

Studies on pollen allergy included in relevant Cochrane reviews but excluded from this review

Study	Reason for exclusion
Armentia-Medina A, Blanco Quiros A, Martin-Santos JM, Alvarez Cuesta E, Moneo Goiri I, Carreira P, <i>et al.</i> Rush immunotherapy with a standardized Bermuda grass pollen extract. <i>Ann Allergy</i> 1989; 63 :127–35	Only 8 out of 30 patients with a history of allergic rhinitis
Caffarelli C, Sensi LG, Marcucci F, Cavagni G. Preseasonal local allergoid immunotherapy to grass pollen in children: a double-blind, placebo-controlled, randomized trial. <i>Allergy</i> 2000; 55 :1142–7	Includes some children with asthma only, not SAR; results not separable for SAR children only
Grammer LC, Shaughnessey MA, Shaughnessy JJ, Patterson R, Grammer LC, Shaughnessey MA, <i>et al.</i> Asthma as a variable in a study of immunotherapy for allergic rhinitis. <i>J Allergy Clin Immunol</i> 1984; 73 :557–60	Placebo and untreated treatment groups combined in the analysis, so not all patients double-blinded
Lizaso Bacaicoa MT, Garcia BE, Gomez B, Zabalegui A, Rodriguez MJ, Tabar AI. [Treatment of allergy to mushrooms.] <i>Anales del Sistema Sanitario de Navarra</i> 2003; 26 (Suppl. 2):129–37	Not all participants had SAR
Meriney DK, Kothari H, Chinoy P, Grieco MH. The clinical and immunologic efficacy of immunotherapy with modified ragweed extract (allergoid) for ragweed hay fever. <i>Ann Allergy</i> 1986; 56 :34–8	Not all patients treatment naive
Pajno GB, Vita D, Parmiani S, Caminiti L, La Grutta S, Barberio G. Impact of sublingual immunotherapy on seasonal asthma and skin reactivity in children allergic to Parietaria pollen treated with inhaled fluticasone propionate. <i>Clin Exp Allergy</i> 2003; 33 :1641–7	Children with SAA only (with or without rhinoconjunctivitis)
Paraskevopoulos G, Jacobson M, Carr V, Calderon M, Till SJ, Francis JN, <i>et al.</i> Grass pollen injection immunotherapy: time course of suppression of allergen-induced late phase skin response. <i>J Allergy Clin Immunol</i> 2005; 115 :S266	No relevant symptom or QoL-related outcomes
Sabbah A, Hassoun S, Lesellin J, Andre C, Sicard H. A double-blind, placebo-controlled trial by the sublingual route of immunotherapy with a standardized grass-pollen extract. <i>Allergy</i> 1994; 49 :309–13	Around half of patients not treatment naive

Other excluded studies (post 2005)

Study	Reason for exclusion
Agostinis F, Foglia C, Bruno ME, Falagiani P. Efficacy, safety and tolerability of sublingual monomeric allergoid in tablets given without up-dosing to pediatric patients with allergic rhinitis and/or asthma due to grass pollen. <i>Eur Ann Allergy Clin Immunol</i> 2009; 41 :177–80	Not double blind
Agostinis F, Forti S, Di BF. Grass transcutaneous immunotherapy in children with seasonal rhinoconjunctivitis. <i>Allergy</i> 2010; 65 :410–11	Transcutaneous administration, not sublingual or subcutaneous

