Allergic Rhinitis and its Impact on Asthma

PROGETTO MONDIALE ARIA. AGGIORNAMENTO ITALIA

Linee-Guida Italiane

Firenze, 8 Marzo 2018

GARD Participant

ALLERGIC RHINITIS AND ITS IMPACT ON ASTHMA AGGIORNAMENTO ITALIA 2018

Coordinatori :
Carlo Lombardi, Giovanni Passalacqua

S.Arasi
I. Baiardini,
R. Bernardini
B. Bilò
S. Bonini
G.W. Canonica
A.G. Caviglia
E. Compalati
M. Cottini
M. Crivellaro
M. Duse
A. Fiocchi
I. Folletti
M. Gelardi
E. Heffler
C. Incorvaia
A. Infantino
M. Landi
G. Leo
E. Maggi
G. Melioli
M. Milanese
A. Musarra
E. Nettis
G. Pajno
G. Pala
D. Peroni
E. Ridolo
G. Rolla
O. Rossi
E. Savi
G. Senna
F. Tesi
M. Triggiani
M. Uberti
M. T. Zedda

Firenze, 8 Marzo 2018

Le ragioni per creare linee guida per la gestione della rinite allergica

- La rinite allergica è un problema sanitario globale che colpisce dal 5 al 35 % della popolazione.
- La sua prevalenza è tendenzialmente in aumento.
- Pur non essendo sempre una malattia grave, la rinite influisce sulla vita sociale ed altera le prestazioni scolastiche e lavorative.
- I costi socio sanitari sono rilevanti.
- La rinite si associa spesso all'asma e costituisce fattore di rischio per la sua insorgenza. Oltre all'asma possono associarsi alla rinite numerose altre co-morbilità.
- La divulgazione e l'applicazione delle linee guida sono in grado di migliorare la gestione dei pazienti.

DEFINIZIONE-PATOGENESI

CLASSIFICAZIONE

EPIDEMIOLOGIA

CLINICA E DIAGNOSTICA

IMPATTO SULLA QoL

TRATTAMENTO

IMPATTO SULL'ASMA

ASPETTI PARTICOLARI

DEFINIZIONE DI RINITE ALLERGICA

Patologia della mucosa nasale indotta da un' infiammazione IgE-mediata conseguente all'esposizione allergenica.

E' caratterizzata clinicamente da rinorrea, starnuti, prurito e ostruzione, reversibili spontaneamente o in seguito a terapia.

RICONOSCIMENTO DALLA MEDICINA INTERNA

The NEW ENGLAND JOURNAL of MEDICINE

CLINICAL PRACTICE

Caren G. Solomon, M.D., M.P.H., *Editor*

Allergic Rhinitis

Lisa M. Wheatley, M.D., M.P.H., and Alkis Togias, M.D.

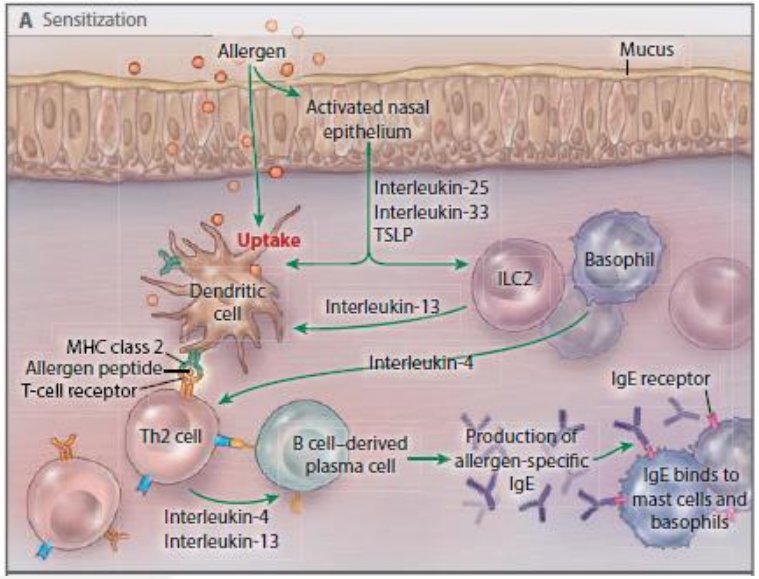
KEY CLINICAL POINTS

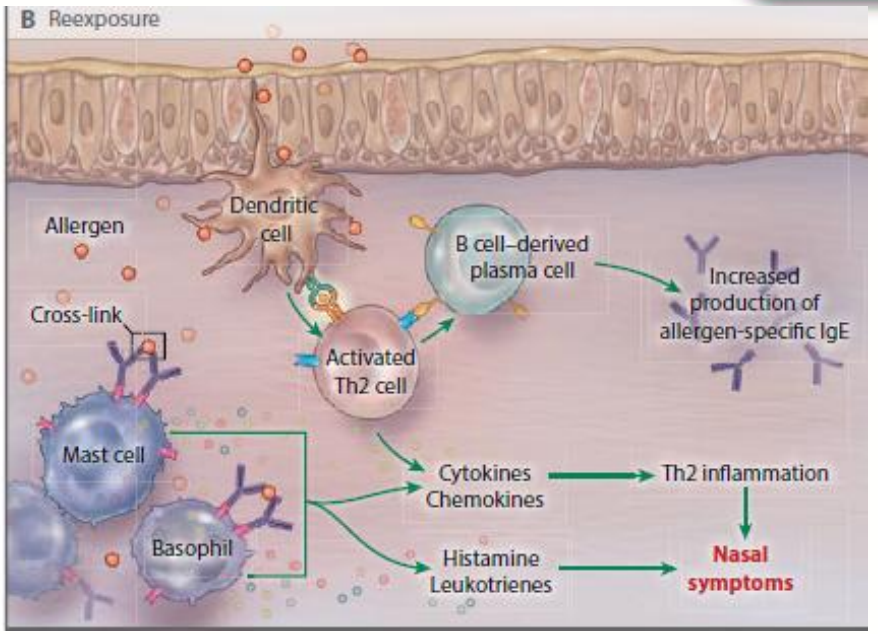
ALLERGIC RHINITIS

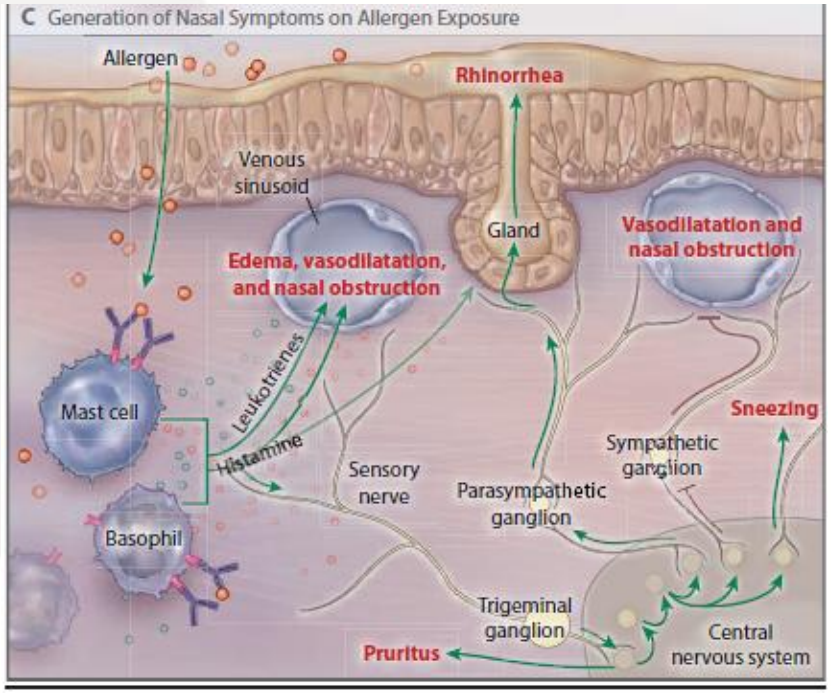
- An estimated 15 to 30% of patients in the United States have allergic rhinitis, a condition that affects productivity and the quality of life in children and adults.
- Allergic rhinitis frequently coexists with asthma and other allergic diseases; most people with asthma have rhinitis.
- Intranasal glucocorticoids are generally the most effective therapy; oral and nasal antihistamines and leukotriene-receptor antagonists are alternatives. However, many patients do not obtain adequate relief with pharmacotherapy.
- Allergen immunotherapy should be used in patients with refractory symptoms or in those for whom pharmacotherapy is associated with unacceptable side effects.
- Two forms of allergen immunotherapy are now available: subcutaneous injections and rapidly dissolving sublingual tablets, the latter limited in the United States to the treatment of grass and ragweed allergy. Both forms of therapy generally provide sustained efficacy after the cessation of treatment.

NEJM 2015 Jan 29;372(5):456-63

MECCANISMI PATOGENETICI PRINCIPALI







The NEW ENGLAND JOURNAL of MEDICINE

CLINICAL PRACTICE

Caren G. Solomon, M.D., M.P.H., *Editor*

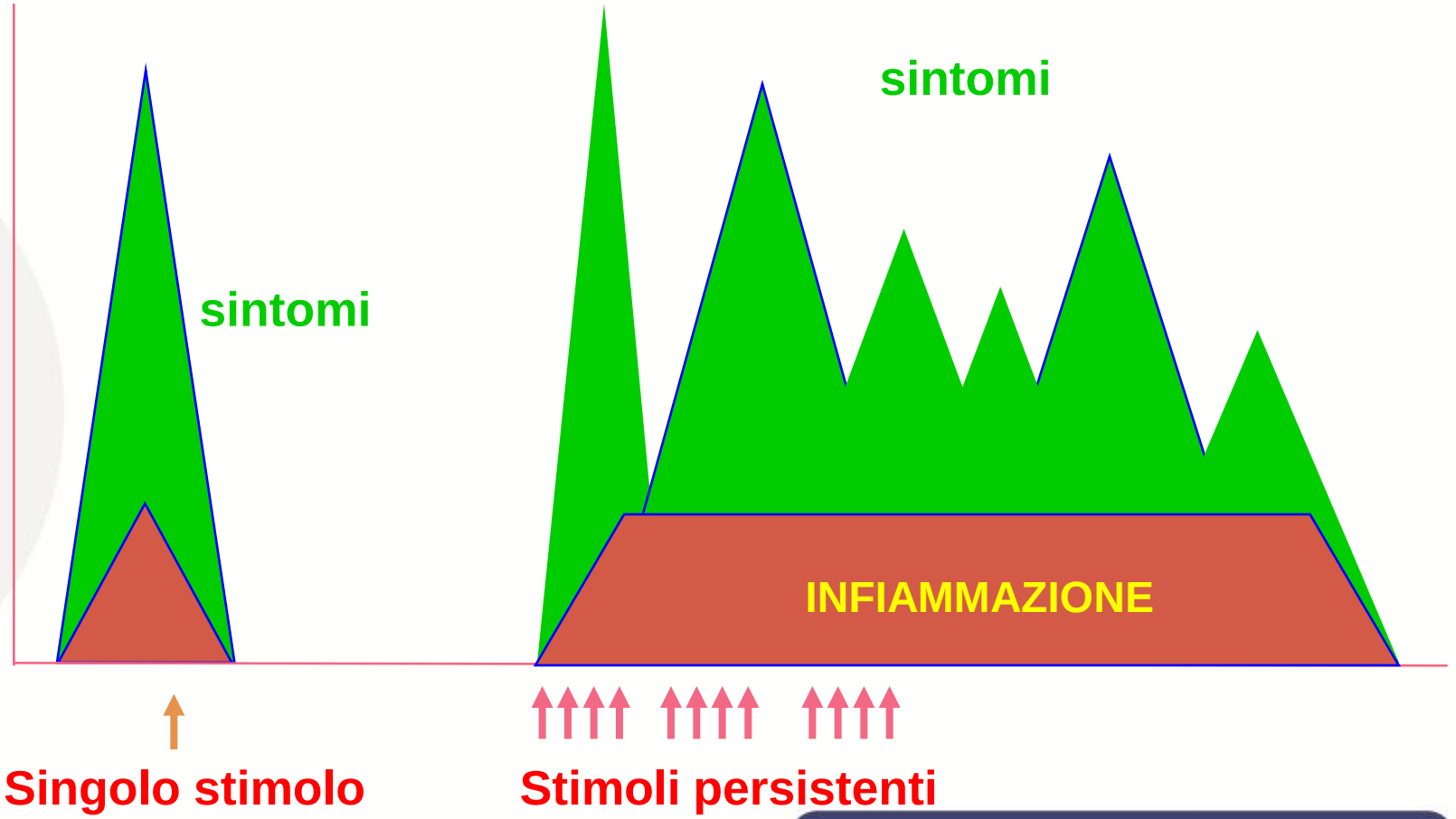
Allergic Rhinitis

Lisa M. Wheatley, M.D., M.P.H., and Alkis Togias, M.D.

NEJM 2015 Jan 29;372(5):456-63

Infiammazione persistente

Se lo stimolo allergenico è protratto nel tempo (come nell'esposizione naturale), l'infiammazione allergica diventa cronica. L'infiammazione mucosale è in larga parte responsabile dell'ostruzione



DEFINIZIONE-PATOGENESI

CLASSIFICAZIONE

EPIDEMIOLOGIA

CLINICA E DIAGNOSTICA

IMPATTO SULLA QoL

TRATTAMENTO

IMPATTO SULL'ASMA

ASPETTI PARTICOLARI

CLASSIFICAZIONE DELLE RINOPATIE
Modificata da: Gelardi M JAP 2012

Infettive Acute, Croniche — Batteriche, Virali, Micotiche

Irritative **da agenti chimico-fisici ambientali**

Allergiche Intermittente, Persistente

Non allergiche (vasomotorie o "cellulari") Neutrofila (NARNE), Eosinofila(NARES), Mastocitaria (NARMA), Eosin/mastocitaria (NARESMA)

Atrofiche

Ormonali Ipotiroidismo, gravidica, premestruale

Iperplastiche/granulomatose Poliposi, polipo antrocoanale, sarcoidosi S. Di Wegener e Churg-Strauss

Neoplastiche Papilloma invertito, Condroma, fibroma Angioma, sarcoma

Iatrogene Vasocostrittori, cocaina, Clonidina, ACE inib, ASA e FANS, contraccettivi, Neurolettici, Ca antagonisti

Altre Gustatoria, emozionale Meccanica (dev.setto, atresia coanale, ipertrofia turbinati) Fibrosi cistica, discinesia ciliare. Decubito, esercizio fisico

Classificazione ARIA della rinite allergica

Intermittente

. < 4 giorni/settimana

. o < 4 settimane

Persistente

. > 4 giorni/settimana

. e > 4 settimane

Lieve

Tutte le seguenti

- Sonno conservato
- Nessuna limitazione nelle attività quotidiane
- Normale attività lavorativa o scolastica
- Non sintomi fastidiosi

Moderata-grave

uno o più dei seguenti

. Alterazioni del sonno

. Limitazioni delle attività quotidiane

. Riduzione prestazioni lavorative/scolastiche

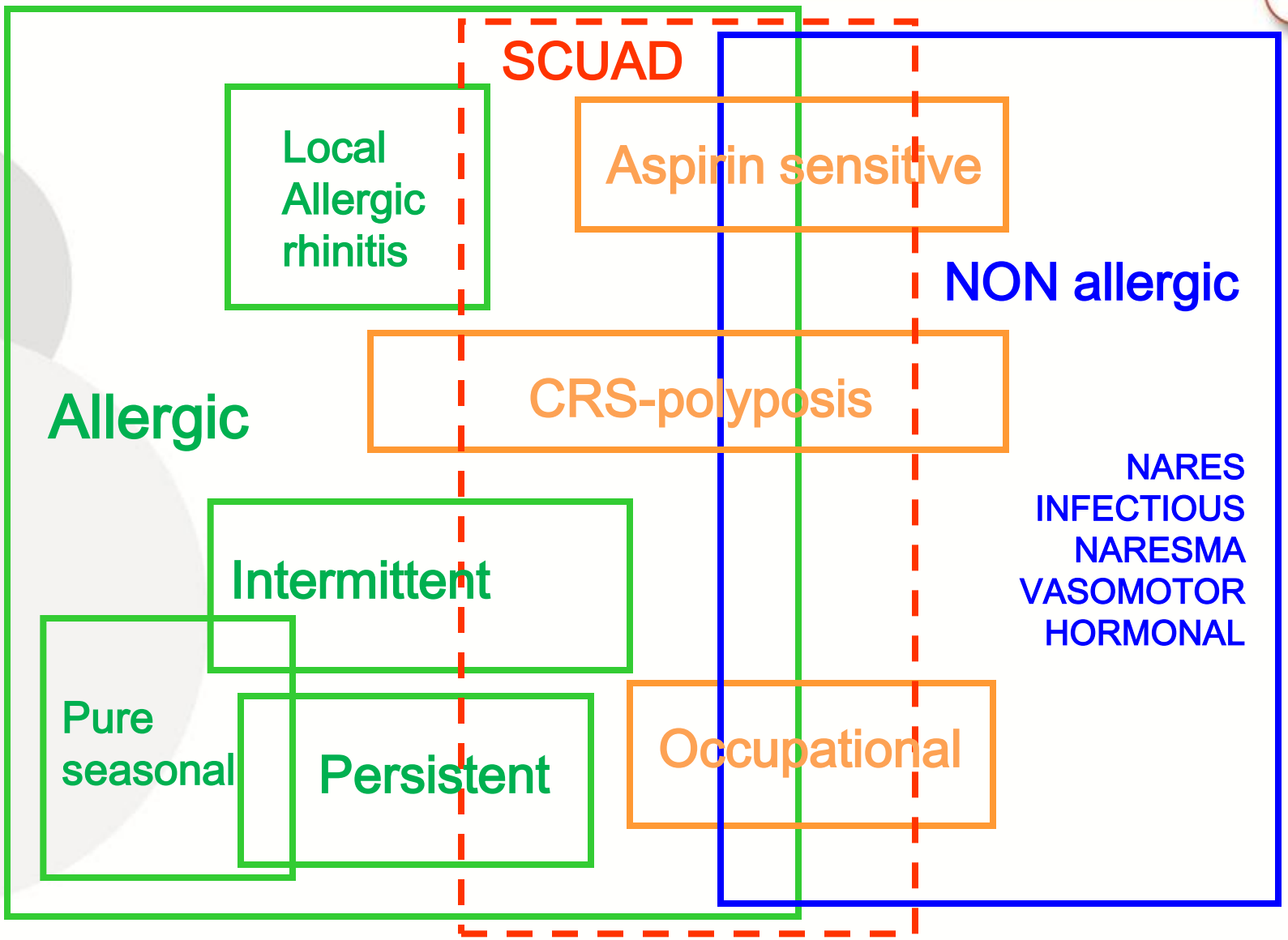
. Sintomi gravi

Nei pazienti non trattati

…" Con poche eccezioni, gli studi clinici fanno riferimento a rinite allergica "stagionale" o "perenne", basandosi più sull'allergene responsabile che sulla gravità e durata dei sintomi. In questo documento, come nelle precedenti versioni, abbiamo mantenuto i termini di rinite allergica "stagionale o perenne" al fine di rendere valutabili in maniera più omogenea gli studi pubblicati fino ad ora.

Brozek J et al.
Allergic Rhinitis and its Impact on Asthma (ARIA) Guidelines – 2016 revision
J Allergy Clin Immunol. 2017 Oct;140(4):950-958.

I possibili fenotipi della rinite (allergica e non allergica)



Fenotipi della Rinite - Practall

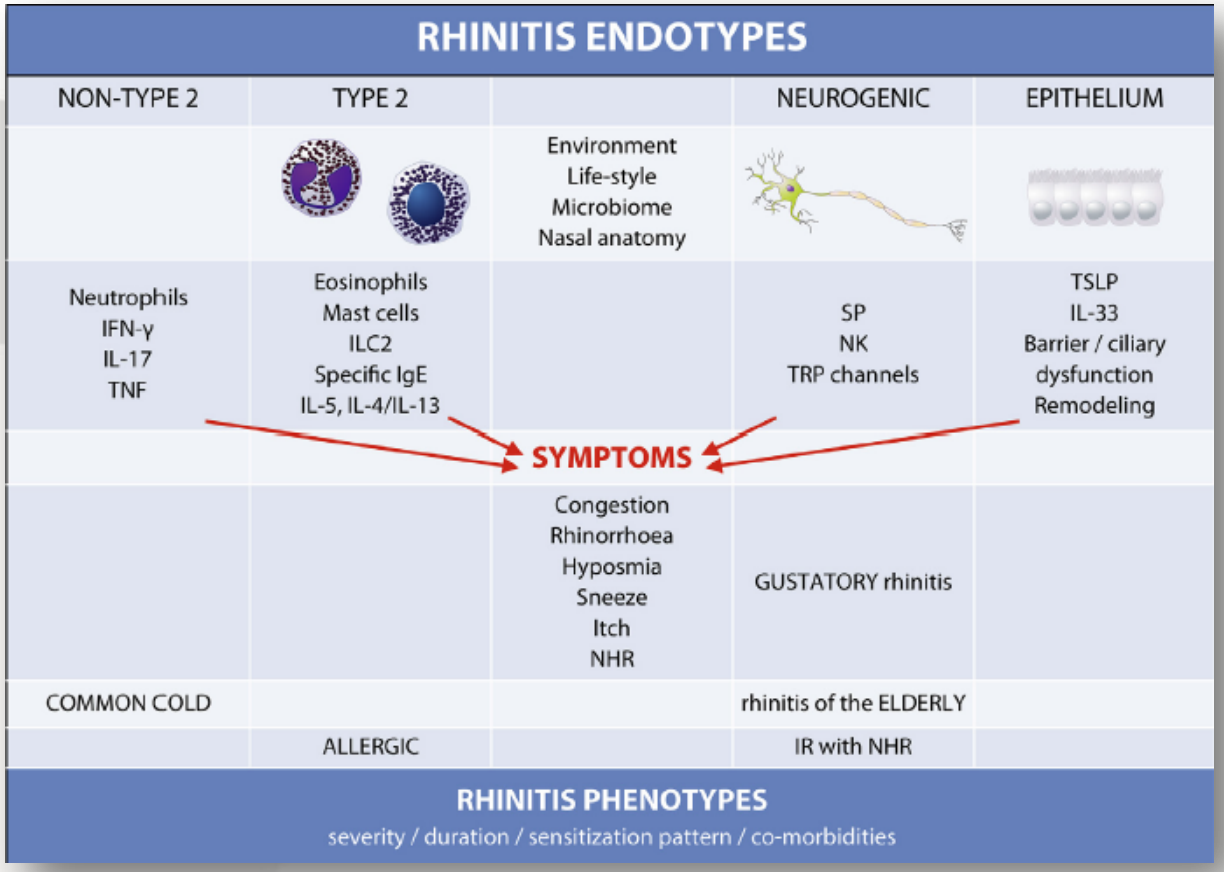
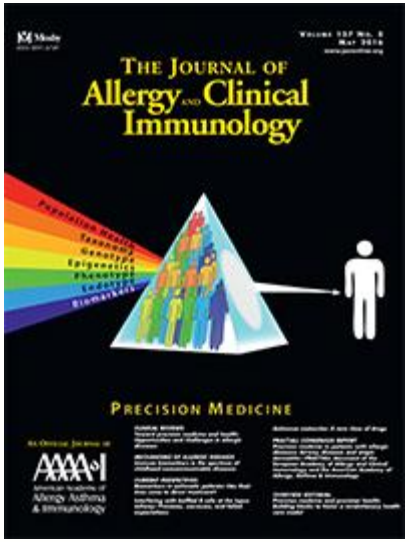


FIG 4. Overview of rhinitis phenotypes and endotypes. Similar to asthma, a type 2 immune response and non–type 2 immune response endotype can be described for rhinitis. Neurogenic and epithelial barrier dysfunction endotypes are particularly relevant for rhinitis. *ILC*, Innate lymphoid cell; *IR*, idiopathic rhinitis; *NHR*, nasal hyperreactivity; *NK*, neurokinin; *SP*, substance P; *TRP*, transient receptor potential.

PRACTALL consensus report

Precision medicine in patients with allergic diseases: Airway diseases and atopic dermatitis—PRACTALL document of the European Academy of Allergy and Clinical Immunology and the American Academy of Allergy, Asthma & Immunology



(Muraro A, et al., J Allergy Clin Immunol 2016;137:1347-58.)

Rinite allergica locale : possibile ulteriore fenotipo

Local allergic rhinitis is an independent rhinitis phenotype: The results of a 10-year follow-up study

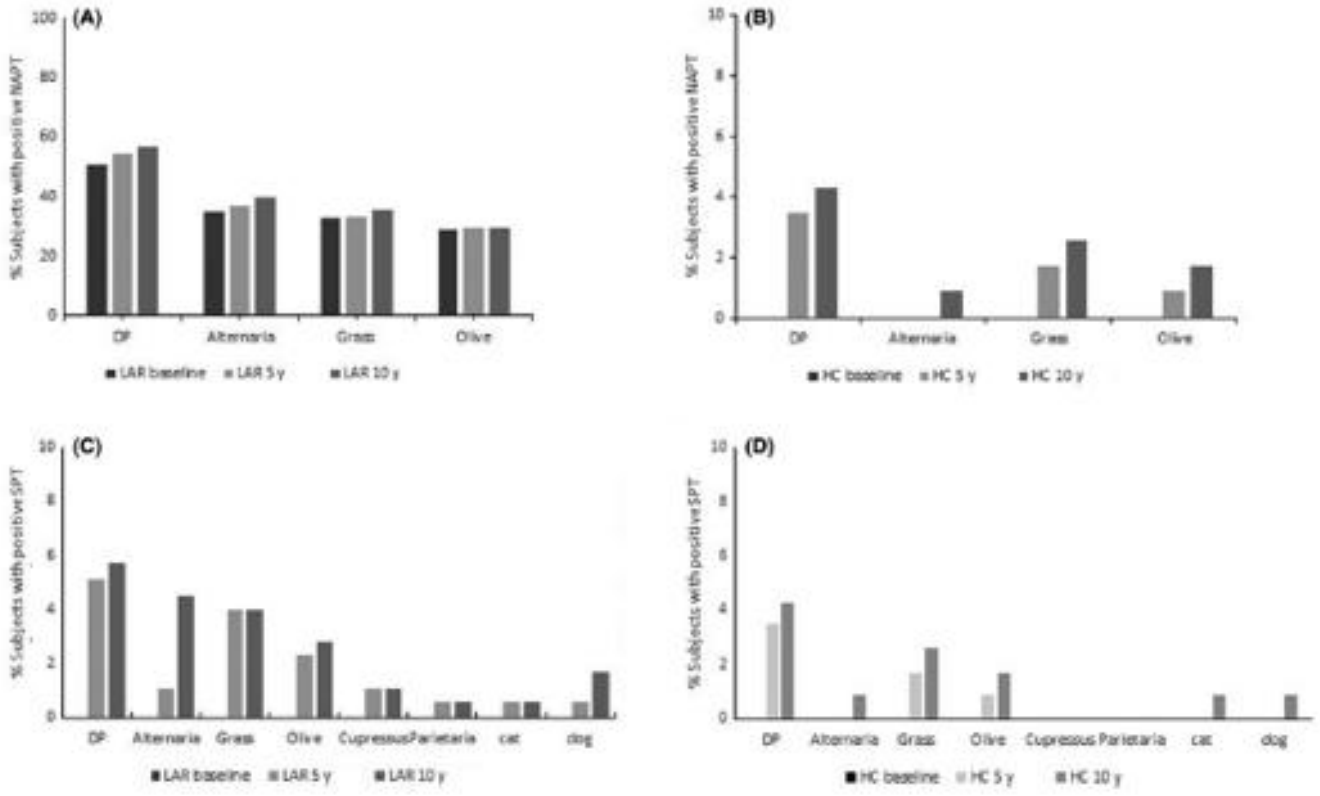


FIGURE 1 Distribution of frequencies of nasal and systemic allergen sensitization in local allergic rhinitis (LAR) patients and healthy controls (HC). Bars represent the following: (A) LAR patients with positive response to nasal allergen provocation test (NAPT) to different allergens; (B) HC with positive response to NAPT; (C) LAR patients with positive skin prick test or serum specific IgE; (D) HC with positive skin prick test or serum sIgE

(Rondon C et al., Allergy 2017)

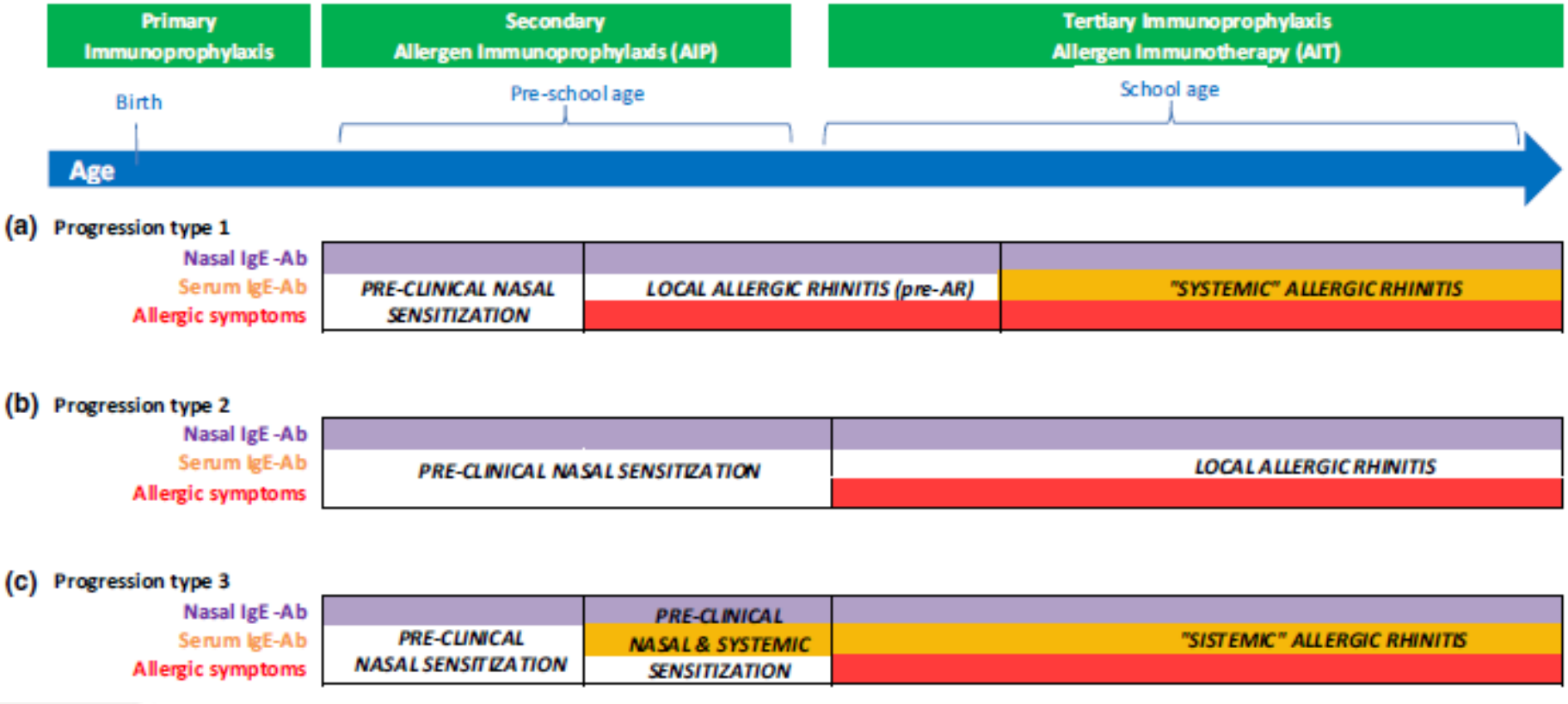
La rinite allergica locale nel bambino

Pediatric Allergy and Immunology

ROSTRUM

Local allergic rhinitis: A critical reappraisal from a paediatric perspective

Stefania Arasi[1,2], Giovanni Battista Pajno[1], Susanne Lau[3] & Paolo Maria Matricardi[2]



Pediatr Allergy Immunol. 2016 Sep;27(6):569-73

Le IgE nasali allergene-specifiche sono presenti anche nei soggetti sani

Gelardi et al. World Allergy Organization Journal (2016) 9:39
DOI 10.1186/s40413-016-0126-z

World Allergy Organization Journal

ORIGINAL RESEARCH Open Access

Local allergic rhinitis: entopy or spontaneous response?

