10	55% reduc-tion	NR	10	ANOVA	NR	No
Grosclaude, Mees, Pinelli, et al., 1997	Cetirizine+ pseudo-ephedrine	Pseudo-ephedrine	TSS	0.85	NR	230	1.14	NR	231	ANOVA	P < 0.001	Yes
Meran, Morse, and Gibbs, 1990	Acrivastine+ pseudo-ephedrine	Pseudo-ephedrine	TSS	1.66	2.25	40	2.92	2.25	40	ANOVA (log-trans-formed scores)	P = 0.014	Yes

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Study	Combination	Mono-therapy	Outcome	Combo mean	Combo SD	Combo n	Mono mean	Mono SD	Mono n	Statistical test	P-value	Possible to calculate ES?
Sussman, Mason, Compton, et al., 1999	Fexofenadine + pseudo-ephedrine	Pseudo-ephedrine	TSS	2.32	NR	215	1.42	NR	218	ANCOVA	P < 0.0001	Yes
Williams, Hull, McSorley, et al., 1996	Acrivastine+ pseudo-ephedrine	Pseudo-ephedrine	TSS	8.5	NR	202	10.8	NR	202	ANCOVA	P < 0.001 (1-sided)	Yes
D. Antihistamine + decongestant combination versus decongestant alone, nasal symptom severity (see also Figure 6)												
Bertrand, Jamart, Marchal, et al., 1996	Cetirizine+ pseudo-ephedrine	Pseudo-ephedrine	Nasal obstruc-tion	Graph	NR	70	Graph	NR	70	CMH (categori-cal)	P = 0.025	No
Bronsky, Boggs, Findlay, et al., 1995	Loratadine+ pseudo-ephedrine	Pseudo-ephedrine	NSS	NR	NR	212	NR	NR	212	ANOVA	P = NS	No
Dockhorn, Williams, and Sanders, 1996	Acrivastine+ pseudo-ephedrine	Pseudo-ephedrine	NSS	3.8	NR	176	4.1	NR	177	ANCOVA (1-sided)	P ~ 0.29	Yes
Falliers and Redding, 1980 (study 1)	Azatadine+ pseudo-ephedrine	Pseudo-ephedrine	NSS	68% reduc-tion	NR	30	62% reduc-tion	NR	30	ANOVA	P ~ 0.72	Yes
Falliers and Redding, 1980 (study 2)	Azatadine+ pseudo-ephedrine	Pseudo-ephedrine	NSS	73% reduc-tion	NR	10	63% reduc-tion	NR	10	ANOVA	P ~ 0.65	Yes
Grosclaude, Mees, Pinelli, et al., 1997	Cetirizine+ pseudo-ephedrine	Pseudo-ephedrine	NSS	1.19	NR	230	1.22	NR	231	ANOVA	P ~ 0.68	Yes

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Study	Combination	Mono-therapy	Outcome	Combo mean	Combo SD	Combo n	Mono mean	Mono SD	Mono n	Statistical test	P-value	Possible to calculate ES?
Meran, Morse, and Gibbs, 1990	Acrivastine+ pseudo-ephedrine	Pseudo-ephedrine	NSS	1.89	NR	40	2.88	NR	40	ANOVA (log-trans-formed scores)	P < 0.01	Yes
Sussman, Mason, Compton, et al., 1999	Fexofenadine+ pseudo-ephedrine	Pseudo-ephedrine	NSS	0.56	NR	215	0.45	NR	218	ANCOVA	P ~ 0.059	Yes
Williams, Hull, McSorley, et al., 1996	Acrivastine+ pseudo-ephedrine	Pseudo-ephedrine	NSS	2.3	NR	202	2.6	NR	202	ANCOVA	P ~ 0.01 (1-sided)	Yes
E. Antihistamine + nasal glucocorticoid versus antihistamine alone, nasal symptom severity (see also Figure 7)												
Backhouse, Finnamore, and Gosden, 1986	Terfenadine+ flunisolide nasal spray	Terfenadine	Nasal con-gestion	1.4	0.7	49	1.8	0.9	50	t-test	P ~ 0.03	Yes
Brooks, Francom, Peel, et al., 1996	Loratadine+ beclo-methasone nasal spray	Loratadine	Nasal con-gestion	NR	NR	20	NR	NR	20	ANOVA	P < 0.001	Yes
Juniper, Kline, Hargreave, et al., 1989	Astemizole+ beclo-methasone nasal spray	Astemizole	Nasal con-gestion	0.322	NR	30	0.594	NR	30	ANOVA	P < 0.05	Yes
Ratner, van Bavel, Martin, et al., 1998	Loratadine+ fluticasone nasal spray	Loratadine	NSS	160	NR	150	232	NR	150	ANOVA	P < 0.01	Yes
Simpson, 1994	Terfenadine+ budesonide nasal spray	Terfenadine	Blocked nose	7	NR	32	14	NR	23	ANOVA	P < 0.05	Yes