Study	Reason for exclusion
Al Ahmed N, Arifhodzic N, Al Ahmed M. Comparison of clinical efficacy and preventive role between subcutaneous and sublingual immunotherapy in children with seasonal allergic rhinitis. <i>Allergy</i> 2010; 65 (XXIX EAACI Congress of the European Academy of Allergy and Clinical Immunology, London, UK, 5–9 June 2010):1550	Not double blind
Ali I, Goksal K, Ozan B, Gulsen D. Long-term allergen-specific immunotherapy correlates with long-term allergen-specific immunological tolerance. <i>Adv Ther</i> 2008; 25 :29–36	Retrospective evaluation
Alvarez-Cuesta E, Bousquet J, Canonica GW, Durham SR, Mailing HJ, Valovirta E. Standards for practical allergen-specific immunotherapy. <i>Allergy</i> 2006; 61 :1–20	Review
Ariano R, Incorvaia C, La GS, Marcucci F, Pajno G, Sensi L, <i>et al.</i> Safety of sublingual immunotherapy started during the pollen season. <i>Curr Med Res Opin</i> 2009; 25 :103–7	Not double blind
Asturias JA, Ferrer A, Arilla MC, Andreu C, Madariaga B, Martinez A. Tolerance and immunological changes of chemically modified allergen vaccine of <i>Parietaria judaica</i> in accelerated schedules. <i>Clin Exp Allergy</i> 2007; 147 :491–6	Not double blind
Bachert C, Vestenbaek U, Christensen J, Griffiths UK, Poulsen PB. Cost-effectiveness of grass allergen tablet (GRAZAX® for the prevention of seasonal grass pollen induced rhinoconjunctivitis: a Northern European perspective. <i>Clin Exp Allergy</i> 2007; 37 :772–9	CEA
Bartosikova L, Necas J, Bartosik T, Pavlik M, Fránová J. [Contribution of allergen immunotherapy using Phostal in the treatment of seasonal allergic rhinitis (two years of use)]. <i>Ceska Slov Farm</i> 2008; 57 :99–102	Not double blind
Bell MC, Jones SM. Efficacy and safety of 5-grass-pollen sublingual immunotherapy tablets in pediatric allergic rhinoconjunctivitis. <i>Pediatrics</i> 2009; 124 :S152	Comment on other study (Wahn <i>et al.</i> ²⁶)
Berto P, Passalacqua G, Crimi N, Frati F, Ortolani C, Senna G, <i>et al.</i> Economic evaluation of sublingual immunotherapy vs symptomatic treatment in adults with pollen-induced respiratory allergy: the Sublingual Immunotherapy Pollen Allergy Italy (SPAI) study. <i>Ann Allergy Asthma Immunol</i> 2006; 97 :615–21	EE
Berto P, Frati F, Incorvaia C, Cadario G, Contiguglia R, Di Gioacchino M, <i>et al.</i> Comparison of costs of sublingual immunotherapy and drug treatment in grass-pollen induced allergy: results from the SIMAP database study. <i>Curr Med Res Opin</i> 2008; 24 :261–6	Cost comparison
Bochenska-Marciniak M, Tworek D, Kupczyk M, Bogacka E, Kuprys Lipinska I, Kuna P. The effectiveness of allergen immunotherapy depending on the regimen on rhinoconjunctivitis and asthma symptoms in allergy to grass pollen. Abstract. <i>Am J Respir Crit Care Med</i> 2009; 179 [April (Meeting Abstracts):A2781 [Monday, Section B31]	Not placebo controlled
Bordignon V, Burastero SE. Multiple daily administrations of low-dose sublingual immunotherapy in allergic rhinoconjunctivitis. <i>Ann Allergy Asthma Immunol</i> 2006; 97 :158–63	Not double blind
Bowser C, Erstein DP, Silverberg JI, Nowakowski M, Joks R. Correlation of plasma complement split product levels with allergic respiratory disease activity and relation to allergen immunotherapy. <i>Ann Allergy Asthma Immunol</i> 2010; 104 :42–9	Not RCT
Burastero SE, Mistrello G, Paolucci C, Breda D, Roncarolo D, Zanotta S, <i>et al.</i> Clinical and immunological correlates of pre-co-seasonal sublingual immunotherapy with birch monomeric allergoid in patients with allergic rhinoconjunctivitis. <i>Int J Immunopathol Pharmacol</i> 2009; 22 :343–52	Not double blind or RCT
Calderon M, Brandt T. Treatment of grass pollen allergy: focus on a standardized grass allergen extract: Grazax. <i>Therapeut Clin Risk Manag</i> 2008; 4 :1255–60	Review
Calderon MA, Birk AO, Andersen JS, Durham SR. Prolonged preseasonal treatment phase with Grazax sublingual immunotherapy increases clinical efficacy. <i>Allergy</i> 2007; 62 :958–61	Post hoc analysis of three trials

Study	Reason for exclusion
Can D, Tanac R, Demir E, Gulen F, Veral A. Efficacy of pollen immunotherapy in seasonal allergic rhinitis. <i>Pediatr Int</i> 2007; 49 :64–9	Not double blind
Canonica GW, Poulsen PB, Vestenbaek U. Cost-effectiveness of GRAZAX® for prevention of grass pollen induced rhinoconjunctivitis in Southern Europe. <i>Respir Med</i> 2007; 101 :1885–94	Cost-effectiveness study
Ciprandi G, Sormani MP, Cirillo I, Tosca M. Upper respiratory tract infections and sublingual immunotherapy: preliminary evidence. <i>Ann Allergy Asthma Immunol</i> 2009; 102 :262–3	Not an RCT
Corren J, Lemay M, Lin YM, Rozga L, Randolph RK. Clinical and biochemical effects of a combination botanical product (ClearGuard™) for allergy: a pilot randomized double-blind placebo-controlled trial. <i>Nutrition J</i> 2008; 7	Single-dose tablet taken for 3 days only
D'Anneo RW, Arena A, Garnmeri E, Bruno ME, Fallagiani P, Riva G, et al. <i>Parietaria</i> sublingual allergoid immunotherapy with a co-seasonal treatment schedule. <i>Allergol Immunopathol</i> 2008; 36 :79–84	Not double blind
Didier A, Montagut A, Fadef R, Melac M. Immunological Biomarkers of Grass Allergen Tablets in Grass Pollen Rhinoconjunctivitis Patients. <i>J Allergy Clin Immunol</i> 2008; 121 (American Academy of Allergy, Asthma and Immunology, 64th Annual Meeting, Philadelphia, PA, USA, 14–18 March, 2008):Abstract 478	No relevant outcomes reported
Durham SR. Allergen immunotherapy (desensitisation) for allergic diseases. <i>Clin Med</i> 2006; 6 :348–51	Review
Durham SR. Sublingual immunotherapy: reply. <i>J Allergy Clin Immunol</i> 2007; 119 :515–17	Author reply/letter
Durham SR, Birk AO, Andersen JS. Days with severe symptoms: an additional efficacy endpoint in immunotherapy trials. <i>Allergy</i> 2011; 66 :120–3	Secondary analysis of data
Ellis AK, Ratz JD, Chowdry C, Day JH. Controlled allergen challenge clinical trials: impact upon seasonal allergic rhinitis symptoms? [P362]. <i>Ann Allergy Asthma Immunol</i> 2009; 103 :A139	Not seasonal exposure (controlled allergen challenge)
Eng PA, Borer-Reinhold M, Heijnen IAFM, Gnehm HPE. Twelve-year follow-up after discontinuation of preseasonal grass pollen immunotherapy in childhood. <i>Allergy</i> 2006; 61 :198–201	Discontinuation study
Friedlander S, Friedlander AS. Clinical effects of ragweed antigen emulsion. A double-blind study. <i>J Allergy</i> 1962; 33 :412–22	Does not appear to be randomised (comparative study)
Halken S, Agertoft L, Seidenberg J, Bauer C-P, Payot F, Martin-Munoz MF, et al. Five-grass pollen 300-IR SLIT tablets: efficacy and safety in children and adolescents. <i>Pediatr Allergy Immunol</i> 2010; 21 :970–6	Further report of Wahn et al. ²⁶ (included in Cochrane review of SLIT); appears to contain no new data, although some more detailed analysis of AE data
Horak F, Ziegelmayer P, Ziegelmayer R, Lemell P, Devillier P, Montagut A et al. Early onset of action of a 5-grass-pollen 300-IR sublingual immunotherapy tablet evaluated in an allergen challenge chamber. <i>J Allergy Clin Immunol</i> 2009; 124 :471–7	Symptoms not measured during natural exposure (allergen challenge chamber)
Horiguchi S, Okamoto Y, Yonekura S, Okawa T, Yamamoto H, Kunii N, et al. A randomized controlled trial of sublingual immunotherapy for Japanese cedar pollinosis. <i>Int Arch Allergy Immunol</i> 2008; 146 :76–84	Not double blind
Howland WC, Hamilton RG, Holdich T. Effect of ultra short course subcutaneous immunotherapy on specific IgG and IgE levels compared with placebo in patients with ragweed pollen-allergic rhinoconjunctivitis. Abstract 17. <i>Ann Allergy Asthma Immunol</i> 2009; 103 :A23	No relevant outcomes reported
Jacobsen L, Niggemann B, Dreborg S, Ferdousi HA, Halken S, Host A, et al. Specific immunotherapy has long-term preventive effect of seasonal and perennial asthma: 10-year follow-up on the PAT study. <i>Allergy</i> 2007; 62 :943–8	Open follow-up study of RCT