Matteo Gelardi[1], Antonio V. N. Guglielmi[1], Lucia Iannuzzi[1], Vitaliano Nicola Quaranta[2], Nicola Quaranta[1], Massimo Landi[3], Mario Correale[4], Annamaria Sonnante[4], Margherita Rossini[5], Maria Addolorata Mariggiò[5], Giorgio Walter Canonica[6] and Giovanni Passalacqua[6*]

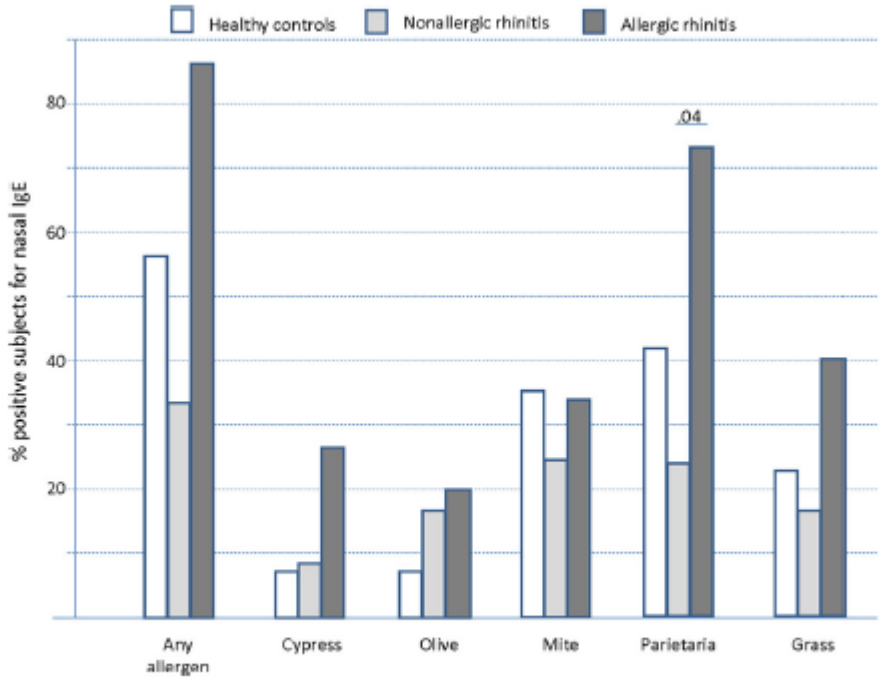
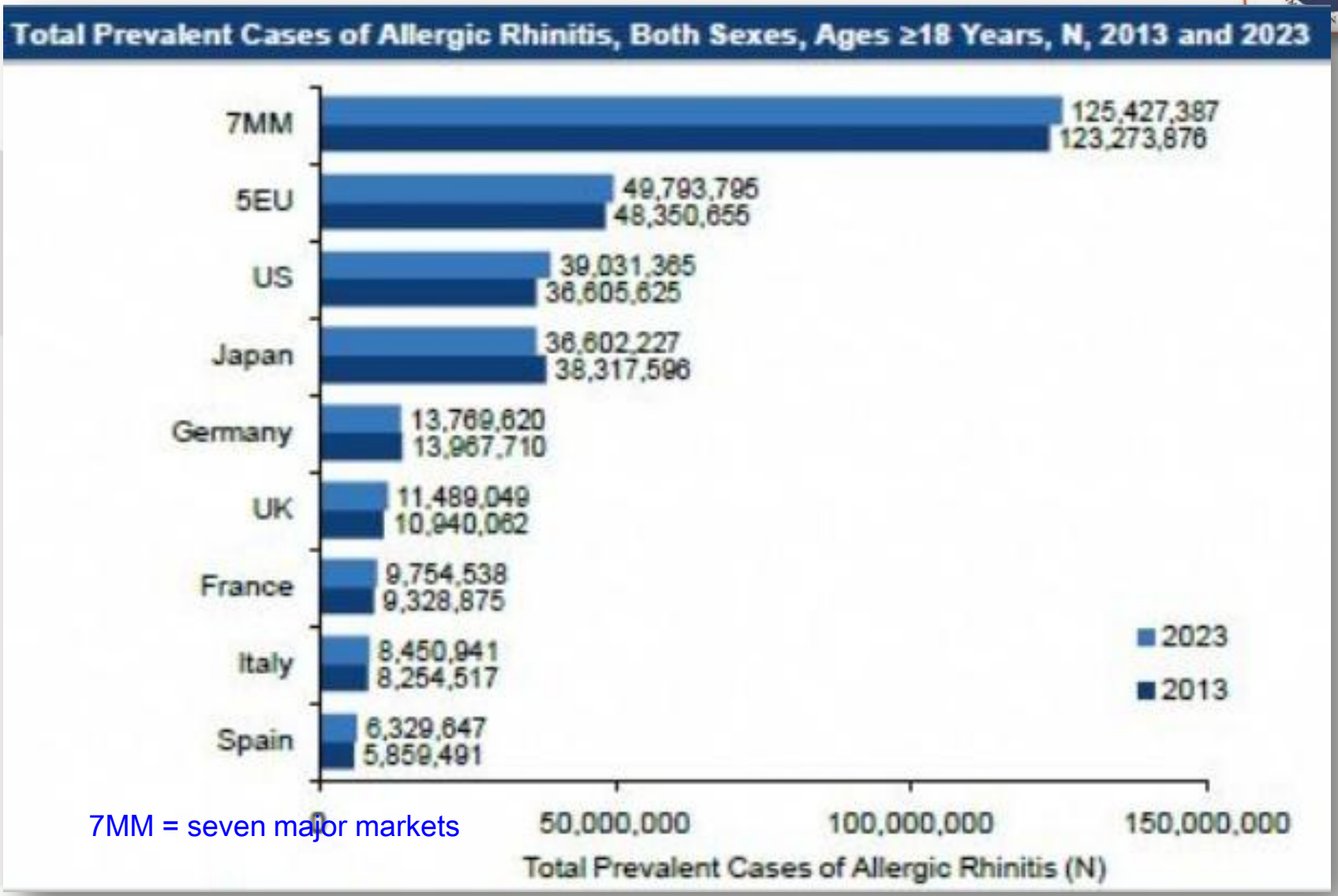


Fig. 2 % of patients with positive assay for nasal IgE, in total and for each single allergen. A significant difference among the 3 groups was detected only for Parietaria. Significant p values are reported above the bars

Gelardi M et al, WAO Journal 2016 2015

DEFINIZIONE-PATOGENESI
CLASSIFICAZIONE
EPIDEMIOLOGIA
CLINICA E DIAGNOSTICA
IMPATTO SULLA QoL
TRATTAMENTO
IMPATTO SULL'ASMA
ASPETTI PARTICOLARI

Epidemiologia Rinite Allergica : 2013-2023

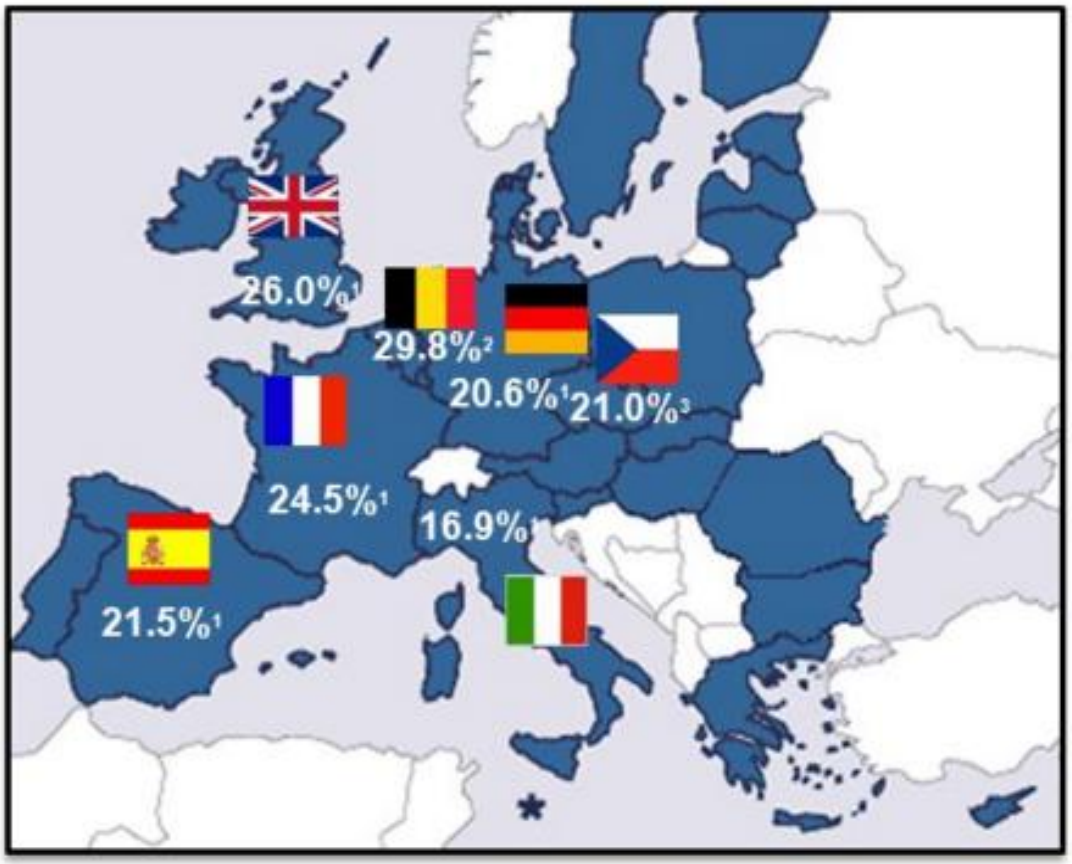


7MM = seven major markets

Source: GlobalData; Bauchau and Durham, 2004; Konno et al., 2012; Nathan et al., 1997.
5EU = France, Germany, Italy, Spain, and UK; 7MM = US, 5EU and Japan

Epidemiologia Rinite Allergica : Area Europea

Prevalence of AR in a population-based survey in 6 EU countries[1]:
UK, Germany, France, Belgium, Italy and Spain

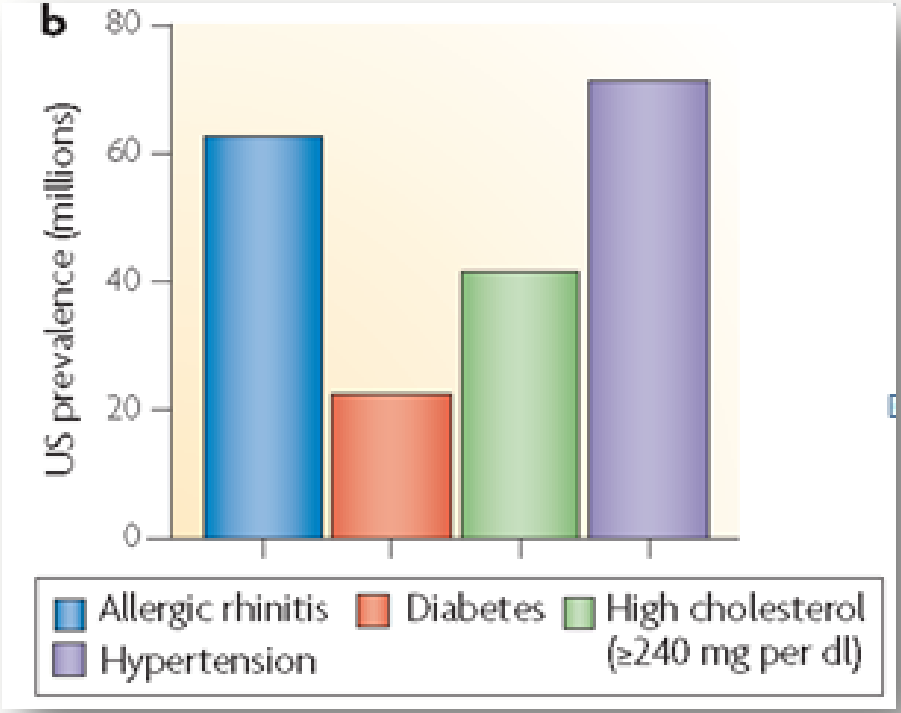


AR European prevalence is **23%**, of which **45%** are undiagnosed[1]

500 million people suffer from AR worlwide

1.Bauchau V., Durham S.R., Eur Respir J 2004:758-764
2.Bachert C. Allergy 2006: 61: 693-698
3.Brehl P. Ind Health 2003 Apr; 41 (2): 121-3

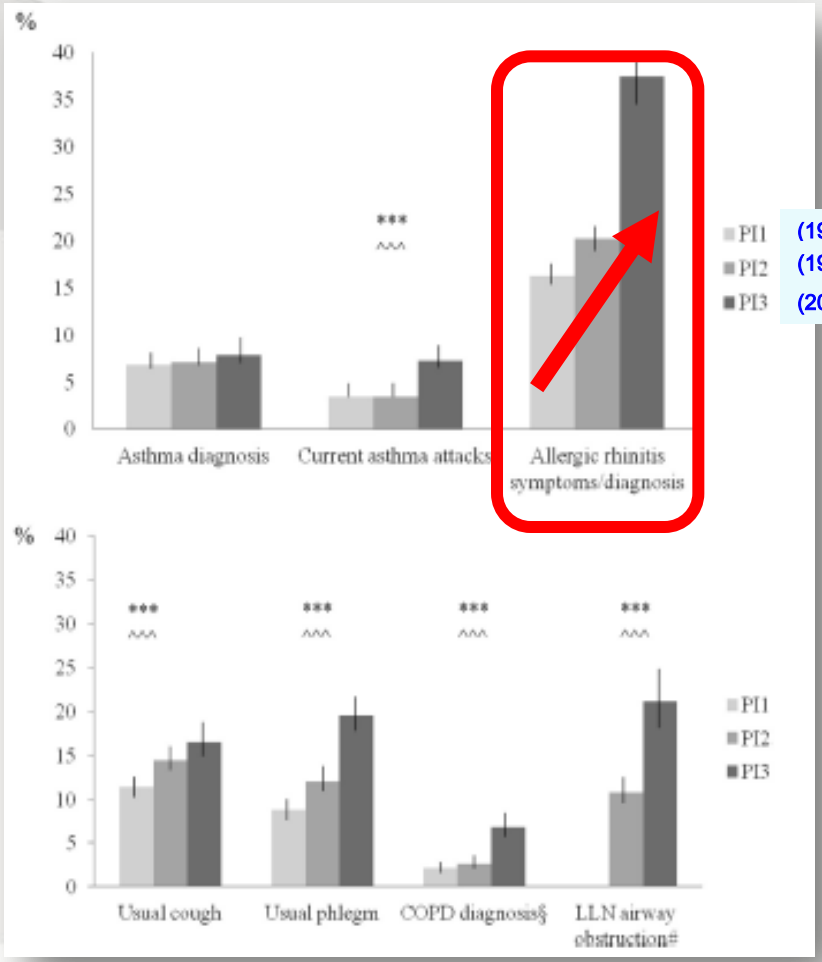
La prevalenza stimata (milioni di pazienti) della rinite allergica negli Stati Uniti, Europa e Giappone e confronto con altre malattie



Nature Reviews Drug Discovery 2009; 8: 271-272

RINITE ALLERGICA IN ITALIA: EPIDEMIOLOGIA

Respiratory symptoms/diseases prevalence is still increasing: a 25-yr population study



1985-88 (n: 3865), 1991-93 (n: 2841), 2009-11 (n:1620).

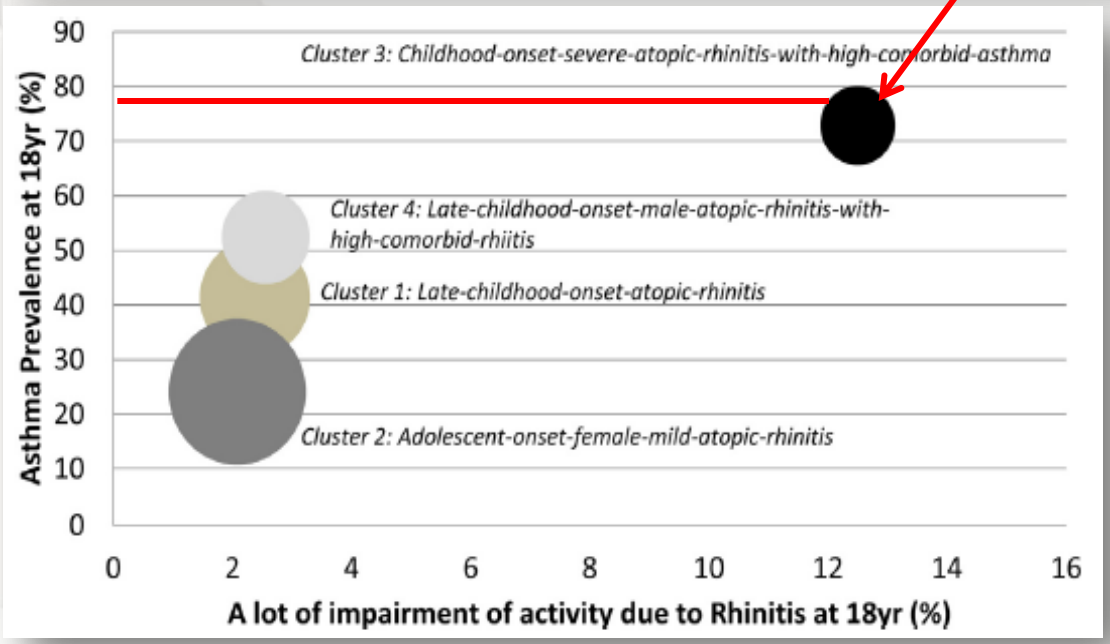
There was an increasing trend in prevalence rates of all respiratory symptoms/diseases throughout the surveys: current asthma attacks (1st – 3rd survey prevalence: 3.4-7.2%), allergic rhinitis (16.2-37.4%), usual phlegm (8.7-19.5%) and COPD (2.1-6.8%) more than doubled.

Maio S. et al., Respiratory Medicine 110 (2016) 58-65

INTERAZIONE FENOTIPI DELLA RINITE E DELL'ASMA

Identifying the heterogeneity of young adult rhinitis through cluster analysis in the Isle of Wight birth cohort

Cluster	Name	Atopy	Eczema	Asthma	Total IgE	BDR	BHR	Persistent rhinitis	High levels of limitation by rhinitis
1	Moderate childhood-onset rhinitis	+++	+++	+	++	+	+	++	+
2	Mild adolescence-onset female rhinitis	+	++	+	+	+	+	+	+
3	Severe earliest-onset rhinitis with asthma	+++	+++	+++	++	+++	+++	+++	+++
4	Moderate childhood-onset male rhinitis with asthma	++	+	++	+++	++	+	++	+



Conclusione:
La RA a esordio precoce si associa a un peggioramento della patologia allergica nell'adulto.

(RJ Kurukulaaratchy et al., J Allergy Clin Immunol 2015;135:143-50)

I COSTI DELLA RINITE ALLERGICA IN EUROPA

Nel contesto del Global Allergy and Asthma European Network (GA²LEN), Zuberbier et al. hanno condotto uno studio dettagliato sull'analisi dei costi del trattamento nell'Unione Europea. I costi totali dei pazienti non trattati opportunamente variano da € 55 a € 151 milioni annuali includendo assenteismo e ridotta produttività.

Questo calcolo fornisce circa € 2,405/anno per ogni paziente non opportunamente trattato.

Il costo del trattamento secondo le linee guida sarebbe di circa € 125 per paziente all'anno, solo il 5% dei costi del non-trattamento.

Il trattamento adeguato dei pazienti allergici è fortemente cost-effective, con un potenziale risparmio di circa € 142 milioni per anno entro l'EU.

Zuberbier T, Lotvall J, Simoens S, Subramanian SV, Church MK.
Economic burden of inadequate management of allergic diseases in the European Union: a GA(2) LEN review.
Allergy 2014;69(10):1275-1279.

PREVALENZA A LIVELLO MONDIALE IN ETA' PEDIATRICA

The International Study of Asthma and Allergies in Childhood (ISAAC) Phase Three: A global synthesis

J. Mallol[a,*], J. Crane[b], E. von Mutius[c], J. Odhiambo[d], U. Keil[e], A. Stewart[f], the ISAAC Phase Three Study Group[◊]

Table 1 Prevalence of current symptoms of asthma, rhinoconjunctivitis and eczema by world region and gender, 6–7-year age group.

Region	Gender	N	Asthma		Rhinoconjunctivitis		Eczema	
			N	%	N	%	N	%
Africa	Male	2979	321	10.8	223	7.5	283	9.5
	Female	2886	268	9.3	230	8.0	262	9.1
Asia-Pacific	Male	30,509	3296	10.8	3712	12.2	2962	10.2[b]
	Female	29,470	2423	8.2	2615	8.9	2796	10.0[b]
Eastern Mediterranean	Male	20,769	2146	10.3	1130	5.4	1001	4.8
	Female	19,804	1678	8.5	968	4.9	943	4.8
Indian Sub-Continent	Male	25,867	1909	7.4	1166	4.5	786	3.0
	Female	24,225	1483	6.1	917	3.8	735	3.0
Latin America	Male	45,926	8691	18.9	6017	13.1	4482	9.8
	Female	47,848	7565	15.8	5914	12.4	4873	10.2
North America	Male	2011	433	21.5	176	8.8	197	9.8
	Female	2001	334	16.7	136	6.8	207	10.3
Northern and Eastern Europe	Male	21,444	2132	9.9	1277	6.0	1286	6.0
	Female	21,104	1583	7.5	1064	5.0	1302	6.2
Oceania	Male	7028	1705	24.3	879	12.5	991	14.1
	Female	6860	1315	19.2	742	10.8	1163	17.0
Western Europe	Male	39,328	4296	10.9	3247	8.3	3018	7.7
	Female	38,394	3191	8.3	2491	6.5	3301	8.6
Male Total		195,861	24,929	12.7	17,827	9.1	15,006	7.7[b]
Female Total		192,592	19,840	10.3	15,077	7.8	15,582	8.2[b]
Global Total[a]		388,811	44,799	11.5	32,928	8.5	30,616	7.9[b]

[a] Includes participants with unknown gender (358).
[b] Percent values calculated using smaller denominators as not all centres included the eczema questionnaire.

Table 2 Prevalence of current symptoms of asthma, rhinoconjunctivitis and eczema by region and gender, 13–14-year age group.

Region	Gender	N	Asthma		Rhinoconjunctivitis		Eczema	
			N	%	N	%	N	%
Africa	Male	32,373	4521	14.0	5087	15.7	3822	11.8
	Female	33,935	4747	14.0	6850	20.2	4640	13.7
Asia-Pacific	Male	49,675	4428	8.9	6208	12.5	2174	4.7[b]
	Female	49,959	4303	8.6	7498	15.0	2692	5.8[b]
Eastern Mediterranean	Male	25,879	2748	10.6	3393	13.1	1627	6.3
	Female	25,826	2053	7.9	3361	13.0	1615	6.3
Indian Sub-Continent	Male	27,432	2362	8.6	3203	11.7	1218	4.4
	Female	28,351	1522	5.4	2762	9.7	916	3.2
Latin America	Male	80,715	11,753	14.6	11,193	13.9	5062	6.3
	Female	85,185	14,597	17.1	17,543	20.6	8631	10.1
North America	Male	69,739	13,793	19.8	906	13.8[b]	421	6.4[b]
	Female	71,270	16,634	23.3	1445	19.6[b]	693	9.4[b]
Northern and Eastern Europe	Male	35,455	3168	8.9	2721	7.7	1356	3.8
	Female	36,602	3841	10.5	3873	10.6	2308	6.3
Oceania	Male	17,837	3060	17.2	2620	14.7	1520	8.5
	Female	18,462	3241	17.6	3547	19.2	2028	11.0
Western Europe	Male	54,741	7545	13.8	6771	12.4	2968	5.4
	Female	52,932	7938	15.0	8835	16.7	4414	8.3
Male Total	Male	393,846	53,378	13.6	42,102	12.7[b]	20,168	6.2[b]
Female Total	Female	402,522	58,876	14.6	55,714	16.5[b]	27,937	8.3[b]
Global Total[a]		798,685	112,630	14.1	97,866	14.6[b]	48,131	7.3[b]

[a] Includes participants with unknown gender (2317).
[b] Percent values calculated using smaller denominators as not all centres included the rhinoconjunctivitis and eczema questionnaires.

Globally, the prevalence for current asthma, rhinoconjunctivitis and eczema in the 13-14 year age group was 14.1%, 14.6% and 7.3%, respectively. In the 6-7-year age group the prevalence for current asthma, rhinoconjunctivitis and eczema was 11.7%, 8.5% and 7.9%, respectively.

Allergol Immunopathol (Madr). 2013;41(2):73-85

DEFINIZIONE-PATOGENESI
CLASSIFICAZIONE
EPIDEMIOLOGIA
CLINICA E DIAGNOSTICA
IMPATTO SULLA QoL
TRATTAMENTO
IMPATTO SULL'ASMA
ASPETTI PARTICOLARI

Sintomi tipici e non tipici della rinocongiuntivite allergica

SINTOMI TIPICI DI RINITE ALLERGICA
- rinorrea acquosa
- starnuti a salve
- ostruzione nasale
- prurito nasale
- congiuntivite concomitante

SINTOMI TIPICI DI CONGIUNTIVITE ALLERGICA
- sintomi di rinite concomitante
- sintomi bilaterali
- lacrimazione
- prurito congiuntivale
- iperemia

SINTOMI NON TIPICI DI RINITE ALLERGICA
- sintomi unilaterali
- ostruzione nasale isolata
- rinorrea mucopurulenta
- rinorrea posteriore isolata
- dolore, anosmia
- epistassi ricorrenti

SINTOMI NON TIPICI DI CONGIUNTIVITE ALLERGICA
- completa assenza di rinite
- sintomi unilaterali
- fotofobia
- bruciore oculare o dolore
- secchezza della congiuntiva

COME INDIRIZZARE L'ANAMNESI

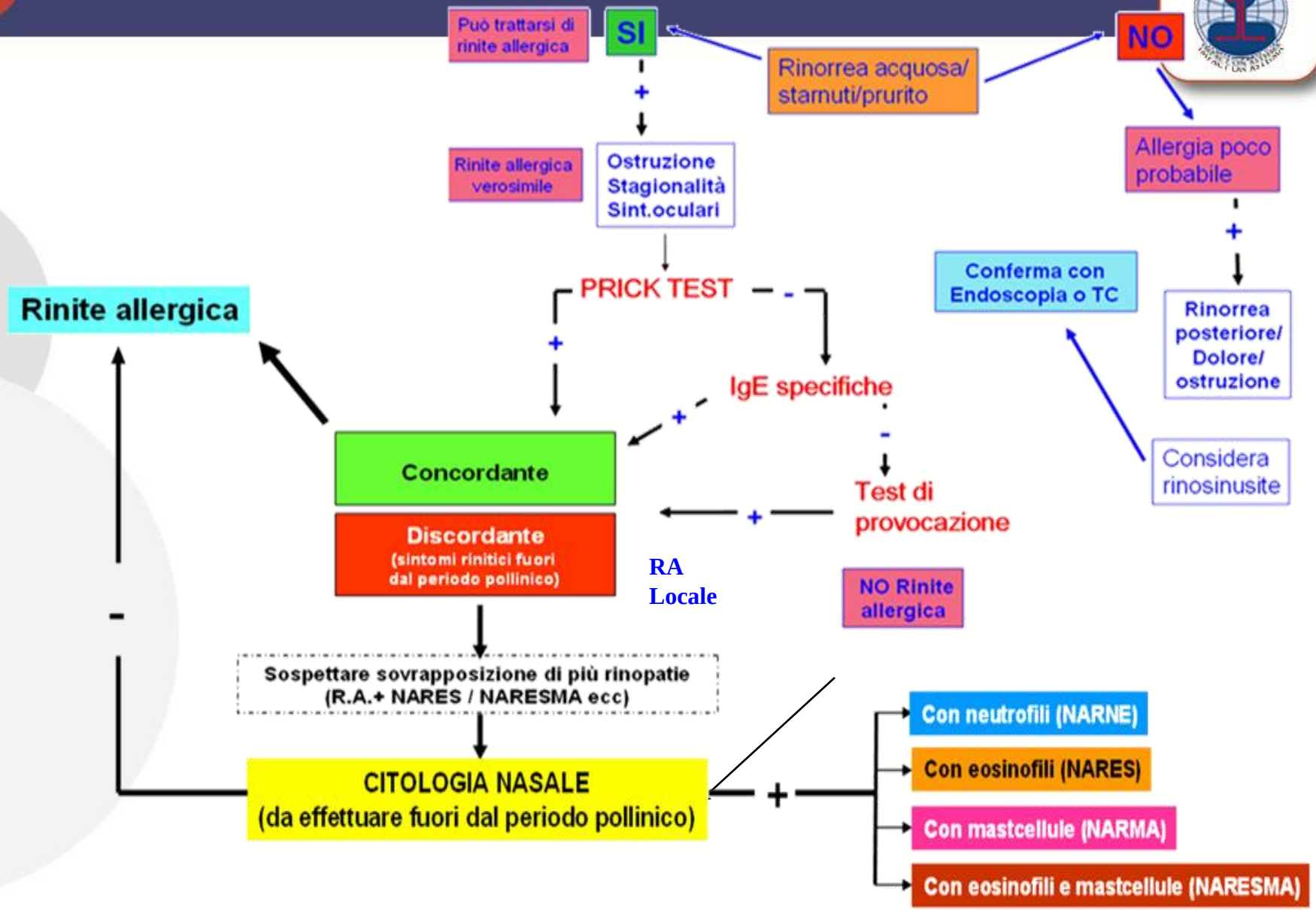
0. E' presente familiarità allergica?

1. E' presente qualcuno dei seguenti sintomi?		
Sintomi solo in una narice	SI	NO
Secrezioni dense, di colore giallo o verdastro	SI	NO
Secrezioni che scendono in gola, specialmente con muco denso	SI	NO
Dolore facciale	SI	NO
Sanguinamenti dal naso	SI	NO
Perdita dell'olfatto	SI	NO
2 E' presente qualcuno di seguenti sintomi almeno un ora al giorno, in molti giorni consecutivi (o durante una particolare stagione dell'anno)?		
Rinorrea acquosa	SI	NO
Starnuti, anche a salve	SI	NO
Naso chiuso	SI	NO
Prurito nasale	SI	NO
Congiuntivite (occhi rossi o che prudono)	SI	NO

La presenza di uno o più sintomi della domanda 1 suggerisce una natura non allergica dei sintomi e richiede valutazione specialistica. Dolore facciale, rinorrea purulenta e iposmia sono spesso associati a rinosinusite, ma non escludono la concomitanza di RA. La rinorrea acquosa con uno o più dei sintomi della domanda 2 suggerisce fortemente la rinite allergica.

AR Reference Guide. Bousquet, Allergy 2008

ALGORITMO DIAGNOSTICO



DA: Journal of Allergy and Clinical Immunology 10.1016/j.jaci.2012.02.032), modificato

La citologia nasale

REVIEW

NASAL cytology: practical aspects and clinical relevance

M. Gelardi[1], L. Iannuzzi[1], N. Quaranta[1], M. Landi[2,3] and G. Passalacqua[4]

[1]Section of Otolaryngology, Department of Basic Medical Science, Neuroscience and Sensory Organs, University of Bari, Bari, Italy, [2]National Pediatric Healthcare System, Turin, Italy, [3]Unit Research of Pediatric Pulmonology and Allergy, Institute of Biomedicine and Molecular Immunology (IBIM), National Research Council, Palermo, Italy and [4]Allergy and Respiratory Diseases, IRCCS San Martino-IST-University of Genoa, Genoa, Italy

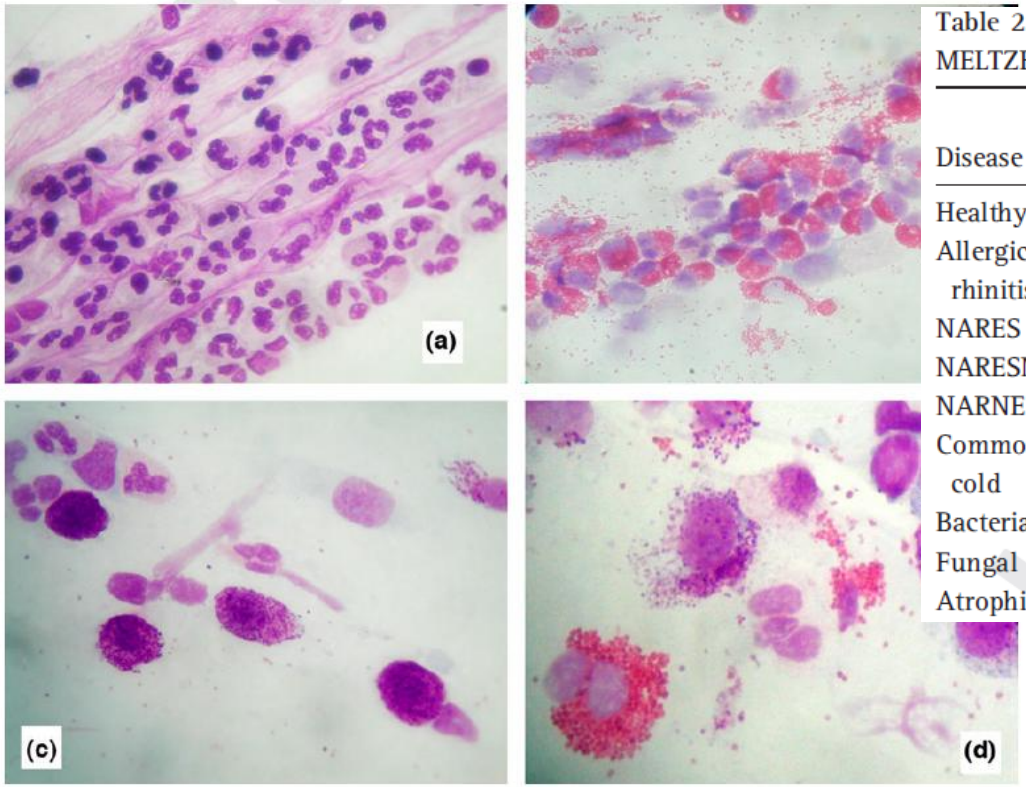


Table 2. Examples of differential diagnoses at NC (Adapted from MELTZER 1988)

Disease	Eosinophils	Mast-cells	Neutrophils	Bacteria	Fungal spores
Healthy	0	0	0–1+	0	0
Allergic rhinitis	2 + /4+	2 + /4+	2 + /4+	0	0
NARES	2 + /4+	0	Variable	0	0
NARESMA	2 + /4+	2 + /4+	Variable	0	0
NARNE	0	0	3 + /4+	0	0
Common cold	0	0	1 + /4+	0	0
Bacterial	0–1+	0	3 + /4+	3 + /4+	0
Fungal	0	0	Variable	0	2 + /4+
Atrophic	0	0	Variable	0	0

Gelardi M et al, CEA 2016

Siti aerobiologia per elaborazione calendari pollinici

ASSOCIAZIONE ITALIANA AEROBIOLOGIA

AIA

La Rete è costituita da Centri di Monitoraggio, distribuiti in tutto il territorio nazionale. I centri gestiti da soci AIA aderiscono alla campagna di campionamento annuale. Altri centri di monitoraggio mettono a disposizione della R.I.M.A.® i propri dati aerobiologici.

Link Utili

- CMA-CRA (ex UCEA)
- Deutscher Pollenflug
- EAS
- European Pollen Info (EPI)
- Federasma
- International Association for Aerobiology (IAA)
- International Ragweed Society
- Meteopolline
- Meteosuisse
- NPARU
- Panamerican Aerobiology Association
- REA
- RNSA
- SIAAIC
- Station d'aerobiologie du Ministere de la Santè

http://www.ilpolline.it/

PollinieAllergia.net
Aerobiologia, ecologia prevenzione ambientale

AIITO
Associazione Allergologi Immunologi Italiani Territoriali e Ospedalieri

MAPPA MOLECOLARE ITALIANA DI DISTRIBUZIONE DEGLI AEROALLERGENI

ALPI E PREALPI

Bet v 1 > Aln g 1 >> Que a 1 > Cor a 1
Fra e 1
Amb a 1; Art v 1
Phl p 1, 5; Cyn d 1
Der p 1, p 2, f 1, f 2
Alt a 1

NORD ADRIATICO

Cor a 1 > Que a 1 > Bet v 1 > Aln g 1
Ole e 1 > Fra e 1
Pla a 1
Amb a 1; Art v 1
Sal k 1
Phl p 1, 5; Cyn d 1
Der p 1, p 2, f 1, f 2
Alt a 1

PIANURA PADANA

Bet v 1 > Aln g 1 > Que a 1 > Cor a 1
Fra e 1
Pla a 1
Amb a 1; Art v 1
Phl p 1, 5; Cyn d 1
Der p 1, p 2, f 1, f 2
Alt a 1

APPENNINO CENTRO-ADRIATICO

Cor a 1 > Aln g 1 > Que a 1 > Bet v 1
Ole e 1 > Fra e 1
Pla a 1
Cup a 1
Par j 1, 2; Art v 1
Phl p 1, 5; Cyn d 1
Der p 1, p 2, f 1, f 2
Alt a 1

NORD TIRRENO

Cor a 1 > Aln g 1 > Que a 1 > Bet v 1
Ole e 1 > Fra e 1
Pla a 1
Cup a 1
Par j 1, 2; Art v 1
Sal k 1
Phl p 1, 5; Cyn d 1
Der p 1, p 2, f 1, f 2
Alt a 1

SUD ADRIATICO - PUGLIA

Cor a 1 > Que a 1
Ole e 1
Cup a 1
Par j 1, 2; Art v 1
Sal k 1
Phl p 1, 5; Cyn d 1
Der p 1, p 2, f 1, f 2
Alt a 1

CENTRO TIRRENO

Que a 1 > Cor a 1
Ole e 1 > Fra e 1
Pla a 1
Cup a 1
Par j 1, 2; Art v 1
Phl p 1, 5; Cyn d 1
Der p 1, p 2, f 1, f 2
Alt a 1

SARDEGNA

Que a 1
Ole e 1
Cup a 1
Par j 1, 2
Phl p 1, 5; Cyn d 1
Der p 1, p 2, f 1, f 2
Alt a 1

SICILIA

Que a 1
Ole e 1
Cup a 1
Par j 1, 2
Sal k 1
Phl p 1, 5; Cyn d 1
Der p 1, p 2, f 1, f 2
Alt a 1

SUD TIRRENO - CALABRIA

Cor a 1 > Que a 1
Ole e 1
Cup a 1
Par j 1, 2; Art v 1
Sal k 1
Phl p 1, 5; Cyn d 1
Der p 1, p 2, f 1, f 2
Alt a 1

(Cecchi et al. Eur Ann Allergy Clin Immunol 2013 supp.2)

DIAGNOSTICA MOLECOLARE : WAO-ARIA-GALEN Consensus Document

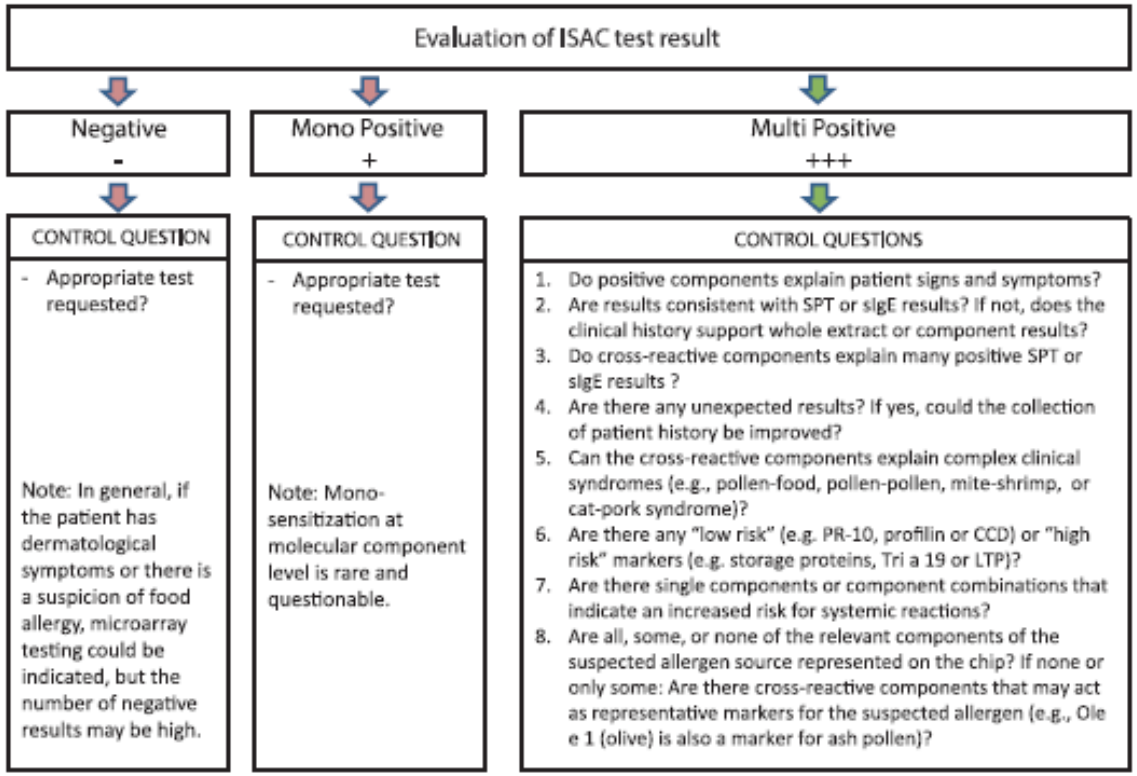
Canonica *et al. World Allergy Organization Journal* 2013, **6**:17
http://www.waojournal.org/content/6/1/17

WAO journal
WORLD ALLERGY ORGANIZATION

CONSENSUS DOCUMENT **Open Access**

A WAO - ARIA - GA²LEN consensus document on molecular-based allergy diagnostics

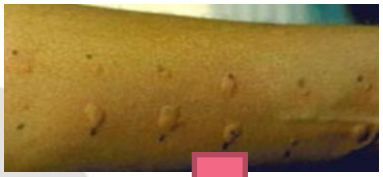
Giorgio Walter Canonica[1*], Ignacio J Ansotegui[2], Ruby Pawankar[3], Peter Schmid-Grendelmeier[4], Marianne van Hage[5], Carlos E Baena-Cagnani[6], Giovanni Melioli[7], Carlos Nunes[8], Giovanni Passalacqua[9], Lanny Rosenwasser[10], Hugh Sampson[11], Joaquin Sastre[12], Jean Bousquet[13], Torsten Zuberbier[14], Katrina Allen[15], Riccardo Asero[16], Barbara Bohle[17], Linda Cox[18], Frederic de Blay[19], Motohiro Ebisawa[20], René Maximiliano-Gómez[21], Sandra González-Diaz[22], Tari Haahtela[23], Stephen Holgate[24], Thilo Jakob[25], Mark Larché[26], Paolo Maria Matricardi[27],

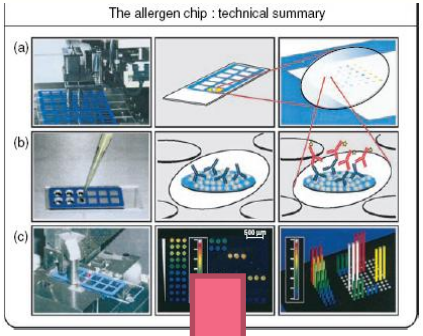


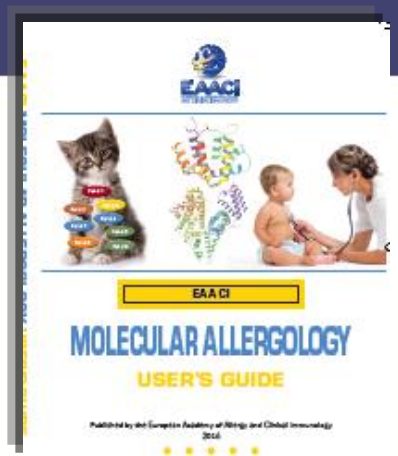
La diagnostica molecolare (con proteine allergeniche purificate/ricombinanti) consente di distinguere le sensibilizzazioni genuine da quelle dovute a cross-reattività.

