



ARIA masterclass
from Guidelines to real-life

Why is the control suboptimal in Allergic Rhinitis?

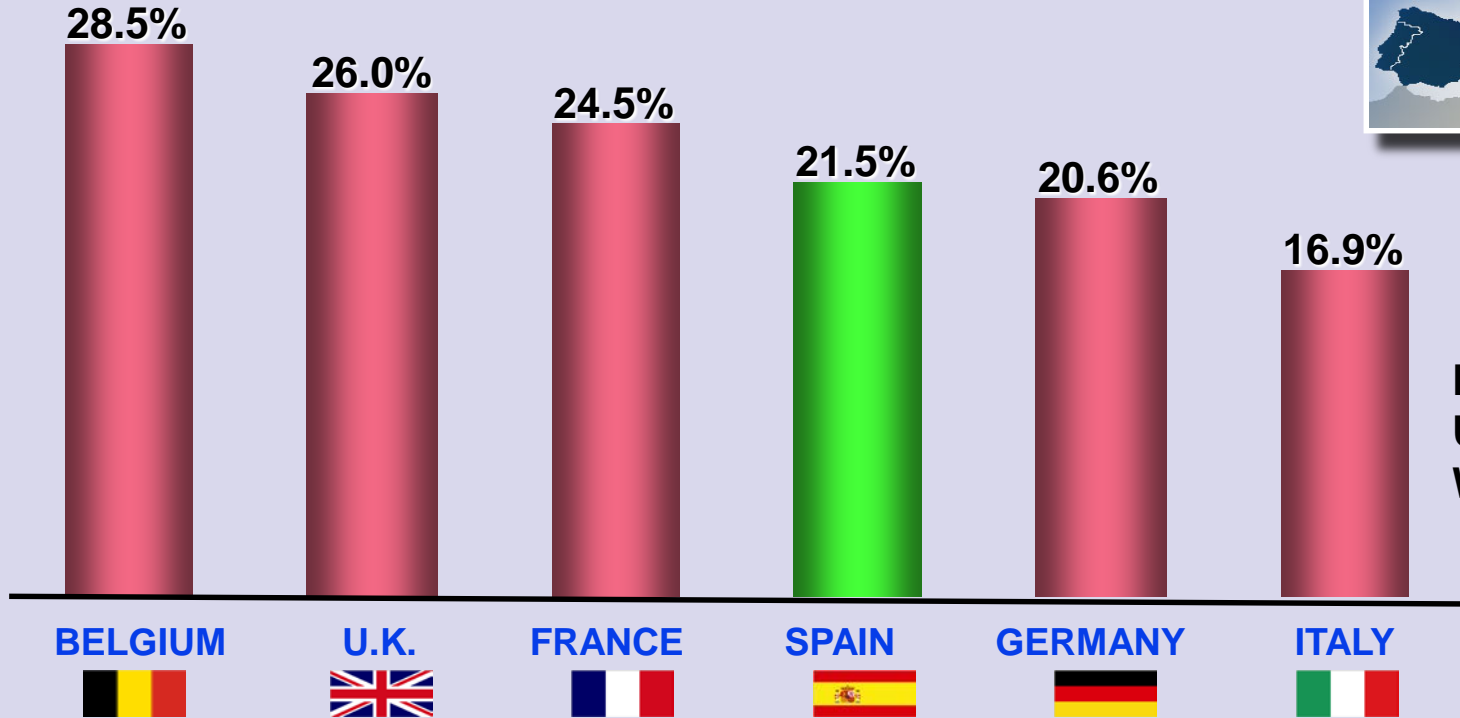


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Epidemiology in the E.U

prevalence of AR - adults



Europe 15-30%
USA 10-30%
World 5-50%

Prevalence of AR - ISAAC phase III

World regions

6-7 yr

13-14 yr

Region	Gender	Rhinoconjunctivitis		Rhinoconjunctivitis	
		N	%	N	%
Africa	Male	223	7.5	5087	15.7
	Female	230	8.0	6850	20.2
Asia-Pacific	Male	3712	12.2	6208	12.5
	Female	2615	8.9	7498	15.0
Eastern Mediterranean	Male	1130	5.4	3393	13.1
	Female	968	4.9	3361	13.0
Indian Sub-Continent	Male	1166	4.5	3203	11.7
	Female	917	3.8	2762	9.7
Latin America	Male	6017	13.1	11,193	13.9
	Female	5914	12.4	17,543	20.6
North America	Male	176	8.8	906	13.8 ^b
	Female	136	6.8	1445	19.6 ^b
Northern and Eastern Europe	Male	1277	6.0	2721	7.7
	Female	1064	5.0	3873	10.6
Oceania	Male	879	12.5	2620	14.7
	Female	742	10.8	3547	19.2
Western Europe	Male	3247	8.3	6771	12.4
	Female	2491	6.5	8835	16.7

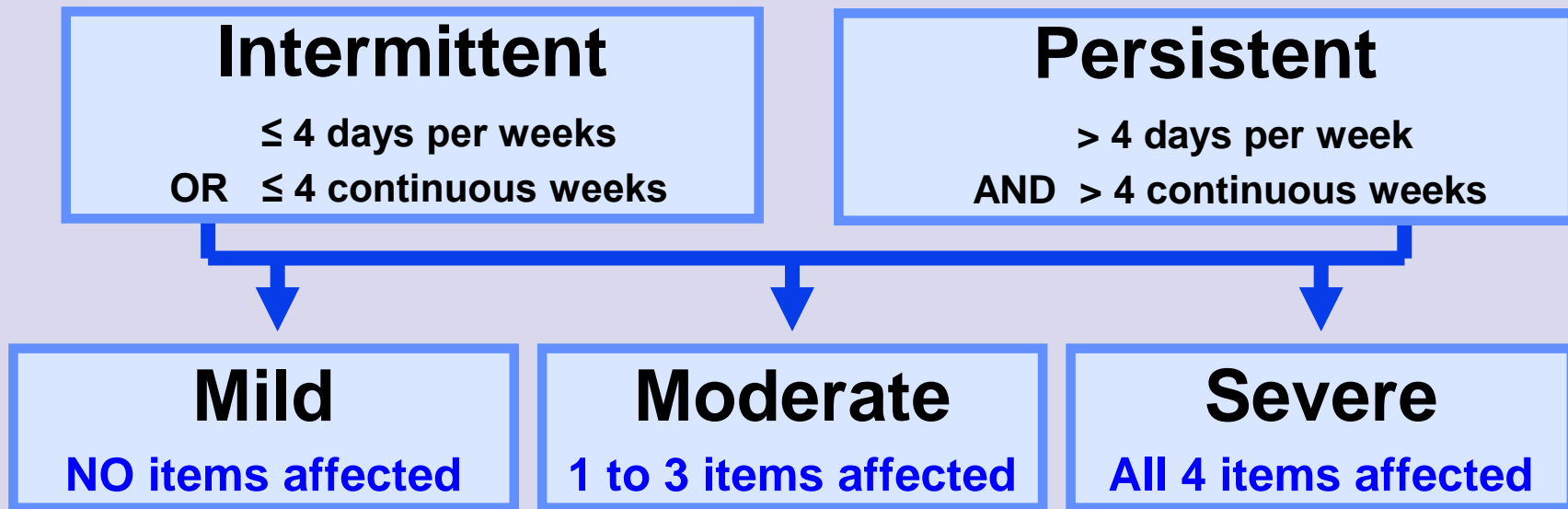


N= 390,000

N= 800,000



ARIA-modified classification



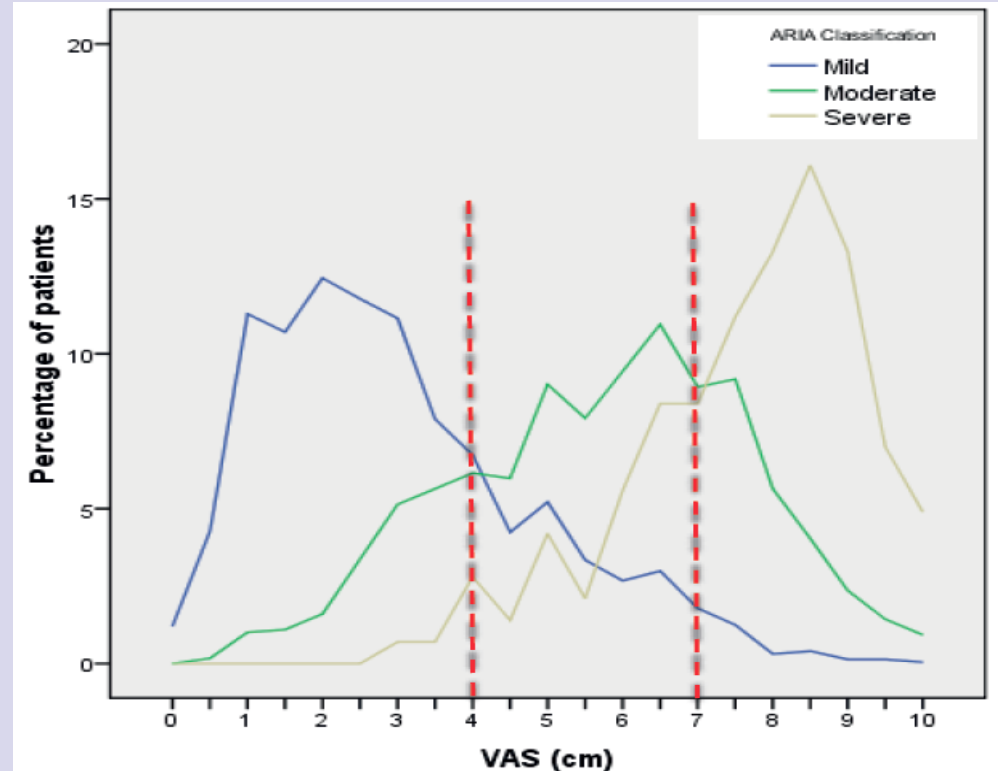
- Abnormal sleep
- Impairment of daily activities, sport, leisure
- Abnormal work and school
- Troublesome symptoms