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Study	Combination	Mono-therapy	Outcome	Combo mean	Combo SD	Combo n	Mono mean	Mono SD	Mono n	Statistical test	P-value	Possible to calculate ES?
Wilson, Dempsey, Sims, et al., 2000	Cetirizine+ mometasone nasal spray	Cetirizine	NSS	1.8	0.6 (SEM)	14	3.5	0.7 (SEM)	13	MANOVA with pairwise comparison	P ~ 0.07	Yes
F. Antihistamine + nasal glucocorticoid versus nasal glucocorticoid alone, nasal symptom severity (see also Figure 8)												
Benincasa and Lloyd, 1994	Cetirizine+ fluticasone nasal spray	Fluticasone nasal spray	NSS	1.5	1.6	227	1.5	1.4	227	t-test	P = 1.0	Yes
Brooks, Francom, Peel, et al., 1996	Loratadine+ beclo-methasone nasal spray	Beclo-methasone nasal spray	Nasal con-gestion	NR	NR	20	NR	NR	20	ANOVA	P = 0.66	Yes
Drouin, Yang, Horak, et al., 1995	Loratadine+ belclo-methasone nasal spray	Beclo-methasone nasal spray	NSS	66% im-proved	NR	76	59% im-proved	NR	78	ANOVA	P = NS	No
Juniper, Kline, Hargreave, et al., 1989	Astemizole+ beclo-methasone nasal spray	Beclo-methasone nasal spray	Nasal con-gestion	0.322	NR	30	0.319	NR	30	ANOVA	P ~ 0.98	Yes
Purello-D'Ambro-sio, Isola, Ricciardi, et al., 1999	Loratadine+ flunisolide nasal spray	Flunisolide nasal spray	Nasal blockage	19.9%	NR	15	20%	NR	15	ANOVA	P ~ 1.0	Yes
Ratner, van Bavel, Martin, et al., 1998	Loratadine+ fluticasone nasal spray	Fluticasone nasal spray	NSS	160	NR	150	192	NR	150	ANOVA	P < 0.05	Yes
Simpson, 1994	Terfenadine+ budesonide nasal spray	Budesonide nasal spray	Blocked nose	7	NR	32	5.5	NR	30	ANOVA	P ~ 0.58	Yes

Abbreviations: ANCOVA = analysis of covariance; ANOVA = analysis of variance; CMH = Cochran-Mantel-Haenszel; ES = effect size; MANOVA = multivariate analysis of variance; n = number of patients; NR = not reported; NS = not significant; NSS = nasal symptom severity; SD = standard deviation; TSS = total symptom score

Table 19. Summary of meta-analysis of randomized controlled trials comparing combination pharmacotherapy to monotherapy for allergic rhinitis

Combination	Comparator drug	Number of studies	Total number of patients	Outcome evaluated	Summary effect size (95% confidence interval
Antihistamine-decongestant	Antihistamine	7	2298	Total symptom score	0.23 (0.15 to 0.32)
Antihistamine-decongestant	Decongestant	6	2154	Total symptom score	0.31 (0.22 to 0.39)
Antihistamine-decongestant	Antihistamine	8	2233	Nasal symptom score	0.33 (0.24 to 0.41)
Antihistamine-decongestant	Decongestant	7	1806	Nasal symptom score	0.16 (0.07 to 0.25)
Antihistamine-nasal glucocorticoid	Antihistamine	6	559	Nasal symptom score	0.44 (0.27 to 0.61)
Antihistamine-nasal glucocorticoid	Nasal glucocorticoid	6	946	Nasal symptom score	0.9 (-0.4 to 0.22)