Study	Reason for exclusion
James LK, Shamji MH, Walker SM, Wilson DR, Wachholz PA, Francis JN, <i>et al.</i> Long-term tolerance after allergen immunotherapy is accompanied by selective persistence of blocking antibodies. <i>J Allergy Clin Immunol</i> 2011; 127 :509–16	Discontinuation study
Jutel M, Cromwell O. Clinical results from vaccination with recombinant grass pollen allergens. <i>Clin Dev Immunol</i> 2006; 13 :389–94.	Further analysis of Jutel 2005, included in Cochrane review
Keiding H, Jorgensen KP. A cost-effectiveness analysis of immunotherapy with SQ allergen extract for patients with seasonal allergic rhinoconjunctivitis in selected European countries. <i>Curr Med Res Opin</i> 2007; 23 :1113–20	Cost-effectiveness analysis
Keith P. Significant improvements in quality of life following mpl-adjuvanted ultra short course subcutaneous immunotherapy (uSCIT) in patients with seasonal grass pollen allergy. Abstract 219. <i>J Allergy Clin Immunol</i> 2009; 123 :S61	No relevant outcomes reported
Keskin O, Tuncer A, Adalioglu G, Sekerel BE, Sackesen C, Kalayci O. The effects of grass pollen allergoid immunotherapy on clinical and immunological parameters in children with allergic rhinitis. <i>Pediatr Allergy Immunol</i> 2006; 17 :396–407	Not double blind
Klunker S, Saggar LR, Seyfert-Margolis V, Asare AL, Casale TB, Durham SR, <i>et al.</i> Combination treatment with omalizumab and rush immunotherapy for ragweed-induced allergic rhinitis: Inhibition of IgE-facilitated allergen binding. <i>J Allergy Clin Immunol</i> 2007; 120 :688–95	No relevant outcomes reported
Kopp MV, Hamelmann E, Zielen S, Kamin W, Bergmann KC, Sieder C, <i>et al.</i> Combination of omalizumab and specific immunotherapy is superior to immunotherapy in patients with seasonal allergic rhinoconjunctivitis and co-morbid seasonal allergic asthma. <i>Clin Exp Allergy</i> 2009; 39 :271–9	Comparison of SIT plus omalizumab vs SIT only
Larenas-Linnemann D. Briefings from ACAAI 2008 annual meeting. The Annual Scientific Meeting of the American College of Allergy, Asthma and Immunology, Seattle, WA, USA, 6–11 November, 2008. <i>Therapy</i> 2009; 6 :279–83	Review
Leonardi S, Spicuzza L, La RM. High-dose sublingual immunotherapy in children at 8-year follow-up. <i>Clin Exp Allergy</i> 2009; 102 :259–60	Discontinuation study
Malling HJ, Montagut A, Melac M, Patriarca G, Panzner P, Seberova E, <i>et al.</i> Efficacy and safety of 5-grass pollen sublingual immunotherapy tablets in patients with different clinical profiles of allergic rhinoconjunctivitis. <i>Clin Exp Allergy</i> 2009; 39 :387–93	Subgroup analysis of included RCTs
Martinez-Canavate Burgos A, Vallenzuella-Soria A, Rojo-Hernandez A. Immunotherapy with <i>Alternaria alternata</i> : present and future. <i>Allergol Immunopathol</i> 2007; 35 :259–63	Review
Martínez Cócera C, Sastre J, Cimarra M, Quirce S, Fernández Rivas M, Enríquez Matas A, <i>et al.</i> Immunotherapy with a <i>Phleum pratense</i> allergen extract induces an immune response to a grass-mix allergen extract. <i>J Investig Allergol Clin Immunol</i> 2010; 20 :13–19.	Not double blind
Mauro M, Russello M, Incorvaia C, Gazzola GB, Di Cara G, Frati F. Comparison of efficacy, safety and immunologic effects of subcutaneous and sublingual immunotherapy in birch pollinosis: a randomized study. <i>Eur Ann Allergy Clin Immunol</i> 2007; 39 :119–22	Not double blind
McCormack PL, Wagstaff AJ. Ultra-short-course seasonal allergy vaccine (Pollinex® Quattro). <i>Drugs</i> 2006; 66 :931–8	Review
Milani M, Leonardi A, Pozzan M, Pecora S. Two years specific sublingual immunotherapy with alternative extracts. Abstract 493. <i>J Allergy Clin Immunol</i> 2008; 21 :S127	Not double blind
Mösger R, Graute V, Christ H, Sieber HJ, Wahn U, Niggemann B. Safety of ultra-rush titration of sublingual immunotherapy in asthmatic children with tree-pollen allergy. <i>Pediatr Allergy Immunol</i> 2010; 21 :1135–8	Report only on subgroup of children with asthma
Naspitz CK, Warner JO. Children are pharmaco-therapeutic orphans. <i>Pediatr Allergy Immunol</i> 2010; 21 :249–50	Editorial