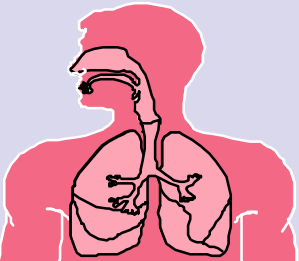


ARIA-modified classification

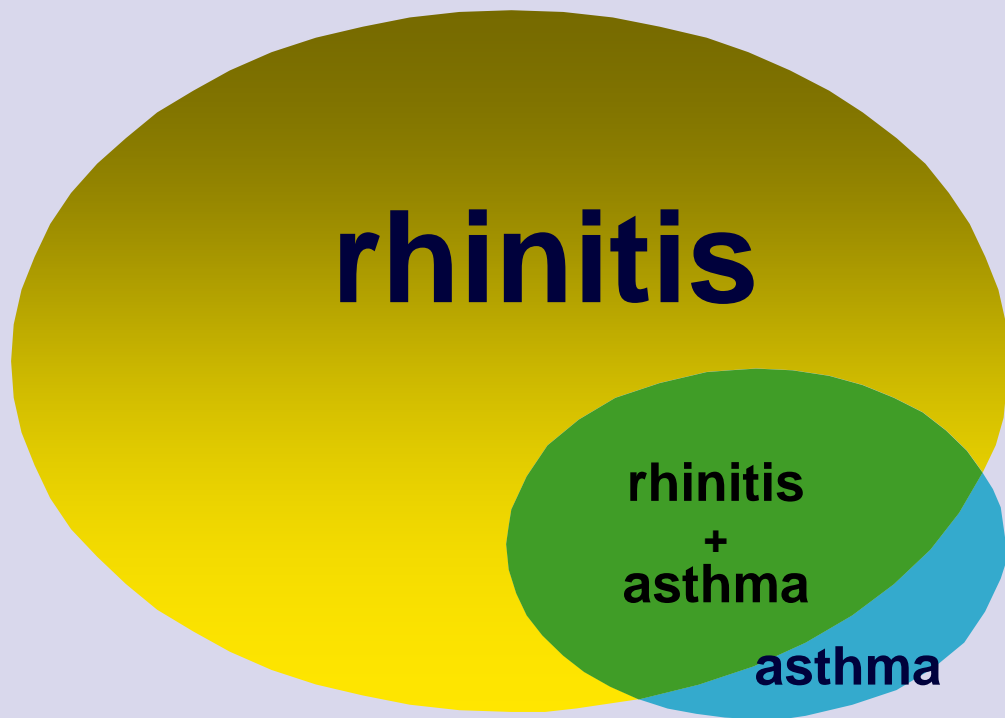
correlation of m-ARIA with VAS

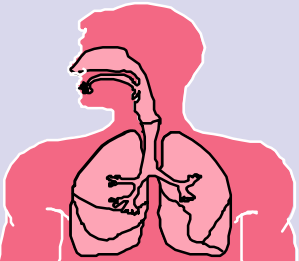
Mild	0 - 4
Moderate	>4 - 7
Severe	>7 - 10





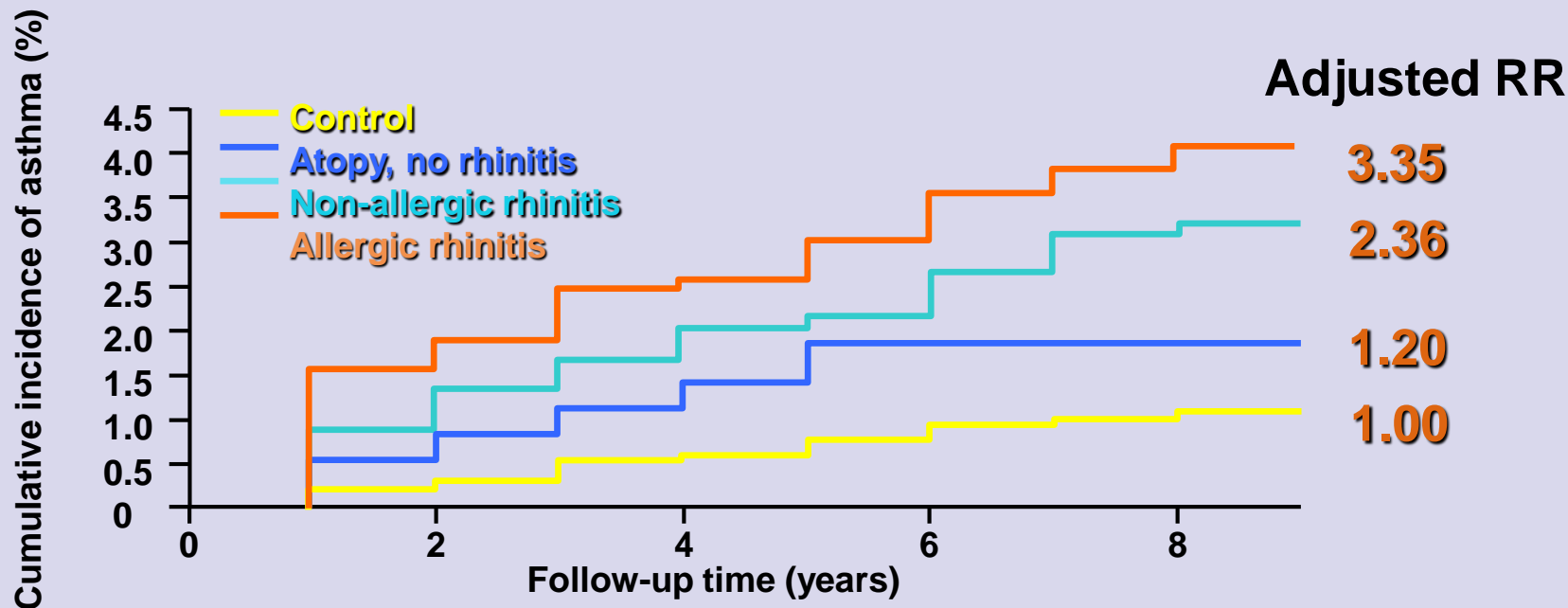
Allergic Rhinitis and Asthma comorbidity





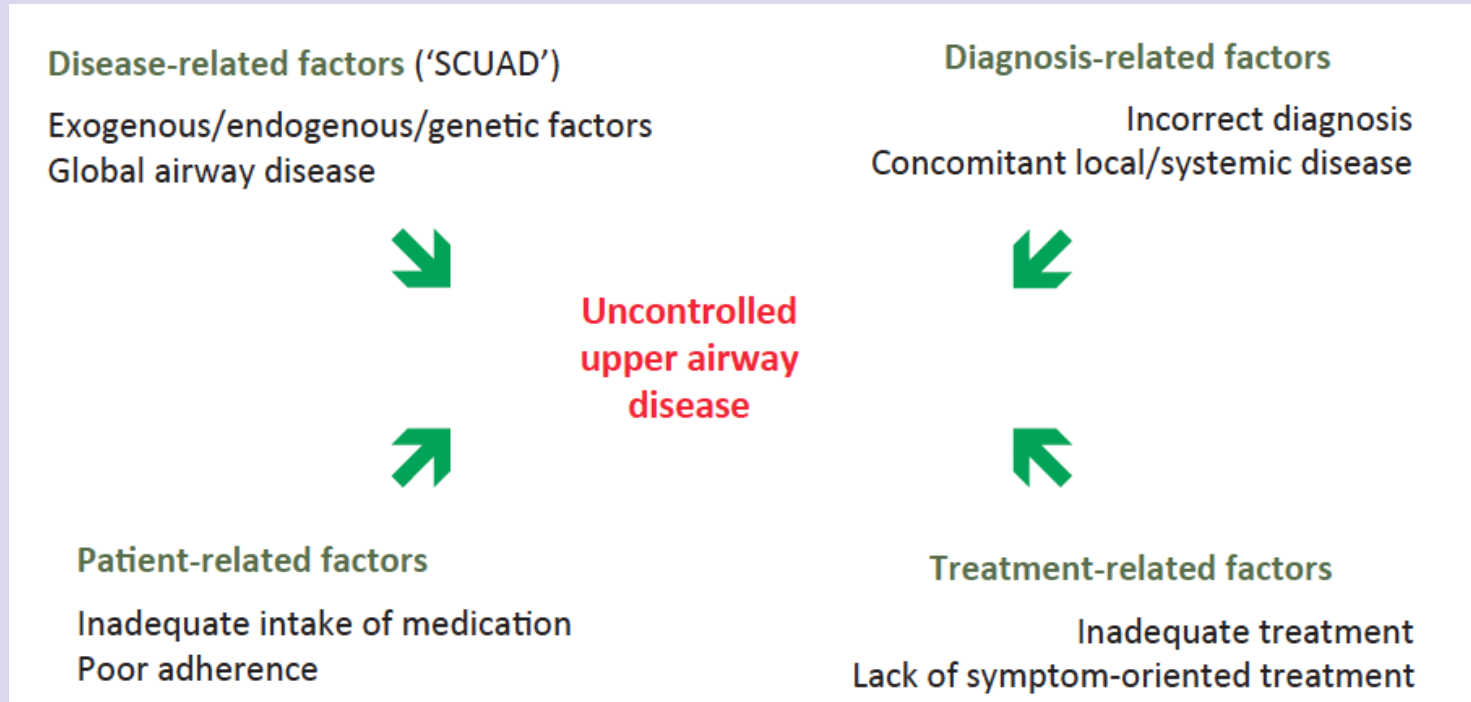
Allergic Rhinitis and Asthma

natural history in Europe



AR severity & control related factors

Uncontrolled rhinitis related factors



Allergic rhinitis adherence to INS in adults

Morisky Medical Adherence Score

Education ^a	MMAS-8
Primary school	3.11
Middle school	6.71
High school	5.63
University/postgraduate	2.43 ^b

Allergy Diary App 6%

		n	MMAS-8 score	p
Age	≤35	30	3.40	0.413
	>35	29	3.89	
Gender	Female	25	3.28	0.387
	Male	34	3.96	
Marital status	Single	19	3.50	0.827
	Married	40	3.71	
Multidrug use	Yes	26	3.75	0.987
	No	33	3.42	
Comorbidities	Yes	20	3.68	0.778
	No	39	3.55	
Daily working hours	≤6 h	33	4.00	0.327
	>6 h	26	3.41	
Children	≤2	35	3.13	0.001 ^a
	>2	24	6.87	
Side effects	Yes	12	5.07	0.150
	No	47	3.23	
Benefit from the drug	Yes	38	2.89	0.001 ^a
	No	21	6.90	
Abroad days per month	≤5 days	36	3.24	0.081
	>5 days	23	4.92	



Watery anterior rhinorrhea & sneezing

The patient
may be allergic

YES



Nasal obstruction



The patient
is likely
to be allergic

Symptoms occurring
at the same time
every year



The patient
is most likely
allergic

Bilateral eye
symptoms :