Utile nel polisensibile in aggiunta alla diagnostica standard, nella sensibilizzazione combinata tra alimenti e inalanti e per la scelta della ITS appropriata.
La diagnostica multiplexed (ISAC) è sempre di terzo livello.

DIAGNOSTICA MOLECOLARE



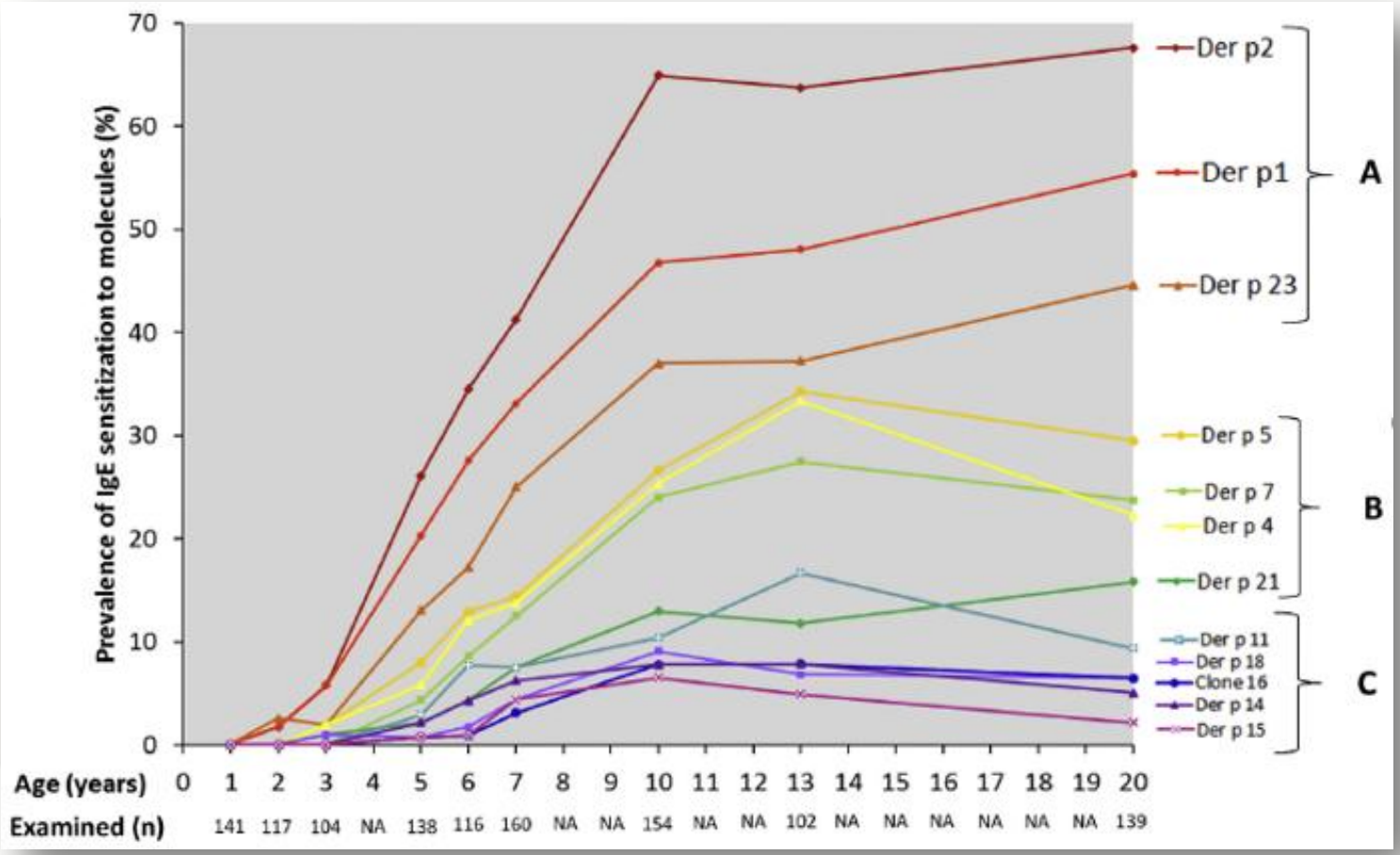




	Extracts	Molecular	Explanations
Absolute Disagreement (qualitative differences)			
A	positive	negative	a) serum IgE binds only to extract's molecules that are not (yet) available in molecular assays; b) molecular assays less analytically sensitive than the extract based assay
B	negative	positive	c) serum IgE binds to molecules tested as components which missing or of low abundance in the extract; d) extract assay less analytically sensitive than the molecular assay
Relative Disagreement (quantitative differences)			
C	positive	negative to major components	serum IgE binds only to highly cross reactive, minor allergenic molecules or CCD determinants
D	lower levels	higher levels	serum IgE binds to molecules tested as components being of low abundance in the extract

Molecular Allergology, EAACI Handbook, 2016

Evolution and predictive value of IgE responses toward a comprehensive panel of house dust mite allergens during the first 2 decades of life

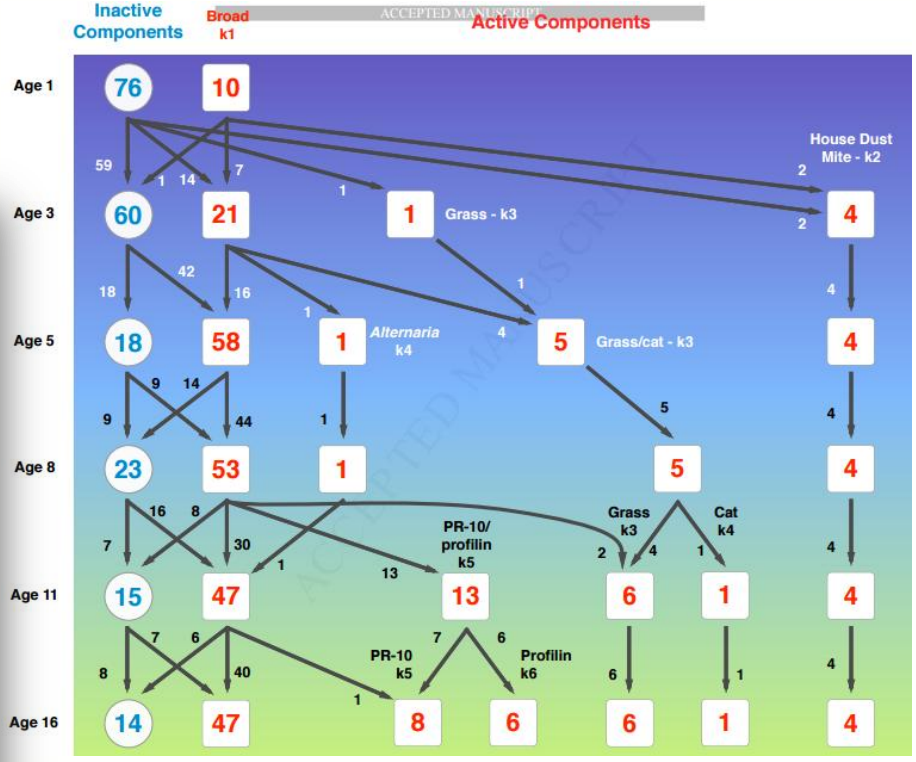


(Posa D et al., JACI february 2017)

Evolution of IgE responses to multiple allergen components throughout childhood

The Authors describe the architecture of the evolution of IgE responses to multiple 50 allergen components throughout childhood, which may facilitate development of better diagnostic and prognostic biomarkers for allergic diseases.

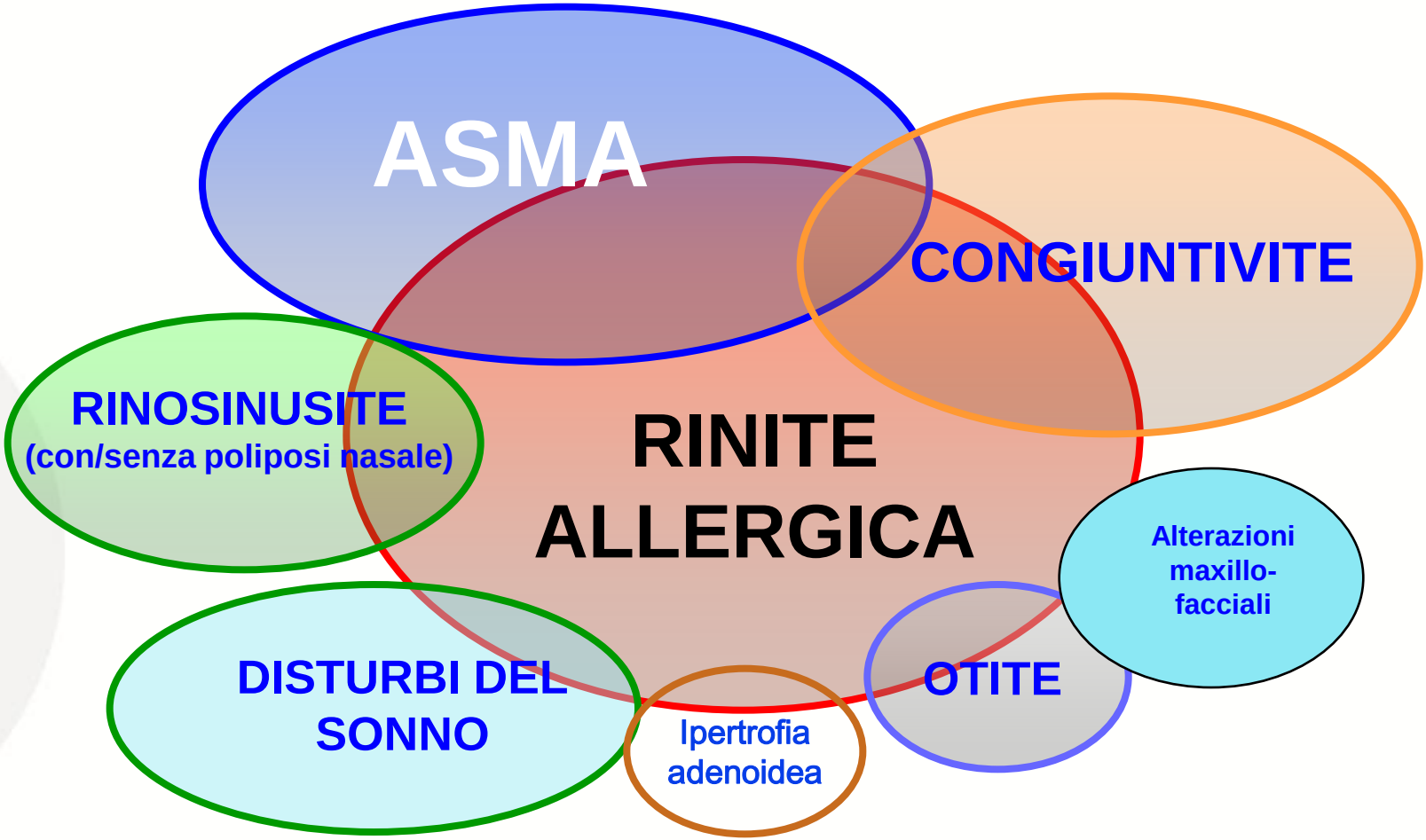
Results: We identified one sensitization cluster at age one, 3 at age three, 4 at ages five and eight, 5 at age 11, and six at age 16 years. "Broad" cluster was the only cluster present at every follow-up, comprising of components from multiple sources. "Dust mite" cluster formed at age three and remained unchanged to adolescence. At age three, a single-component "Grass" cluster emerged, which at age five absorbed additional grass components and Fel d 1 to form the "Grass/cat" cluster. Two new clusters formed at age 11: "Cat" cluster and "PR-10/profilin" (which divided at age 16 into "PR-10" and "Profilin"). The strongest contemporaneous associate of asthma at age 16 years was sensitization to "Dust mite" cluster (OR [95% CI]: 2.6 [1.2-6.1], $P<0.05$), but the strongest early-life predictor of subsequent asthma was sensitization to "Grass/cat" cluster (3.5 [1.6–7.4], $P<0.01$).



Clustering active IgE components throughout childhood. Cluster membership was determined using a Bernoulli Mixture Model applied to binarized sensitization data from all subjects.

Howard R, Belgrave D, Papastamoulis P, Simpson A, Rattray M, Custovic A, Journal of Allergy and Clinical Immunology (2018)

PRINCIPALI COMORBILITA’



Anamnesi/Esame obiettivo

Ha mai avuto attacchi di respiro sibilante ?
Ha tosse "secca" ?
Ha tosse o sibili dopo esercizio fisico ?
Ha senso di oppressione al petto ?

Se positivi o suggestivi

Spirometria

- **ostruzione** → **TEST DI REVERSIBILITA'**
- **normale** → **VALUTARE PER EVENTUALE TEST DI BRONCODILATAZIONE E/O TEST DI PROVOCAZIONE ASPECIFICO**

Cheratocongiuntivite atopica e primaverile (AKC e VKC) vs congiuntivite allergica (AC)

	AC	AKC	VKC<
Sintomi	+		+++
Segni	+ (vasodilatazione/edema)		+++ (proliferazione)
Interessamento corneale	-		+
Malattia preferenz.associata	Rinite		Eczema, asma
IgE totali	+		++/+++
IgE specifiche	++		+/-
Eosinofili	-/+		++/+++
Reattività congiunt. non-specifica	+/-		+/++
Risposta a terapia antiallergica	++/+++		-/+

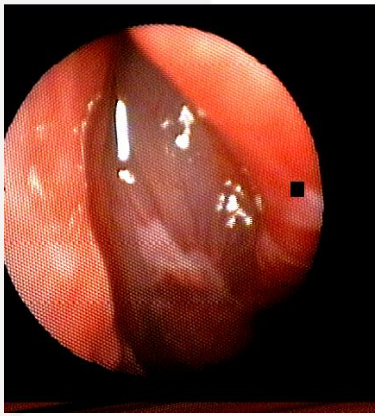
Legenda

RINOSINUSITE (E POLIPOSI): DIAGNOSI
La radiografia standard non è raccomandata

ALMENO due o più SINTOMI, di cui almeno uno di:

a)ostruzione nasale e/o rinorrea ant. o post.

b)ipo-anosmia e/o dolore facciale



ED EVIDENZA ENDOSCOPICA DI:

- **poliposi e/o**
- **scolo purulento dal meato medio e/o**
- **edema mucosale nel meato medio**

E/O EVIDENZA TC DI:

- **interessamento sinusale od ostio-meatale**

EP3OS, Rhinology 2012

Congestione nasale e disturbi del sonno

Congestion and Sleep Impairment in Allergic Rhinitis

Timothy J. Craig • Amir Sherkat • Sahar Safaee

La congestione/ostruzione nasale è la principale responsabile delle alterazioni del sonno nel rinitico.

Dal 30 al 40% dei rinitici ha alterazioni del sonno

I principali problemi sono: apnee ostruttive, russamento, sonno non ristoratore, risvegli.

Le alterazioni del sonno possono causare sonnolenza diurna e ridotta performance lavorativa o scolastica

DEFINIZIONE-PATOGENESI
CLASSIFICAZIONE
EPIDEMIOLOGIA
CLINICA E DIAGNOSTICA
IMPATTO SULLA QoL
TRATTAMENTO
IMPATTO SULL'ASMA
ASPETTI PARTICOLARI

QoL: Questionari per la rinite

QUESTIONARIO	BIBLIOGRAFIA	N di items	ETA'
Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ)	Juniper *JACI, 1999*	28	Adulti
Mini Rhinoconjunctivitis Quality of Life Questionnaire (Mini-RQLQ)	Juniper *Clin Exp Allergy 2000*	14	Adulti
Pediatric Rhinoconjunctivitis Quality of Life Questionnaire (PRQLQ)	Juniper *JACI, 1998*	23	Bambini (6-12)
Adolescent Rhinoconjunctivitis Quality of Life Questionnaire	Juniper *JACI, 1994*	25	Adolescenti (12-17)
Multiattribute rhinitis utility index	Revicki *Qual Life Res, 1998*	10	Adulti
Nocturnal Rhinoconjunctivitis QoL questionnaire (NRQLQ)	Juniper *JACI, 2003*	16	Adulti
Rhinasthma	Baiardini *Allergy, 2003*	30	Adulti
Rhinasthma adolescenti	*La Grutta PAI 2014*	30	Adolesc.
RAPP	*Braido, Allergy 2012*	10	Adulti

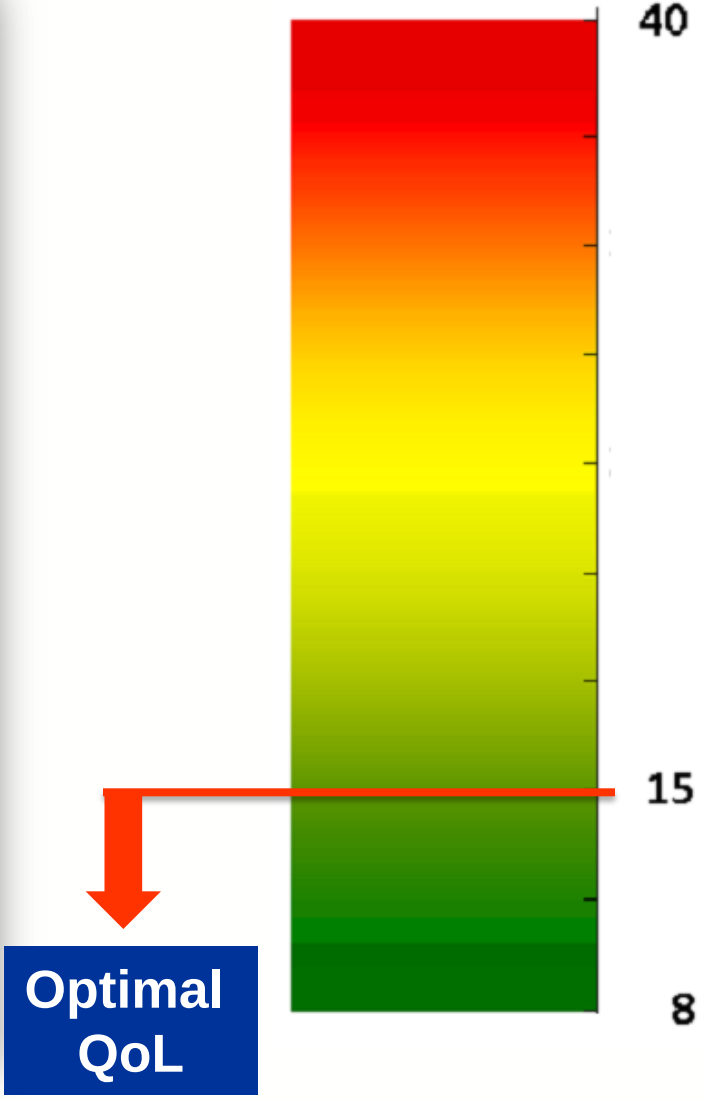
Come è strutturato il questionario RAPP (Rhinitis Asthma Patient Perspective)

RAPP

Rhinitis & Asthma Patient Perspective

Il seguente questionario ha lo scopo di valutare l'impatto della rinite e dell'asma nella vita quotidiana.
Indichi con una crocetta quanto è stato disturbato/a nelle ultime 2 settimane da:

	Per niente	Poco	Abbastanza	Molto	Moltissimo	PUNTEGGIO
1. Naso chiuso o che cola, starnuti o prurito al naso	1	2	3	4	5	
2. Prurito agli occhi, lacrimazione, bruciore, occhi arrossati	1	2	3	4	5	
3. Difficoltà a concentrarti	1	2	3	4	5	
4. Respiro sibilante, tosse, oppressione al torace, difficoltà a respirare	1	2	3	4	5	
5. Sonno disturbato (es. risvegli notturni)	1	2	3	4	5	
6. Dal dover evitare certi ambienti	1	2	3	4	5	
7. Dal dover prendere farmaci	1	2	3	4	5	
8. Dalle limitazioni nello svolgere attività (lavoro, studio, attività sportiva)	1	2	3	4	5	
						TOTALE



(Allergy 2012 Nov; 67(11):1443-50)

Qualità della vita e fenotipo della rinite

Burden of allergic respiratory disease: a systematic review

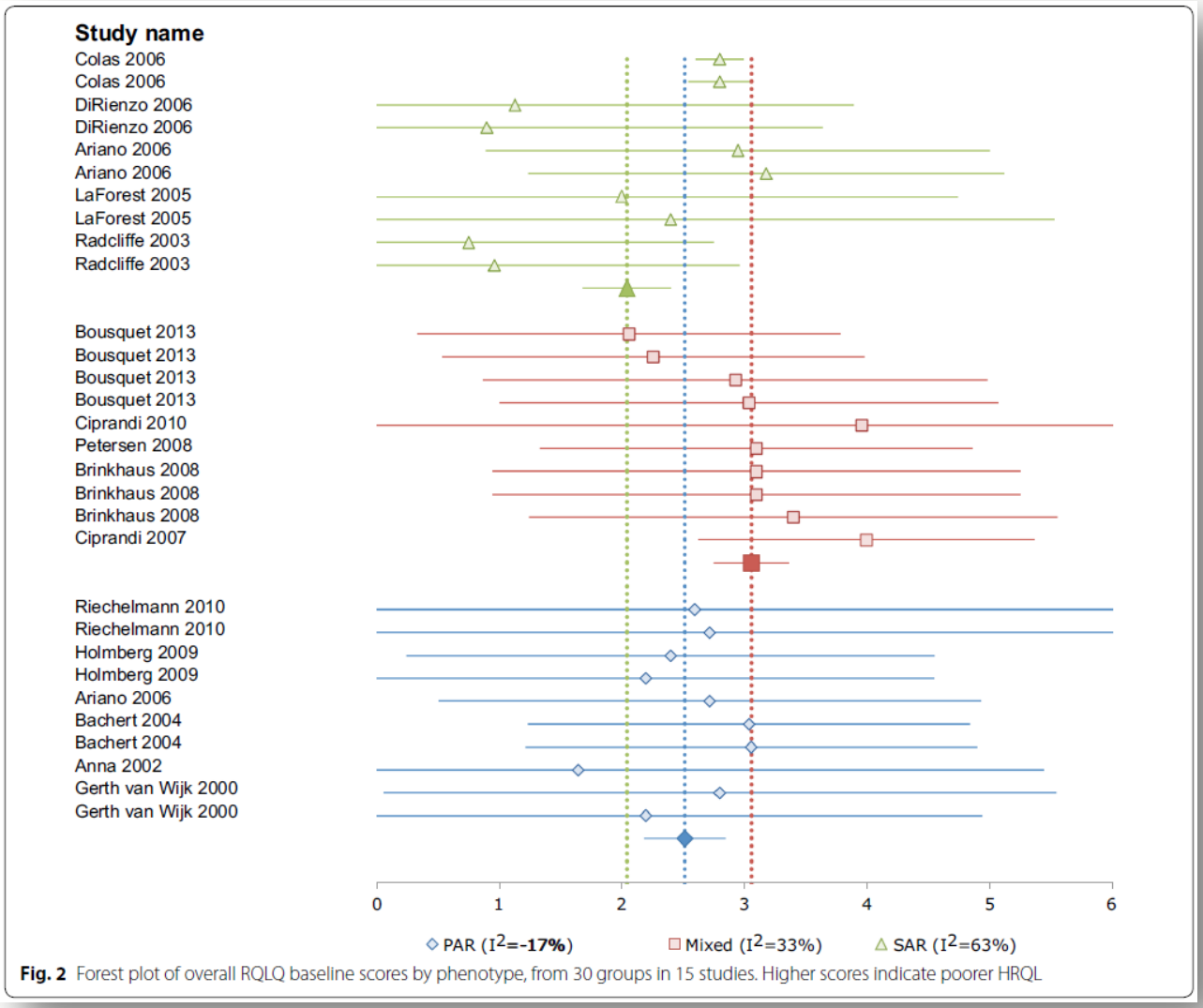


Fig. 2 Forest plot of overall RQLQ baseline scores by phenotype, from 30 groups in 15 studies. Higher scores indicate poorer HRQL

La QoL è sempre peggiore nella RA perenne che in quella stagionale. Peggiora ulteriormente nelle forme «miste»

(Linneberg A et al., Clin Mol Allergy 2016; sept. 28; 14:12)

Il controllo della rinite allergica nella «real life»

The control of allergic rhinitis in real life: a multicenter cross-sectional Italian study

Federica Gani[1*], Carlo Lombardi[2], Laura Barrocu[1], Massimo Landi[3], Erminia Ridolo[4], Massimo Bugiani[5], Giovanni Rolla[6], Gianenrico Senna[7] and Giovanni Passalacqua[8]

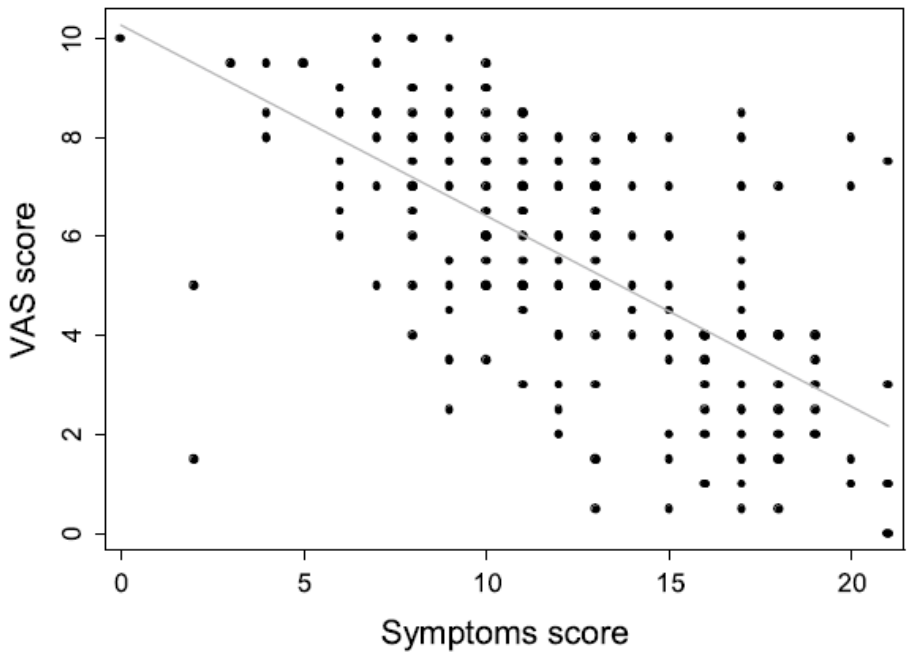


Fig. 1 Median regression of VAS score versus symptoms-score

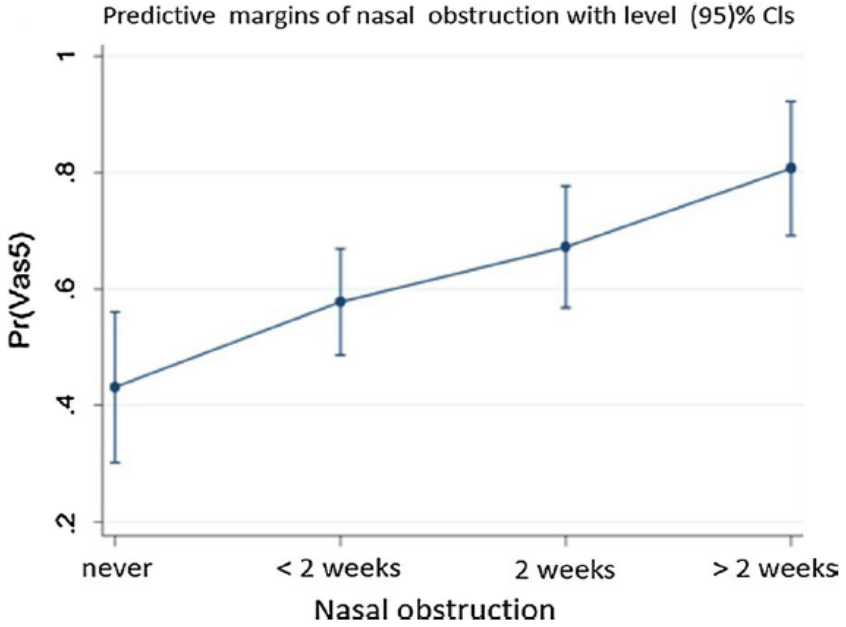


Fig. 2 Probability of VAS score > 5 by nasal obstruction frequency, adjusted for other CARAT items by means of logistic regression analysis

This survey, conducted in a real-life setting, confirmed that AR is overall poorly controlled. The VAS assessment well correlates with the structured CARAT questionnaire and with the relevant symptoms of AR.

(Clin Mol Allergy (2018) 16:4)

Impatto sulla produttività lavorativa

Impact of Rhinitis on Work Productivity: A Systematic Review

This systematic review provides summary estimates of the magnitude of work productivity impairment due to AR and identifies its main determinant factors.

TABLE III. Pooled analysis of the impact of rhinitis on work productivity: estimates weighted for variance

	Absenteeism, %*				Impaired presenteeism, %*				Overall work productivity impairment, %*			
Study type	N studies (references)	N strata	N participants	Mean % (95% CI)	N studies (references)	N strata	N participants	Mean % (95% CI)	N studies (references)	N strata	N participants	Mean % (95% CI)
All studies	6[19,25,31,37,39,43]	8	1666	3.6 (2.4; 4.8)	8[17,19,25,31,34,37,39,43]	15	4563	35.9 (29.7; 42.1)	11[17,19,25,31,33-37,39,43]	22	6535	39.4 (34.8; 44.0)
By study design:												
Observational	3[19,25,43]	3	676	4.3 (1.0; 7.7)	4[17,19,25,43]	7	2803	28.6 (19.8; 37.5)	4[17,19,25,43]	7	2802	29.3 (21.3; 37.4)
Interventional	3[31,37,39]	5	990	3.2 (1.9; 4.4)	4[31,34,37,39]	8	1760	42.2 (34.9; 49.6)	7[31,33-37,39]	15	3733	44.2 (39.9; 48.4)
By disease pattern:												
IAR/SAR	4[31,37,39,43]	6	1054	2.9 (1.8; 4.0)	5[17,31,37,39,43]	9	2113	37.5 (23.8; 51.3)	7[17,31,33,35,37,39,43]	14	3523	41.2 (33.7; 48.6)
PAR	1[43]	1	NA	NA	3[17,34,43]	5	2015	28.0 (19.8; 36.2)	4[17,34,36,43]	7	2522	33.7 (26.4; 40.9)
By disease severity:												
Mild AR	1[43]	1	NA	NA	2[17,43]	3	168	16.3 (8.9; 23.7)	2[17,43]	3	168	16.5 (9.6; 23.5)
M/S AR	5[25,31,37,39,43]	7	1347	3.1 (2.1; 4.1)	7[17,25,31,34,37,39,43]	12	4094	38.1 (31.5; 44.8)	10[17,25,31,33-37,39,43]	19	6066	41.4 (36.7; 46.0)

AR, Allergic rhinitis; *CI*, confidence interval; *IAR*, intermittent AR; *M/S*, moderate/severe AR; *NA*, not appropriate; *PAR*, persistent AR; *SAR*, seasonal AR.
*Assessed using the Work Productivity and Activity Impairment-Allergy Specific (WPAI-AS) questionnaire.

Pooled analysis of Work Productivity and Activity Impairment (WPAI)-based studies found an estimated 3.6% missed work time and 35.9% had impairment in at-work performance due to AR.