Study	Reason for exclusion
Nasser S, Vestenbaek U, Beriot MA, Poulsen PB. Cost-effectiveness of specific immunotherapy with Grazax in allergic rhinitis co-existing with asthma. <i>Allergy</i> 2008; 63 :1624–9	Cost-effectiveness study
Niederberger V, Reisinger J, Valent P, Krauth MT, Pauli G, van HM, et al. Vaccination with genetically modified birch pollen allergens: immune and clinical effects on oral allergy syndrome. <i>J Allergy Clin Immunol</i> 2007; 119 :1013–16	Relates to food allergy
Nieminen K, Valovirta E, Savolainen J. Clinical outcome and IL-17, IL-23, IL-27 and FOXP3 expression in peripheral blood mononuclear cells of pollen-allergic children during sublingual immunotherapy. <i>Pediatr Allergy Immunol</i> 2010; 21 :E174–84	Secondary analysis of data
Nunes C, Ladeira S. Pre-seasonal Specific Immunotherapy in rhino-conjunctivitis versus placebo. <i>J Allergy Clin Immunol</i> 2010; 125 :AB236	Not double blind
Nunes C, Ladeira S. Pre-seasonal specific short-term immunotherapy versus placebo in seasonal rhino-conjunctivitis. <i>Rev Port Imunoalergol</i> 2010; 18 :39–56	Not double blind
Panzner P, Petras M, Sykora T, Lesna IK, Liska M. Both sublingual and supralingual routes of administration are effective in long-term allergen-specific immunotherapy. <i>Allergy Asthma Proc</i> 2011; 32 :142–50	Not double blind
Passali D, Mösges R, Passali GC, Passali FM, Ayoko G, Bellussi L. Safety, tolerability and efficacy of sublingual allergoid immunotherapy with three different shortened up-dosing administration schedules. <i>Acta Otorhinolaryngol Ital</i> 2010; 30 :131–7	Not double blind
Patel P, Salapatek AMF. Pollinex® Quattro: a novel and well-tolerated, ultra short-course allergy vaccine. <i>Expert Rev Vaccine</i> 2006; 5 :617–29	Review
Penagos M, Compalati E, Tarantini F, Baena-Cagnani R, Huerta J, Passalacqua G, et al. Efficacy of sublingual immunotherapy in the treatment of allergic rhinitis in pediatric patients 3 to 18 years of age: a meta-analysis of randomized, placebo-controlled, double-blind trials. <i>Ann Allergy Asthma Immunol</i> 2006; 97 :141–8	Review
Petersen KD, Gyrd-Hansen D, Linneberg A, Dahl R, Larsen JN, Lowenstein H, et al. Willingness to pay for allergy-vaccination among Danish patients with respiratory allergy. <i>Int J Technol Assess Health Care</i> 2010; 26 :20–9.	Economic study
Pfaar O, Klimek L, Fischer I, Sieber J, Amoroso S, Aguilar CM, et al. Safety of two cluster schedules for subcutaneous immunotherapy in allergic rhinitis or asthma patients sensitized to inhalant allergens. <i>Int Arch Allergy Immunol</i> 2009; 150 :102–8	Open-label study (safety)
Piconi S, Trabattoni D, Rainone V, Borgonovo L, Passerini S, Rizzardini G, et al. Immunological effects of sublingual immunotherapy: clinical efficacy is associated with modulation of programmed cell death ligand 1, IL-10, and IgG4. <i>J Immunol</i> 2010; 185 :7723–30	Not double blind. Different treatment schedules compared
Pilette C, Nouri-Aria KT, Jacobson MR, Wilcock LK, Detry B, Walker SM, et al. Grass pollen immunotherapy induces an allergen-specific IgA2 antibody response associated with mucosal TGF-beta expression. <i>J Immunol</i> 2007; 178 :4658–66	No relevant outcomes reported
Pokladnikova J, Krcmova I, Vlcek J. Economic evaluation of sublingual vs subcutaneous allergen immunotherapy. <i>Clin Exp Allergy</i> 2008; 100 :482–9	EE based on open-label study
Pozzan M, Milani M. Efficacy of sublingual specific immunotherapy in patients with respiratory allergy to <i>Alternaria alternata</i> : A randomised, assessor-blinded, patient-reported outcome, controlled 3-year trial. <i>Curr Med Res Opin</i> 2010; 26 :2801–6	Not double blind
Pree I, Reisinger J, Focke M, Vrtala S, Pauli G, van HM, et al. Analysis of epitope-specific immune responses induced by vaccination with structurally folded and unfolded recombinant Bet v 1 allergen derivatives in man. <i>J Immunol</i> 2007; 179 :5309–16	No relevant outcomes (in vitro study)
Purohit A, Niederberger V, Kronqvist M, Horak F, Gronneberg R, Suck R, et al. Clinical effects of immunotherapy with genetically modified recombinant birch pollen Bet v 1 derivatives. <i>Clin Exp Allergy</i> 2008; 38 :1514–25	Not standard SIT