- ± pruritus
- ± tearing
- ± redness

**Confirm diagnosis of allergic rhinitis
by skin tests or serum-specific IgE**

NO



Postnasal
drip



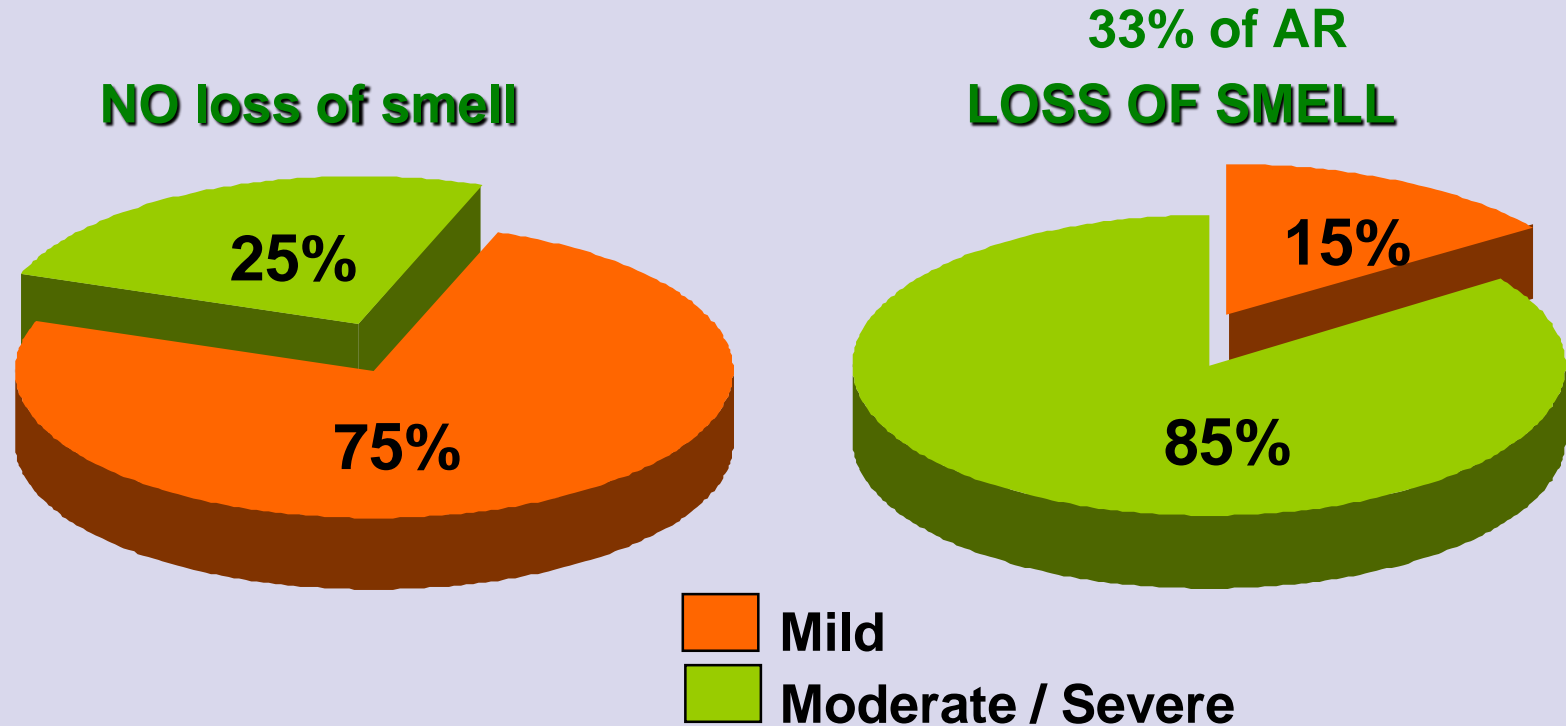
Coloured
discharge and/or
facial pain

The patient
is unlikely
to be allergic

**Suspect
chronic
rhinosinusitis**

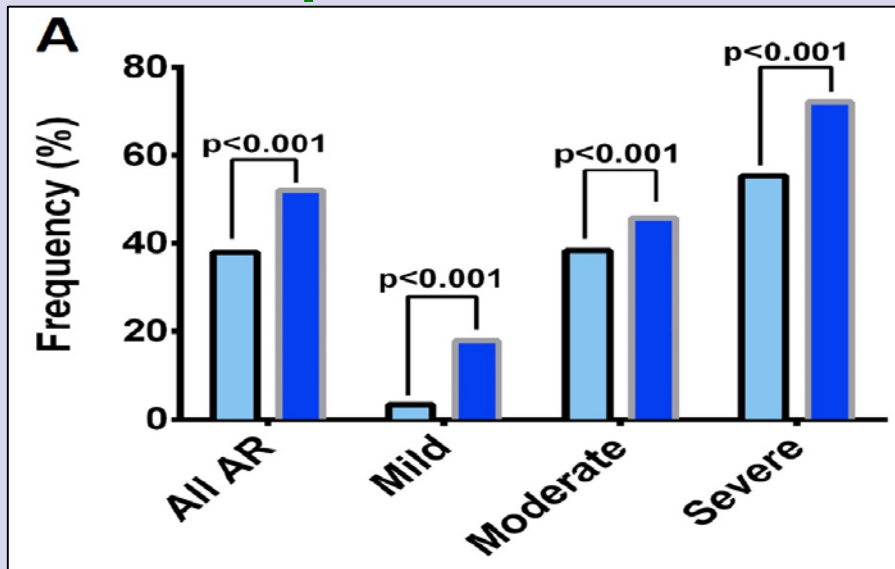
**Confirm diagnosis of rhinosinusitis
by ENT examination - CT scan**

Smell loss in adult PER

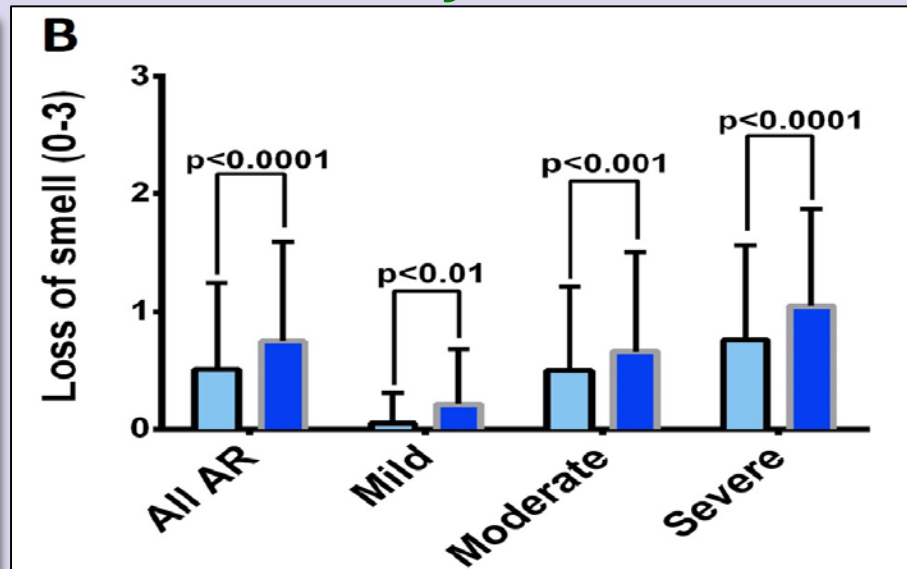


Smell loss in paediatric AR (6-12yo)