(Vandenplas et al., J Allergy Clin Immunol Pract 2017)

DEFINIZIONE-PATOGENESI
CLASSIFICAZIONE
EPIDEMIOLOGIA
CLINICA E DIAGNOSTICA
IMPATTO SULLA QoL
TRATTAMENTO
IMPATTO SULL'ASMA
ASPETTI PARTICOLARI

I 4 cardini dell'approccio terapeutico

Allontanamento dell'allergene
indicato quando possibile

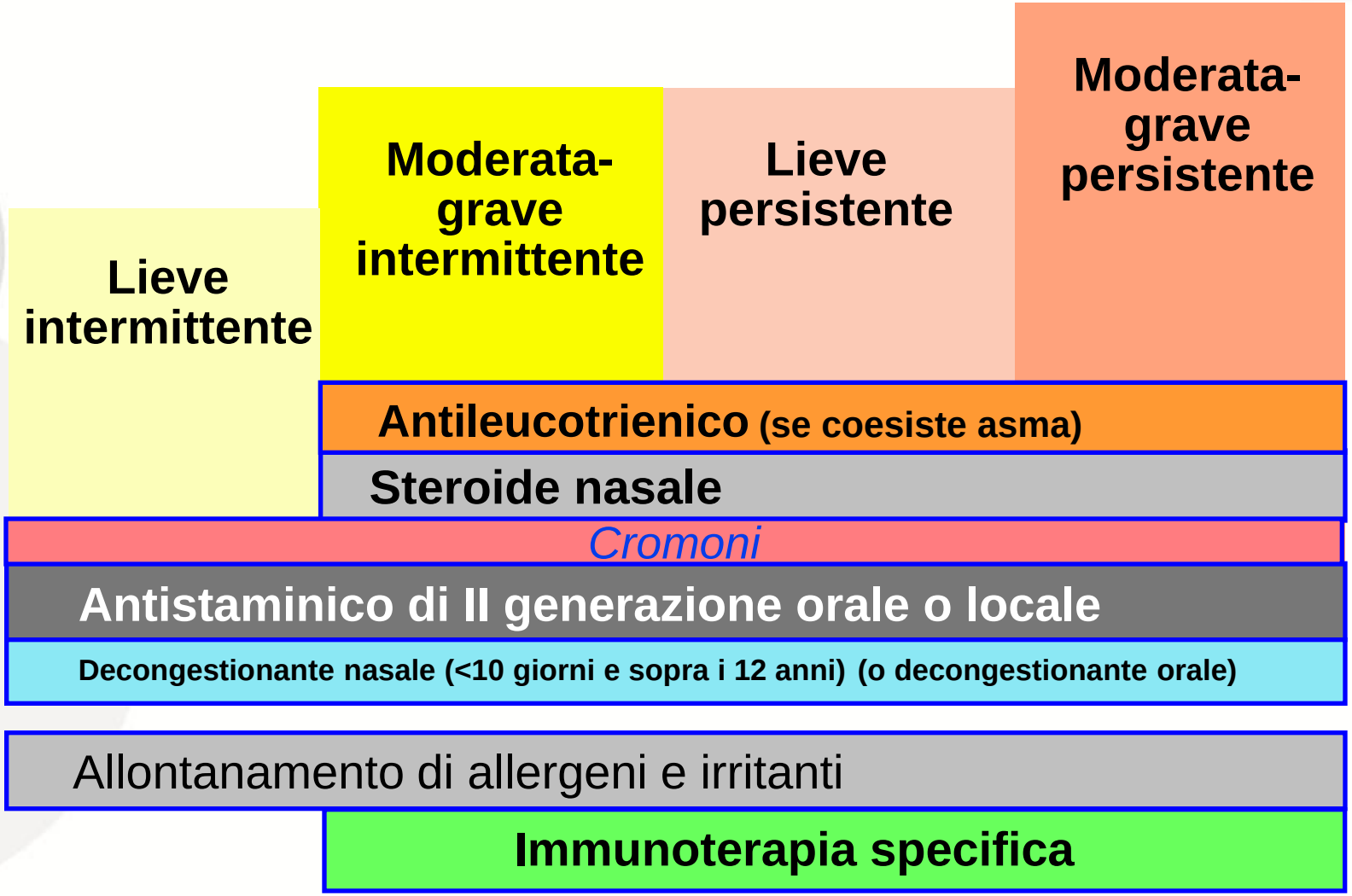
Immunoterapia
- *efficacia*
- *prescrizione specialist.*
- *può modificare la storia naturale*

costi

Farmacoterapia
- *sicurezza*
- *efficacia*
- *facilità di somministrazione*

Educazione del paziente
sempre indicata

Trattamento stepwise della rinite allergica



Educazione del paziente con RA

La comunicazione e l'educazione del paziente hanno un ruolo centrale nella gestione della rinite allergica, per ottenere un adeguato livello di compliance alle prescrizioni e di delegare al paziente adeguati spazi di autocontrollo e autogestione, sotto la supervisione del medico curante.

Il percorso dell'educazione terapeutica che guiderà il paziente o la sua famiglia verso un cambiamento nello stile di vita, adattandolo alle esigenze che la patologia richiede:

- **Valutazione clinica e diagnosi documentata di RA**
- **Comunicazione della Diagnosi e descrizione della malattia.** Spiegazione del rapporto tra l'allergene e i sintomi e delle possibili reazioni crociate (pollini/alimenti).
- **Indicazione dei rischi**, compresa la possibilità di un'evoluzione naturale della malattia o dello sviluppo di comorbidità.
- **Comunicazione delle migliori strategie per prevenire i sintomi**
- **Comunicazione della strategia terapeutica più adeguata**
- **Educazione all'autogestione** nell'uso corretto dei farmaci e dei dispositivi medici.
- **Valutazione periodica** del paziente e verifica delle competenze acquisite

Home Environmental Interventions for House Dust Mite

I. Bedroom
   a. Cover mattress with plastic or fine woven fabric; cover pillows and comforters with fine woven fabric; mattress pads, sheets and all blankets should be suitable for washing every 1-2 weeks
   b. Remove carpet if possible; decrease upholstered furniture, drapes, clothing, etc.
   c. Room air cleaner; best to use HEPA filter placed on polished floor

II. Whole House
   a. Decrease to 45% relative humidity or less
   b. Ventilate house at times when there is low outside humidity
   c. Choose a house with 2nd floor bedrooms
   d. Avoid concrete slabs except in the basement and certainly avoid fitted carpets on a concrete slab

III. Specific questions beyond the bedroom
   a. Carpets should be area rugs if possible; ideally they should be cleaned or put out in the sun and beaten
   b. Vacuum carpets twice weekly
   c. Avoid upholstered furniture as much as possible and reduce clutter to facilitate cleaning

Priorities in the approach to decrease dust mite exposure

TABLE II. Successful trials of dust mite avoidance in the management of asthma

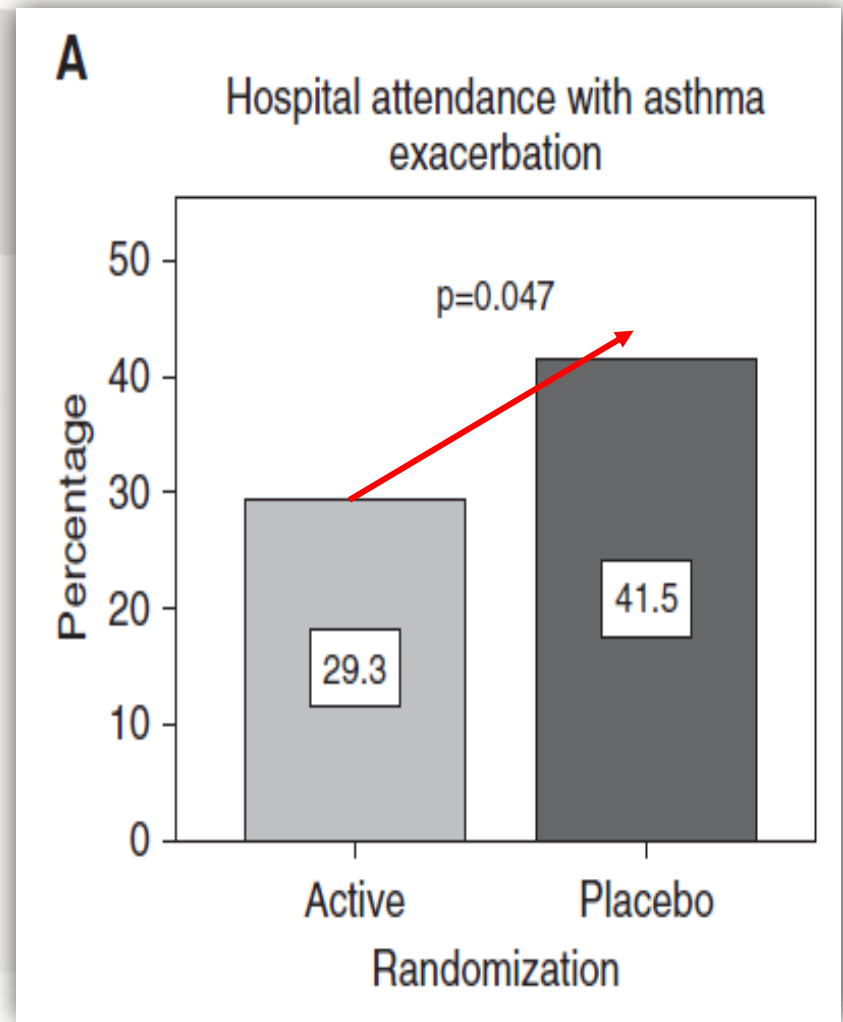
Authors	Length	Methods	Participants	Decrease in mite	Outcome
Walshaw and Evans,[73] 1986	1 y	Physical barriers	22/10	++	PEFR/BHR
Ehnert et al,[74] 1992	1 y	Physical barriers	8/16	++	PEFR/BHR
Htut et al,[75] 2001	1 y	Heat treatment	10/10/10	++	BHR
Morgan et al,[76] 2004	1 y	Multiple measures	425/441	++	Symptoms
Murray et al,[77] 2017	1 y	Physical barriers	146/138	ND	Acute exacerbations

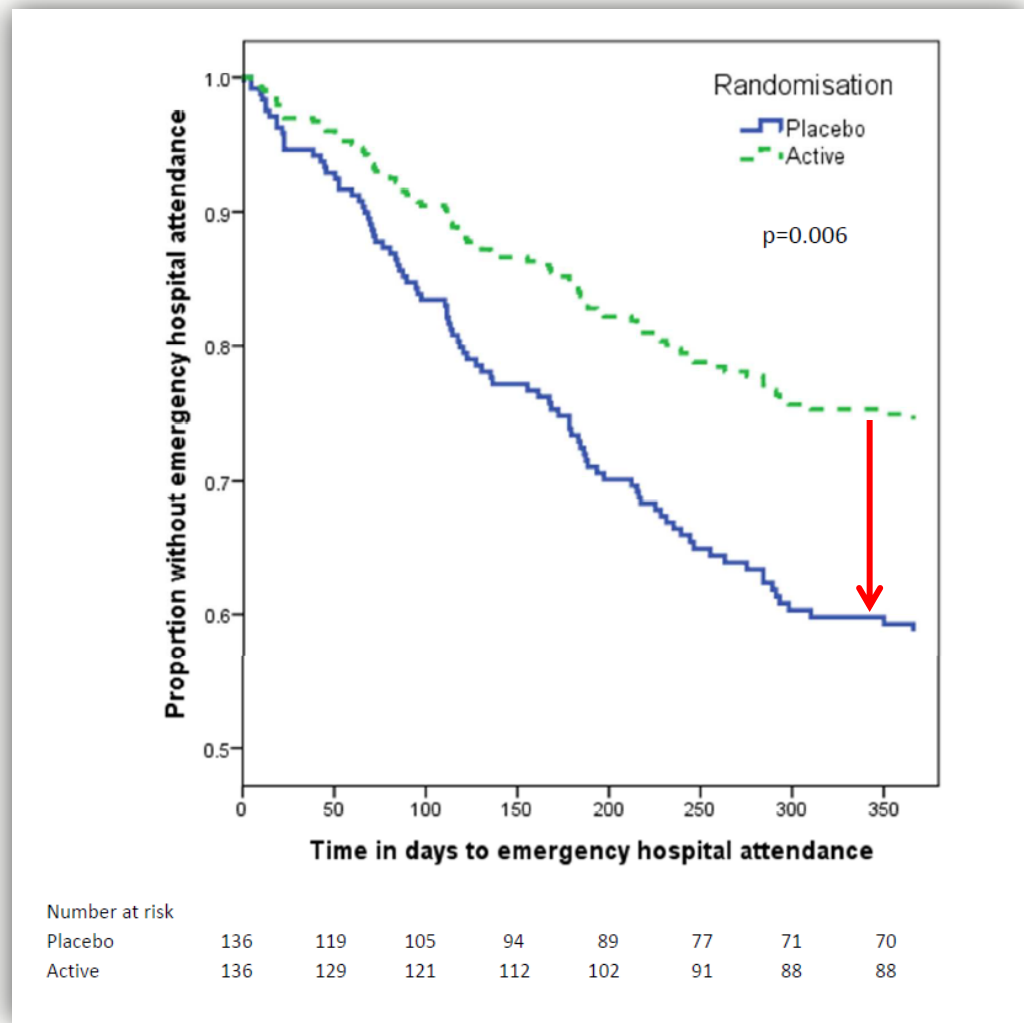
ND, Not determined; *PEFR*, peak expiratory flow rate.

(Wilson JM et al., J Allergy Clin Immunol Pract 2018;6:1-7)

Preventing severe asthma exacerbations in children with mite-impermeable bedcovers

146 active; 138 placebo





(Murray, AJRCCM 2017;196:150)

FORZA DELLE RACCOMANDAZIONI PER ALCUNI FARMACI PER LA RINITE ALLERGICA

	RINITE STAGIONALE		RINITE PERENNE	
FARMACO	ADULTI	BAMBINI	ADULTI	BAMBINI
Antistaminico orale	A	A	A	A
Antistaminico nasale	A	A	A	A
Antistaminico oculare	A	A	B	B
Steroide nasale	A	A	A	A
Steroide orale	A	B	B	B
Steroide i.m.	A	B	B	B
Cromone nasale	A	A	A	B
Cromone oculare	A	A	B	B
NAAGA oculare	B	C	C	C
Decongestionante nasale	C	C*	C	C*
Decongestionante orale	A			
Decongestionante orale * antiH1	A	B*	B	B*
Anticolinergico			A	A

* Solo > 12 anni

Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines—2016 revision

Recommendation	Assumed values and preferences	Explanations and other considerations
Question 1: Should a combination of an oral H1-antihistamine (OAH) and intranasal corticosteroid (INCS) vs INCS alone be used for treatment of AR?		
Recommendation 1A: In patients with SAR, we suggest either a combination of an INCS with an OAH or an INCS alone (conditional recommendation | low certainty of evidence).	ARIA guideline panel acknowledged that the choice of treatment would depend mostly on patient preferences and local availability and cost of treatment. Panel members assumed that in the majority of situations, potential net benefit would not justify spending additional resources.	This is a conditional recommendation, and thus different choices will be appropriate for different patients. In settings in which the additional cost of an OAH is not large and/or patients' values and preferences differ from those assumed by guideline panel members, a combination therapy might be a reasonable choice, especially in patients whose symptoms are not well controlled with an INCS alone, those with pronounced ocular symptoms, or those commencing treatment because of likely faster onset of treatment effects. This recommendation concerns regular use of newer and less sedative OAHs and INCSs in patients with SAR. For older OAHs with more sedative effects, the balance of desirable and undesirable effects may be different.
Recommendation 1B: In patients with PAR, we suggest an INCS alone rather than a combination of an INCS with an OAH (conditional recommendation | very low certainty of evidence).	—	Currently available evidence suggests that there is no additional benefit from a combination therapy compared with INCS alone, and there might be additional undesirable effects. This recommendation is conditional because of sparse information and thus very low certainty of the estimated effects.

(Brozek J et al., J Allergy Clin Immunol 2017;140:950-8)

Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines—2016 revision

Recommendation	Assumed values and preferences	Explanations and other considerations
Question 2: Should a combination of an intranasal H_1-antihistamine (INAH) and INCS vs an INCS alone be used for treatment of AR?		
Recommendation 2A: In patients with SAR, we suggest either a combination of an INCS with an INAH or an INCS alone (conditional recommendation | moderate certainty of evidence).	The panel members acknowledged that the choice of treatment will mostly depend on patient preferences and local availability and cost of treatment. At initiation of treatment (approximately the first 2 weeks), a combination of an INCS with an INAH might act faster than an INCS alone and thus might be preferred by some patients.	This is a conditional recommendation, and thus different choices will be appropriate for different patients. In settings in which the additional cost of combination therapy is not large and/or patients value potential benefits more than any increased risk of adverse effects, a combination therapy might be a reasonable choice.
Recommendation 2B: In patients with PAR, we suggest either a combination of an INCS with an INAH or an INCS alone (conditional recommendation | very low certainty of evidence).	The panel members acknowledged that the choice of treatment will mostly depend on patient preferences and local availability and cost of treatment.	This is a conditional recommendation because of the very low certainty of the evidence. At the initiation of treatment (approximately the first 2 weeks), combination of an INCS with an INAH might act faster than an INCS alone and thus might be preferred by some patients.

(Brozek J et al., J Allergy Clin Immunol 2017;140:950-8)

Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines—2016 revision

Recommendation	Assumed values and preferences	Explanations and other considerations
Question 3: Should a combination of an INAH and INCS vs an INAH alone be used for treatment of AR?		
Recommendation 3A: In patients with SAR, we suggest a combination of an INCS with an INAH rather than an INAH alone (conditional recommendation | low certainty of evidence).	This recommendation places higher value on additional reduction of symptoms and improved quality of life with a combination therapy compared with an INAH alone. It places a lower value on avoiding additional cost (expenditure of resources).	This is a conditional recommendation, and thus different choices will be appropriate for different patients. In settings in which the additional cost of a combination therapy is large, an alternative choice (ie, and INAH alone) might be equally reasonable. One panel member thought that the recommendation should be conditional for either the intervention or comparison.
Question 4: Should a leukotriene receptor antagonist (LTRA) vs an OAH be used for treatment of AR?		
Recommendation 4A: In patients with SAR, we suggest either an LTRA or an OAH (conditional recommendation | moderate certainty of evidence).	Panel members acknowledged that the choice of an LTRA or OAH will mostly depend on patient preferences and local availability and cost of specific medications. In many settings an OAH might still be more cost-effective, but this will largely depend on availability of generic LTRAs and the local cost of various newer-generation OAHs and LTRAs.	Some patients with AR who have concomitant asthma, especially exercise-induced and/or aspirin-exacerbated respiratory disease, might benefit from an LTRA more than from an OAH. However, this recommendation applies to treatment of AR but not to treatment of asthma. Patients with asthma who have concomitant AR should receive an appropriate treatment according to the guidelines for the treatment of asthma.

(Brozek J et al., J Allergy Clin Immunol 2017;140:950-8)

Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines—2016 revision

Recommendation	Assumed values and preferences	Explanations and other considerations
Question 5: Should an INAH vs an INCS be used for treatment of AR?		
Recommendation 5A: In patients with SAR, we suggest an INCS rather than an INAH (conditional recommendation | moderate certainty of evidence).	This recommendation places a higher value on likely small but greater reduction of symptoms and improvement of quality of life with an INCS compared with an INAH and a lower value on avoiding larger cost of treatment with an INCS in many jurisdictions.	This is a conditional recommendation, and thus different choices will be appropriate for different patients. Clinicians must help each patient to arrive at a decision consistent with her or his values and preferences, considering local availability and costs.
Recommendation 5B: In patients with PAR, we suggest an INCS rather than an INAH (conditional recommendation | low certainty of evidence).	This recommendation places a higher value on probably greater reduction of nasal symptoms with an INCS compared with an INAH, although the overall difference is likely small. It places a lower value on avoiding larger cost of treatment with an INCS in many jurisdictions.	This is a conditional recommendation, and thus different choices will be appropriate for different patients. Clinicians must help each patient to arrive at a decision consistent with her or his values and preferences, considering local availability and costs.
Question 6: Should an INAH vs an OAH be used for treatment of AR?		
Recommendation 6A: In patients with SAR, we suggest either an INAH or OAH (conditional recommendation | low certainty of evidence).	The panel members acknowledged that the choice of treatment will depend mostly on patient preferences and local availability and cost of treatment.	This is a conditional recommendation, and thus different choices will be appropriate for different patients. Clinicians must help each patient to arrive at a decision consistent with her or his preferences, considering local availability, coverage, and costs.
Recommendation 6B: In patients with PAR, we suggest either an INAH or OAH (conditional recommendation | very low certainty of evidence).	The panel members acknowledged that the choice of treatment will mostly depend on patient preferences and local availability and cost of treatment.	This is a conditional recommendation, and thus different choices will be appropriate for different patients. Clinicians must help each patient to arrive at a decision consistent with her or his preferences, considering local availability, coverage, and costs.

(Brozek J et al., J Allergy Clin Immunol 2017;140:950-8)

Terapia farmacologica
RACCOMANDAZIONI GENERALI

- Gli antistaminici orali o topici di seconda generazione sono raccomandati per il trattamento della rinite e della congiuntivite in adulti e bambini.

- Gli steroidi nasali sono raccomandati per il trattamento della rinite allergica in adulti e bambini; sono i farmaci più efficaci nella rinite allergica.

ARIA, Allergy 2008

RACCOMANDAZIONI GENERALI

•Gli steroidi depot non sono raccomandati.

• Gli steroidi sistemici non devono essere utilizzati per periodi lunghi per motivi di sicurezza.

• I cromoni possono essere usati per il trattamento della rinite e della congiuntivite allergica, ma la loro efficacia è modesta.

• L'ipratropio può essere utilizzato per trattare la rinorrea, se questa è importante.

• I decongestionanti topici possono essere usati (sopra i 12 anni), solo per brevi periodi, se l'ostruzione nasale è molto severa.

ARIA, Allergy 2008

TRATTAMENTI FARMACOLOGICI

Gli antistaminici di II generazione sono efficaci su rinorrea, starnuti e prurito. Alcuni di essi possiedono attività antinfiammatorie e agiscono in parte anche sull'ostruzione.

Nayak, Allergy 2001; Wilson, Allergy 2002; Simons, JACI 2003; Potter, Allergy 2003; Hore, Clin Exp Allergy 2005

I corticosteroidi nasali sono efficaci sull'ostruzione. Il massimo effetto richiede 24-48 ore, ma possono agire sui sintomi già a partire dalle 12 ore circa.

Jen, Ann Allergy Asthma Immunol 2000; Denkewicz, JACI 2003

Alcuni corticosteroidi nasali (beclometasone dipropionato, mometasone furoato e fluticasone furoato) hanno mostrato di poter migliorare anche gli eventuali sintomi oculari concomitanti.

Kaiser et al. JACI 2007;119; Bielory Ann Allergy 2008; Weinstein et al., Allergy Asthma Proc.2014

STEROIDI NASALI : le differenti biodisponibilità

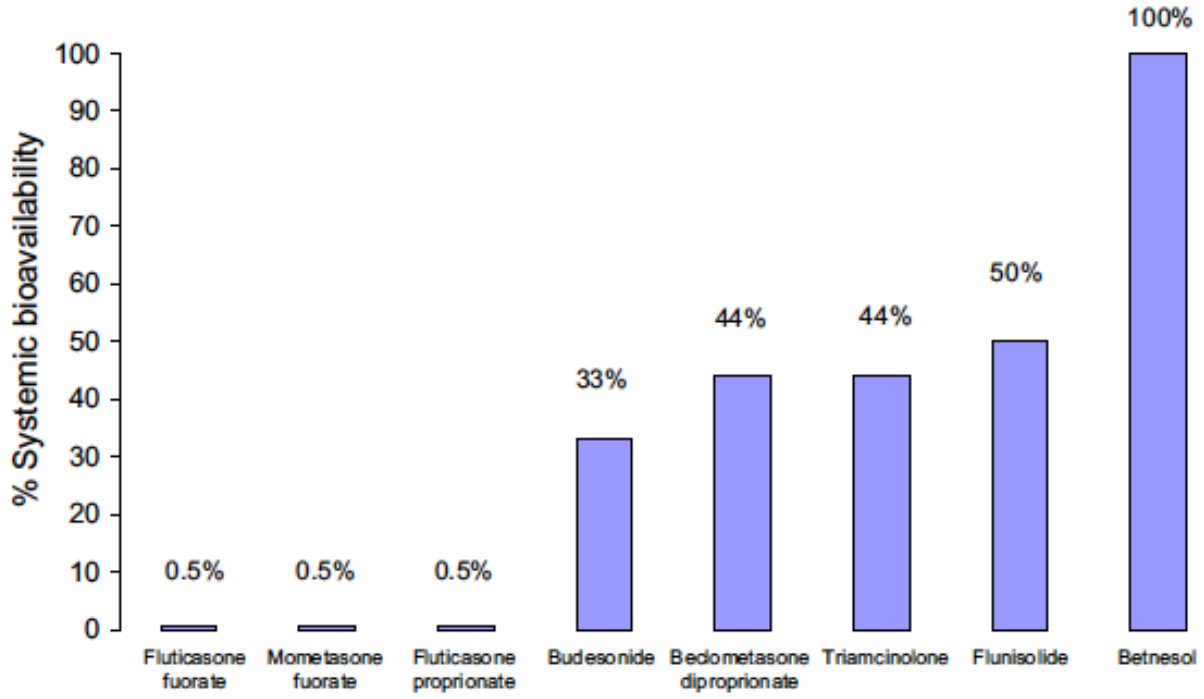


FIGURE 3 Bioavailability of intranasal corticosteroids. The more recent molecules have little systemic uptake and are suitable for use in children and for long-term therapy (Grade A evidence)

Scadding GC, et al. BSACI guideline for the diagnosis and management of allergic and non-allergic rhinitis (Revised Edition 2017; First edition 2007)
Clin Exp Allergy. 2008 Jan;38(1):19-42.

Nuova indicazione pediatrica di Mometasone

- Mometasone spray nasale è indicato nel trattamento dei sintomi della rinite allergica stagionale o perenne negli adulti e nei bambini dai **3 anni di età**.

GU N° 14 del 2-2-2016

No effect on linear height over 12 months. Pediatrics, 2000

NESSUN EFFETTO MISURABILE SULLA CRESCITA LINEARE ANCHE IN ETA' PRECOLARE

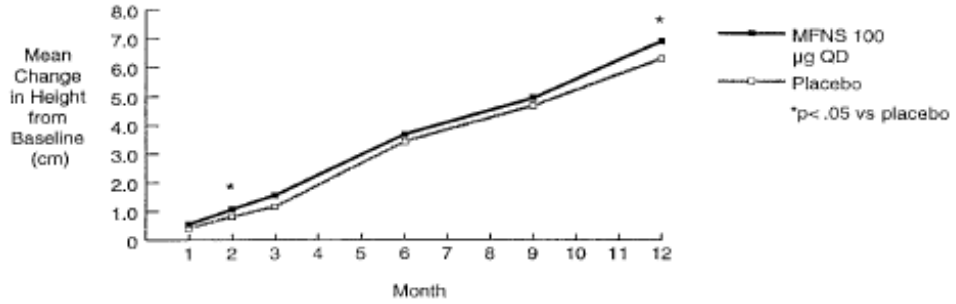


Fig 1. Mean change in standing height from baseline measured by stadiometer over 1 year of treatment with MFNS 100 µg QD or placebo.

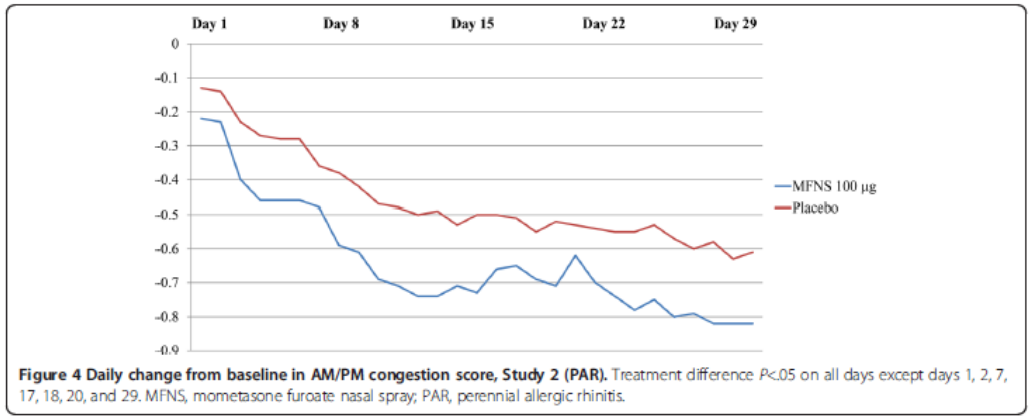
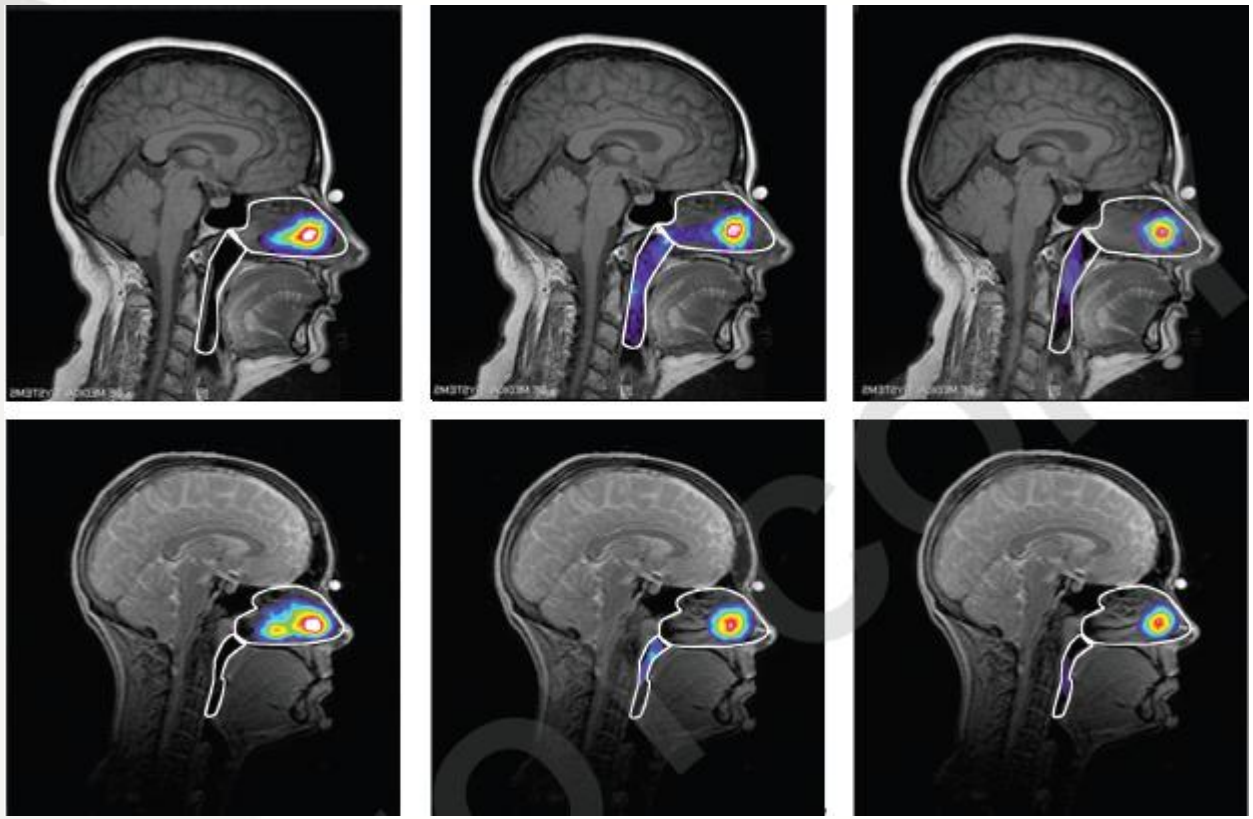


Figure 4 Daily change from baseline in AM/PM congestion score, Study 2 (PAR). Treatment difference *P*<.05 on all days except days 1, 2, 7, 17, 18, 20, and 29. MFNS, mometasone furoate nasal spray; PAR, perennial allergic rhinitis.

EFFETTO SIGNIFICATIVO SULLA CONGESTIONE NASALE ANCHE NEI BAMBINI

Ages 3–11 years with perennial AR [PAR] ≥1 year)

Regional deposition of mometasone furoate nasal spray suspension in humans



Initial human deposition images of MFS radiolabeled formulation (left) and after 20 and 60 minutes (center and right) of two subjects (above, below).

Mometasone Furoate nasal suspension deposited significant drug into the posterior nasal cavity. Both nasal cast validation and mucociliary clearance confirm the radiolabel deposition distribution method accurately represented corticosteroid nasal deposition.

Table 4. **Mean radiolabel remaining (standard deviation) in the nasal cavity as a percentage of the initial radiolabel counts in the nasal cavity**

Time (min)	Nasal Spray Suspension
0	100.00 (0)
15	41.11 (18)
20	37.02 (17)
30	30.71 (14)
45	26.42 (11)
60	25.00 (11)
90	23.04 (10)
120	20.54 (9)
180	17.37 (7)
360	13.32 (7)

(Shah et al. , Allergy and Asthma Proceedings, 2015)

Onset of action of the fixed combination intranasal azelastine-fluticasone propionate in an allergen exposure chamber

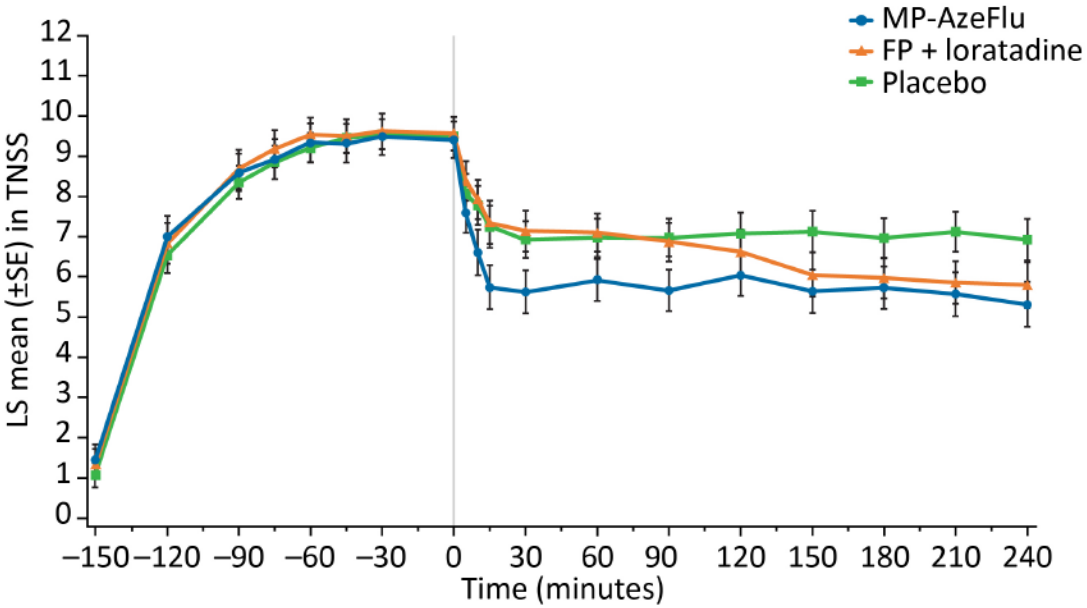
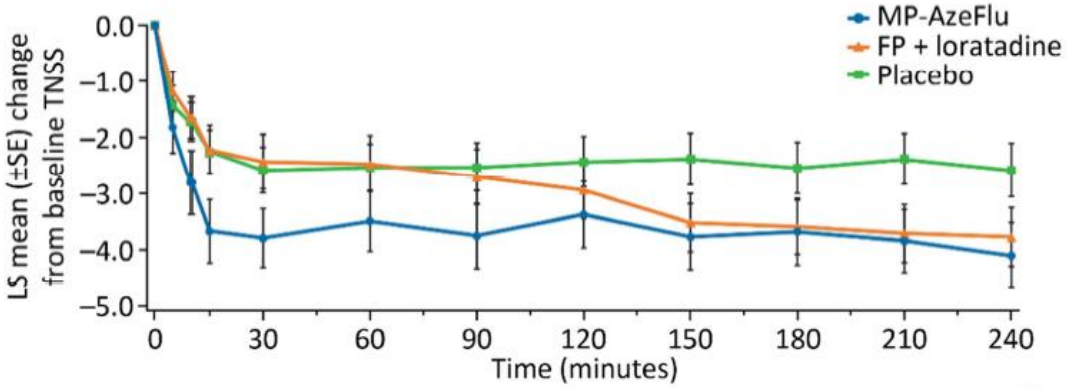
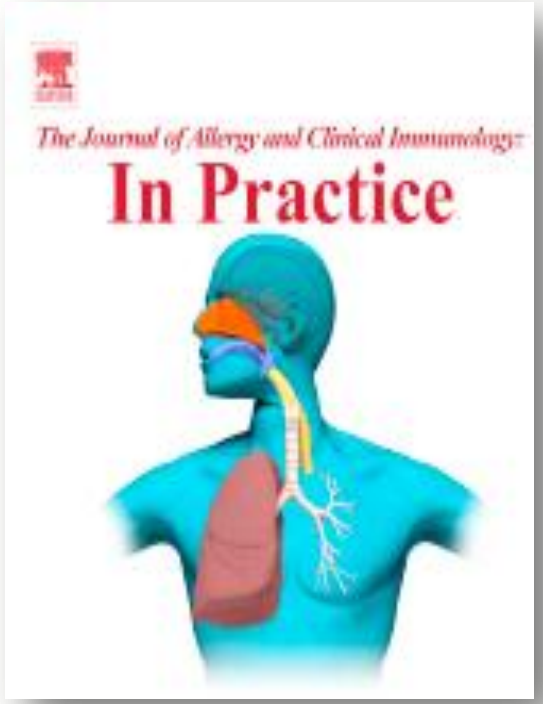


Figure 1B:





Bousquet J et al.,
J Allergy Clin Immunol Pract.
2018 Feb 6

Azalastina+fluticasone propionato vs. fluticasone propionato

Practice Guideline

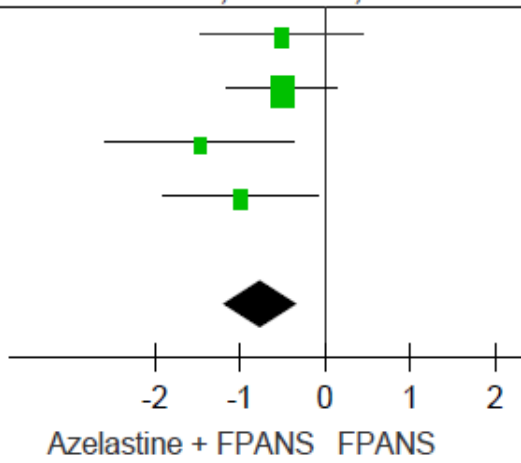
Treatment of seasonal allergic rhinitis
An evidence-based focused 2017 guideline update

Mark S. Dykewicz, MD; Dana V. Wallace, MD; Fuad Baroody, MD; Jonathan Bernstein, MD; Tim Craig, DO; Ira Finegold, MD; Faith Huang, MD; Desiree Larenas-Linnemann, MD; Eli Meltzer, MD; Gary Steven, MD, PhD; David I. Bernstein, MD; Joann Blessing-Moore, MD; Chitra Dinakar, MD; Matthew Greenhawt, MD, MBA; Caroline C. Horner, MD; David A. Khan, MD; David Lang, MD; John Oppenheimer, MD; Jay M. Portnoy, MD; Christopher R. Randolph, MD; Matthew A. Rank, MD; Workgroup Chair and Cochair: Mark S. Dykewicz, MD; Dana V. Wallace, MD

	Azelastine + FPANS			FPANS				Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Carr 2012a	-5.5	5.2	207	-5	4.7	207	20.0%	-0.50 [-1.45, 0.45]	
Carr 2012b	-5.6	5.2	448	-5.1	4.7	450	43.5%	-0.50 [-1.15, 0.15]	
Hampel 2010	-5.31	5.08	153	-3.84	4.76	151	14.9%	-1.47 [-2.58, -0.36]	
Meltzer 2012	-5.54	4.617	193	-4.55	4.617	194	21.6%	-0.99 [-1.91, -0.07]	
Total (95% CI)			**1001**			**1002**	**100.0%**	**-0.75 [-1.18, -0.32]**	

Heterogeneity: Tau² = 0.00; Chi² = 2.72, df = 3 (P = 0.44); I² = 0%

Test for overall effect: Z = 3.44 (P = 0.0006)



Modificazioni del total nasal symptom score

(Ann Allergy Asthma Immunol; november 2017 : 1-23)

Practice Guideline

Treatment of seasonal allergic rhinitis

An evidence-based focused 2017 guideline update

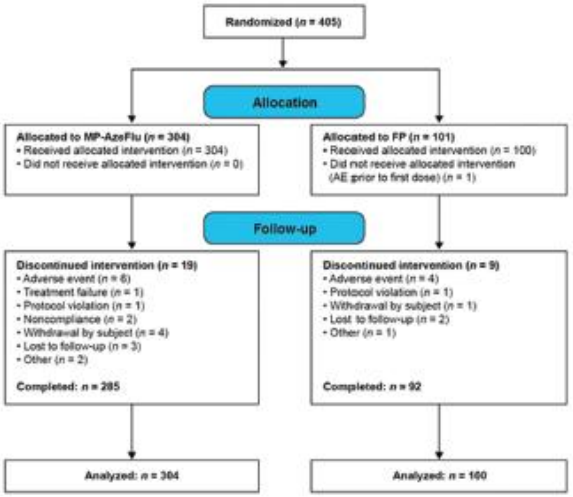
Mark S. Dykewicz, MD; Dana V. Wallace, MD; Fuad Baroody, MD; Jonathan Bernstein, MD; Tim Craig, DO; Ira Finegold, MD; Faith Huang, MD; Desiree Larenas-Linnemann, MD; Eli Meltzer, MD; Gary Steven, MD, PhD; David I. Bernstein, MD; Joann Blessing-Moore, MD; Chitra Dinakar, MD; Matthew Greenhawt, MD, MBA; Caroline C. Horner, MD; David A. Khan, MD; David Lang, MD; John Oppenheimer, MD; Jay M. Portnoy, MD; Christopher R. Randolph, MD; Matthew A. Rank, MD; Workgroup Chair and Cochair: Mark S. Dykewicz, MD; Dana V. Wallace, MD

Conclusion

In summary, from our review of specific management strategies for AR, the following conclusions are warranted. When monotherapy is being considered, INCSs are a more effective choice than LTRAs. When a patient is already taking an INCS, yet the patient's condition is not optimally controlled, and is considering the addition of an antihistamine, the best additional therapy is an INAH not an oral antihistamine.