Study	Reason for exclusion
Railey MD, Adair MA, Burks AW. Allergen immunotherapy for allergic rhinitis. <i>Curr Allergy Asthma Rep</i> 2008; 8 :1–3	Comment
Rak S, Heinrich C, Scheynius A. Comparison of nasal immunohistology in patients with seasonal rhinoconjunctivitis treated with topical steroids or specific allergen immunotherapy. <i>Allergy</i> 2005; 60 :643–9	Not placebo controlled with rescue medication (SIT + placebo steroids vs placebo SIT + steroids)
Reha CM, Ebru A. Specific immunotherapy is effective in the prevention of new sensitivities. <i>Allergol Immunopathol</i> 2007; 35 :44–51	Not double blind
Roberts G, Hurley C, Turcanu V, Lack G. Grass pollen immunotherapy as an effective therapy for childhood seasonal allergic asthma. <i>J Allergy Clin Immunol</i> 2006; 117 :263–8	SAA, not rhinitis
Roder E, Berger MY, de Groot H, van Wijk RG. Sublingual immunotherapy in youngsters: adherence in a randomized clinical trial. <i>Clin Exp Allergy</i> 2008; 38 :1659–67	Analysis of adherence data from trial reported elsewhere
Rodriguez F, Boquete M, Ibanez MD, Torre-Martinez F, Tabar AI. Once daily sublingual immunotherapy without uposing: a new treatment schedule. <i>Int Arch Allergy Immunol</i> 2006; 140 :321–6	Results for patients with SAR not separable
Rolinck-Werninghaus C, Keil T, Kopp M, Zielen S, Schauer U, von Berg A, et al. Specific IgE serum concentration is associated with symptom severity in children with seasonal allergic rhinitis. <i>Allergy</i> 2008; 63 :1339–44	RCT of omalizumab vs placebo
Romaniuk LI, DuBuske IV, DuBuske LM. Comparative efficacy of subcutaneous immunotherapy, sublingual immunotherapy and combined subcutaneous and sublingual immunotherapy in patients with seasonal allergic rhinitis and cross-reactive food allergy. Abstract 82. <i>J Allergy Clin Immunol</i> 2009; 123 :S25	Results for patients with SAR with not separable from those with food allergy
Rossi RE, Monasterolo G, Coco G, Silvestro L, Operti D. Evaluation of serum IgG4 antibodies specific to grass pollen allergen components in the follow up of allergic patients undergoing subcutaneous and sublingual immunotherapy. <i>Vaccine</i> 2007; 25 :957–64	Not double blind
Sager A, Braeutigam M, Badorrek P, Krug N. Efficacy of a rush immunotherapy with a depigmented polymerized extract of grass pollen using an environmental challenge chamber (ECC). Abstract 485. <i>J Allergy Clin Immunol</i> 2008; 21 :S125	No natural exposure-allergen chamber
Serra P, Martino M, Muggianu E, Corrias C, Manconi P, Milani M. Efficacy of SQ-standardised grass allergy immunotherapy tablet treatment on basophil activation test in subjects with grass pollen induced rhinoconjunctivitis. <i>Allergy</i> 2010; 65 (XXIX, EAACI, Congress of the European Academy of Allergy and Clinical Immunology, London, UK, 5–9 June 2010):684	No relevant outcomes
Simons FER, HayGlass KT. Immunotherapy with a ragweed vaccine [2]. <i>New Eng J Med</i> 2007; 356 :86–7	Correspondence
Sjolin I, Haugaard L, Kopp T, Jansen A, Brüning H, Smedegaard AB, et al. High patient compliance on a once daily treatment regimen with the hay fever drug Grazax. <i>J Allergy Clin Immunol</i> 2008; 121 (American Academy of Allergy, Asthma and Immunology 64th Annual Meeting, Philadelphia, PA, USA, 14–18 March, 2008, S128):Abstract 495	Not double blind
Skripak J, Wood RA. A prospective, randomized, double-blind, placebo-controlled multi-centre study on the efficacy and safety of sublingual immunotherapy (SLIT) in children with seasonal allergic rhinoconjunctivitis to grass pollen. Commentary. <i>Pediatrics</i> 2006; 118 :S22	Comment on another study
Stelmach I, Kaczmarek-Wozniak J, Majak P, Olszowiec-Chlebna M, Jerezynska J. Efficacy and safety of high-doses sublingual immunotherapy in ultra-rush scheme in children allergic to grass pollen. <i>Clin Exp Allergy</i> 2009; 39 :401–8	Patients with SAA
Stosovic R, Bogic M, Tomic-Spiric V. Long-term efficacy and safety of sublingual immunotherapy in seasonal allergic rhinitis. <i>Allergy</i> 2008; 63 (XXVII EAACI, Congress of the European Academy of Allergology and Clinical Immunology, Barcelona, Spain, 7–11 June, 2008):Abstract 1065	Not double blind

Study	Reason for exclusion
Thien F. Sublingual immunotherapy with a grass allergen tablet improved symptoms and quality of life in allergic rhinoconjunctivitis. <i>Evid Base Med</i> 2006; 11 :173	Commentary
Wahn U, Bauer C, Agertoft L, Melac M, Le Gall M. Agreement of efficacy assessments for five grass pollen sublingual immunotherapy (SLIT) tablets in children and adolescents with grass pollen rhinoconjunctivitis and with or without mild asthma. Abstract 214. <i>J Allergy Clin Immunol</i> 2009; 123 :S59	Secondary analysis of data
Williams A, Henzgen M, Rajakulasingam K, Williams A, Henzgen M, Rajakulasingam K. Additional benefit of a third year of specific grass pollen allergoid immunotherapy in patients with seasonal allergic rhinitis. <i>Eur Ann Allergy Clin Immunol</i> 2007; 39 :123–6	Open-label continuation of trial
Zuberbier T, Sussman G. Epidemiological characteristics and allergen sensitisation patterns in subjects with intermittent allergic rhinitis in the international ACCEPT1 study in association with GA2LEN. <i>Allergy</i> 2008; 63 (XXVII EAACI, Congress of the European Academy of Allergology and Clinical Immunology, Barcelona, Spain, 7–11 June 2008):Abstract	Not SIT