prevalence



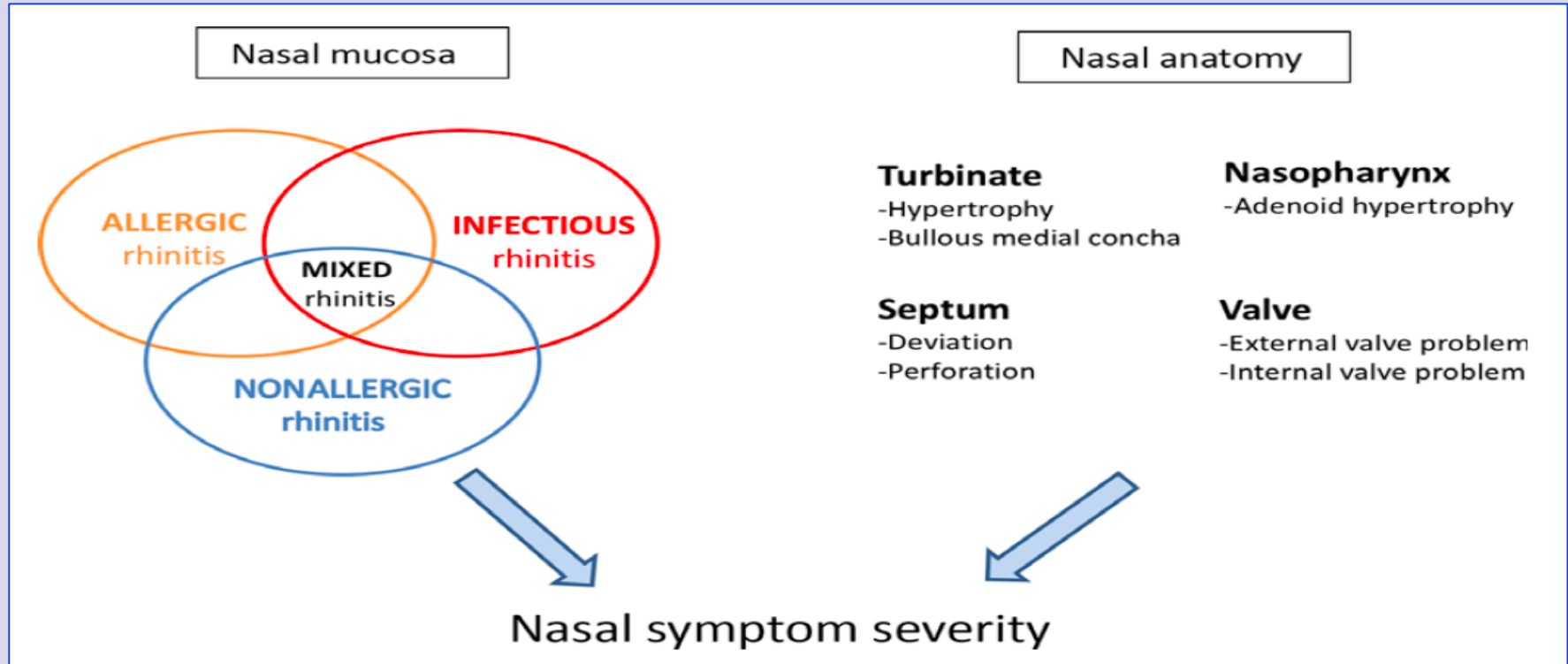
intensity - score



N= 1,260

IAR
PER

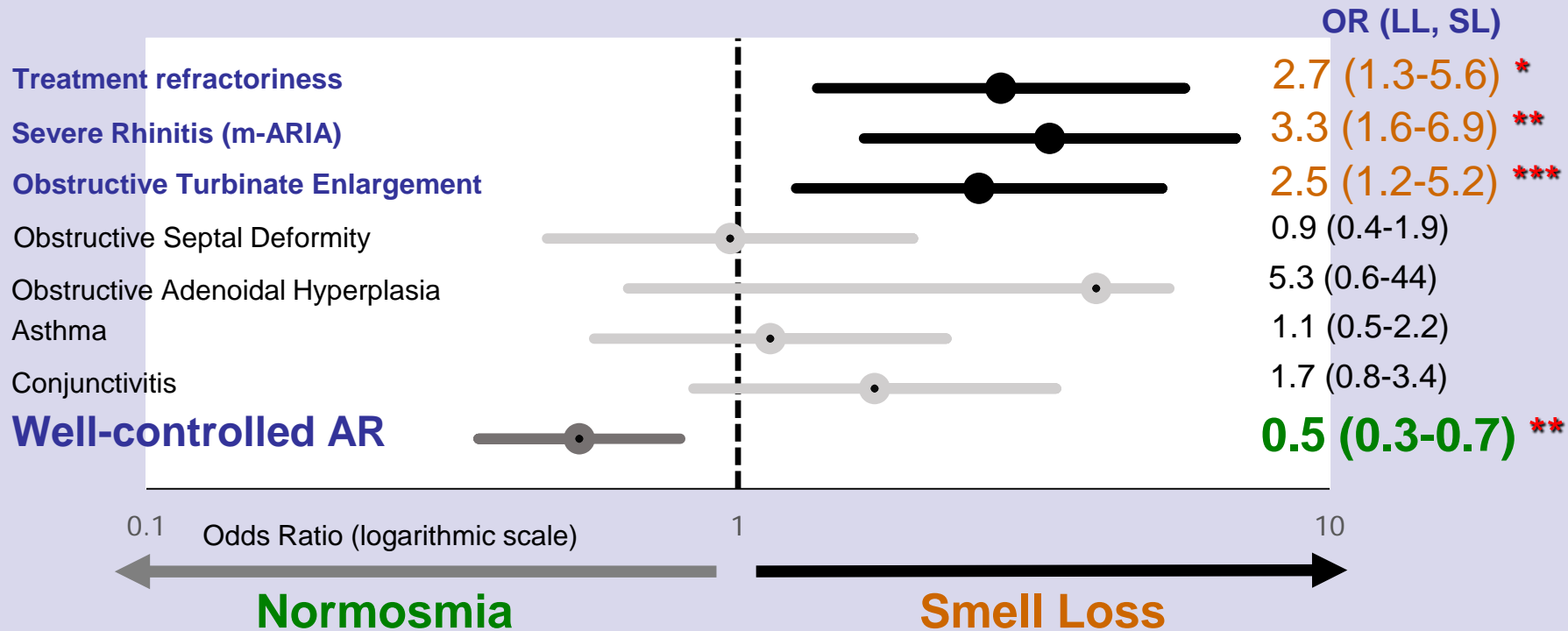
Uncontrolled rhinitis related factors





Loss of smell in AR

clinical marker of severity & refractoriness



AR severity & control
impact of treatment

Allergic Rhinitis landscape

Most patients have '**moderate/severe**' AR



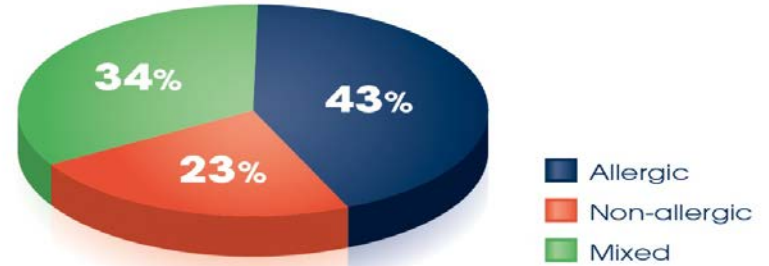
European Survey

- 67.2% = moderate or severe
- 42.5% = persistent disease

Many patients have **mixed forms** of AR



Many patients are becoming **polysensitized**



Evolution of **treatment-resistant** phenotypes

- Severe Chronic Upper Airway Disease (SCUAD)

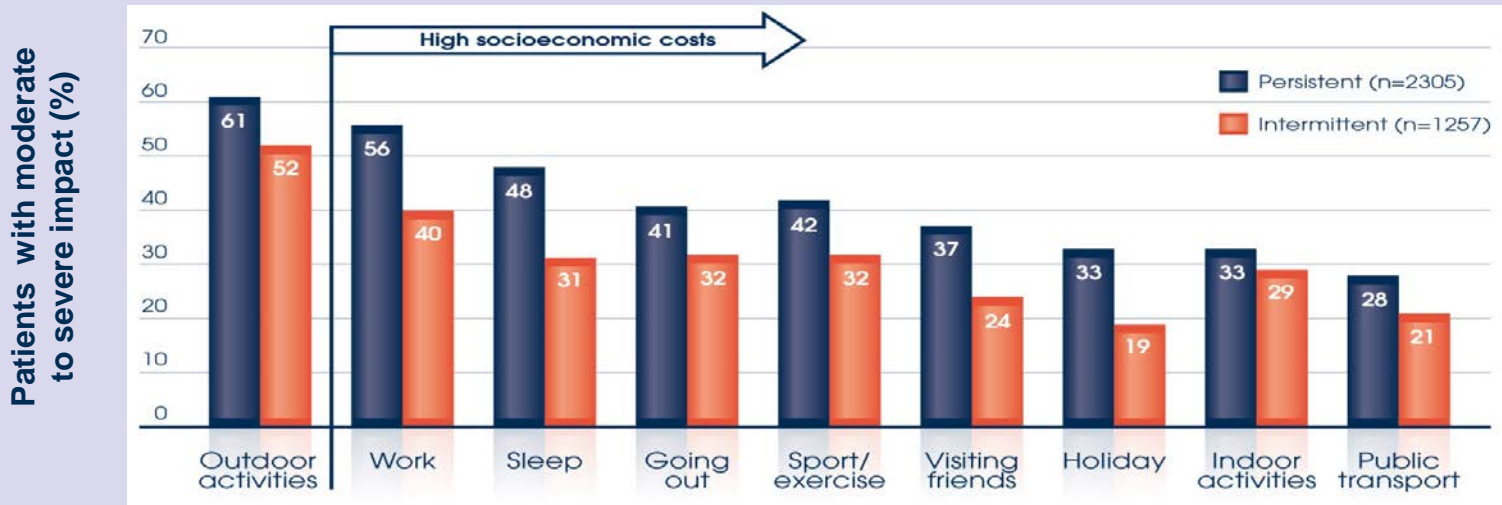


SCUAD

- approx. **30%** of AR patients

Allergic Rhinitis – Finland landscape

the patient's voice allergy survey



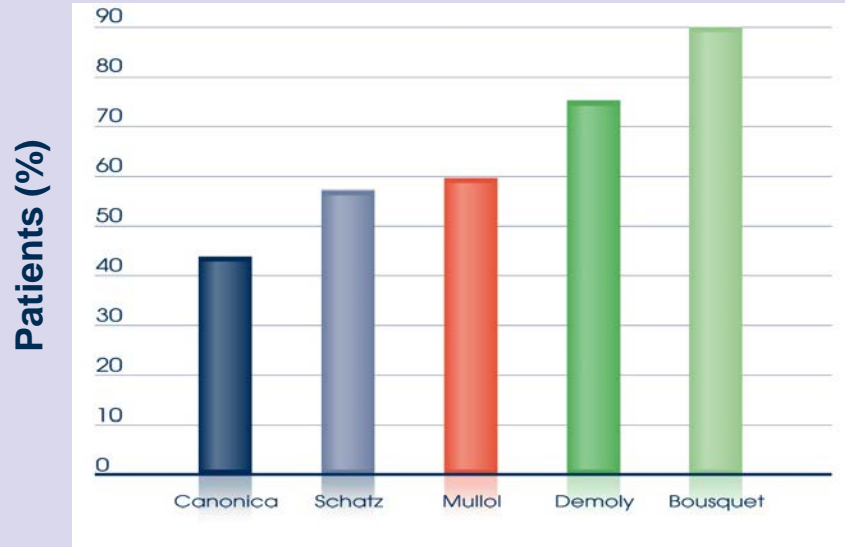
**In Sweden, the cost of rhinitis is
2.7 billion €/ yr in terms of lost productivity**

Allergic Rhinitis landscape

need of multiple medications to achieve control

- up to **90% of AR patients** take ≥ 2 medication to treat AR
- **60% of all AR patients** are “very interested” in finding a new medication
- **25%** “constantly” trying different medications

patients taking ≥ 2 medications



Canonica et al. Allergy 2007

Mullol et al. J Invest Allergol Clin Immunol 2009

Bousquet et al. Int Arch Allergy Immunol 2012

Marple et al. Otolaryngol Head Neck Surg 2007

Schatz et al. Allergy 2007

Demoly et al. Allergy 2002

Bousquet et al. Allergy 2008

Allergic Rhinitis – France landscape

need for more effective medications

- 990 AR patients recruited by 161 GPs in France
- **72.5%** were currently taking allergic rhinitis medication

The majority of treated AR patients **remain symptomatic**

89%	rhinorrhea
82%	sneezing
82%	nasal congestion
68%	nasal itching
68%	ocular symptoms

Global discomfort caused by AR during the previous week (VAS)

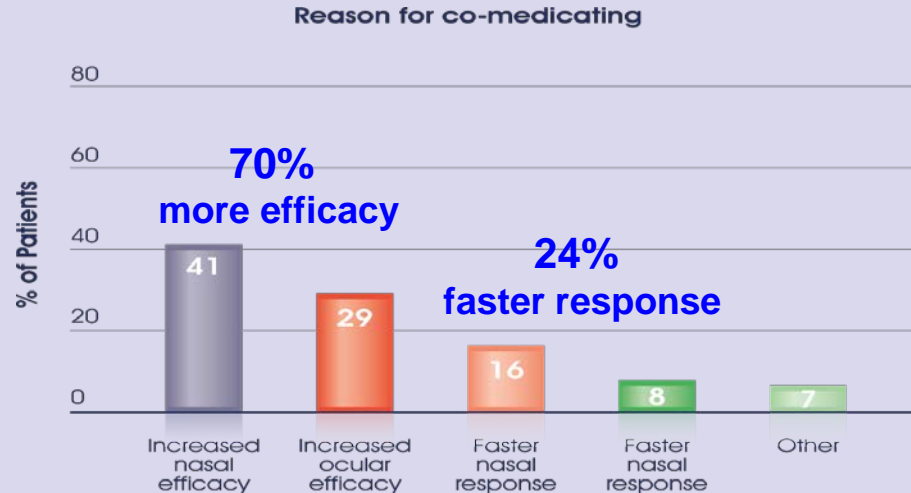
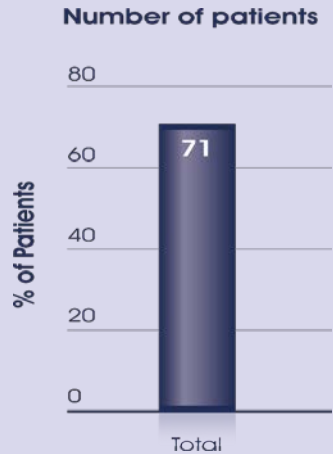


Uncontrolled

Allergic Rhinitis – UK landscape

use of multiple medications to control ...