(Ann Allergy Asthma Immunol; november 2017 : 1-23)

Safety of azelastine + fluticasone in children



Safety of a novel intranasal formulation of azelastine hydrochloride and fluticasone propionate in children: A randomized clinical trial

The intranasal formulation of AZE and FP was safe and well tolerated after 3 months' continuous use in children with allergic rhinitis.

	All Age Strata		Ages ≥4 to <6 y		Ages ≥6 to <9 y		Ages ≥9 to <12 y	
	MP-AzeFlu (*n* = 304)	FP (*n* = 100)	MP-AzeFlu (*n* = 40)	FP (*n* = 11)	MP-AzeFlu (*n* = 128)	FP (*n* = 44)	MP-AzeFlu (*n* = 136)	FP (*n* = 45)
Any TEAE, no. (%)	124 (41)	37 (37)	18 (45)	5 (45)	51 (40)	15 (34)	55 (40)	17 (38)
Epistaxis	30 (10)	9 (9)	4 (10)	1 (9)	12 (9)	4 (9)	14 (10)	4 (9)
Headache	20 (7)	3 (3)	2 (5)	0 (0)	10 (8)	3 (7)	8 (6)	0 (0)
Cough	11 (4)	3 (3)	3 (8)	0 (0)	4 (3)	2 (5)	4 (3)	1 (2)
Pyrexia	10 (3)	2 (2)	2 (5)	0 (0)	4 (3)	0 (0)	4 (3)	2 (4)
Oropharyngeal pain	9 (3)	0 (0)	0 (0)	0 (0)	4 (3)	0 (0)	5 (4)	0 (0)
Otitis media	9 (3)	3 (3)	3 (8)	0 (0)	5 (4)	1 (2)	1 (<1)	2 (4)
Vomiting	9 (3)	2 (2)	0 (0)	1 (9)	6 (5)	0 (0)	3 (2)	1 (2)
Upper abdominal pain	8 (3)	2 (2)	0 (0)	1 (9)	5 (4)	1 (2)	3 (2)	0 (0)
URTI	8 (3)	1 (1)	2 (5)	1 (9)	2 (2)	0 (0)	4 (3)	0 (0)
Diarrhea	4 (1)	4 (4)	0 (0)	2 (18)	1 (<1)	1 (2)	3 (2)	1 (2)

TEAE = treatment-emergent adverse event; MP-AzeFlu = Meda Pharma's azelastine hydrochloride and fluticasone propionate; FP = fluticasone propionate; URTI = upper respiratory tract infection.
**TEAEs recorded are those reported by ≥3% of the subjects in either treatment group.*

(Berger et al., Allergy Asthma Proc 39 :110 –116, 2018)

ASSOCIAZIONE DESLORATADINA + PSEUDOEFEDRINA

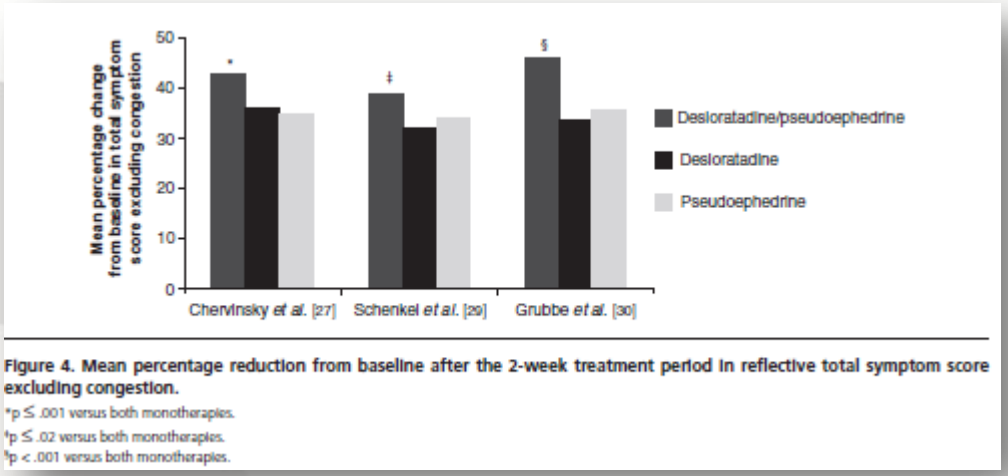


Figure 4. Mean percentage reduction from baseline after the 2-week treatment period in reflective total symptom score excluding congestion.

*p ≤ .001 versus both monotherapies.
‡p ≤ .02 versus both monotherapies.
§p < .001 versus both monotherapies.

Desloratadine and pseudoephedrine combination therapy as a comprehensive treatment for allergic rhinitis and nasal congestion

…"Administration of the second-generation antihistamine desloratadine in combination with the decongestant pseudoephedrine may be regarded as an efficacious and convenient option for patients with AR who are particularly troubled by nasal congestion".

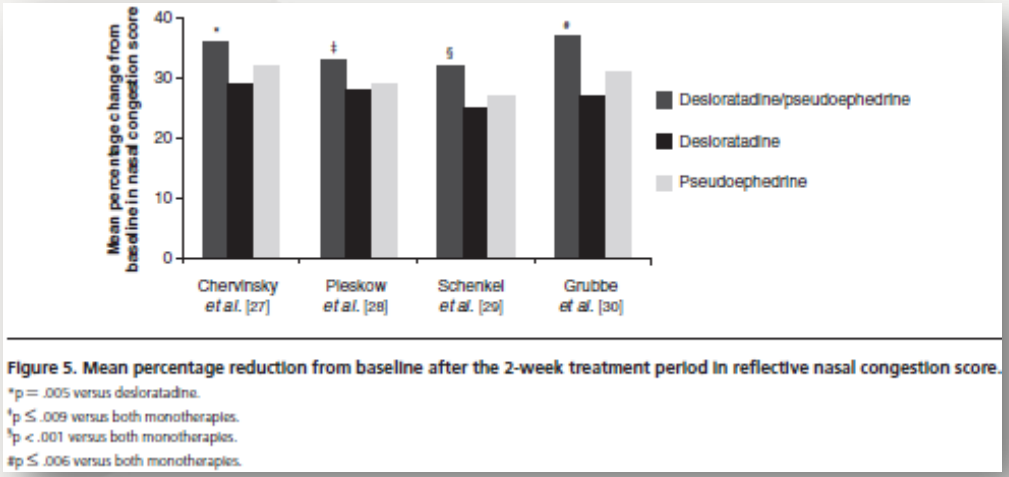


Figure 5. Mean percentage reduction from baseline after the 2-week treatment period in reflective nasal congestion score.

*p = .005 versus desloratadine.
‡p ≤ .009 versus both monotherapies.
§p < .001 versus both monotherapies.
#p ≤ .006 versus both monotherapies.

L'associazione è più efficace dei due singoli farmaci, soprattutto sul sintomo ostruzione.
Particolare attenzione alla durata del trattamento (non superiore ai 5 giorni consecutivi). Possibili (anche se rari) effetti avversi cardiovascolari.

R. Anolik, *Expert Opin. Drug Metab. Toxicol. (2009) 5(6):683-694*

ANTILEUCOTRIENICI

Possono essere utilizzati nel trattamento della rinite quando coesistono i sintomi di asma bronchiale (**A**). *Nota AIFA 82*

Nella rinite gli antileucotrienici hanno efficacia inferiore agli steroidi topici (**A**).

Come farmaci aggiuntivi possono incrementare il beneficio ottenuto con la terapia standard (antistaminici) (**B**).

Il profilo di sicurezza è ottimale. Il rapporto costo/beneficio deve essere considerato caso per caso.
Gli antileucotrienici sono sicuri in gravidanza (categoria di rischio FDA: B)

Anti-IgE (Omalizumab) : impatto favorevole sulla coesistenza rinite-asma

Omalizumab management beyond clinical trials: The added value of a network model

Marco Caminati [a,*], Gianenrico Senna [a], Fulvia Chieco Bianchi [b], Maria Rita Marchi [b], Andrea Vianello [b], Claudio Micheletto [c], Carlo Pomari [d], Silvia Tognella [e], Francesca Savoia [b], Valentina Mirisola [f], Andrea Rossi [g], on behalf of NEONET Study Group [1]

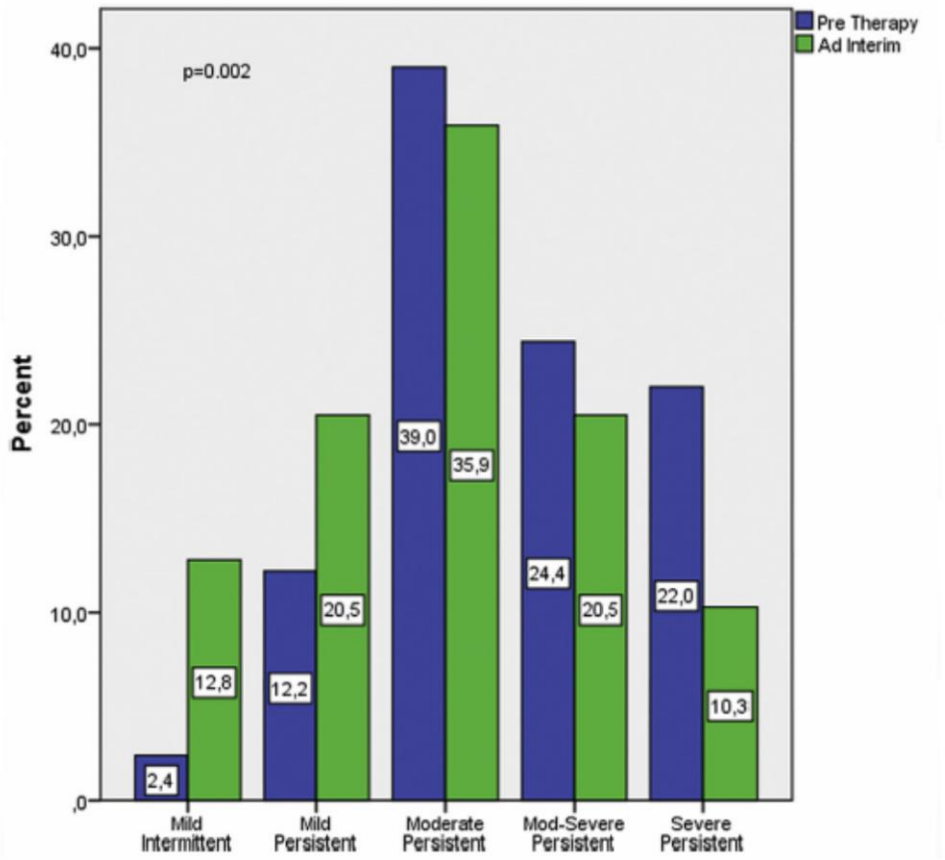
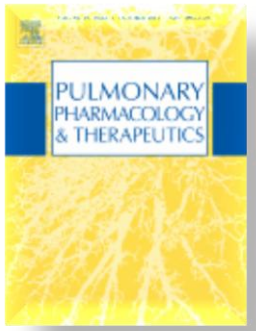


Fig. 6. ARIA classification of rhinitis severity at baseline (pre-therapy) and at the time of analysis (ad interim). Percent = percentage of patients.

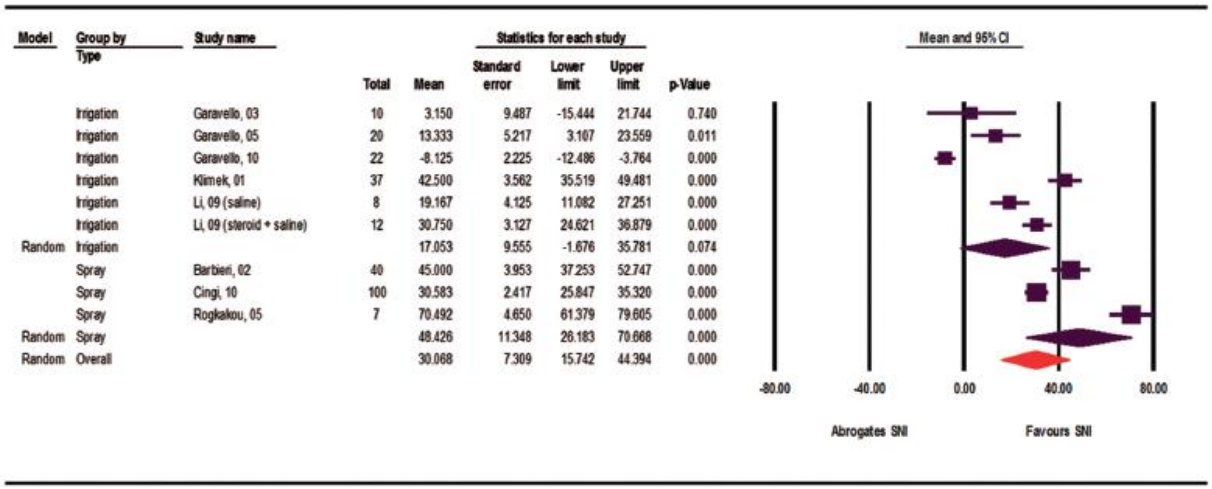


LAVAGGIO NASALE

Nasal irrigation as an adjunctive treatment in allergic rhinitis: A systematic review and meta-analysis

Kristina E. Hermelingmeier, M.D.,[2] Rainer K. Weber, Ph.D.,[1] Martin Hellmich, Ph.D.,[2] Christine P. Heubach, M.D.,[2] and Ralph Mösges, Ph.D.[2]

Am J Rhinol Allergy 2012



Model	Group by Type	Study name	Total	Mean	Standard error	Lower limit	Upper limit	p-Value
	Irrigation	Garavello, 03	10	3.150	9.487	-15.444	21.744	0.740
	Irrigation	Garavello, 05	20	13.333	5.217	3.107	23.559	0.011
	Irrigation	Garavello, 10	22	-8.125	2.225	-12.486	-3.764	0.000
	Irrigation	Klimek, 01	37	42.500	3.562	35.519	49.481	0.000
	Irrigation	Li, 09 (saline)	8	19.167	4.125	11.082	27.251	0.000
	Irrigation	Li, 09 (steroid + saline)	12	30.750	3.127	24.621	36.879	0.000
Random	Irrigation			17.053	9.555	-1.676	35.781	0.074
	Spray	Barbieri, 02	40	45.000	3.953	37.253	52.747	0.000
	Spray	Cingi, 10	100	30.583	2.417	25.847	35.320	0.000
	Spray	Rogkakou, 05	7	70.492	4.650	61.379	79.605	0.000
Random	Spray			48.426	11.348	26.183	70.668	0.000
Random	Overall			30.068	7.309	15.742	44.394	0.000

3.4.4.3. Nasal or antral irrigation

The results between the groups were compared. Most of them offer evidence that nasal washouts or irrigations with isotonic or hypertonic saline are beneficial in terms of alleviation of symptoms. Hypertonic saline is preferred to isotonic saline in the treatment of rhinosinusitis by some authors in the USA, mostly based on a paper indicating that it significantly improves nasal mucociliary clearance measured by saccharine testing in healthy volunteers [329].

European Position Paper on Rhinosinusitis and Nasal Polyps 2012

ERS / EAACI guidelines for acute and chronic rhinosinusitis with and without nasal polyps based on systematic review

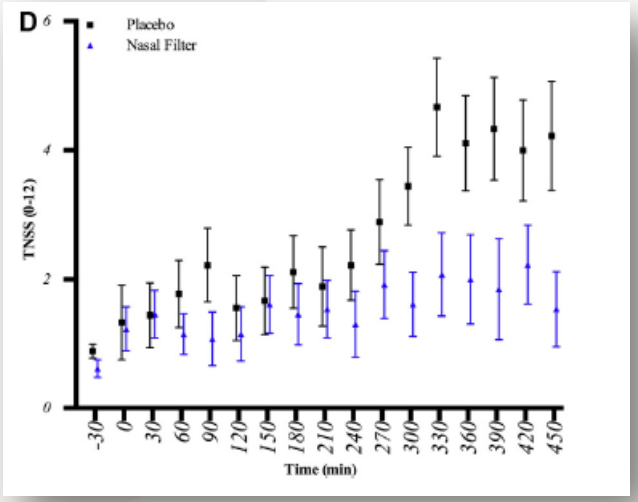
Aspetti particolari: i filtri nasali possono limitare i sintomi della rinite allergica stagionale

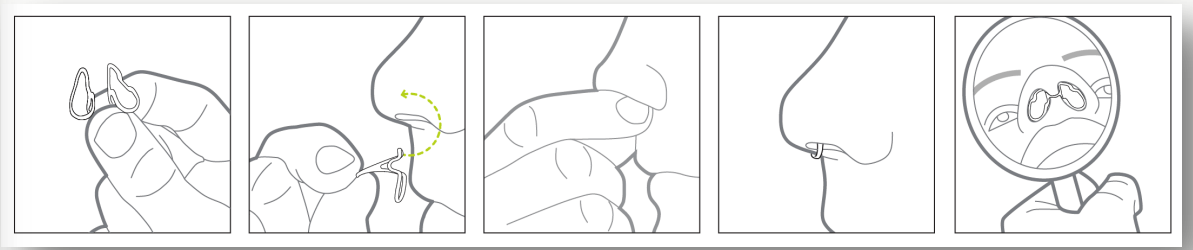
Preventive effect of nasal filters on allergic rhinitis: A randomized, double-blind, placebo-controlled crossover park study

Peter Kenney, BSc,[a,b] Ole Hilberg, MD, DMSci,[c] Anne Cathrine Laursen, BSc,[d] Robert George Peel, PhD,[e] and Torben Sigsgaard, MD, PhD[a] *Aarhus and Roskilde, Denmark*

Studio condotto in due giornate di esposizione in un parco nella stagione delle Graminacee in 76 soggetti affetti da rinite allergica da Graminacee.

L'impiego del filtro nasale riduceva il punteggio totale di sintomi nasali (TNSS) del 40% ($p< 0.02$), dell'83% gli starnuti ($p < 0.001$), del 75% la secrezione lacrimale ($p< 0.02$) e del 53% la rinorrea ($p< 0.005$) rispetto al placebo. Il filtro era ben tollerato.





Rhinix; Rhinix ApS, Aarhus, Denmark

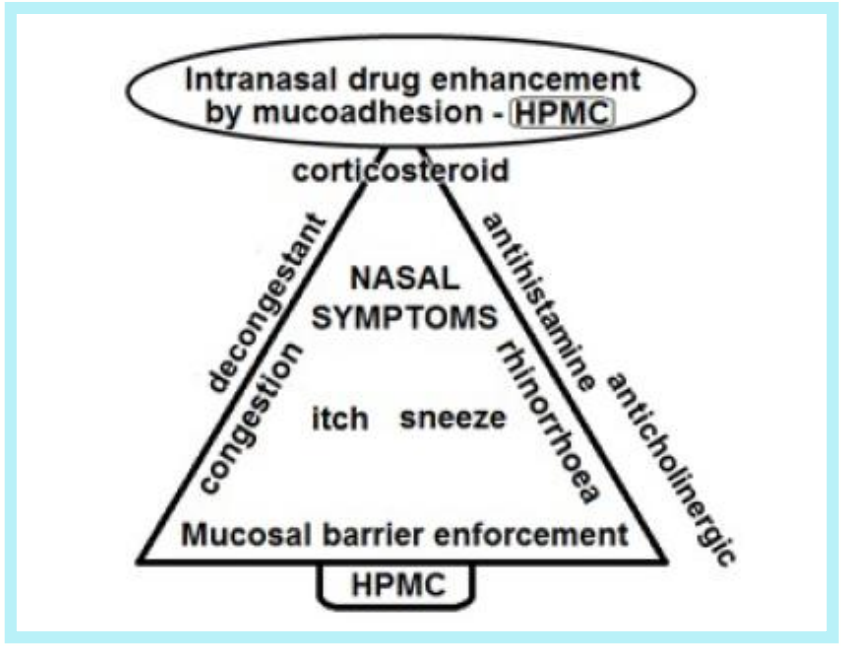
J Allergy Clin Immunol. 2015 Dec;136(6):1566-72

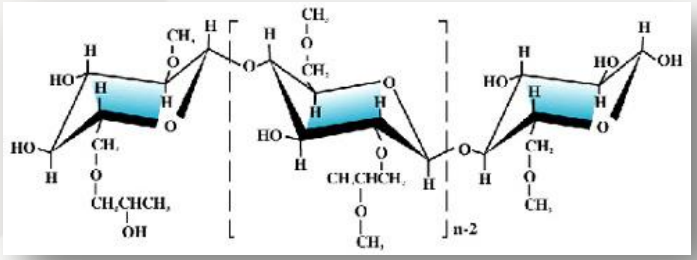
Nuovi approcci terapeutici

Methyl-cellulose powder for prevention and management of nasal symptoms

Todor A. Popov, Nils Åberg, Jean Emberlin, Peter Josling, Natalia I. Ilyina, Nikolai P. Nikitin & Martin Church

La somministrazione nasale di idrossi propil-metil-cellulosa (**HPMC-p**) crea una barriera fisica mucosale, riduce i sintomi e favorisce l'effetto dei farmaci topici.





ISSN: 1747-6348 (Print) 1747-6356 (Online) Journal homepage: http://www.tandfonline.com/loi/ierx20

Nuovi approcci terapeutici

Methyl-cellulose powder for prevention and management of nasal symptoms

Todor A. Popov, Nils Åberg, Jean Emberlin, Peter Josling, Natalia I. Ilyina, Nikolai P. Nikitin & Martin Church

- Twenty-six studies with hydroxy-propyl-methyl-cellulose powder (HPMC-p) were critically appraised to obtain an updated characteristic of the product.

- Most studies assessed the efficacy of HPMC-p as a nasal barrier enforcing measure.

- The studies, using either nasal allergen challenge or natural exposure of patients to environmental allergen, support the hypothesis that HPMC-p possesses barrier enforcing properties

- Also, acute and clinical experiments indicated that intra-nasal application of HPMC-p following local relief medications enhances their ability to suppress symptoms and reduces their long-term use

ISSN: 1747-6348 (Print) 1747-6356 (Online) Journal homepage: http://www.tandfonline.com/loi/ierx20

Assessment of control in untreated symptomatic patient

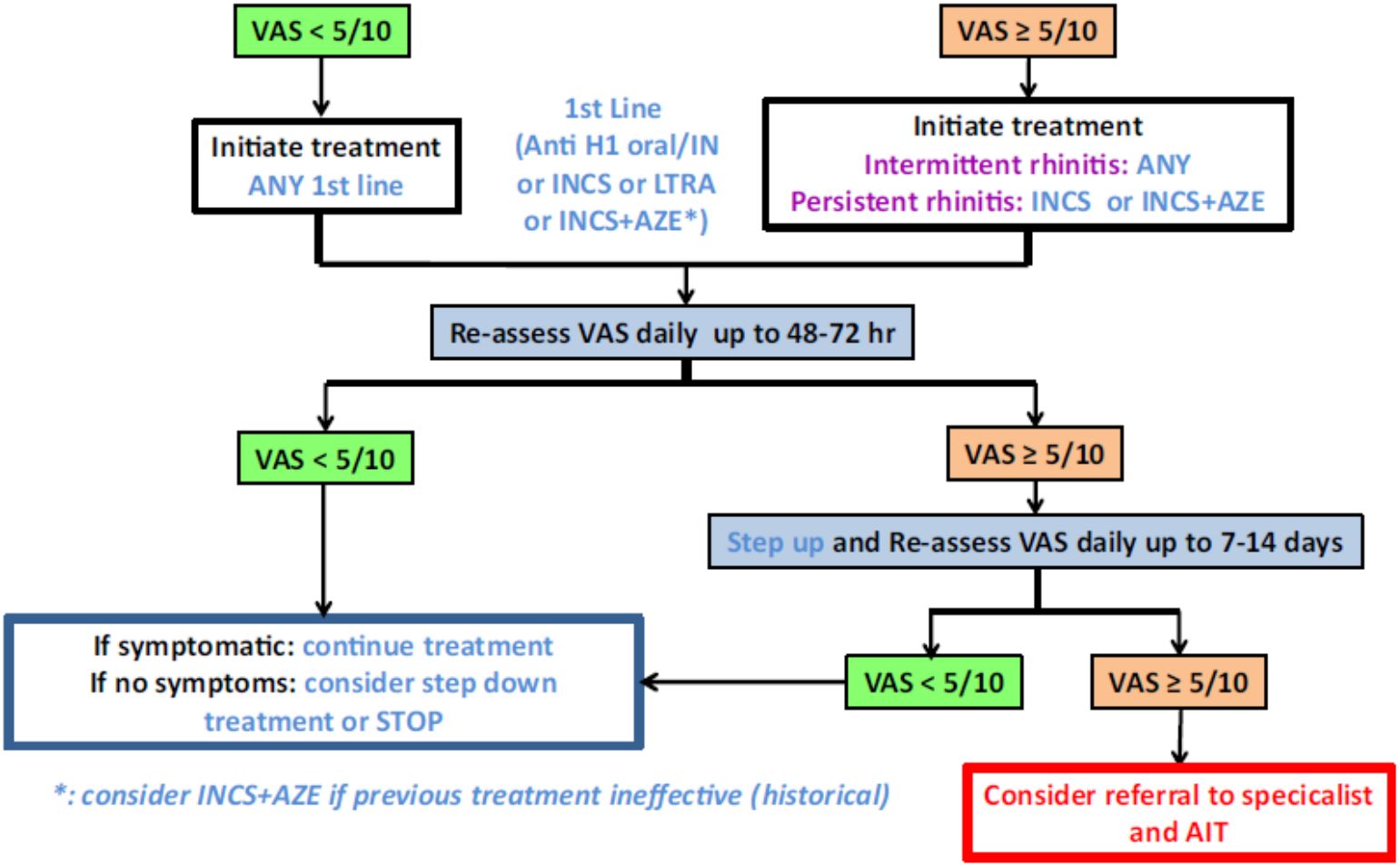
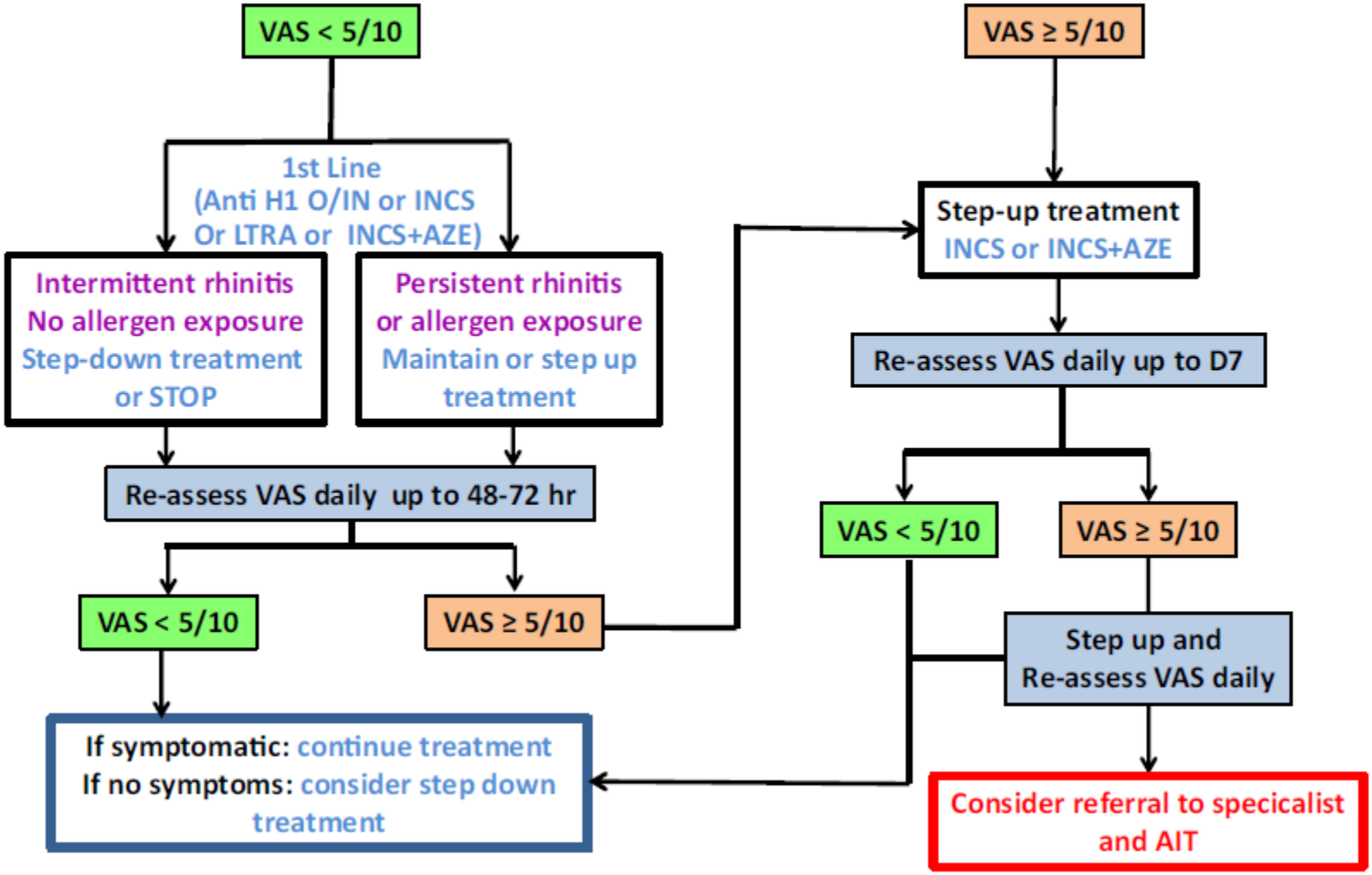


FIG 1. Step-up algorithm in untreated patients using the VAS (adolescents and adults). The proposed algorithm considers the treatment steps and patient preference and VAS levels in ratio. If ocular symptoms remain, add intraocular treatment.