Unobtainable studies (reference incorrect or inaccurate and therefore unable to locate, or British Library unable to supply at the time of ordering)

Arbesman CE. Hyposensitization therapy including repository: a double-blind study *J Allergy Clin Immunol* 1964;**35**:12–17

Arbesman CE, Reisman RE, Kunz ML. Clinical and immunologic evaluation of a purified fraction of ragweed pollen (delta). A double-blind study. *J Allergy Clin Immunol* 1965;**36**:29–38

Ariano R, Panzani RC, Augeri G. Efficacy and safety of oral immunotherapy in respiratory allergy to *Parietaria judaica* pollen. A double-blind study. *J Investig Allergol Clin Immunol* 1998;**8**:155–60

Bachert C. New Clinical Documentation on Alk Grass Allergen Tablet. *Drugs of Today* 2008;**44**:57–60

Basomba A. [Immunotherapy in pollenosis: a double-blind study.] *Rev Espanol Alergol Inmunol Clin* 1991;**6**:22–7

Corthay P, Gumowski PI, Bodmer R, Clot B. Efficacy of sublingual versus subcutaneous immunotherapy to pollen allergens after 3 consecutive years of treatment. Annual Meeting of the Swiss Society for Allergology and Immunology, 1996

Durham SR, Hamid QA. The effect of immunotherapy on allergen induced late responses. *Arbeiten aus dem Paul Ehrlich Institut zu Frankfurt a M* 1997;**33**–9

Frank E, Williams A, Cromwell O, Atkinson P, Rajakulasingam K. Effectiveness of a pre-seasonal allergoid immunotherapy in patients with seasonal allergic rhinitis due to grass pollen. *J Allergy Clin Immunol* 2001;**107**:S260 POSTER no. 851 (Tuesday 20 March). American Association of Asthma, Allergy & Immunology, 57th Annual Meeting, 2001

Franklin W, Lowell FC. Comparison of two dosages of ragweed extract in the treatment of pollenosis. *J Am Med Assoc* 1967;**201**:915–17

Hordijk GJ, Antvelink JB, Luwema RA. A placebo controlled study on the efficacy of sublingual immunotherapy with standardized grass pollen allergens (Oralgen). XVI Congress of the European Rhinologic Society; VIII Congress of the International Rhinologic Society, Ghent, Belgium, 7–13 June 1996:150

Khinchi MS, Poulsen LK, Carat F, Andre C, Malling HJ. Clinical efficacy of sublingual-swallow and subcutaneous immunotherapy in patients with allergic rhinoconjunctivitis due to birch pollen. A double-blind, double-dummy placebo-controlled study. *Allergy* 2000;**54**:24

Klimek L, Pfaar O, Sieber J, Amoroso S, Carmen MA, Sges R. A prospective trial to evaluate the safety of two cluster regimens in subcutaneous immunotherapy in patients with allergic rhinitis and mild or moderate allergic asthma to grass pollen, tree pollen or mites. *Allergy* 2006;**61**:Abstract (XXV Congress of the European Academy of Allergology and Clinical Immunology)

Leonardi S, Arena A, Bruno ME, Cannaò PM, D'Anneo RW, Falagiani P, et al. Olea sublingual allergoid immunotherapy administered with two different treatment regimens. *Allergy Asthma Proc* 2010;**31**:e25–9

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- Matuska J. Cluster immunotherapy. SR theophylline in prevention of systemic reactions. *Eur Respir J* 2001;**18**:430
- Monzon S, Venturini M, Colas C, Lezaun A, Casanovas M, Reichelt C, et al. Specific immunotherapy with modified *Salsola kali* extract: preliminary results. *Alergol Immunol Clin* 2003;**18**:20–4
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- Rak S, Stender A, Dahl R. Confirmed clinical safety and efficacy of grass allergen tablets. *Eur Respir J* 2005;**26** (15th European Respiratory Society Annual Congress, Copenhagen, Denmark, 17–21 September, 2005):Abstract
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- Torres Lima M, Wilson DR, Pitkin L, Roberts A, Nouri-Aria KT, Jacobson M, et al. Grass pollen immunotherapy (SLIT) for seasonal rhinoconjunctivitis: a randomised controlled trial. *Clin Exp Allergy* 2001;**31**:42
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- Yuksel H, Tanac R, Gousseinov A, Demir E. Sublingual immunotherapy and influence on urinary leukotrienes in seasonal pediatric allergy. *J Investig Allergol Clin Immunol* 1999;**9**:305–13
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Studies not identified in Cochrane reviews