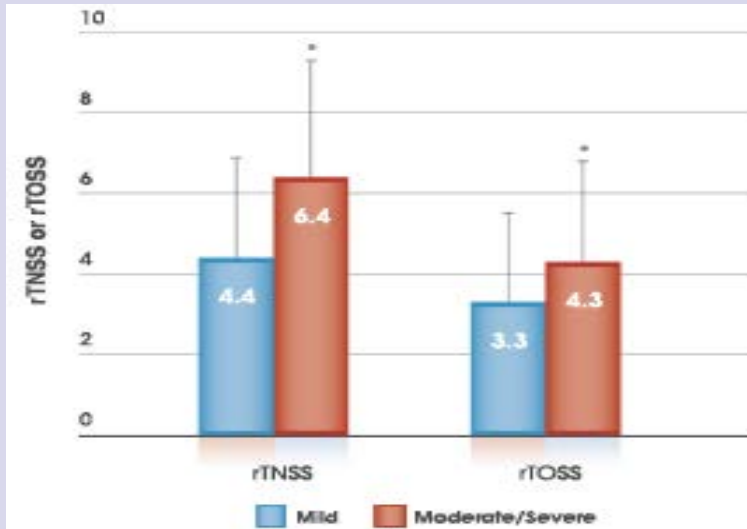
moderate/severe AR patients on ≥ 2 medications (N=1,000 p)



The need for **MORE** and **FASTER** effective treatment was the primary reason for co-medicating

Allergic Rhinitis – UK landscape

... remain symptomatic on treatment



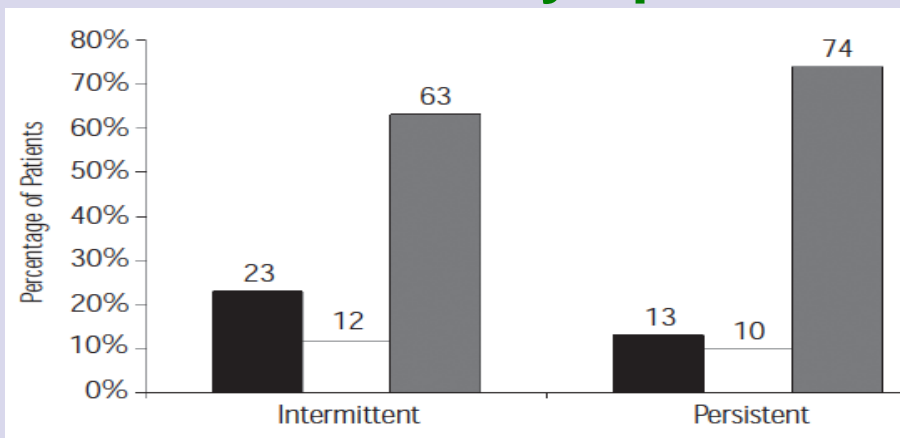
- 96.2% of AR patients were on treatment
- 70.5% were using multiple treatments (mainly INCS and oral antihistamines)

Allergic rhinitis was poorly controlled with current mono- and multiple-therapies