Bousquet J et al JACI 2016

Assessment of control in treated symptomatic patient



Bousquet J et al JACI 2016

Cenni storici sull'immunoterapia allergene-specifica

NOON

FRANKLAND

ISHIZAKA

LICHTENSTEIN

UK CSM

EMPIRICAL USE | 1st RDBPC trial | IgE | Randomized trials | VIT | Allergoids

1911 | 1954 | 1965 | 1978 | 1986

SLIT 1st RDBPC trial

T_H1/T_H2

ROMAGNANI

DURHAM

Mechanisms

SLIT tablets

Canonica-Passalacqua

WHO

Pos Pap

Liposomes

Adjuvants

Allergoids

1986 | 1998 | 2000

Recombinants

DNA-ITS

Creticos

ARIA

Peptides

Preventive effect

FOOD ALLERGY →

SLIT BIG TRIALS →

WAO SLIT Pos Pap

ILIT

EPIT

Senti & Kundig

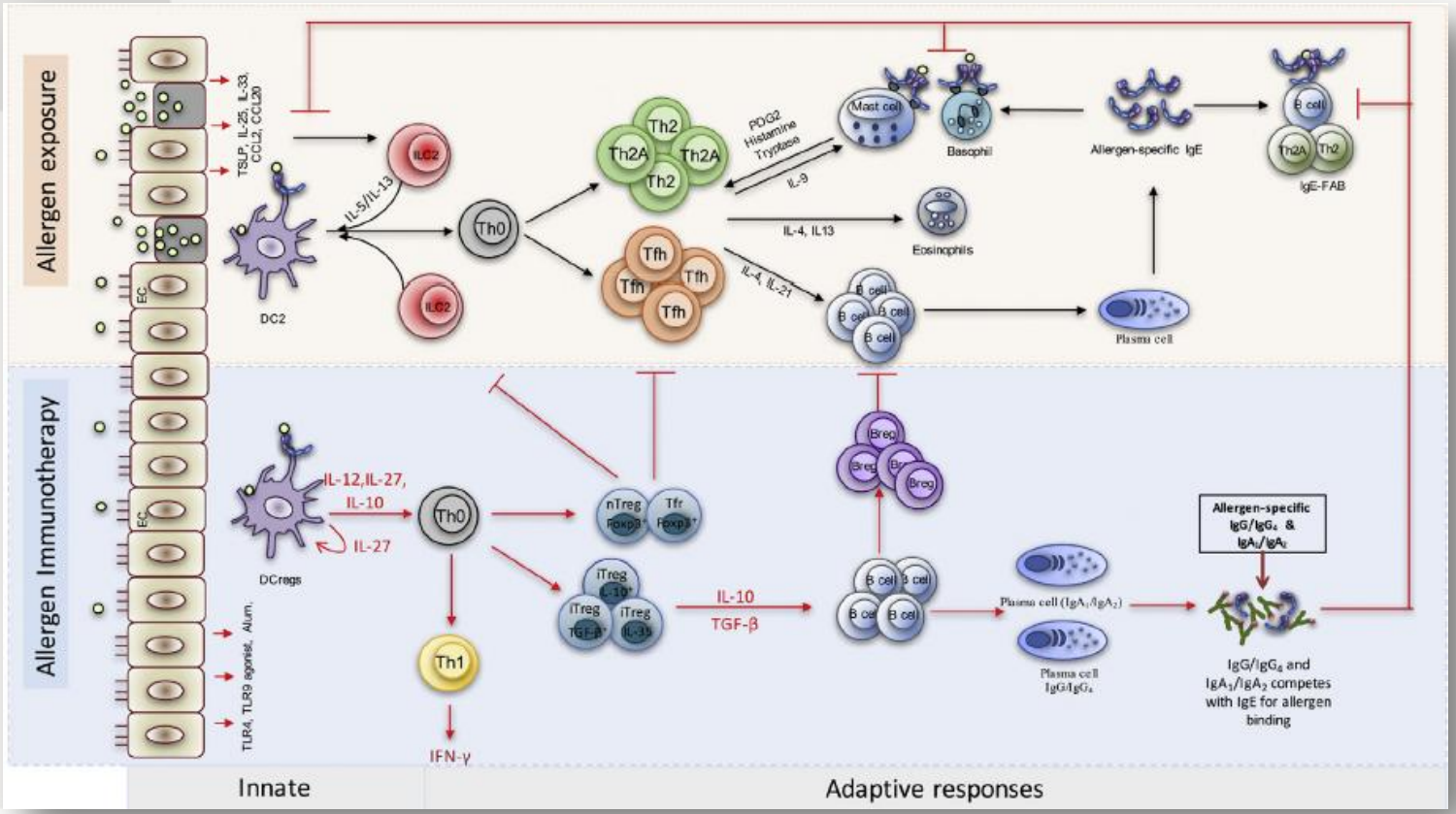
FDA

FDA SLIT APPROVAL

2000 | 2009 | 2014

Immunological mechanisms of AIT

Mechanisms of allergen immunotherapy for inhaled allergens and predictive biomarkers



High-dose allergen exposure by AIT restores DC function, which produces IL-12, IL-27, and IL-10 and promotes immune deviation from a TH2 to TH1 response and induction of Treg and Breg cells (including other B-cell subsets) that produce IgA, IgG, and IgG4 blocking antibodies.

(Shamji MH & Durham SR, JACI 2017;140:1485-98).

AIT : UN MODELLO PER LA "PRECISION MEDICINE"

Passalacqua & Canonica CMA 2015

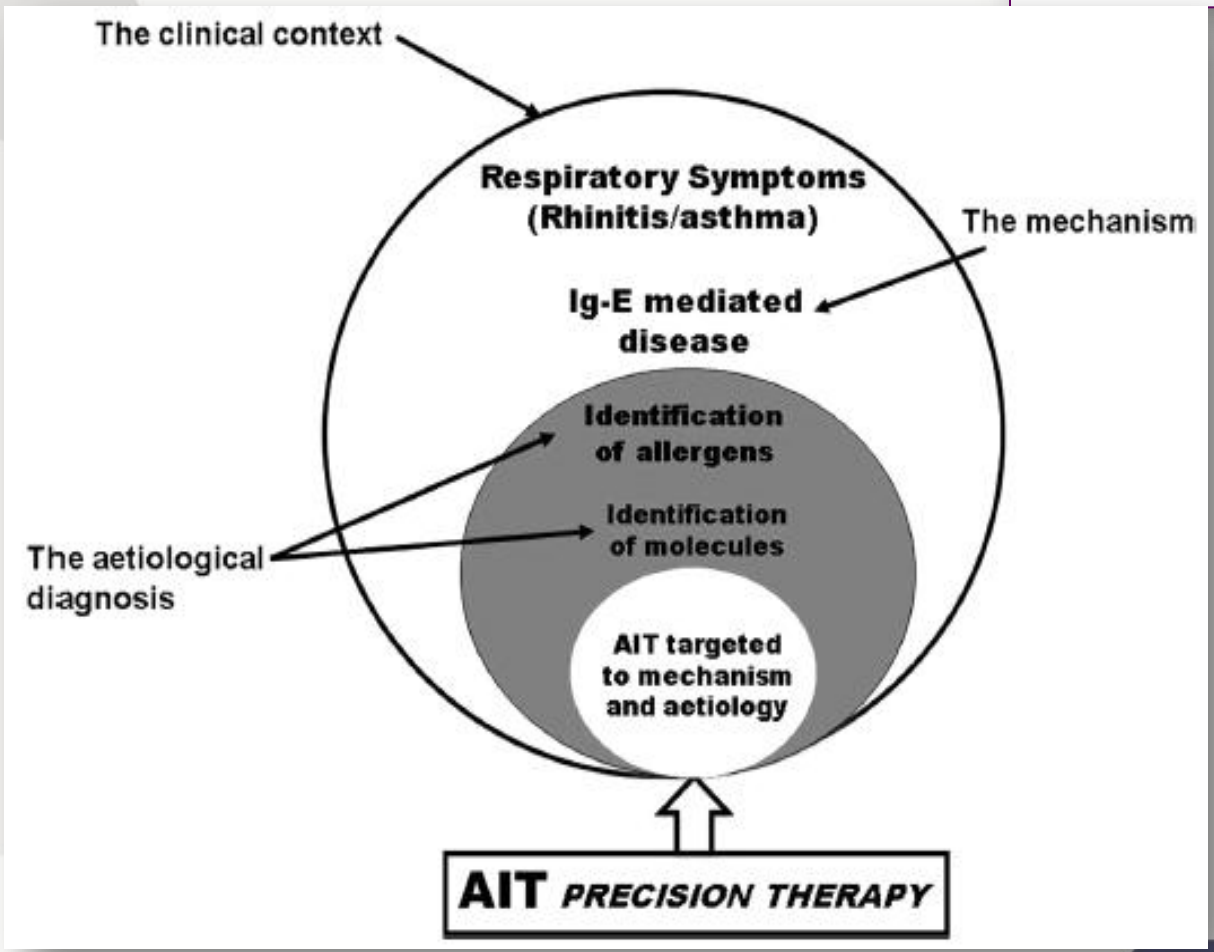
Passalacqua and Canonica *Clin Mol Allergy* (2015) 13:24
DOI 10.1186/s12948-015-0028-6

CLINICAL AND MOLECULAR ALLERGY

COMMENTARY Open Access

AIT (allergen immunotherapy): a model for the "precision medicine"

Giovanni Passalacqua* and Giorgio Walter Canonica



Il ruolo dell'AIT come medicina di precisione

FATTORI DA CONSIDERARE PER LA PRESCRIZIONE DELL'ITS

1. Meccanismo IgE accertato (skin test/CAP)
2. Chiara relazione causale tra esposizione all'allergene e sintomatologia
3. Esclusione di altri fattori scatenanti
4. Gravità dei sintomi (inclusi effetti su attività lavorativa o scolastica)
5. Risposta alla farmacoterapia
6. Disponibilità di estratto standardizzato di cui sia stata dimostrata efficacia.
7. Assenza di controindicazioni (trattamento con beta-bloccanti, malattie immunologiche sistemiche, asma grave, accertata mancanza di compliance)
8. Rapporto Costo/Beneficio

Allergic Rhinitis & AIT :

EAACI Guidelines on Allergen Immunotherapy : Executive Statement

Allergic rhinoconjunctivitis (8)

- AIT should be considered in patients with allergic rhinitis (AR), with or without conjunctivitis; evidence of IgE-sensitization to one or more clinically relevant allergens; and moderate-to-severe symptoms despite regular and/or avoidance strategies.
- An individual product-based evaluation of evidence for efficacy is recommended before treatment with a specific product is initiated.
- The following can be recommended for AR for short-term benefit:
  - Continuous SCIT for seasonal (Grade A for adults, B for children) or perennial (Grade B for adults, C for children) allergens.
  - Pre- and pre-/co-seasonal SCIT (Grade A for adults, B for children).
  - Modified (allergoids) and unmodified allergen SCIT extracts (Grade A for adults, B for children).
  - SLIT aqueous solutions for grass and tree pollens (Grade B for adults, A in children).
- The following can be recommended for AR for short- and long-term benefit:
  - Continuous grass pollen SCIT (Grade A for adults, B for children).
  - Continuous grass pollen SLIT tablets or SLIT solution (Grade A).
  - HDM SLIT tablet (but not aqueous solution) for short-term (Grade A) and long-term benefit (Grade B for adults, C for children).
- To achieve long-term efficacy, it is recommended that a minimum of 3 years of therapy is used (Grade A).
- SCIT and initial SLIT dosage should be administered by competent staff with patients waiting in the clinic for at least 30 minutes after dose (Grade C).
- Many gaps in the evidence base exist, particularly around long-term benefit and use in children.

(Muraro et al., Allergy, Accepted manuscript online : 30 January 2018)

SICUREZZA

L'immunoterapia sottocutanea (SCIT) ha un lieve margine di rischio per effetti collaterali gravi. Risulta comunque un trattamento sicuro, se praticato con le opportune precauzioni ed attenzioni.

L'immunoterapia sublinguale (SLIT) ha una incidenza di effetti avversi minore rispetto alla SCIT. Sono stati segnalati ad oggi solo 12 casi di anafilassi, e nessuna reazione mortale.
Con la SLIT, la maggioranza degli effetti collaterali sono locali (prurito, bruciore, modesto edema della lingua) e scompaiono dopo le prime dosi

La prima dose di SLIT dovrebbe essere somministrata sotto controllo medico.

Controindicazioni assolute e relative

Allergy EUROPEAN JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY

POSITION PAPER

Clinical contraindications to allergen immunotherapy: a EAACI position paper

C. Pitsios[1], P. Demoly[2,3], M. B. Bilò[4], R. Gerth van Wijk[5], O. Pfaar[6,7], G. J. Sturm[8], P. Rodriguez del Rio[9], M. Tsoumani[10], R. Gawlik[11], G. Paraskevopoulos[12], F. Ruëff[13], E. Valov N. G. Papadopoulos[15,16] & M. A. Calderón[17]

Pregnancy (initiation of AIT)	A	A	A
Pregnancy (continuation of AIT)	No	No	No
Children (<2 years of age)	A	A	A
Children (2–5 years of age)	R	R	R
Any other age groups	No	No	No
HIV (A, B stages; $CD4^+$ >200/μl)	R	R	R
AIDS	A	A	A

Table 2 Absolute (A) and relative (R) contraindications for AIT

	Aeroallergens		Venom
Medical condition	SCIT	SLIT	immunotherapy
Asthma (partially controlled)	R	R	R
Asthma (uncontrolled)	A	A	A
Autoimmune disorders in remission	R	R	R
Autoimmune disorders in active forms (nonresponding to treatment)	A	A	A
Malignant neoplasias	A	A	R
β-Blockers	R	R	No
ACE inhibitors	No	No	R
MAOIs	No	No	No
Cardiovascular diseases	R	R	No
Pregnancy (initiation of AIT)	A	A	A
Pregnancy (continuation of AIT)	No	No	No
Children (<2 years of age)	A	A	A
Children (2–5 years of age)	R	R	R
Any other age groups	No	No	No
HIV (A, B stages; $CD4^+$ >200/μl)	R	R	R
AIDS	A	A	A
Psychiatric and/or mental disorders	R	R	R
Chronic infections	R	R	R
Immunodeficiencies	R	R	R
Use of immunosuppressive drugs	R	R	R

AIT, allergen immunotherapy; MAOIs, monoamine oxidase inhibitors; SCIT, subcutaneous immunotherapy; SLIT, sublingual immunotherapy; A, absolute contraindication; R, relative contraindication; No, no contraindication.

AIT: prevenzione dello sviluppo di asma

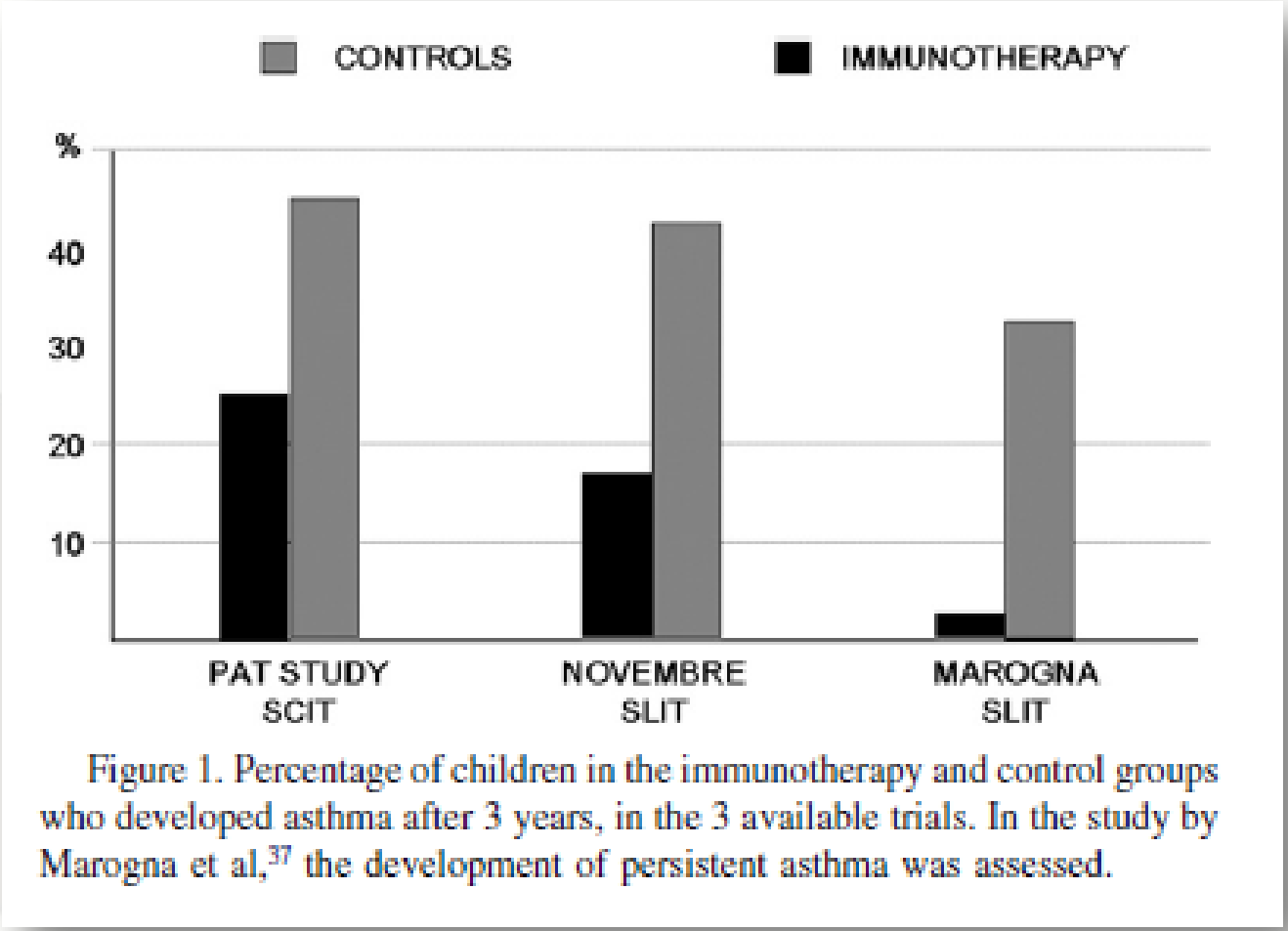


Figure 1. Percentage of children in the immunotherapy and control groups who developed asthma after 3 years, in the 3 available trials. In the study by Marogna et al,[37] the development of persistent asthma was assessed.

Passalacqua G. Ann Allergy Asthma Immunol. 2011;107:401– 406.

SLIT tablets in AR reduces the risk of asthma

Sublingual immunotherapy provides long-term relief in allergic rhinitis and reduces the risk of asthma: A retrospective, real-world database analysis

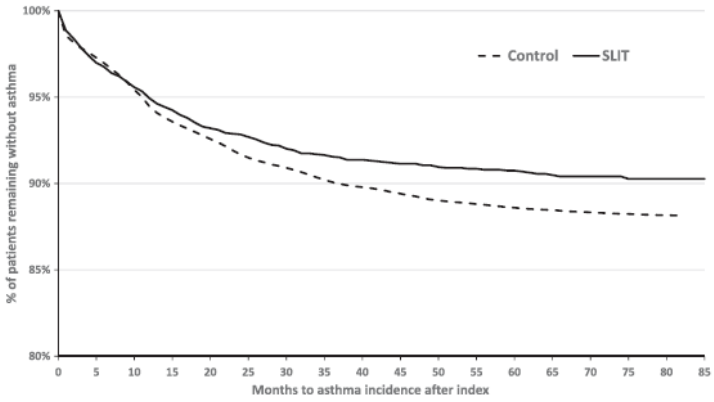


FIGURE 3 Time to asthma onset, defined as time to the date of first prescriptions of short-acting β-agonists or inhaled corticosteroids for sublingual immunotherapy (SLIT) and non-AIT groups during the full analysis period, in patients without asthma at the index date (note the offset of the y-axis)

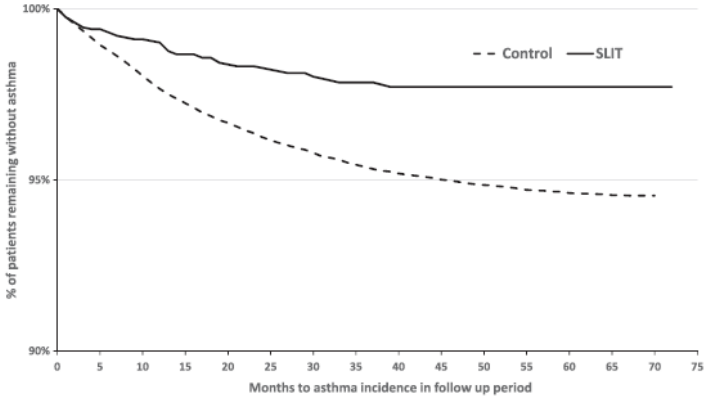


FIGURE 4 Time to asthma onset, defined as time to the date of first prescriptions of short-acting β-agonists or inhaled corticosteroids for sublingual immunotherapy (SLIT) and non-AIT groups during the follow-up period, in patients without asthma at the end of treatment period (note the offset of the y-axis)

Real-world treatment of AR patients with grass pollen SLIT tablets was associated with slower AR progression, less frequent asthma onset, and slower asthma progression.

(Zielen et al., Allergy. 2018;73:165–177)

GAP trial

Results from the 5-year SQ grass sublingual immunotherapy tablet asthma prevention (GAP) trial in children with grass pollen allergy

Erkka Valovirta, MD,[a,b] Thomas H. Petersen, MD,[c] Teresa Piotrowska, MD,[d] Mette K. Laursen, MSc,[e] Jens S. Andersen, MSc, PhD,[e] Helle F. Sørensen, MSc, PhD,[e] and Rabih Klink, MD,[f] on behalf of the GAP investigators*

Turku, Finland, Kolding and Hørsholm, Denmark, Białystok, Poland, and Laon, France

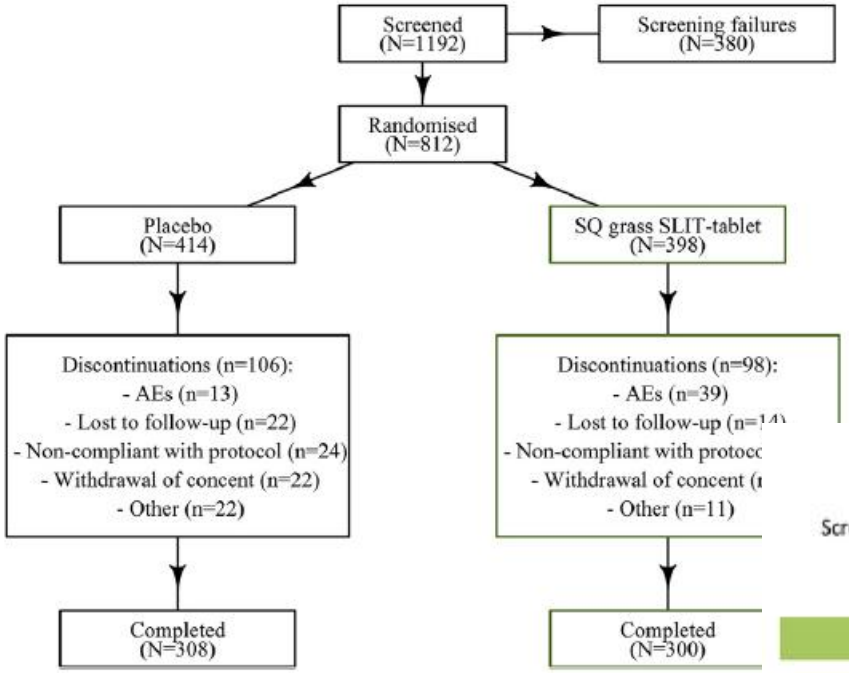


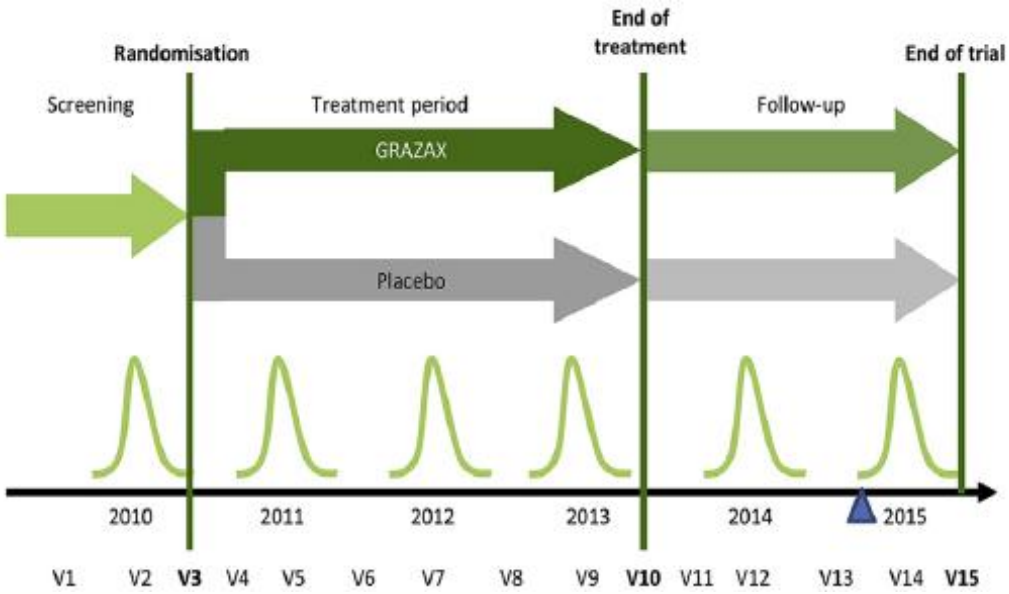
TABLE I. Asthma endpoints

Primary endpoint: time to onset of asthma by protocol definition (FAS)

		Diagnosed with asthma				
Group	n	n	Proportion	HR*	95% CI	*P* value
Placebo	414	39	9.42	0.9	0.57-1.43	.667
SQ grass SLIT tablet	398	34	8.54			

Secondary endpoint: asthma symptom and medication status since last visit at end of trial (assessed at GPS visit in year 5)†

	With asthma



GAP study: randomizzato controllato, doppio cieco/placebo per valutare se AIT per graminacee riduce l'insorgenza di asma nel bambino sensibilizzato e con rinite allergica- 3 Anni di trattamento e 2 anni di osservazione Valovirta et al., J Allergy Clin Immunol 2017)

FIG 3. OR for experiencing asthma symptoms, using asthma medication, and both, shown for the entire trial period and for the 2-year follow-up period.

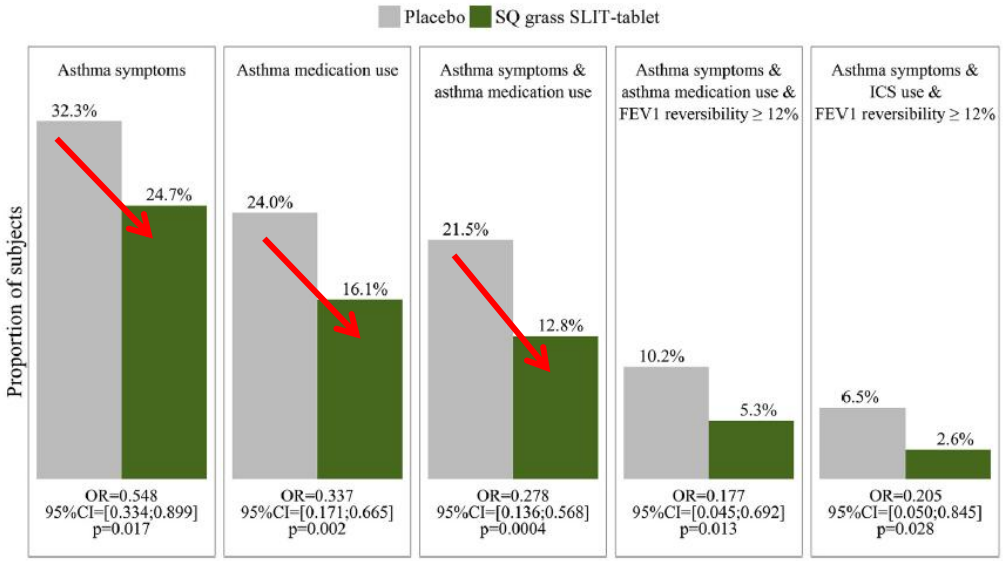
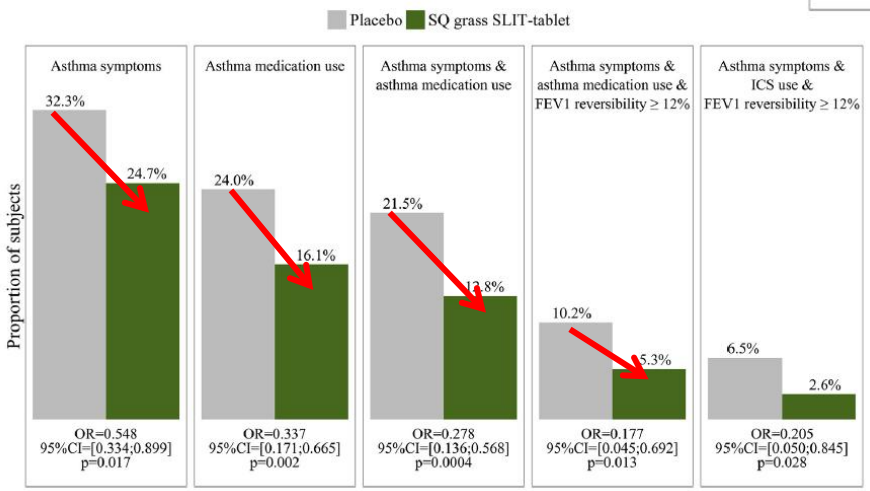


FIG 3. OR for experiencing asthma symptoms, using asthma medication, and both, shown for t trial period and for the 2-year follow-up period.



(Valovirta et al., J Allergy Clin Immunol 2017)

GAP trial

Results from the 5-year SQ grass sublingual immunotherapy tablet asthma prevention (GAP) trial in children with grass pollen allergy

Conclusions:

Treatment with the SQ grass sublingual immunotherapy tablet reduced the risk of experiencing asthma symptoms and using asthma medication, and had a positive, long-term clinical effect on rhinoconjunctivitis symptoms and medication use but did not show any difference in time to onset of asthma.

(Valovirta et al., J Allergy Clin Immunol 2017)

Immunoterapia nei polisensibili

- Dal 51% all'81% dei pazienti americani ed europei è polisensibilizzato.Ciò non implica che tutte le sensibilizzazioni siano responsabili di sintomatologia.
- In Europa le formulazioni sono prevalentemente basate su estratti a singolo allergene (anche per il paziente polisensibile), mentre negli USA contengono in media 8 componenti differenti.

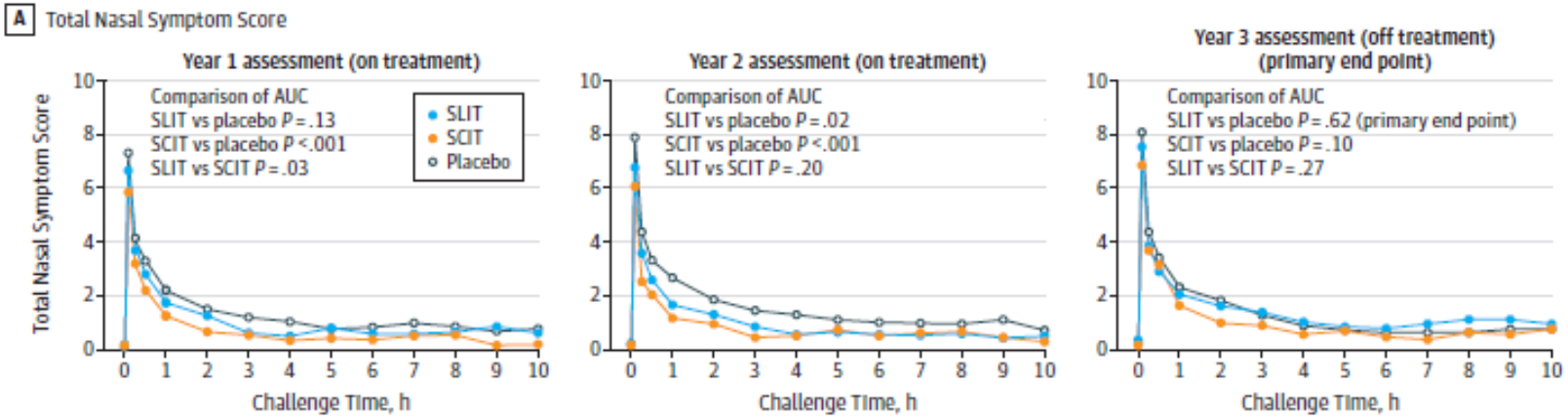
- In recenti studi, ampi e ben disegnati, l'ITS per graminacee ha dimostrato di essere sicura ed efficace in pazienti polisensibili.

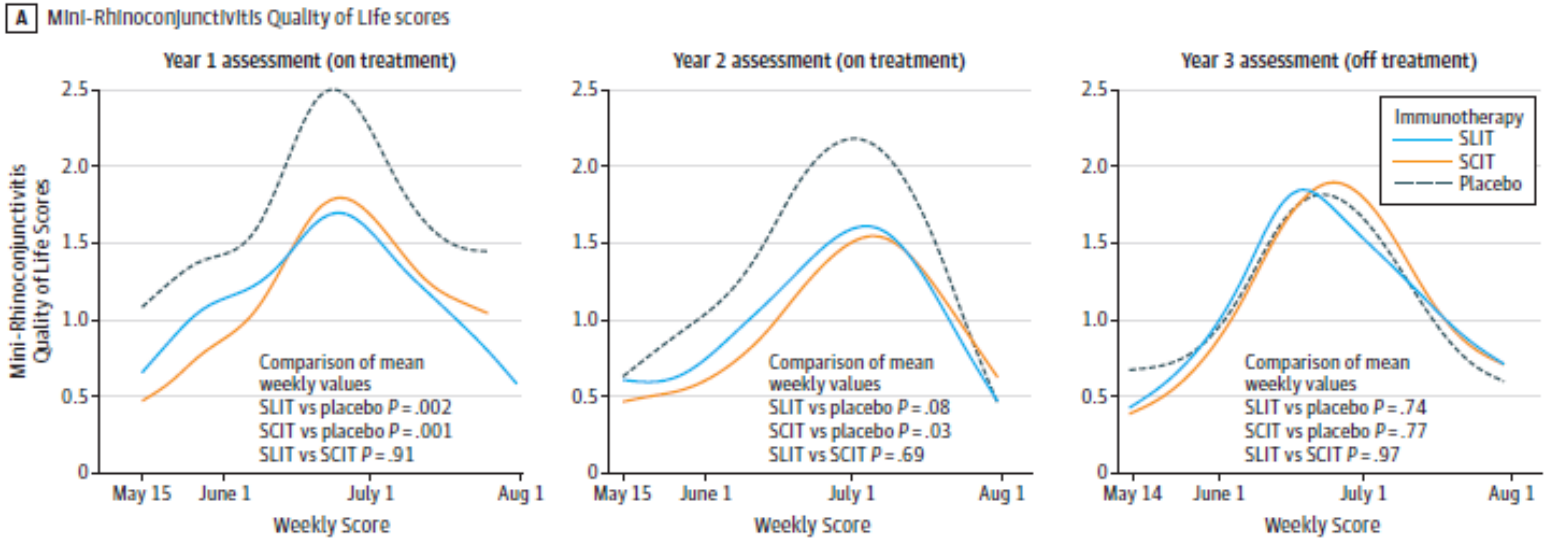
- La validità di SLIT e SCIT con estratti multipli in pazienti polisensibili necessita di ulteriori dati provenienti da ampi trial clinici.

Calderon, Cox, Casale, Mointgeon, Demoly. J Allergy Clin Immunol 2012

DURATA DELL'AIT

Due soli anni di immunoterapia (SCIT o SLIT) per Graminacee non bastano ad avere un effetto long-lasting (al III anno non vi è significativo effetto sui sintomi indotti dal TPN e sulla qualità di vita)





AIT : ITALIAN CONSENSUS REPORTS

Italian Consensus on specific immunotherapy

- La via di somministrazione, SCIT o SLIT: ambedue hanno ampia evidenza di efficacia, la SLIT ha superiore sicurezza. La scelta deve essere discussa con il paziente dopo adeguata informazione
- Il prodotto da utilizzare: l'efficacia dimostrata dai trial con un dato prodotto non può essere traslata ad altri, pur contenenti gli stessi allergeni, poiché le modalità di produzione degli estratti allergenici presentano ampie differenze e rendono i prodotti finali non paragonabili tra loro

A Musarra, MB Bilò, S Bonini, GW. Canonica, G.E. Senna

REVIEW Open Access

Clinical practice recommendations for allergen-specific immunotherapy in children: the Italian consensus report

Giovanni Battista Pajno[1*], Roberto Bernardini[2], Diego Peroni[3], Stefania Arasi[1,4], Alberto Martelli[5], Massimo Landi[6,7], Giovanni Passalacqua[8], Antonella Muraro[9], Stefania La Grutta[7], Alessandro Fiocchi[10], Luciana Indinnimeo[11], Carlo Caffarelli[12], Elisabetta Calamelli[13], Pasquale Comberiati[14], Marzia Duse[11] and Allergen-specific Immunotherapy panel of the Italian Society of Pediatric Allergy and Immunology (SIAIP)

It J Pediatrics 2017

Table 3 Indications for allergen-specific immunotherapy (AIT) for pediatric allergic rhinitis, conjunctivitis with/without asthma

AIT should be considered for patients with evidence of specific IgE sensitization towards one or few clinically relevant allergen(s).

The decision to start AIT depends on various factors including:

- Children's (and caregivers) preference and acceptability
- Adherence to treatment
- Severity of symptoms and pharmacotherapy requirements
- Efficacy of avoidance measures (e.g. house dust mites, pollens)
- Asthma and co-existent rhinitis

Potential indications:

- Possible prevention of new sensitizations in mono-sensitized patients
- IgE-associated food allergy
- Extrinsic atopic dermatitis

Immunoterapia allergene specifica (AIT) nei bambini

L'immunoterapia (AIT) è efficace e ben tollerata nei bambini

L'AIT dovrebbe essere presa in considerazione insieme alla farmacoterapia nei bambini con rinite, rinocongiuntivite con o senza asma allergica.