Subcutaneous immunotherapy

Reference	Details
Bachert C. [Influence of specific immunotherapy on inflammation of the nasal mucosa.] <i>Allergy J</i> 1997; 6 :157–8	Appears to be report of study reported elsewhere but unclear. Thirty-four patients. Patient-related outcomes reported
Crimi N, Li GF, Mangano G, Paolino G, Mastruzzo C, Vancheri C, <i>et al.</i> A randomized, controlled study of specific immunotherapy in monosensitized subjects with seasonal rhinitis: effect on bronchial hyperresponsiveness, sputum inflammatory markers and development of asthma symptoms. <i>Ann Ital Med Int</i> 2004; 19 :98–108	Possible duplicate of studies listed as excluded in Cochrane review (non-relevant outcomes.) In this study, SSs and MSs are presented. Thirty patients
Dreborg S, Agrell B, Foucard T, Kjellman NI, Koivikko A, Nilsson S. A double-blind, multicenter immunotherapy trial in children, using a purified and standardized <i>Cladosporium herbarum</i> preparation. Clinical results. <i>Allergy</i> 1986; 41 :131–40	Duplicate of Karlsson <i>et al.</i> 1986 listed as excluded in Cochrane review, as not SAR. Study is in <i>Cladosporium herbarum</i> , a mould; authors mention July–September as peak mould season, so does appear to have seasonal aspect
Durham SR, Varney V, Gaga M, Frew AJ, Jacobson M, Kay AB. Immunotherapy and allergic inflammation. <i>Clin Exp Allergy</i> 1991; 21 :206–10	Duplicate of study included in Cochrane review (Varney 1991)
Frew AJ, Powell RJ, Durham SR. Alutard SQ grass demonstrates clinical efficacy in subjects with seasonal allergic rhinoconjunctivitis in a large-scale double-blind placebo controlled study of specific allergy vaccination (the AVANZ study). Abstract 317. <i>J Allergy Clin Immunol</i> 2004; 113 :S105	Abstract of study included in Cochrane review (Frew <i>et al.</i> 2006 ¹⁶¹)
Horst M, Hejjaoui A, Horst V, Michel FB, Bousquet J, Horst M <i>et al.</i> Double-blind, placebo-controlled rush immunotherapy with a standardized <i>Alternaria</i> extract. <i>J Allergy Clin Immunol</i> 1990; 85 :460–72	Appears to be relevant RCT in 24 patients. Unclear if published elsewhere
Jean F, Bousquet J, Hejjaoui A, Guerin B, Maasch HJ, Michel FB. Double-blind placebo controlled rush immunotherapy trial with grass-pollen allergen and allergoid. <i>J Allergy Clin Immunol</i> 1985; 75 :164	Abstract. Likely duplicate of study included in Cochrane review
Munro-Ashman D, McEwen H, Feinberg JG. The patient self (P-S) test. Demonstration of a rise in blocking antibodies after treatment with Allpyral. <i>Int Arch Allergy Appl Immunol</i> 1971; 40 :448–53	Appears to be relevant RCT in 21 patients
Polosa R, Li Gotti F, Mangano G, Paolino G, Mastruzzo C, Vancheri C, <i>et al.</i> Effect of immunotherapy on asthma progression, BHR and sputum eosinophils in allergic rhinitis. <i>Allergy</i> 2004; 59 :1224–8	Duplicate publication of Crimi <i>et al.</i> 2004, listed above
Rozniecka M, Kowalski M, Grzegorzczak J, Wojciechowska B, Sliwinska-Kowalska M, Rozniecki J. [Characteristics of hay fever during pollen season with regard to the influence of specific immunotherapy. I. Clinical course and biochemical changes in nasal lavage.] <i>Pneumonol Alergol Pol</i> 1995; 63 :135–43	Appears to be relevant RCT in 27 patients

Sublingual immunotherapy

Reference	Details
Amar SM, Harbeck R, Sills M, O'Brien H, Nelson HS. The response to sublingual immunotherapy with grass pollen extract administered as a single extract or as part of a multi-allergen extract in patients with seasonal allergic rhinitis caused by grass pollen. <i>J Allergy Clin Immunol</i> 2009; 123 (American Academy of Allergy, Asthma and Immunology 65th Annual Meeting. Washington, USA, 13–17 March 2009):Abstract 277	Further abstract of Amar 2009 included in Cochrane review
Ariano R, Panzani RC, Mistrello G. Efficacy of sublingual coseasonal immunotherapy with a monomeric allergoid in Cupressaceae pollen allergy: preliminary data. <i>Eur Ann Allergy Clin Immunol</i> 2005; 37 :103–8	Not identified in Cochrane review; 30 patients
Dahl R, Kapp A, Colombo G, de Monchy JGR, Rak S, Emminger W, <i>et al.</i> Sublingual grass allergen tablet immunotherapy provides sustained clinical benefit with progressive immunologic changes over 2 years. <i>J Allergy Clin Immunol</i> 2008; 121 :512–18	Further publication of GT–08 trial; not listed as included study, but mentioned in text
de Blay F, Barnig C, Kanny G, Purohit A, Leynadier F, De Lara JMT, <i>et al.</i> Sublingual-swallow immunotherapy with standardized 3-grass pollen extract: a double-blind, placebo-controlled study. <i>Ann Allergy Asthma Immunol</i> 2007; 99 :453–61	Full text of abstract included in Cochrane review
Horak F, Siegfried J, Worm M, Melac M, Didier A. Clinical efficacy of sublingual immunotherapy (SLIT) with grass pollen tablets in patients with rhinoconjunctivitis throughout the pollen season and at peak pollen. <i>Allergy</i> 2008; 63 (XXVII EAACI Congress of the European Academy of Allergology and Clinical Immunology, Barcelona, Spain, 7–11 June 2008):Abstract 586	Abstract of Didier <i>et al.</i> ²⁴ included in Cochrane review
Horiguchi S, Okamoto Y, Yonekura S, Okawa T, Kunii N, Yamamoto H, <i>et al.</i> [Lowered effectiveness of immunotherapy for cypress pollinosis by using Japanese cedar pollen extract.] <i>Jp J Allergol</i> 2008; 57 :558–61	Japanese paper identified as likely to be included after preliminary translation. Full translation not obtained
Larsen TH, Poulsen LK, Melac M, Combebias A, Andre C, Malling HJ. Safety and tolerability of grass pollen tablets in sublingual immunotherapy: a phase-1 study. <i>Allergy</i> 2006; 61 :1173–6	Not identified in Cochrane review; 30 patients
Moreno-Ancillo A, Moreno C, Ojeda P, Dominguez C, Barasona MJ, Garcia-Cubillana A, <i>et al.</i> Efficacy and quality of life with once-daily sublingual immunotherapy with grasses plus olive pollen extract without uposing. <i>J Investig Allergol Clin Immunol</i> 2007; 17 :399–405	Not identified in Cochrane review; 105 patients
Mösger R, Brüning H, Hessler HJ, Götz G, Knaussmann HG. Sublingual immunotherapy in pollen-induced seasonal rhinitis and conjunctivitis: a randomized controlled trial. <i>Acta Dermatovenerol Alp Panonica Adriat</i> 2007; 16 :143–8	Not identified in Cochrane review; 105 patients
Palma-Carlos AG, Santos AS, Branco-Ferreira M, Pregal AL, Palma-Carlos ML. Monoid sublingual immunotherapy. <i>Eur Ann Allergy Clin Immunology</i> 2006; 38 :87–9	Likely duplicate publication of Palma-Carlos 2006 in Cochrane review
Rak S, Yang WH, Pedersen MR, Durham SR. Once-daily sublingual allergen-specific immunotherapy improves quality of life in patients with grass pollen-induced allergic rhinoconjunctivitis: A double-blind, randomised study. <i>Qual Life Res</i> 2007; 16 :191–201	Report of Durham 2006 included in Cochrane review
Roder E, Berger MY, Hop WCJ, de GH, Gerth van Wijk R. Efficacy of sublingual immunotherapy (SLIT) with grass pollen allergen in children and adolescents. <i>J Allergy Clin Immunol</i> 2006; 117 (American Academy of Allergy, Asthma and Immunology 62nd Annual Meeting, Miami Beach, FL, USA, 3–7 March 2006:S89): Abstract 346	Duplicate of study in Cochrane review
Sieber J, Merk H, Ott H. Seasonal sublingual immunotherapy is efficacious in allergic rhinitis from the first treatment season on also under high grass pollen exposure: the ECRIT study. <i>Allergy</i> 2008; 63 (XXVII EAACI Congress of the European Academy of Allergology and Clinical Immunology, Barcelona, Spain, 7–11 June 2008):Abstract 597	Abstract of included study