Allergic Rhinitis - Spain landscape

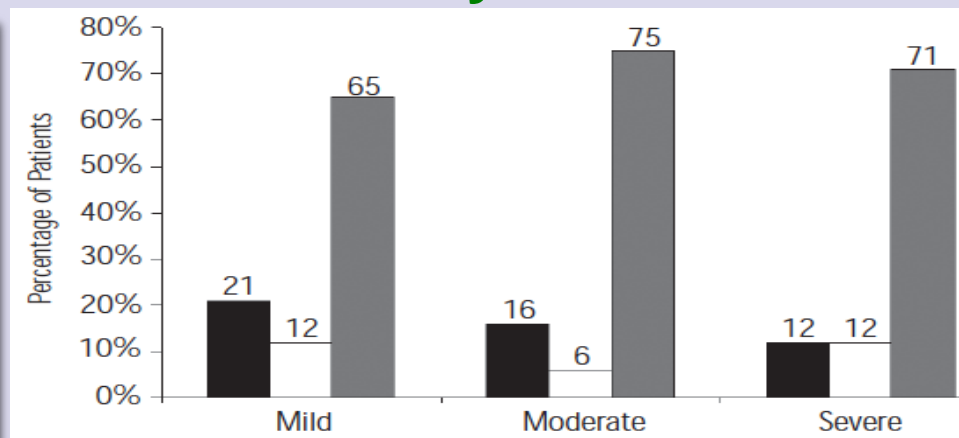
use of ≥ 2 medications for control

duration of symptoms



■ AH $P < .0001$
 □ ICS $P < .05$
 ■ AH+ICS $P < .0001$

severity of disease

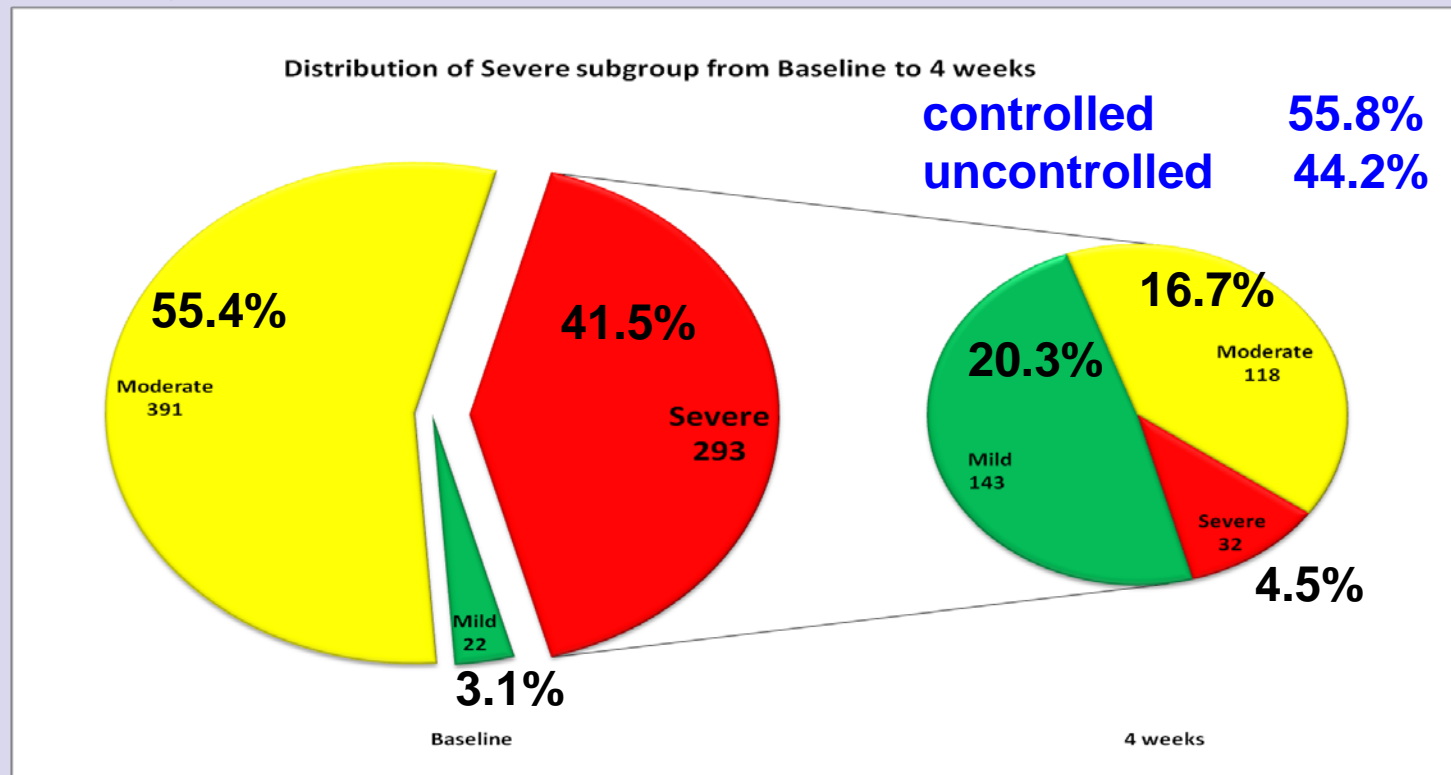


■ AH $P < .05$
 □ ICS $P < .01$
 ■ AH+ICS $P < .001$

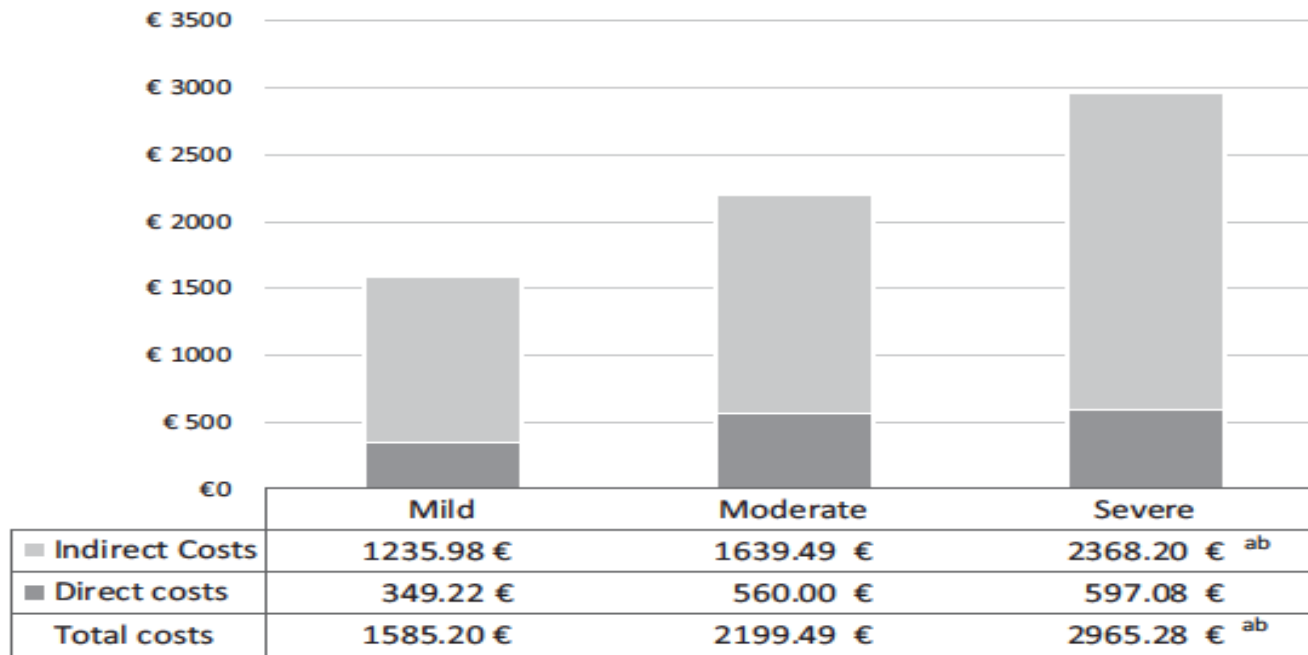
N= 1,008 physicians

Allergic Rhinitis - Spain landscape

poorly controlled despite optimal treatment



Allergic Rhinitis - Spain landscape costs according to AR severity – FERIN



a. $P < 0.05$ compared with mild severity.

b. $P < 0.05$ compared with moderate severity.

**methods to assess
control of AR**

Allergic rhinitis

perceived shortcomings of disease

- **AR SEVERITY** (untreated)
level / degree of symptoms, impact on Quality of Life
- **AR CONTROL** (impact of treatment)
assessment or not of treatment objectives
combining: severity, QoL, nasal function, exacerbations
- **RESPONSIVENESS TO TREATMENT**
assessment of treatment objectives

Allergic rhinitis

questionnaires to assess control

- **CARAT** (Control of AR and Asthma Test)

AR and asthma / 10 items / 4-point scale

Fonseca JA, et al. *Clin Transl Allergy* 2012

- **RCAT** (Rhinitis Control Assessment Test)

allergic rhinitis / 6 items / 5-point scale

Meltzer EO, et al. *J Allergy Clin Immunol* 2013

- **ARCT** (AR Control Test)

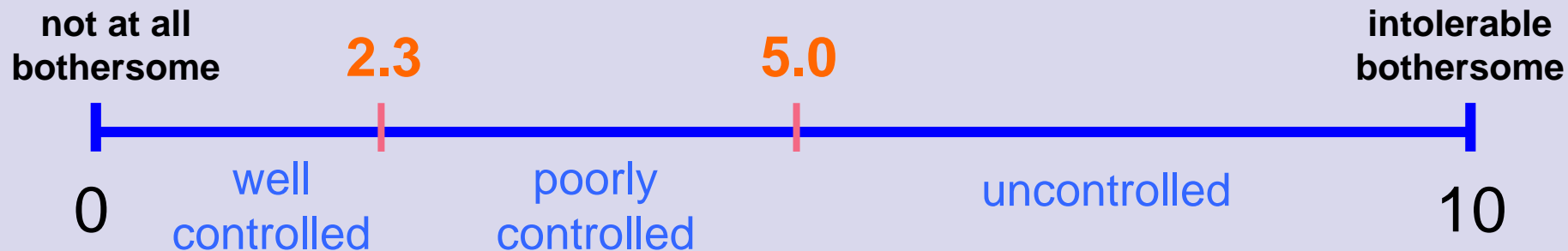
allergic rhinitis / 6 items / 5-point scale

Demoly P, et al. *Clin Exp Allergy* 2011

Allergic rhinitis

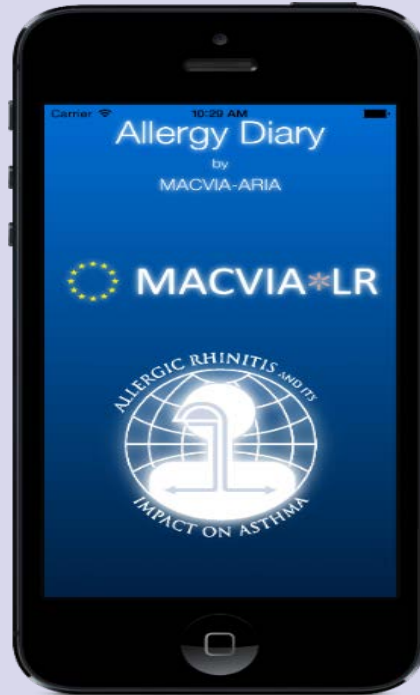
control by Visual Analogue Scale (VAS)

In general, how bothersome are today
your symptoms of allergic rhinitis ?



Allergic rhinitis

control by Visual Analogue Scale (VAS)



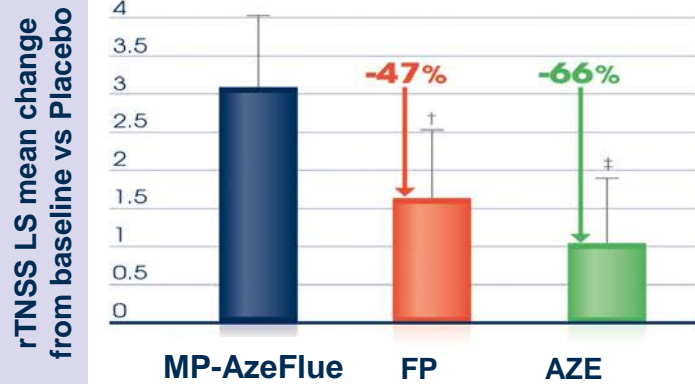
Bousquet J, ..., Mullol J, et al. *Clin Exp Allergy* 2017
Caimmi D, Mullol J, et al, Bousquet J. *Clin Exp Allergy* 2017

Impact of treatment on the control of AR

Seasonal Allergic Rhinitis

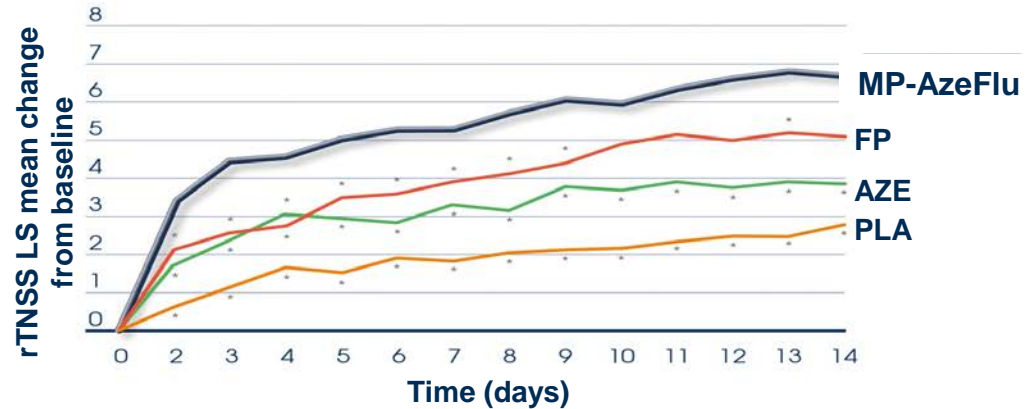
MP-AzeFlu better than first-line treatment

MP-AzeFlu provided significantly greater nasal symptom relief than FP or AZE alone (day 14)