- **E' stato dimostrato che l'AIT può prevenire l'insorgenza di nuove sensibilizzazioni, specialmente nei pazienti inizialmente monosensibilizzati ad acaro della polvere**
- **Le vie di somministrazione attualmente disponibili ed accettate per le allergopatie respiratorie sono quella sublinguale (SLIT) e quella sottocutanea (SCIT)**
- **L'asma rimane un disordine multifattoriale. Occorrono ulteriori e dettagliati studi disegnati specificamente a valutare l'effetto dell'AIT sulla progressione da rinite ad asma.**

Uso di prodotti AIT di qualità comprovata

Table 2 Criteria for a recommendable product for SIT

Minimum expectations for a SIT product to be used in adults:

At least one successful state-of-the-art DBPCR trial in adults for the first year of treatment, best preceded by a dose–response study (nasal provocation testing or allergen exposure chambers may be used for the dose finding)

Additional claims can be justified as follows:

Claims on sustained effects of a product should be based on a successful DBPCR study, based on appropriate sample size calculation, over 3 years of treatment

Claims on disease modifying effects: such studies need be followed up blindly for at least two consecutive years without treatment while maintaining monitoring symptoms

Claims for efficacy in asthmatics should be based on an appropriate successful DBPCR study in the appropriate patient group. For claims on tolerability in asthmatics only, the study can also be performed in allergic rhinitis subjects with comorbid asthma.

Minimum expectations for a SIT product to be used in children:

At least one state-of-the-art DBPCR confirmatory trial in children for the first year of treatment

Additional claims can be justified as follows:

Claims on sustained effects of a product should be based on a successful DBPCR study, based on appropriate sample size calculation, over 3 years of treatment

Claims on disease modifying effects: such studies have to be followed up at least two consecutive years without treatment while maintaining monitoring symptoms

Bachert et al. World Allergy Organization Journal (2015) 8:29
DOI 10.1186/s40413-015-0078-8

WAO journal
WORLD ALLERGY ORGANIZATION

POSITION ARTICLE AND GUIDELINES Open Access

Allergen immunotherapy on the way to product-based evaluation—a WAO statement

Claus Bachert[1*], Mark Larché[2], Sergio Bonini[3], Giorgio Walter Canonica[4], Thomas Kündig[5], Desiree Larenas-Linnemann[6], Dennis Ledford[7], Hugo Neffen[8], Ruby Pawankar[9] and Giovanni Passalacqua[4]

Table 1 Reasons for the use of products supported by evidence-based evaluation of safety and efficacy

The efficacy of the product is known and sufficient (it may fulfill the WAO criteria of 20 % over placebo for rhinitis [3] and appropriate criteria for asthma and other organ manifestations)

The safety of the product is known and favorable; risks for the patient can be evaluated

If efficacy and safety in children are known, the usefulness of the product in children can be evaluated

If information on long-term effects is available for the product, the information can be used for calculations of the socio-economic impact

If the tolerability or the efficacy in asthma patients is known, the usefulness and risks of the product for therapy in asthmatic populations can be estimated

DEFINIZIONE-PATOGENESI
CLASSIFICAZIONE
EPIDEMIOLOGIA
CLINICA E DIAGNOSTICA
IMPATTO SULLA QoL
TRATTAMENTO
IMPATTO SULL'ASMA
ASPETTI PARTICOLARI

The “UNITED AIRWAYS DISEASE”

La rinite e l’asma sono aspetti clinici differenti di un unico disordine immuno-mediato dell’apparato respiratorio.

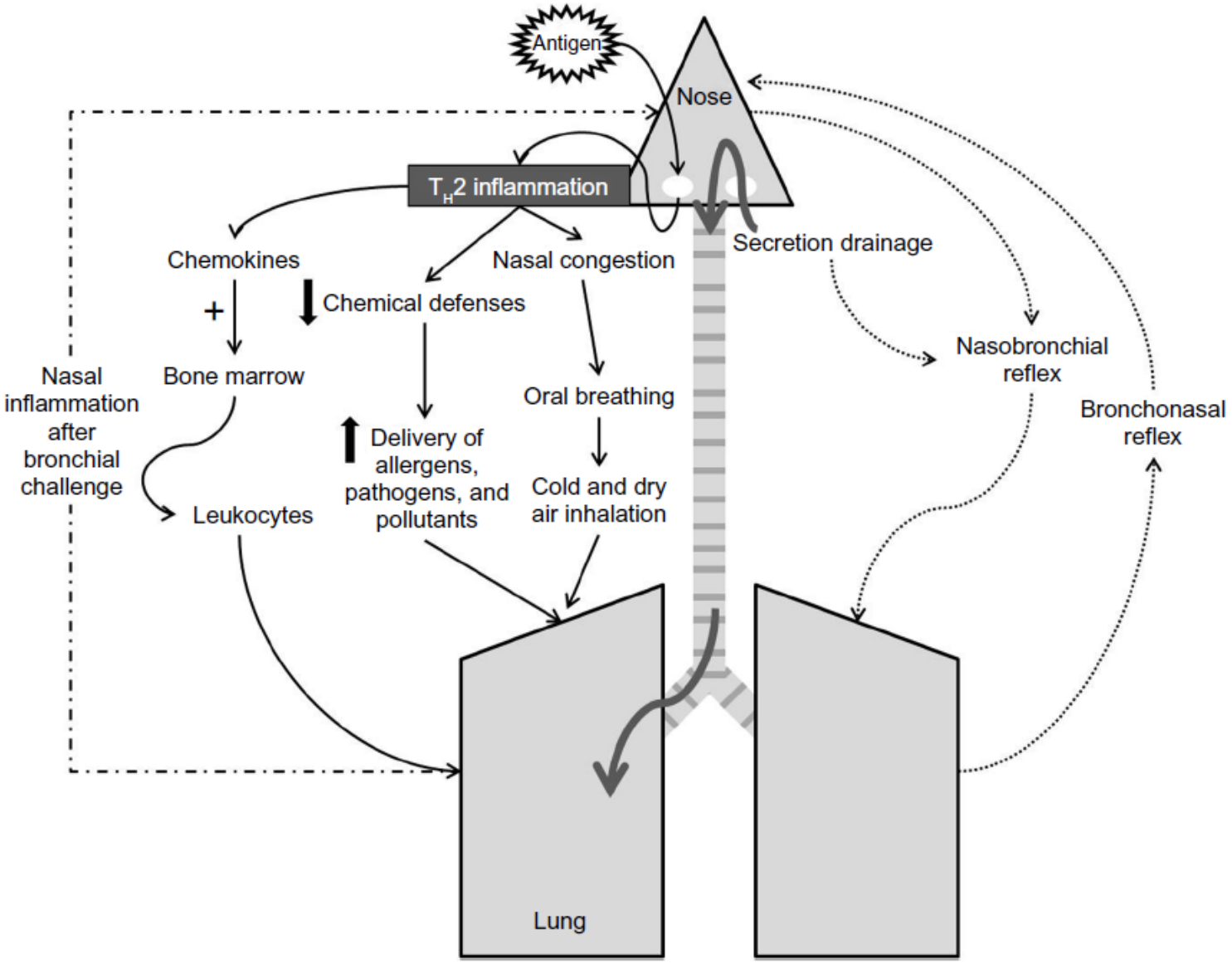
- **Dati epidemiologici**
- **Immunologia**
- **Aspetti funzionali**

La rinite rappresenta un fattore certo di rischio per asma, anche indipendentemente dall’atopia. La forma allergica è quella associata al rischio maggiore. La sensibilizzazione ad allergeni perenni comporta un rischio maggiore di asma rispetto a quella ad allergeni stagionali.

La rinite allergica si può associare ad iperreattività bronchiale aspecifica

Leynaert B et al, JACI 1999
Peroni D et al, Clin Exp Allergy 2003
Guerra S t al, JACI 2002
Ciprandi G, Int Arch Allergy Immunol 2004

Interazioni naso-bronchi



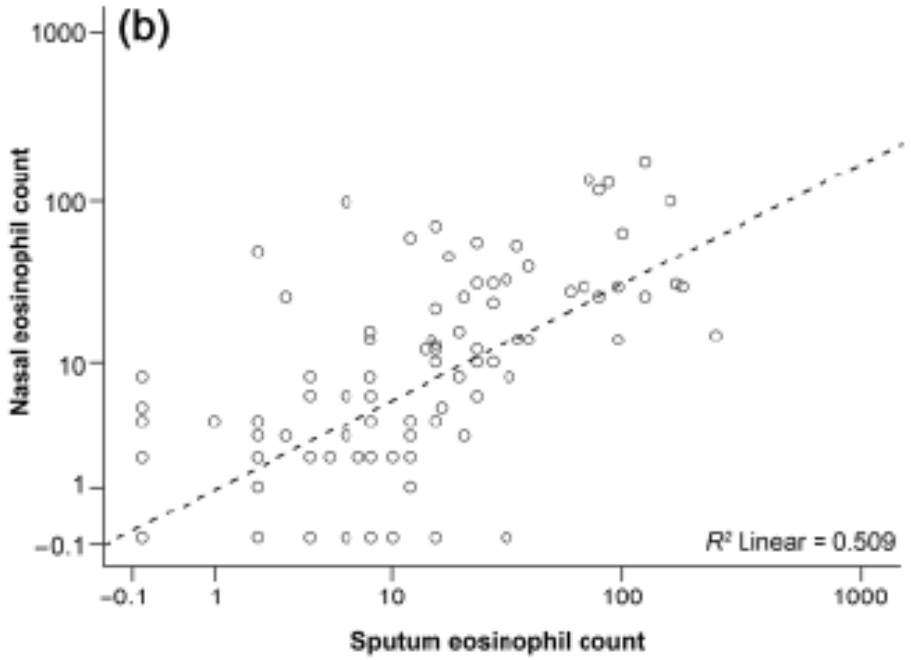
Journal of Asthma and Allergy 2016:9 93–100

Eosinofilia nasale e bronchiale

Nasal eosinophilia: an indicator of eosinophilic inflammation in asthma

M. M. Amorim, A. Araruna, L. B. Caetano, A. C. Cruz, L. L. Santoro and A. L. G. Fernandes

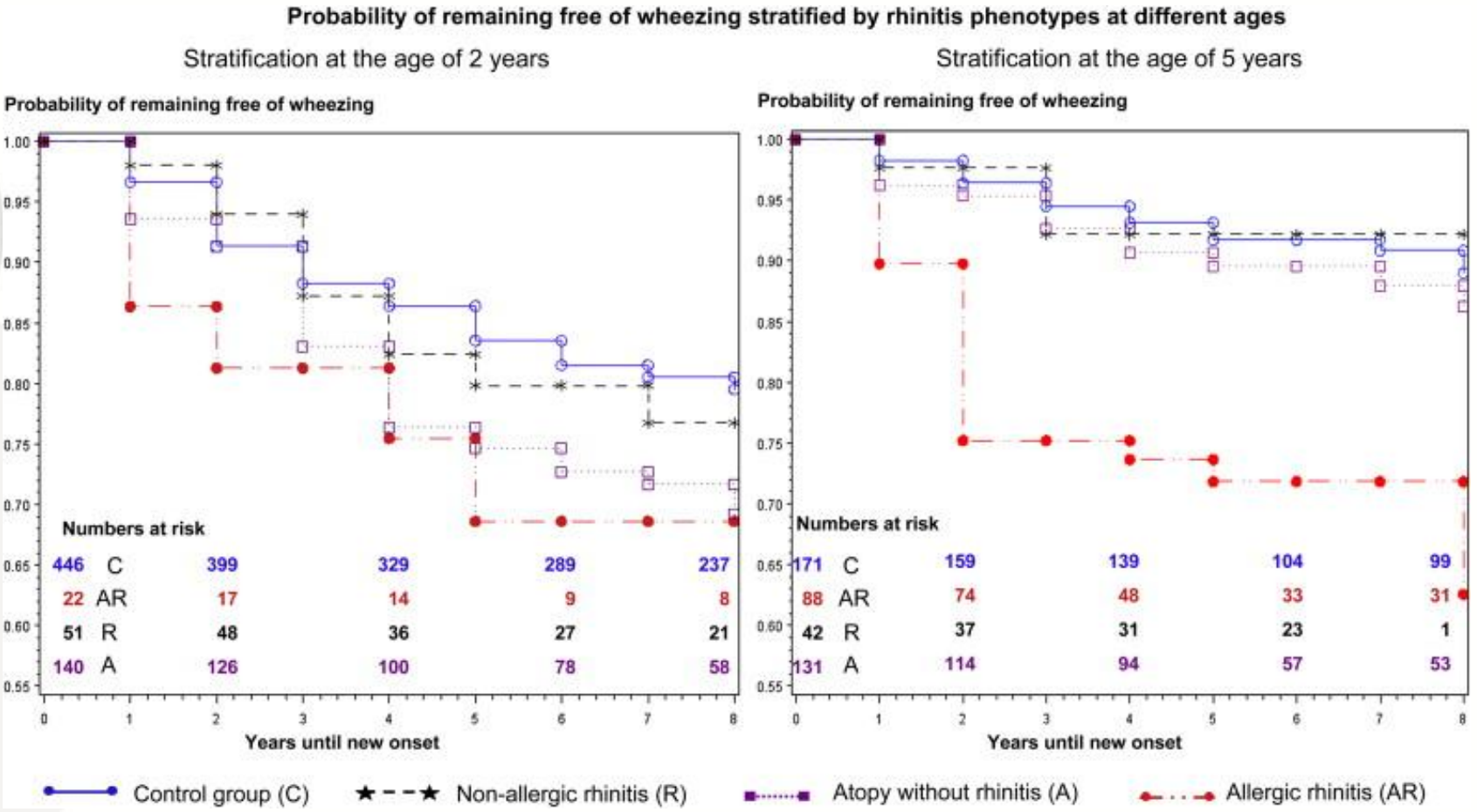
Asthma Research Group Respiratory Division – Federal University of São Paulo-Brazil (UNIFESP), São Paulo, Brazil



Questo studio aggiunge evidenza al fatto che le vie aeree superiori sono una componente importante nell'asma.

Clin Exp Allergy 2010

Rinite allergica è predittiva di insorgenza di wheezing in età scolare



Rochat et al, JACI 2010

Small-airway dysfunction precedes the development of asthma in children with allergic rhinitis

E. Skylogianni[a], M. Triga[a], K. Douros[b], K. Bolis[a], K.N. Priftis[b], S. Fouzas[a,*,1], M.B. Anthracopoulos[a,1]

Male sex	0.9 (0.4–2.6)
Eczema	3.3 (1.1–9.4)
Parental asthma	9.8 (2.9–34)
Sensitisation	
Seasonal	0.8 (0.2–3.0)
Perennial	2.2 (0.8–6.6)
Seasonal and perennial	1.8 (0.7–4.9)
Multiple	1.7 (0.5–5.4)
SAD*	16.8 (4.9–57)

Feb 2018

We suggest that the detection of SAD by means of respiratory impedance in allergic children who perceive only nasal symptoms, may assist in identifying those who are at risk of developing asthma and, thus, in planning targeted follow-up strategies for these patients.

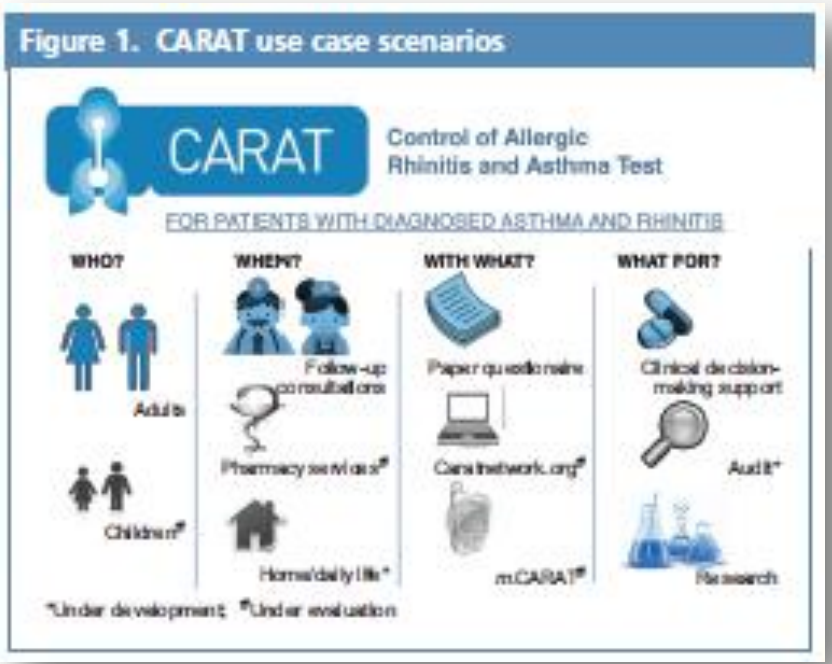
Control of Allergic Rhinitis and Asthma Test (CARAT): dissemination and applications in primary care

Table 1. CARAT characteristics and properties

	Instrument	CARAT
Content	Symptom frequency	Yes
	Rescue therapy use	Yes
	Sleep interference	Yes
	Activity limitation	Yes
	Exacerbations	No
	Physiologic measures	No
	Other	No
Characteristics	Number of questions Response format	10 4-point Likert scale
	Scoring method	Score sum 0-30
	Target population; age	≥18 years
	Time to complete	<3 min
	Patient report?	Yes
	How is it administered?	Self-administered (paper, internet, smart phone)
	Recall period	4 weeks
	Languages	Portuguese (PT), French, Turkish, Italian, Dutch, Portuguese (BR), English (UK), Spanish, Greek, English (US), German, Swedish, Finnish, Slovenian, Indian
	Cost to use	FREE for clinical use
Measurement properties COSMIN[12] requirements	Internal consistency Reliability	Cronbach's alpha was 0.85 [10] ICC 0.82 [11]
	Content validity	Face and content [9,10]
	Criterion validity Hypothesis-testing	Met a priori prediction for correlation coefficients ranging from 0.58 to 0.79; AUC 0.82 [10]
	Structural validity	Assessed using exploratory factor analysis [10]
	Cross-cultural validity	See text
	Floor and ceiling effects	Not present [10]
	Responsiveness	Significant within-patient change of CARAT[10] scoring in clinically unstable patients (95% confidence interval [-5.08; -1.31], p=0.002). The Guyatt's responsiveness index was 1.54[11]
	Interpretability	Clinically meaningful [11]
Instrument summary	Main advantage	Simple, simultaneous evaluation of asthma and rhinitis in accordance with ARIA guidelines
	Additional information needed	Minimal important difference Sub score cut-off values clinical validation of electronic versions

L'asma è frequentemente associata con la rinite allergica. Pertanto dovrebbe essere sempre suggerito un approccio combinato e integrato.
Il Control of Allergic Rhinitis and Asthma Test (CARAT), è il primo questionario che valuta contemporaneamente il livello di controllo di entrambe le patologie.

Figure 1. CARAT use case scenarios



Prim Care Respir J 2013

Relazione tra gravità dell'asma e rinite

The complex link between severity of asthma and rhinitis in mite allergic patients

Leonardo Antonicelli [a,*], Maria Chiara Braschi [a], Megon Bresciani [b], Martina Bonifazi [a], Sandra Baldacci [b], Anna Angino [b], Anna Paola Pala [b], Giovanni Viegi [c]

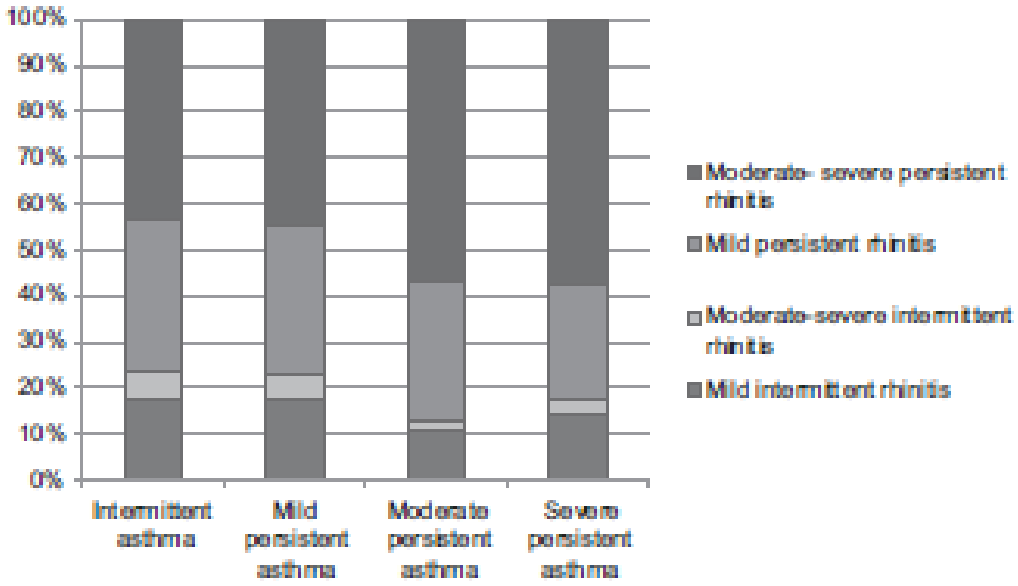


Figure 1 Percentage distribution of rhinitis severity according to the severity of coexistent asthma.

Respir Med 2013

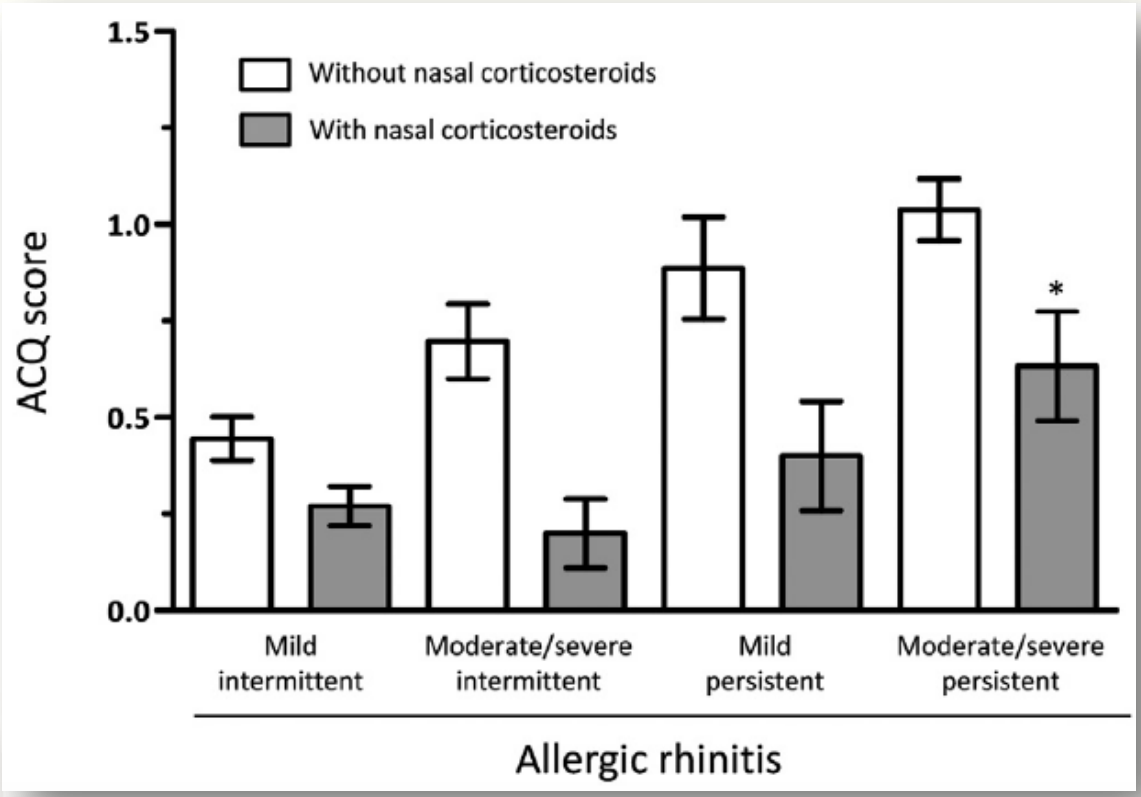
Il trattamento della rinite allergica migliora l'asma? I pochi studi disponibili non sono conclusivi.

A. A. Cruz[1], T. Popov[2], R. Pawankar[3], I. Annesi-Maesano[4], W. Fokkens[5], J. Kemp[6], K. Ohta[7], D. Price[8], J. Bousquet[9] on behalf of ARIA Initiative Scientific Committee

Authors	Location	Number of subjects	Study design	Benefit	Comments
Adams et al. (177)	USA	13 844	Retrospective cohort	RR 0.7 (emergency department visits)	For subjects using nasal glucocorticosteroids
Crystal-Peters et al. (178)	USA	4944	Retrospective cohort	RR 0.5 (emergency visits/hospitalizations)	Nothing remarkable
Corren et al. (179)	USA		Nested case–control	RR 0.56 (hospitalizations)	For subjects using nasal corticosteroids
Moller et al. (187)	Europe	205	Randomized trial	RR 0.40* (of having asthma)	Three years study with immunotherapy
Grembiale et al. (191)	UK	44	Randomized trial	Reduced BHR to Mch	Two years study with immunotherapy
Polosa et al. (192)	Italy	30	Randomized trial	Reduced BHR to AMP but not to Mch	Three years study with immunotherapy
Dahl et al. (171)	Europe	262	Randomized trial	Nonsignificant trend to improvement	Treatment with intranasal fluticasone
Lombardi et al. (193)	Italy	51	Open controlled trial	Reduced BHR to Mch	Three years study with immunotherapy
Taramarcaz and Gibson (170)	Cochrane (multiple)	425	Systematic review of randomized trials	Nonsignificant trend to improvement	Assessment of 11 trials to evaluate the effect of nasal steroids

Allergy 2007: 62 (Suppl. 84): 1–41

Determinants of Incomplete Asthma Control in Patients with Allergic Rhinitis and Asthma



In conclusion, the persistence and severity of AR and the use of NCSs were associated with the level of asthma control in patients with AR and asthma. Despite AR's impact on asthma control and quality of life, it is still undertreated. Evaluation of the activity of AR in patients with asthma and adequate treatment with NCSs are likely to improve asthma condition.

(Oka A. et al., J Allergy Clin Immunol Pract 2017;5:160-4)

Rinite allergica e omeopatia

The aim of this study was to evaluate the efficacy and effectiveness of homeopathic intervention in the treatment of seasonal or perennial allergic rhinitis

Eleven studies were eligible for systematic review. All trials were placebo-controlled except one. Six trials used the treatment approach known as isopathy, but they were unsuitable for meta-analysis due to problems of heterogeneity and data extraction. The overall standard of methods and reporting was poor: 8/11 trials were assessed as "high risk of bias"; only one trial, on isopathy for seasonal AR, possessed reliable evidence. Three trials of variable quality (all using Galphimia glauca for seasonal AR) were included in the meta-analysis: nasal symptom relief at 2 and 4 weeks (RR = 1.48 [95% CI 1.24-1.77] and 1.27 [95% CI 1.10-1.46], respectively) favored homeopathy compared with placebo; ocular symptom relief at 2 and 4 weeks also favored homeopathy (RR = 1.55 [95% CI 1.33-1.80] and 1.37 [95% CI 1.21-1.56], respectively). The single trial with reliable evidence had a small positive treatment effect without statistical significance. A homeopathic and a conventional nasal spray produced equivalent improvements in nasal and ocular symptoms.

CONCLUSIONS: The low or uncertain overall quality of the evidence warrants caution in drawing firm conclusions about intervention effects. Use of either Galphimia glauca or a homeopathic nasal spray may have small beneficial effects on the nasal and ocular symptoms of AR. The efficacy of isopathic treatment of AR is unclear.

Homeopathy for Allergic Rhinitis: A Systematic Review.

DEFINIZIONE-PATOGENESI
CLASSIFICAZIONE
EPIDEMIOLOGIA
CLINICA E DIAGNOSTICA
IMPATTO SULLA QoL
TRATTAMENTO
IMPATTO SULL'ASMA
ASPETTI PARTICOLARI

ASPETTI SPECIALI: Rinite professionale (RP)

- È una malattia infiammatoria del naso caratterizzata da sintomi intermittenti o persistenti e/o da riduzione variabile del flusso aereo nasale e/o da ipersecrezione. E' dovuta a cause e a situazioni attribuibili ad un particolare ambiente di lavoro e non a stimoli presenti al di fuori di esso. Può essere allergica e non allergica.

- La prevalenza stimata è **2-4 volte superiore all'asma professionale**, cui è frequentemente associata (fino al 70-80% dei casi). Considerata **marker precoce di asma professionale**, tuttavia uno studio recente evidenzia la necessità di ulteriori dati a supporto di tale ipotesi (*Balogun RA, AJIM 2018*). Rinite e asma correlate al lavoro sono più frequenti nei soggetti con rinite e/o iperreattività bronchiale pre-esistenti (*Moscato G, Allergy 2008 e 2011*) e la gravità della rinite influenza quella dell'asma professionale (*Moscato G, J Occup Health 2016)*.

- Rinite e rinosinusite sono cause frequenti di **tosse cronica correlata al lavoro** (*Moscato G, Allergy 2014*).

- Nelle riniti insorte in età adulta ogni medico deve considerare la possibilità di un'origine professionale (*Bousquet J, Allergy 2008 - Siracusa A, Curr Opin Allergy Clin Immunol 2013*), per la sua rilevanza epidemiologica e le implicazioni medico-legali (*Moscato G, Curr Opin Otolaryngol Head Neck Surg 2011*), tra cui il possibile **abbandono del posto di lavoro** (*Gerth van Wijk R, Allergy 2011*).

ASPETTI SPECIALI: Rinite professionale (RP)

- I pazienti con RP che continuano a essere esposti all'agente causale hanno uno **scadimento della QoL** (Rhinasthma e RAND-36). Il solo trattamento farmacologico non è sufficiente al miglioramento della QoL, ma è necessario ridurre o cessare l'esposizione (*Airaksinen LK, J Occup Environ Med 2009*).

- Il modello della **"United Airway Disease"** sembra essere applicabile anche in ambito professionale. I soggetti con sospetta AP dovrebbero essere indagati anche per RP (*Castano R,Thorax 2009; Moscato G, Allergy 2009; Ameille J , Occup Environ Med 2013*).

- I giovani devono essere educati ad adottare tutte le misure possibili per limitare l'esposizione ad agenti sensibilizzanti e irritanti respiratori e a riconoscere precocemente e riferire sintomi suggestivi dell'insorgenza di patologie respiratorie allergiche professionali o dell'aggravamento sul posto di lavoro di patologie pre-esistenti (*Moscato G, Allergy 2011)*. Gli apprendisti parrucchieri, in particolare, hanno un rischio aumentato di sviluppare rinite professionale conseguente all'esposizione agli agenti decoloranti sin dal primo anno di attività. Le scuole professionali dovrebbero, pertanto, metter a punto delle strategie per ridurre l'esposizione a tali prodotti *(Foss-Skiftesvik MH, Int Forum Allergy Rhinol 2017)*.

- Nonostante l'evidenza del coinvolgimento degli agenti occupazionali nelle patologie delle vie aeree superiori, sono stati effettuati pochi studi sulla loro prevalenza e sul possibile effetto dannoso di alcune sostanze usate sul lavoro (*Hox V, Allergy 2014*).

ASPETTI SPECIALI: Rinite professionale (RP)

J Occup Health 2016; 58: 310-313

Journal of Occupational Health

Brief Report

Occupational rhinitis affects occupational asthma severity

Gianna Moscato[1], Gianni Pala[2], Ilenia Folletti[3], Andrea Siracusa[4] and Santiago Quirce[5]

Table 2. Distribution of severity of occupational asthma and rhinitis

	Occupational rhinitis [a]	
	Absence, intermittent or mild persistent, n (%) n=47	Moderate-severe persistent, n (%) n=25
Occupational asthma [b]		
Intermittent	15 (32)	2 (8)
Mild persistent	14 (30)	7 (28)
Moderate-severe peristent [c]	18 (38)	16 (64)

[a] Severity of occupational rhinitis assessed by ARIA guidelines
[b] Severity of occupational asthma assessed by GINA guidelines
[c] Chi-Square=6.25; p value<0,005

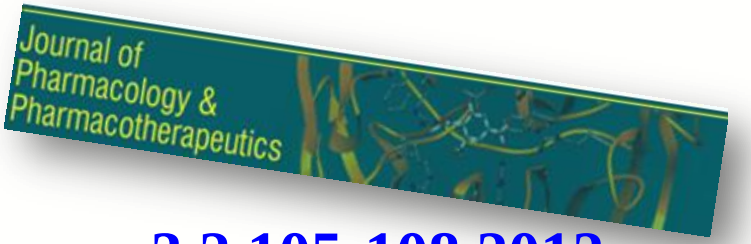
Antistaminici in gravidanza

Drug name	Pregnancy category
Chlorpheniramine	B
Cyproheptadine	B
Dexchlorpheniramine	B
Hydroxyzine	C
Promethazine	C
Tripelennamine	B

FDA pregnancy category classification for the first-generation antihistamines

Drug name	Pregnancy category
Cetirizine	B
Fexofenadine	C
Loratidine	B
Levocetrizine	B
Desloratidine	C

FDA pregnancy category classification for second-generation antihistamines[10]



3,2,105-108,2012

* Categoria di rischio FDA
B: assenza di teratogenicità nell'animale, non studi nelle donne gravide o rischio teratogeno nell'animale ma accertata assenza di rischio nella donna gravida.
C: Rischio teratogeno nell'animale e assenza di studi nella donna gravida (con beneficio/rischio comunque favorevole) o assenza di studi umani e animali

Sicurezza degli steroidi nasali in gravidanza.

Le meta-analisi concludono che gli steroidi inalatori non aumentano il rischio di parto pre-termine, malformazioni, basso peso alla nascita o ipertensione gestazionale.

Per beclometasone, budesonide e fluticasone propionato l'assenza di rischio teratogeno è convincente. I dati per triamcinolone, flunisolide e mometasone sono più limitati.

E' ragionevole continuare in gravidanza lo steroide nasale che ha controllato i sintomi precedentemente.

Se si inizia lo steroide nasale durante la gravidanza, dovrebbe essere preferita budesonide (categoria di rischio B).

La prescrizione di steroidi nasali in gravidanza dovrebbe essere comunque fatta solo se strettamente necessaria, e dopo attenta valutazione del rapporto beneficio/rischio

Rhinitis Practice Parameters, JACI, 2008

Taylor & Francis
Taylor & Francis Group

Expert Review of Clinical Pharmacology

ISSN: 1751-2433 (Print) 1751-2441 (Online) Journal homepage: http://www.tandfonline.com/loi/ierj20

Allergic rhinitis: pharmacotherapy in pregnancy and old age

E Ridolo, M Caminati, I Martignago, V Melli, C Salvottini, O Rossi, AR Dama, M Schiappoli, C Bovo, C Incorvaia & G Senna

- Allergic rhinitis (AR) affects 20-30% of women in reproductive age and may worsen during pregnancy.
- In pregnancy, drug avoidance should be carefully balanced with the need for AR optimal control.
- Topical drugs are suggested as a first approach.
- The safety and tolerability profile of second-generation antihistamines is well supported.
- If allergen immunotherapy (AIT) is ongoing and well tolerated, there is no reason for stopping it. AIT initiation in pregnancy is not recommended.

Prevalenza della rinite negli atleti

Study population (n)	Prevalence	Diagnostic method	Reference
Australian Olympics (185)	8.6%	Medical records analysis	Fitch, 1984
Australian Olympics (106)	7.5%	Medical records analysis	Fitch, 1984
Swiss athletes (2060)	16.8%	Questionnaire	Helbling et al, 1990
Swiss athletes (1530)	19.7%	Questionnaire	Kaelin et al, 1993
US swimmers (738)	19.0%	Questionnaire	Potts, 1996
Finish summer athletes (162)	29.6%	Skin prick tests with medical diagnosis	Helenius et al, 1998
US Olympic team (699)	16.9%	Questionnaire	Weiler et al., 1998
US winter Olympic team (196)	13.3%	Questionnaire	Weiler et al., 2000
Australian Olympic team (214)	41.0%	Skin prick tests with medical diagnosis	Katelaris et al., 2000
Italian Pre-Olympic team (265)	25.3%	Skin prick tests with medical diagnosis	Lapucci et al., 2003
Finnish Olympic athletes (446)	26.5%	Self reported medical diagnosis	Alaranta et al. 2005
Finnish marathon runners (141)	17.3%	Self reported medical diagnosis	Moreira et al. 2007
Italian preOlympics (98)	34.7%	Skin prick tests with medical diagnosis	Bonini et al. 2007
Italian Olympic athlets (659)	26.2%	Skin prick tests with medical diagnosis	Bonini et al. 2015

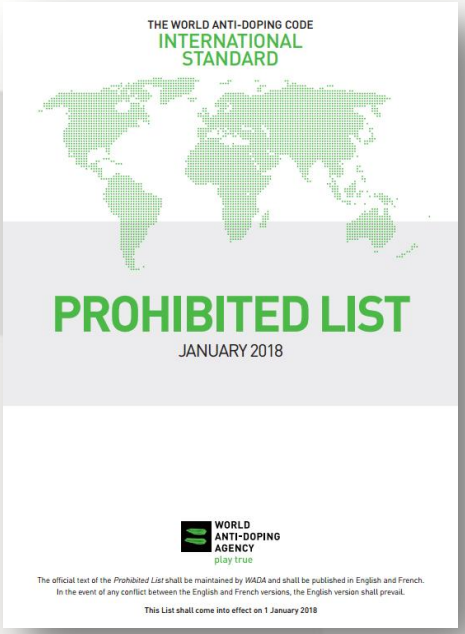
Lista dei "farmaci antiallergici" regolamentati dalla World Anti-Doping Agency aggiornata al 1 gennaio 2018.