Reference	Details
Valovirta E, Ljorring C, Jacobsen L. Double-blind, placebo-controlled dose-response study of clinical efficacy and safety of sublingual immunotherapy (SLIT) with tree pollen extract in children suffering from tree pollen induced hay fever with or without SAA. <i>Allergy</i> 2003; 58 (XXII Congress of the European Academy of Allergology and Clinical Immunology)	Likely abstract of included study
Worm M. Efficacy and tolerability of high dose sublingual immunotherapy in patients with rhinoconjunctivitis. <i>Eur Ann Allergy Clin Immunology</i> 2006; 38 :355–60	Not identified in Cochrane review; 188 patients.

Studies excluded from Cochrane review but meeting our inclusion criteria (not included in this report as not part of update)

Subcutaneous immunotherapy

Reference	Details
Polosa R, Li Gotti F, Mangano G, Mastruzzo C, Pistorio MP, Crimi N. Monitoring of seasonal variability in bronchial hyper-responsiveness and sputum cell counts in non-asthmatic subjects with rhinitis and effect of specific immunotherapy. <i>Clin Exp Allergy</i> 2003; 33 :873–81	Excluded from Cochrane review as 'other outcomes investigated'. Do give symptom/medication scores, but not usable in meta-analysis
Varney VA, Hamid QA, Gaga M, Ying S, Jacobson M, Frew AJ, et al. Influence of grass-pollen immunotherapy on cellular infiltration and cytokine messenger-RNA expression during allergen-induced late-phase cutaneous responses. <i>J Clin Invest</i> 1993; 92 :644–51	Excluded from Cochrane review as 'other outcomes investigated'. Do give symptom/medication scores, but not usable in meta-analysis
Weyer A, Donat N, L'Heritier C, Juilliard F, Pauli G, Soufflet B, et al. Grass pollen hyposensitization versus placebo therapy. I. Clinical effectiveness and methodological aspects of a pre-seasonal course of desensitization with a four-grass pollen extract. <i>Allergy</i> 1981; 36 :309–17	Excluded from Cochrane review as different immunotherapy preparations used. 'The first five doses were administered as aqueous preparations, whereas the 12 subsequent higher doses were injected in their AlOH ₃ -adsorbed form in order to avoid systemic reactions'
Fontana VJ, Holt LE Jr, Mainland D, Fontana VJ, Holt LEJ, Mainland D. Effectiveness of hyposensitization therapy in ragweed hay-fever in children. <i>J Am Med Assoc</i> 1966; 195 :985–92	Excluded from Cochrane review as not standardised allergen extract

Sublingual immunotherapy

Reference	Details
Okubo K, Gotoh M, Fujieda S, Okano M, Yoshida H, Morikawa H, et al. A randomized double-blind comparative study of sublingual immunotherapy for cedar pollinosis. <i>Allergol Int</i> 2008; 57 :265–75	Excluded from Cochrane review as 'additional data not available'. States that 1–20 drops of extract dropped on to pieces of bread, which were held sublingually for 2 minutes
Van Niekerk CH, De Wet JI, Van Niekerk CH, De Wet JI. Efficacy of grass-maize pollen oral immunotherapy in patients with seasonal hay-fever: a double-blind study. <i>Clin Allergy</i> 1987; 17 :507–13	Excluded from Cochrane review as 'not SLIT'; states in paper that 1–15 drops taken sublingually, kept in the mouth for at least 1 minute then swallowed