†, $p=0.0031$ vs MP-AzeFlu
‡, $p<0.0001$ vs MP-AzeFlu

Superiority of MP-AzeFlu present from day 1 and sustained



*, $p \leq 0.04$ vs MP-AzeFlu

Allergic rhinitis

INS + anti-H₁ intranasal formulations

- **MP-AzeFlu (FP+AZE intranasal formulation)**

Carr W, et al. *J Allergy Clin Immunol* 2012

Meltzer EO, et al. *Int Arch Allergy Immunol* 2013

- **Fluticasone propionate + olopatadine**

LaForce CF, et al. *Allergy Asthma Proc* 2010

- **Fluticasone furoate + levocabastine**

Murdoch RD, et al. *Clin Exp Allergy* 2015

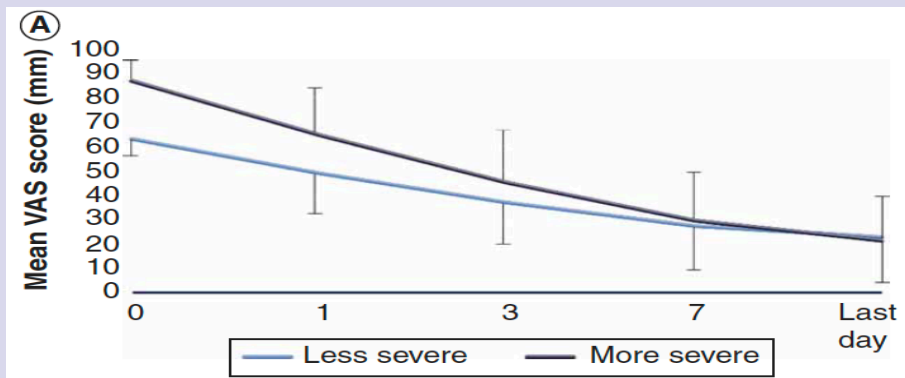
- **Mometasone furoate + olopatadine**

US 20040097474 A1

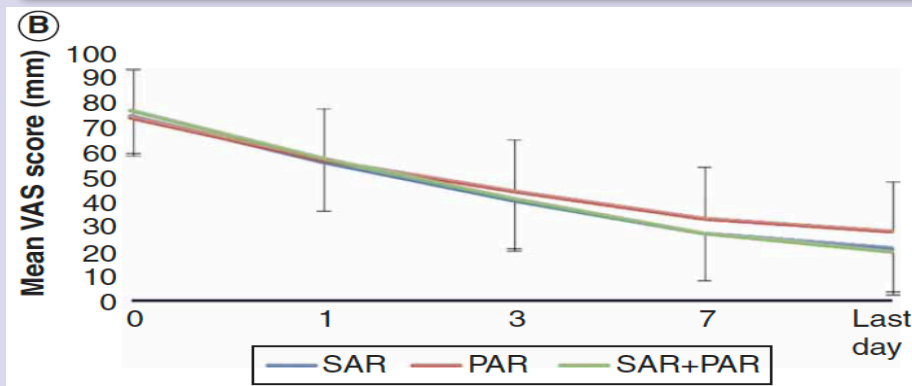
Allergic rhinitis

MP-AzeFlu improves VAS control

severity
phenotype



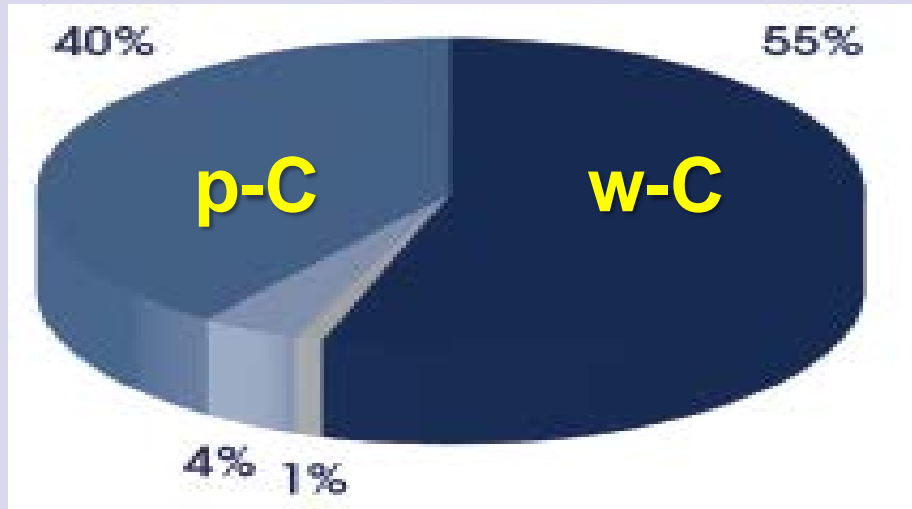
allergen season
phenotype



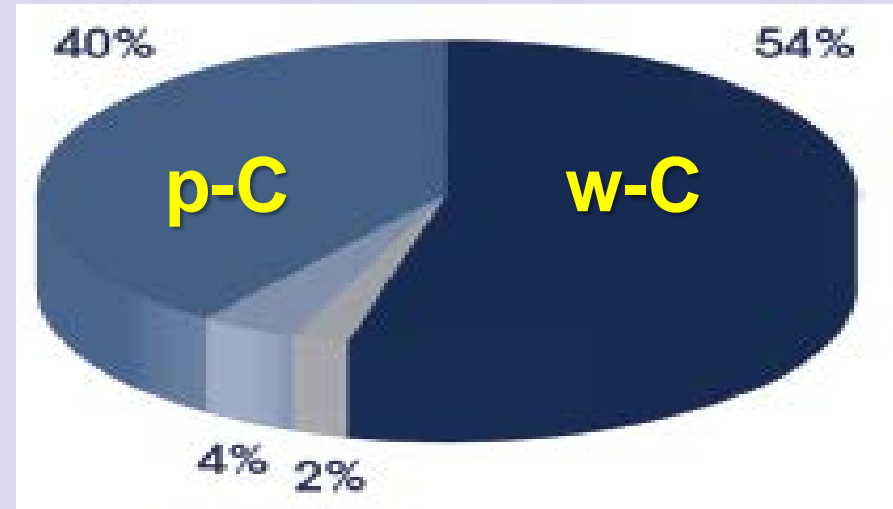
Allergic rhinitis

MP-AzeFlu improves VAS control (day 3)

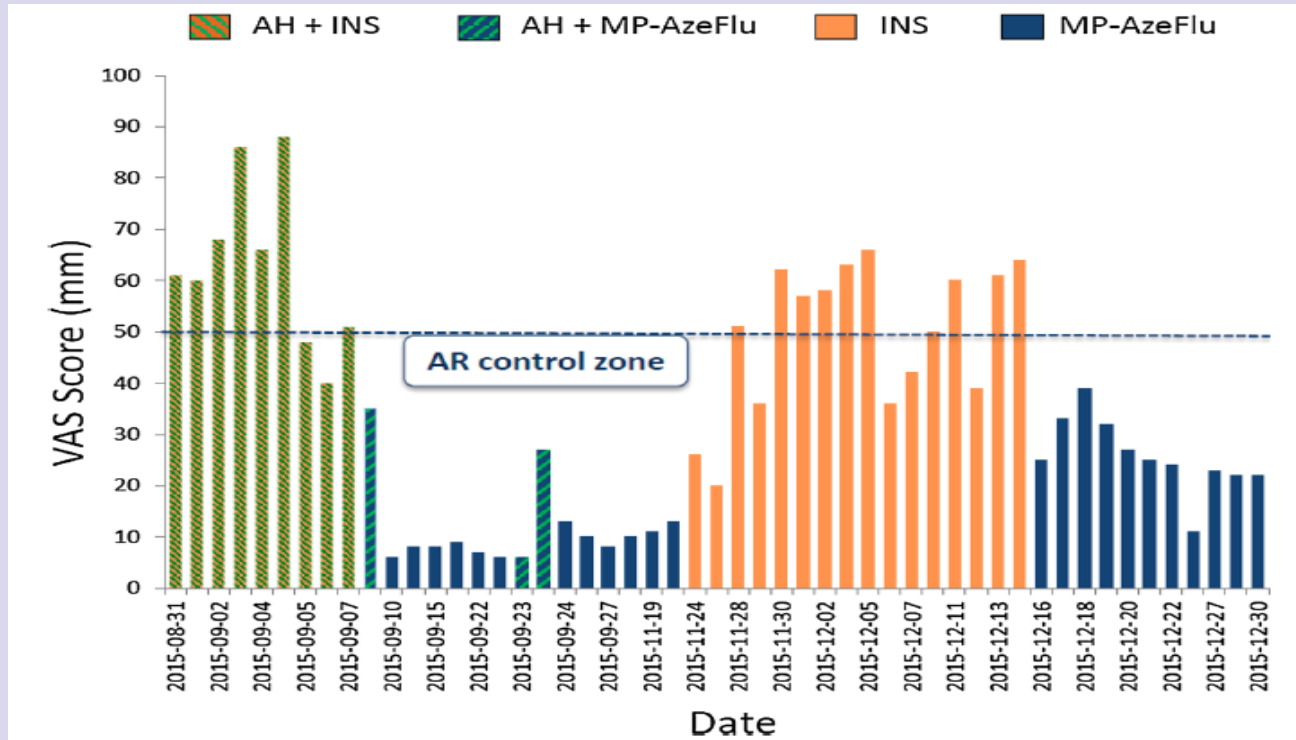
seasonal AR



perennial AR



AR control according to treatment evolution of a single *Allergy Diary App* user



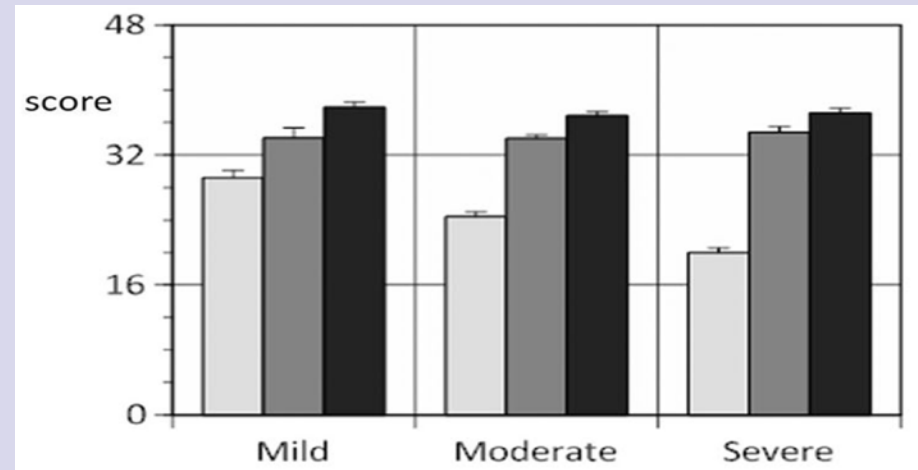
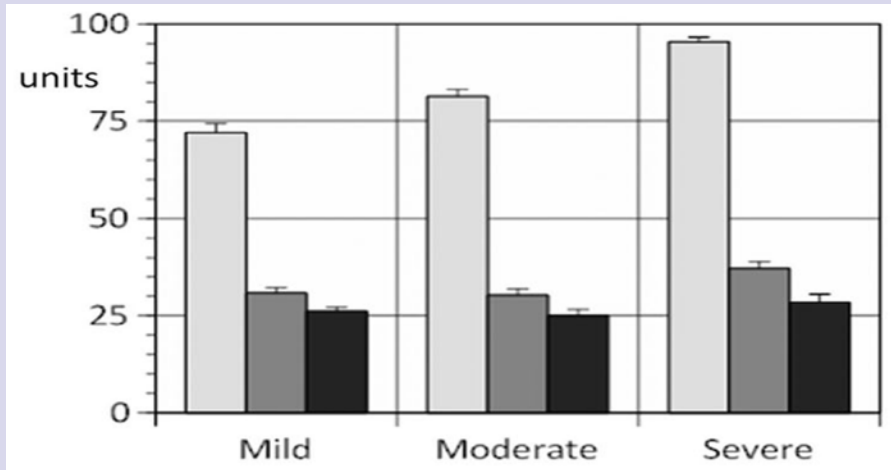
Persistent allergic rhinitis

MP-AzeFlu on severity & smell loss

reduces severity (VAS)