TRATTAMENTO	REGOLAMENTO WADA	NOTE
Antistaminici	Permessi senza limitazioni	Gli antistaminici di prima generazione possono influire sulle prestazioni dell'atleta.
β_2-agonisti per via orale	**Proibiti**	
β_2-agonisti per via inalatoria		
Salbutamolo	Dosaggio massimo di 1600 mcg nelle 24 ore, divisi in dose che non eccedano gli 800 mcg nelle 12 ore	La presenza nelle urine di oltre 1000 ng/mL di salbutamolo è ritenuto doping. Per questo motivo, se fosse necessario un dosaggio giornaliero maggiore di salbutamolo, sarà necessario redigere un TUE.
Formeterolo	Dosaggio massimo di 54 mcg nelle 24 ore	La presenza nelle urine di oltre 40 ng/mL di formeterolo è ritenuto doping. Per questo motivo, se fosse necessario un dosaggio giornaliero maggiore di formeterolo, sarà necessario redigere un TUE.
Salmeterolo	Dosaggio massimo di 200 mcg nelle 24 ore	
Altri β_2-agonisti	**Proibiti**	
Corticosteroidi per via orale	**Proibiti** nelle competizioni ufficiali	Necessità di TUE
Corticosteroidi per via inalatoria	Permessi senza limitazioni	
Anti-leucotrienici	Permessi senza limitazioni	
Anti-colinergici	Permessi senza limitazioni	
Cromoni	Permessi senza limitazioni	
Immunoterapia specifica	Permessa senza limitazioni	
Farmaci biologici	Permessi senza limitazioni	Non è stata provata l'efficacia dei farmaci biologici anti-IgE e anti-IL5 negli atleti. Inoltre è inusuale che questi farmaci siano utilizzati in atleti, visto che sono dedicati a forme severe di asma che non permetterebbero l'esercizio fisico.

WADA = World Anti-Doping Agency; TUE = *Therapeutic Use Exemption*; mcg = microgrammi; ng = nanogrammi; mL = millilitro; anti-IgE = anti-immunoglobuline E; anti-IL5 = anti-interleuchina 5.

The world anti-doping code. Prohibited list (January 2018). https://www.wada-ama.org/sites/default/files/prohibited_list_2018_en.pdf. 2018;

ASPETTI PARTICOLARI; RINITE/ASMA E SPORT. DOCUMENTO AGGIORNATO WADA 2018)



S3 BETA-2 AGONISTS

All selective and non-selective beta-2 agonists, including all optical isomers, are prohibited.

Including, but not limited to:

Fenoterol;
Formoterol;
Higenamine;
Indacaterol;
Olodaterol;
Procaterol;
Reproterol;
Salbutamol;
Salmeterol;
Terbutaline;
Tulobuterol;
Vilanterol.

Except:

- Inhaled salbutamol: maximum 1600 micrograms over 24 hours in divided doses not to exceed 800 micrograms over 12 hours starting from any dose;
- Inhaled formoterol: maximum delivered dose of 54 micrograms over 24 hours;
- Inhaled salmeterol: maximum 200 micrograms over 24 hours.

The presence in urine of salbutamol in excess of 1000 ng/mL or formoterol in excess of 40 ng/mL is not consistent with therapeutic use of the substance and will be considered as an *erse Analytical Finding* (*AAF*) unless the *Athlete* proves, ough a controlled pharmacokinetic study, that the ormal result was the consequence of a therapeutic dose (by inhalation) up to the maximum dose indicated above.

S9 GLUCOCORTICOIDS

All glucocorticoids are prohibited when administered by oral, intravenous, intramuscular or rectal routes.

Including but not limited to:

Betamethasone;
Budesonide;
Cortisone;
Deflazacort;
Dexamethasone;
Fluticasone;
Hydrocortisone;
Methylprednisolone;
Prednisolone;
Prednisone;
Triamcinolone.

www.wada-ama.org

ASPETTI PARTICOLARI: RINITE NELL'ANZIANO

Drugs Aging (2017) 34:21–28
DOI 10.1007/s40266-016-0425-7

REVIEW ARTICLE

Pharmacological Management of Allergic Rhinitis in the Elderly

Andrzej Bozek[1]

Allergic diseases in the elderly: biological characteristics and main immunological and non-immunological mechanisms

Maria Teresa Ventura[1], Nicola Scichilone[2], Roberto Paganelli[3], Paola Lucia Minciullo[4*], Vincenzo Patella[5,6], Matteo Bonini[7], Giovanni Passalacqua[8], Carlo Lombardi[9], Livio Simioni[10], Erminia Ridolo[11], Stefano R. Del Giacco[12], Sebastiano Gangemi[4] and Giorgio Walter Canonica[8]

Ventura MT et al. Clin Molecular Allergy 2017

Key Points

Allergic rhinitis is undertreated in elderly patients.

Antihistamines and nasal glucocorticosteroids are the first-line therapies in patients over 60 years of age.

Attention should be paid to the use of oral antihistamines in patients with comorbidities and polymedication.

ASPETTI PARTICOLARI: RINITE NELL'ANZIANO

Treating rhinitis in the older population: special considerations
Slavin RG. Allergy Asthma & Clin Immunol 2009

La rinite è un disturbo comune e spesso trascurato nell'anziano.
Uno dei provvedimenti più importanti è mantenere idratata la mucosa.
Di solito sono ben tollerati gli antl-H1 di seconda generazione, i corticosteroidi nasali, gli antleucotrienici e l'ipratropio.
Occorre cautela con i decongestionanti.

Fattori che possono modificare gli outcome della terapia

- Polifarmacoterapia
- Decadimento cognitivo
- Insuff. epatica e/o renale
- Alterazioni della massa magra
- Costi e risorse

Tipi di rinite dell'anziano

- Allergica
- Atrofica
- Vasomotoria
- Da farmaci (ASA/Fans, doxazosina, aceinibitori, Ca antagonisti,β bloccanti, idroclorotiazide, risperidone, cloropromazina, amitriptilina, sildenafil)
- NARES

Phenotyping asthma in the elderly: allergic sensitization profile and upper airways comorbidity in patients older than 65 years

Carlo Lombardi, MD [*]; Elena Raffetti, MD [†]; Marco Caminati, MD [‡]; Gennaro Liccardi, MD [§]; Gianni Passalacqua, MD, PhD [‖]; Federico Reccardini, MD [¶]; Erminia Ridolo, MD, PhD [#]; GianEnrico Senna, MD [‡]; Gundi Steinhilber, MD [**]; and M. Milanese, MD [††] on behalf of the ELSA Study Group

Demographic and clinical characteristics of subjects with asthma and in relation to COPD-like features

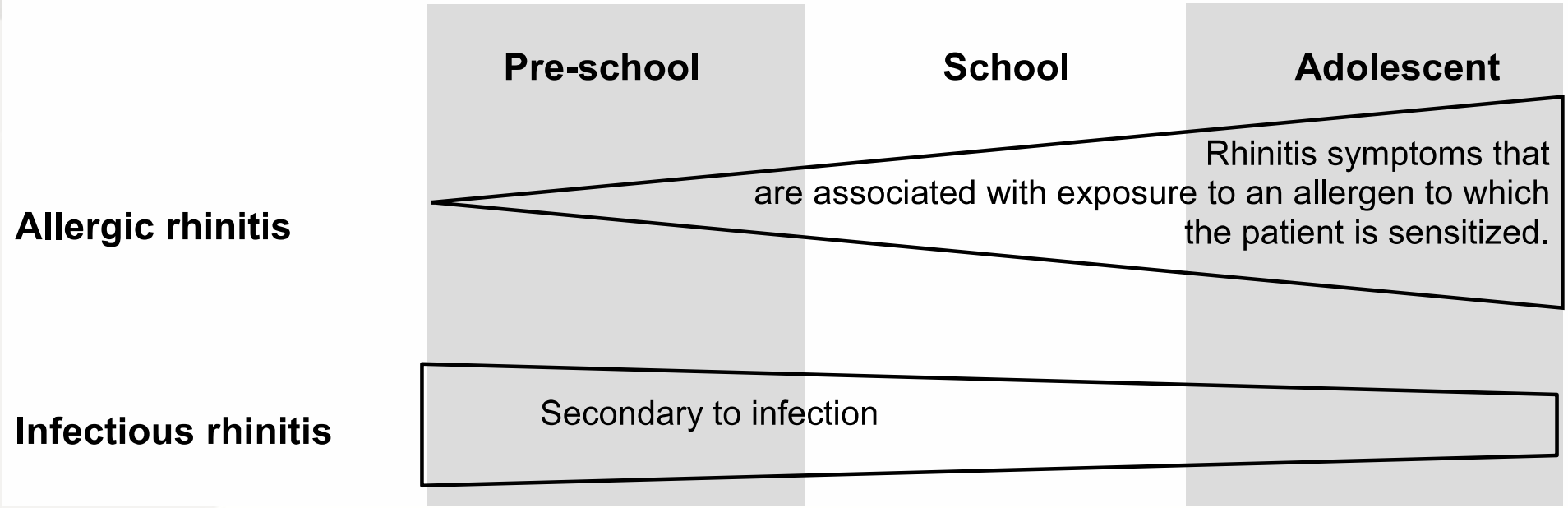
Variables	Categories	Total subjects, n (%)[a]	Without COPD-like features, n (%)[a]	With COPD-like features, n (%)[a]	*P* value by χ^2 test
Total		368 (100.0)	267 (72.5)	101 (27.5)	
Sex	Men	235 (63.9)	172 (64.4)	63 (62.4)	NS
Age (y)	65–69	122 (33.2)	94 (35.2)	28 (27.7)	.025[b]
	70–74	126 (34.2)	96 (36.0)	30 (29.7)	
	≥75	120 (32.6)	77 (28.8)	43 (42.6)	
	Mean (SD)	72.4 (5.4)	72.0 (5.3)	73.6 (5.4)	
Rhinitis	Yes	217 (59.0)	154 (57.7)	63 (62.4)	NS
Age at rhinitis onset (y)		49.0 (18.0)	49.0 (17.9)	49.1 (18.2)	NS[c]
Allergic rhinitis	Yes	175 (47.6)	127 (47.6)	48 (47.5)	NS
Nonallergic rhinitis	Yes	42 (11.4)	27 (10.1)	15 (14.9)	NS
Sensitization	Yes	193 (52.4)	140 (52.4)	53 (52.5)	NS
Polysensitization	Yes	117 (31.8)	85 (31.8)	32 (31.7)	NS
HDM	Yes	117 (31.8)	77 (28.8)	40 (39.6)	.048
Parietaria species	Yes	63 (17.1)	44 (16.5)	19 (18.8)	NS
Grass	Yes	72 (19.6)	56 (21.0)	16 (15.8)	NS
Birch	Yes	39 (10.6)	28 (10.5)	11 (10.9)	NS
Alternaria species	Yes	14 (3.8)	12 (4.5)	2 (2.0)	NS
Cat	Yes	24 (6.5)	14 (5.2)	10 (9.9)	NS
Other allergens	Yes	65 (17.7)	47 (17.6)	18 (17.8)	NS

Conclusion: Approximately 60% of elderly subjects with asthma had rhinitis, mainly allergic and often untreated, whose onset preceded asthma symptoms by a mean of approximately 10 years. Nonallergic asthma was better controlled than allergic asthma. However, HDM sensitization was greater in subjects with asthma with features resembling chronic obstructive pulmonary disease (39% vs 28%). When restricting analysis to this group, the negative role of HDM in overall asthma control (forced expiratory volume in first second and Asthma Control Test) was significant.

Ann Allergy Asthma Immunol march 2016

ASPETTI PARTICOLARI: pediatria

DEFINIZIONE
La rinite allergica può sovrapporsi a quadro infettivo con diversa prevalenza a seconda dell'età



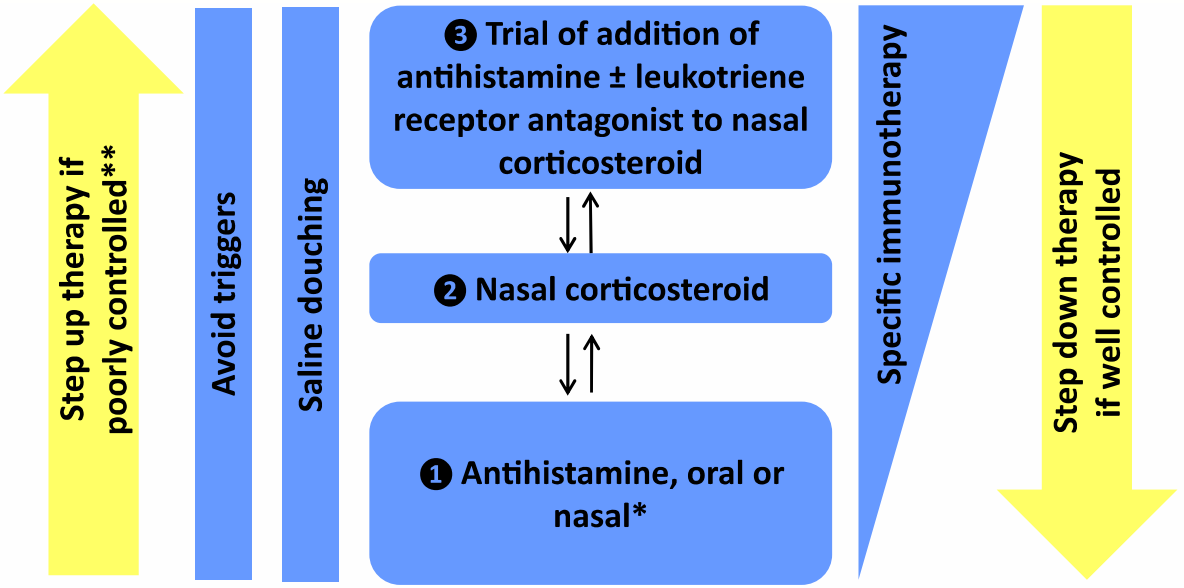
Roberts G et al. Allergy 2013; 68: 1102–1116,.

ASPETTI PARTICOLARI: diagnosi differenziale in pediatria

Diagnosis	Pre-school	School	Adolescent
Choanal atresia or stenosis	Obstruction without other features of allergic rhinitis		
Immuno-deficiency	Persisting mucopurlent discharge		
Encephalocoele	Unilateral nasal “polyp”		
Adenoidal hypertrophy	Mouth breathing, discoloured nasal secretions, snoring in the absence of other features of allergic rhinitis		
Foreign body	Unilateral discoloured nasal secretions, foul smell		
Rhinosinusitis		Discoloured nasal secretions, headache, facial pain, poor smell, halitosis, cough	
Cystic fibrosis	Bilateral nasal polyps, poor smell, chest symptoms, symptoms of malabsorption, failure to thrive		
Primary ciliary dyskinesia	Persisting mucopurlent discharge without respite between “colds”, bilateral stasis of mucus and secretions at the nasal floor, symptoms from birth		
CSF leakage	Colourless nasal discharge often with a history of trauma		
Coagulopathy	Recurrent epistaxis with minimal trauma		
Septal deviation		Obstruction in the absence of other features of allergic rhinitis	

Roberts G et al. Allergy 2013; 68: 1102–1116,.

ASPETTI PARTICOLARI: terapia in pediatria



Roberts G et al. Allergy 2013; 68: 1102–1116,.

Antistaminici orali di seconda generazione possono essere utilizzati dal secondo anno di vita
Antistaminici nasali possono essere utilizzati dal 12° anno di vita
In Italia, gli steroidi nasali possono essere utilizzati dal sesto anno di vita (mometasone dal terzo anno)(registrazione italiana)
Antileucotrienici possono essere utilizzati specialmente in caso di asma associato

DEFINIZIONE

La rinite allergica è una patologia della mucosa nasale indotta da una infiammazione IgE mediata conseguente all'esposizione allergenica.

SINTOMI TIPICI DI RINITE ALLERGICA
- Rinorrea acquosa
- Starnuti a salve
- Prurito nasale
- Ostruzione nasale
- Congiuntivite concomitante

SINTOMI TIPICI DI CONGIUNTIVITE ALLERGICA
- Rinite concomitante
- Sintomi bilaterali
- Lacrimazione
- Prurito congiuntivale
- Iperemia

CLASSIFICAZIONE (paziente non trattato)

Per durata dei sintomi
- Intermittente: < 4 giorni/settimana o < 4 settimane
- Persistente: > 4 giorni/settimana e 4 settimane

Per gravità dei sintomi
- Moderata-grave. Uno o più fra: alterazioni del sonno, limitazioni delle attività quotidiane, riduzione prestazioni lavorative/scolastiche, sintomi gravi.
- Lieve. Nessuna delle caratteristiche cliniche della forma moderata-grave.

ESSENTIALIA per il Medico di Medicina Generale

DIAGNOSI

- Anamnesi personale (sintomi tipici) e famigliare
- Rinoscopia anteriore
- documentazione della sensibilizzazione ad aeroallergeni e correlazione con la clinica

TERAPIA FARMACOLOGICA

- Prevalente ostruzione nasale: corticosteroide topico
- Prevalenti rinorrea e starnuti: antistaminico anti H1 non sedativo per os

FOLLOW-UP (controllo, non necessariamente visita, dopo 2-4 settimane)

- Se migliora: continua terapia precedentemente impostata
- Se non migliora: cambio o aggiunta di farmaco/invio a consulenza

COMORBILITA' RINITE-ASMA

- Nei pazienti con rinite persistente verificare la coesistenza di asma con anamnesi mirata (respiro sibilante, tosse secca, sintomi dopo esercizio, senso di oppressione al torace). Se positiva/suggestiva: spirometria. I pazienti con asma devono essere valutati per eventuale rinite concomitante.

IMMUNOTERAPIA SPECIFICA

- E' l'unico trattamento allergene orientato ad effetto precoce. Riduce i sintomi e il consumo di farmaci. Può modificare l'eventuale progressione da rinite ad asma. Ha un effetto long-lasting.

Percezione e prescrizioni nella RA da parte di MMG e farmacisti in Italia

Canonica *et al. Clin Mol Allergy (2015) 13:25*
DOI 10.1186/s12948-015-0029-5

CLINICAL AND MOLECULAR ALLERGY

RESEARCH Open Ac

360 degree perspective on allergic rhinitis management in Italy: a survey of GPs, pharmacists and patients

G. Walter Canonica[1*], Massimo Triggiani[2] and GianEnrico Senna[3]

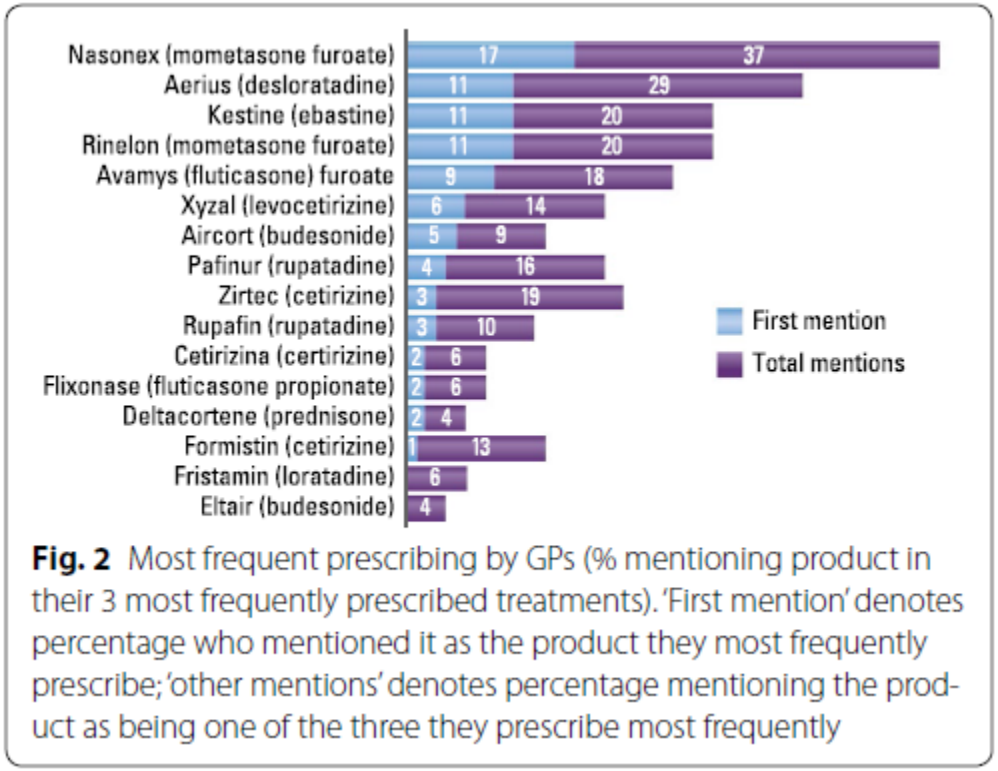


Fig. 2 Most frequent prescribing by GPs (% mentioning product in their 3 most frequently prescribed treatments). 'First mention' denotes percentage who mentioned it as the product they most frequently prescribe; 'other mentions' denotes percentage mentioning the product as being one of the three they prescribe most frequently

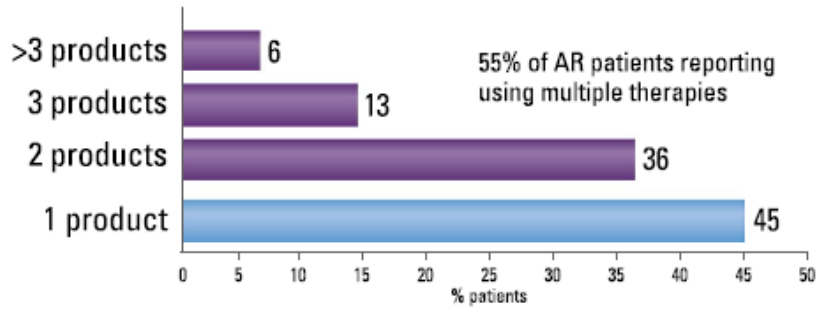
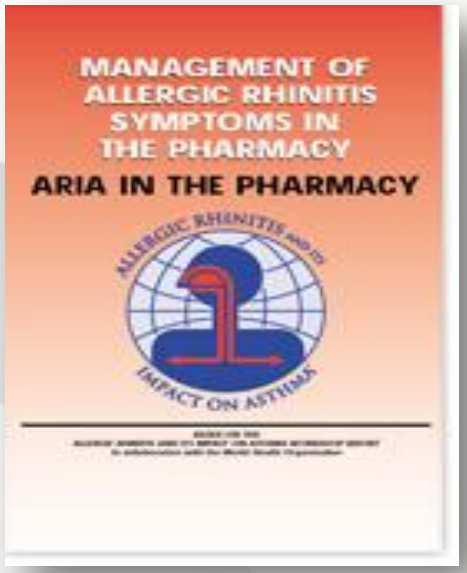
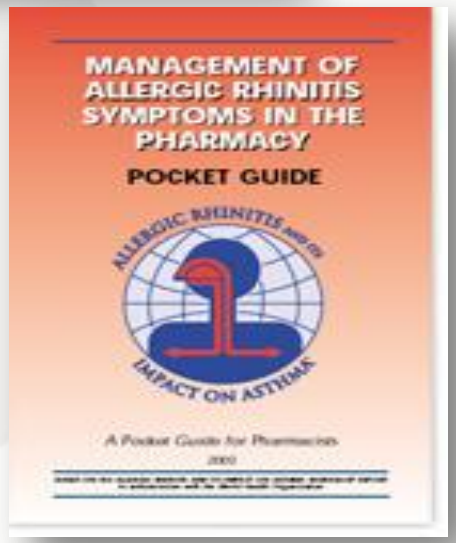


Fig. 4 Proportion of patients using multiple therapies

Progetto ARIA in Farmacia





COSA DOVREBBE CHIEDERE IL FARMACISTA PER EROGARE L' AUTOMEDICAZIONE?

- Ci sono i sintomi tipici di rinite allergica?
- Ci sono sintomi atipici? *
- È presente una stagionalità? Familiari allergici?
- E presente anche congiuntivite?
- Sono presenti sintomi sospetti per asma? *
- Il trattamento sintomatico funziona? **

* Inviare al medico.

** Se no entro 2 settimane inviare al medico

Mobile (m)-health : l'avvento delle Apps

European Summit on the Prevention and Self-Management of Chronic Respiratory Diseases: report of the European Union Parliament Summit (29 March 2017)

Peter W. Hellings[1,2], David Borrelli[3], Sirpa Pietikainen[4], Ioana Agache[5], Cezmi Akdis[6,7], Claus Bachert[8], Michael Bewick[9], Erna Botjes[10], Jannis Constantinidis[11], Wytske Fokkens[2], Tari Haahtela[12], Claire Hopkins[13], Maddalena Illario[14], Guy Joos[15], Valerie Lund[16], Antonella Muraro[17], Benoit Pugin[18], Sven Seys[18,19], David Somekh[20], Pär Stjärne[21], Arunas Valiulis[22,23], Erkka Valovirta[24] and Jean Bousquet[25,26,27*]

mySinusitisCoach: a EUFOREA mobile application

Patient Educational Platform

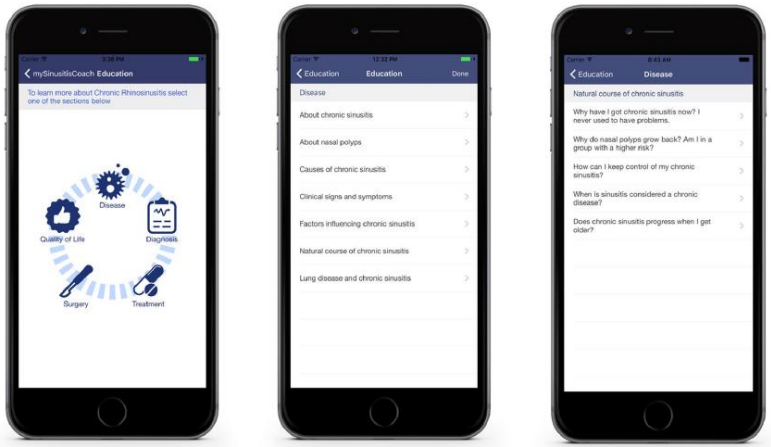
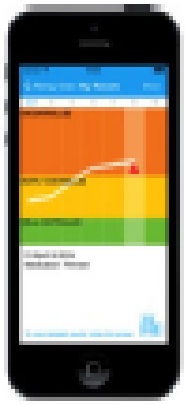


Fig. 4 EUFOREA 'mySinusitisCoach'

Clin Transl Allergy. 2017; 7: 49.

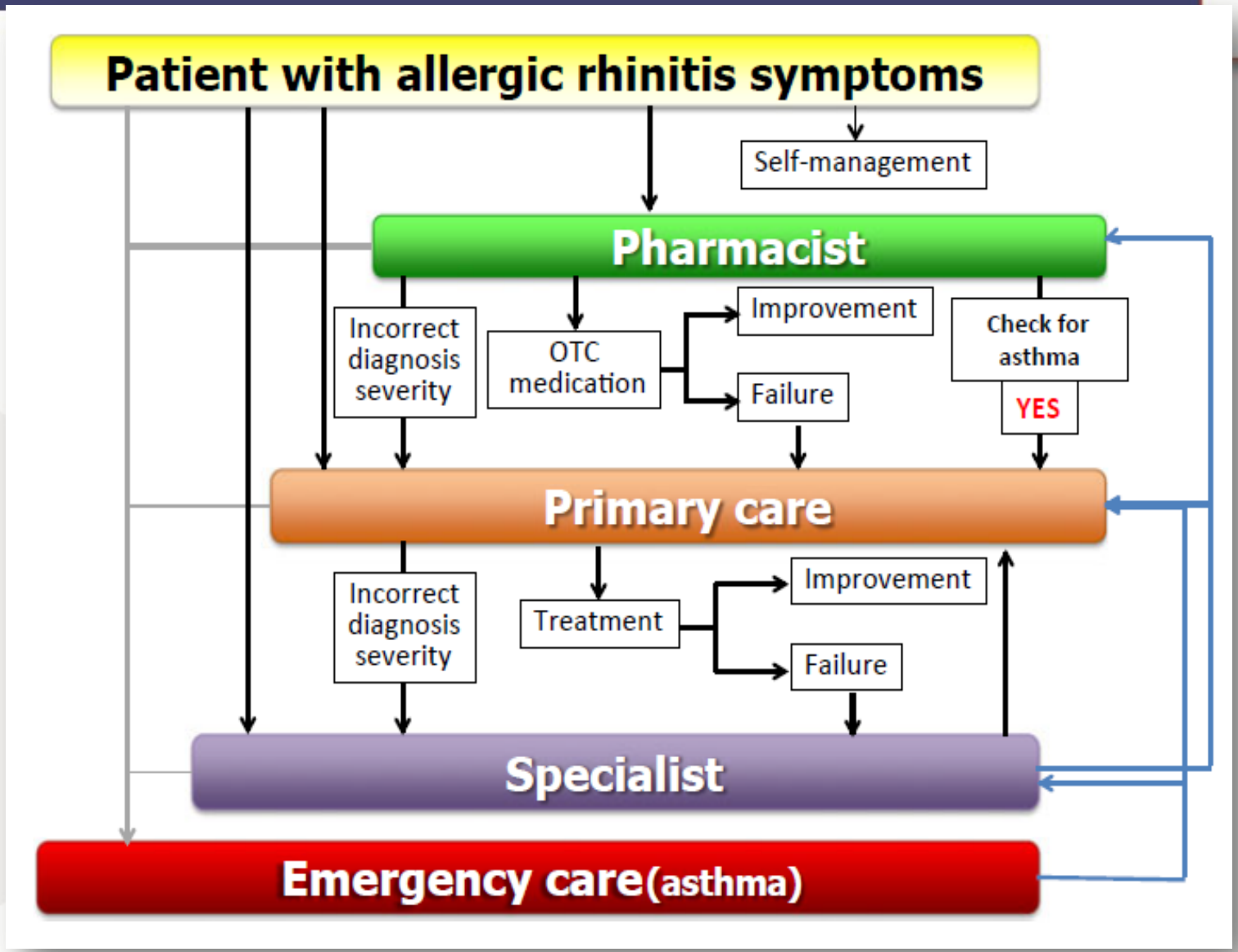
- In case of continued high scores the feedback message will display an appropriate message in red type and a warning icon will mark the graph
- Prompts users to discuss their diary data with their health care provider



Aim: get to "green" and stay there

MASK-rhinitis (MACVIA-ARIA Sentinel NetworK for allergic rhinitis) è un sistema centrato sul paziente, che usa tecnologie informatiche e di comunicazione (ICT) per uno strumento di montoraggio e di decisione clinica (CDSS) in base ai sintomi. Tale sistema ha l'aspetto di un'App che consente la registrazione quotidiana dei sintomi, del controllo e del trattamento della RA

Modello integrato di management del paziente con RA



(Allergy 70 (2015) 1372–1392)

«Choosing wisely» per la rinite allergica
Talvolta il meglio è peggio del bene

Heffler *et al. Clin Mol Allergy (2015) 13:28*
DOI 10.1186/s12948-015-0034-8

CLINICAL AND MOLECULAR ALLERGY

RESEARCH Open Access

Choosing wisely in Allergology: a Slow Medicine approach to the discipline promoted by the Italian Society of Allergy, Asthma and Clinical Immunology (SIAAIC)

Enrico Heffler[1*], Massimo Landi[2], Silvana Quadrino[3,6], Cristoforo Incorvaia[4], Stefano Pizzimenti[5], Sandra Vernero[6], Nunzio Crimi[1], Giovanni Rolla[7] and Giorgio Walter Canonica[8]

Table 1 The list of identified 5 most inappropriate allergological procedures

Do not perform allergy tests for drugs (including anhestetics) and/or foods when there are neither clinical history nor symptoms suggestive of hypersensitivity reactions
Do not perform the so-called "food intolerance tests" (apart from those which are validated for suspect celiac disease or lactose enzymatic intolerance)
Do not perform serological allergy tests (i.e.: total IgE, specific IgE, component-resolved diagnosis) as first-line tests or as "screening" of inhalant & food immediate hypersensitivity assays
Do not treat patients sensitized to allergens or aptens if there is not a clear correlation between exposure to that specific allergen/apten and symptoms suggestive of allergic reaction. This recommendation is particularly strong for allergen immunotherapy and elimination diets
Do not diagnose asthma without having performed lung function tests (including bronchodilating test and/or bronchial challenge)

Choosing wisely & Pediatria

Table 1 Five Recommendations of the Italian Society of Pediatric Allergy and Immunology – SIAIP

1 Avoid contraindicating routinely vaccination in case of allergies.

A history of allergies or mild allergic reactions are not contraindications to vaccination.

Local and mild systemic reactions (redness of the injection site and/or fever) after vaccination reactions are common and do not contraindicate the administration of doses of vaccine in the future. Special precautions should be followed only in the case of persons who have presented serious systemic reactions with risk of life (severe dyspnea, stridor, cyanosis, mental status changes, hypote… protein is not a contraindication to vaccination against measles, mumps and rubella.

Kelso et al. 2012 [11], Kelso et al. 2013 [12]

2 Avoid performing routinely allergy testing in children with acute urticaria.

The diagnosis of acute urticaria is basically clinical and infections (in particular viral infections) account the far most common cause during childhood. Testing patients for allergies is indicated only when there is a close temporal relationship between food ingestion and the appearance of urticarial eruption: laboratory investigations are not indicated in first instance, it is appropriate to limit allergologic tests to the skin test (SPT) by using commercial extracts or fresh food (prick by prick).

Zuberbier et al. 2009 [13], Capra et al. 2012 [14], Zuberbier et al. 2009 [15]

3 Avoid prescribing mucolytics in children with bronchial asthma.

Inflammation, mucosal edema and mucus hypersecretion increase the narrowing of the bronchial lumen with the formation of mucus plugs that worsen bronchial obstruction in patients with asthma. Studies conducted on the effectiveness of mucolytics to treat asthma and its exacerbations have demonstrated their poor effectiveness and the possibility of dangerous side effects. The most important International guidelines (GINA, ATS, BTS) don't include mucolytics in the "management" of children with bronchial asthma. Mucolytics agents are also contraindicated under 2 years of age due to the risk of a substantial deterioration of respiratory function for a difficult bronchial drainage.

Balsamo et al. 2010 [16], Aliyali et al. 2010 [17], Linee guida GINA italiane 2013 [18]

4 Avoid prescribing routinely immunological tests in children with recurrent respiratory infections.

Immunological and genetic investigations are not need when the child is suffering from undifferentiated common viral infections affecting the upper airways and when there is no family history of primary lung diseases or hereditary immunodeficiencies. The decision to perform tests should be based not only on the number of infections, but expecially on their severity, on the presence of unusual or opportunistic germs, on the protracted course and on the occurrence of infections beyond the age of primary socialization. Complete blood cell count and the dosage of immunoglobulins are considered first level tests, together with the sweat test in patients with recurrence of ear infections, bacterial sinusitis, bronchopneumonia or other invasive infections.

Notarangelo 2009 [19], Brand et al. 2012 [20], Bousfiha et al. 2013 [21]

5 Avoid ruling out a food from the diet only for the positivity of skin prick tests and/or specific serum IgE.

An accurate medical history is essential for the diagnosis of food allergy, in particular should be investigated a framework compliant with food allergy and a temporal relationship between the introduction of food and the appearance of symptoms. The presence of skin test (prick test) and/or positive serum specific IgE against foods indicates only a sensitization, condition that can be compatible with the intake of a food. For a correct diagnosis of food allergy an oral food challenge test must be provided (if the history and skin prick tests/specific serum IgE are not exhaustive for diagnosis).

Boyce et al. [22], Burks et al. 2012 [23], Heinzerling et al. 2013 [24]

Beyond the "Choosing wisely": a possible attempt

Bernardini et al., Italian Journal of Pediatrics (2016) 42:55