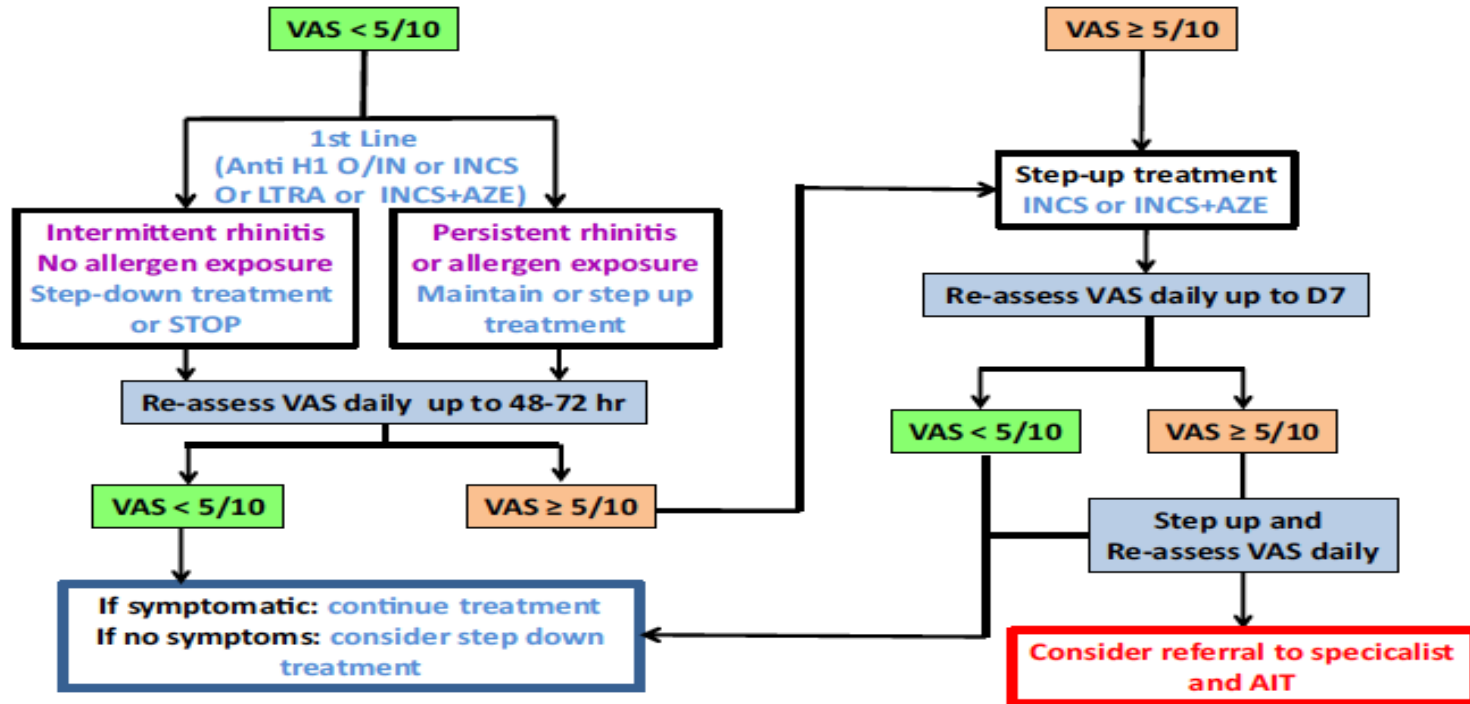
improves smell (TDI score)



Treatment recommendations to control AR

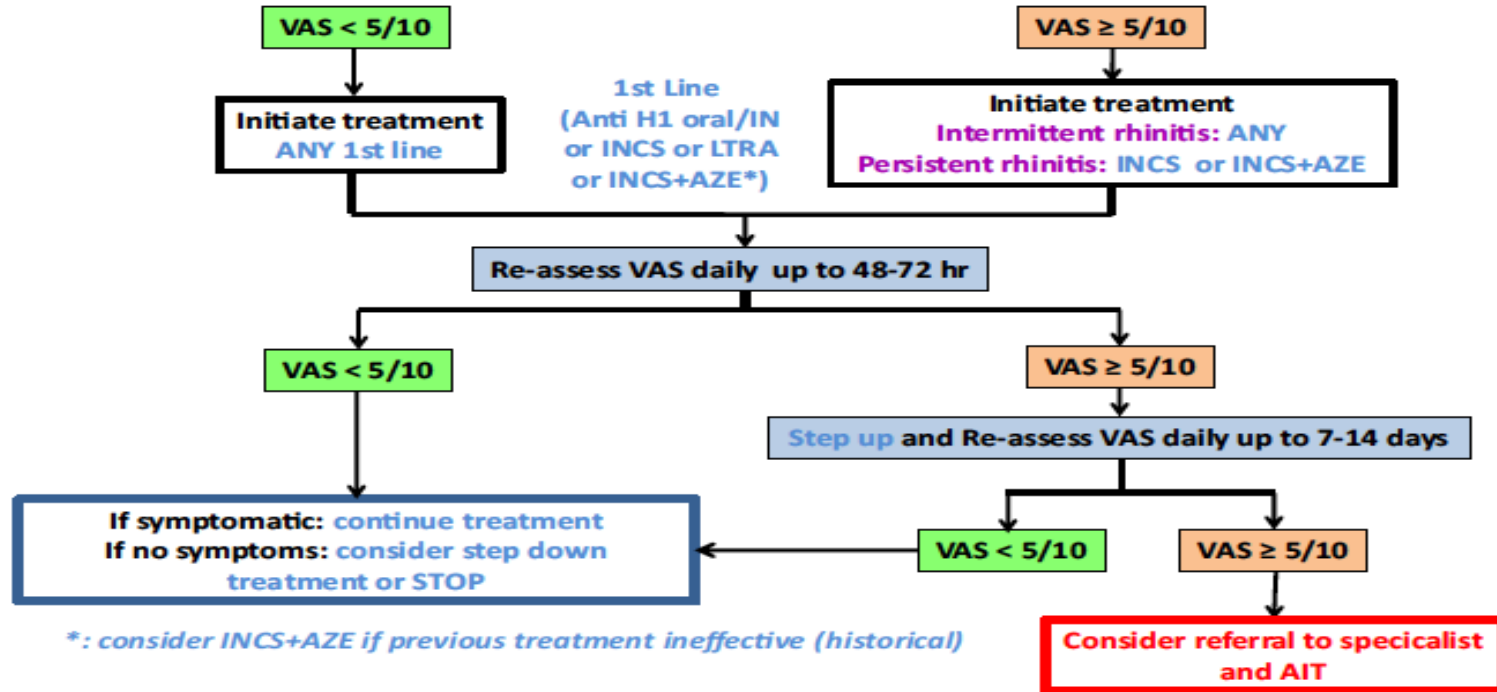
treatment algorithm based on AR control

Assessment of control in treated symptomatic patient



treatment algorithm based on AR control

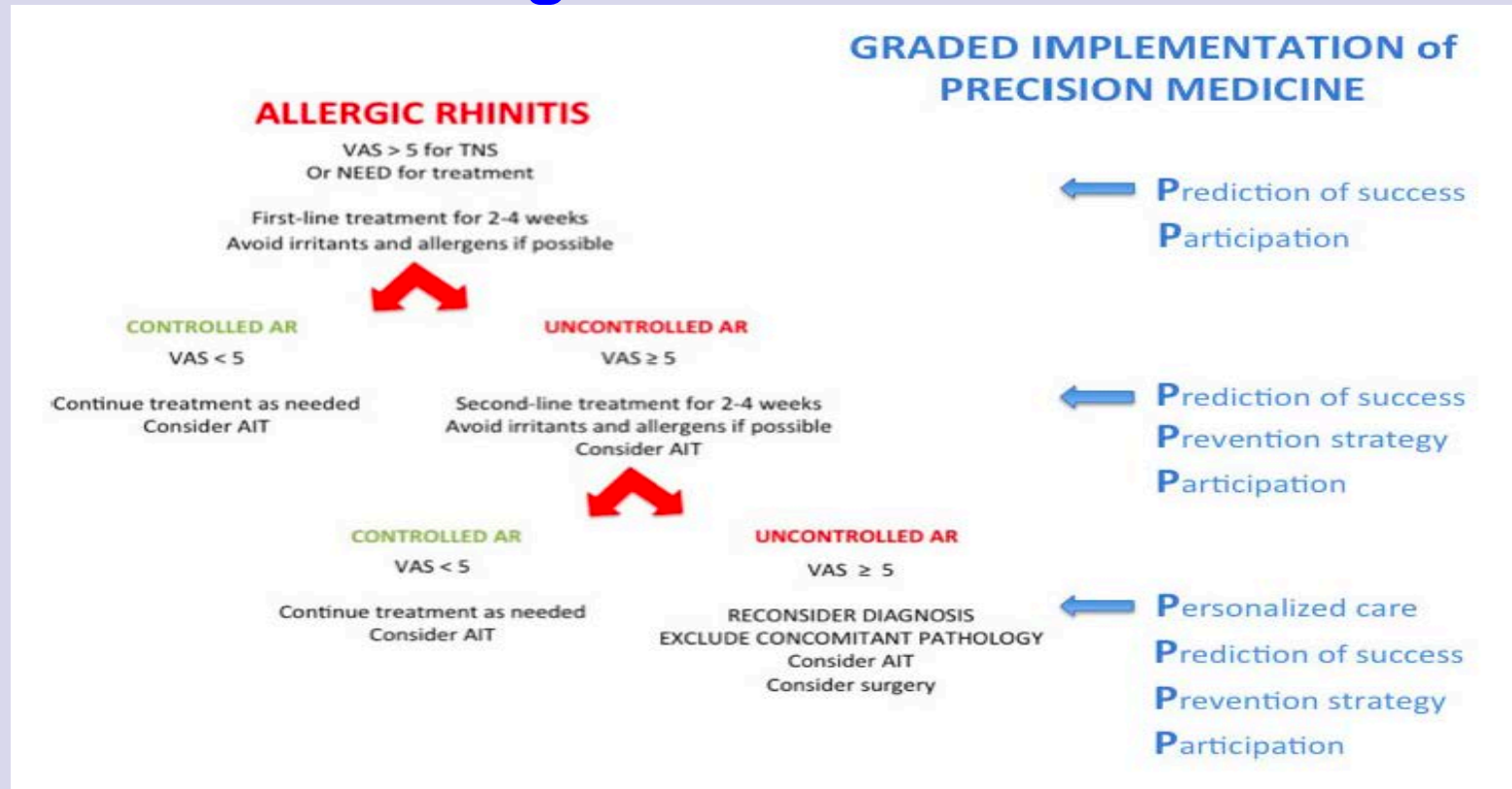
Assessment of control in untreated symptomatic patient





Precision Medicine

treatment algorithm based on AR control



Precision Medicine

multidisciplinary AR treatment algorithm

