



Innovative Approaches in Anaphylaxis



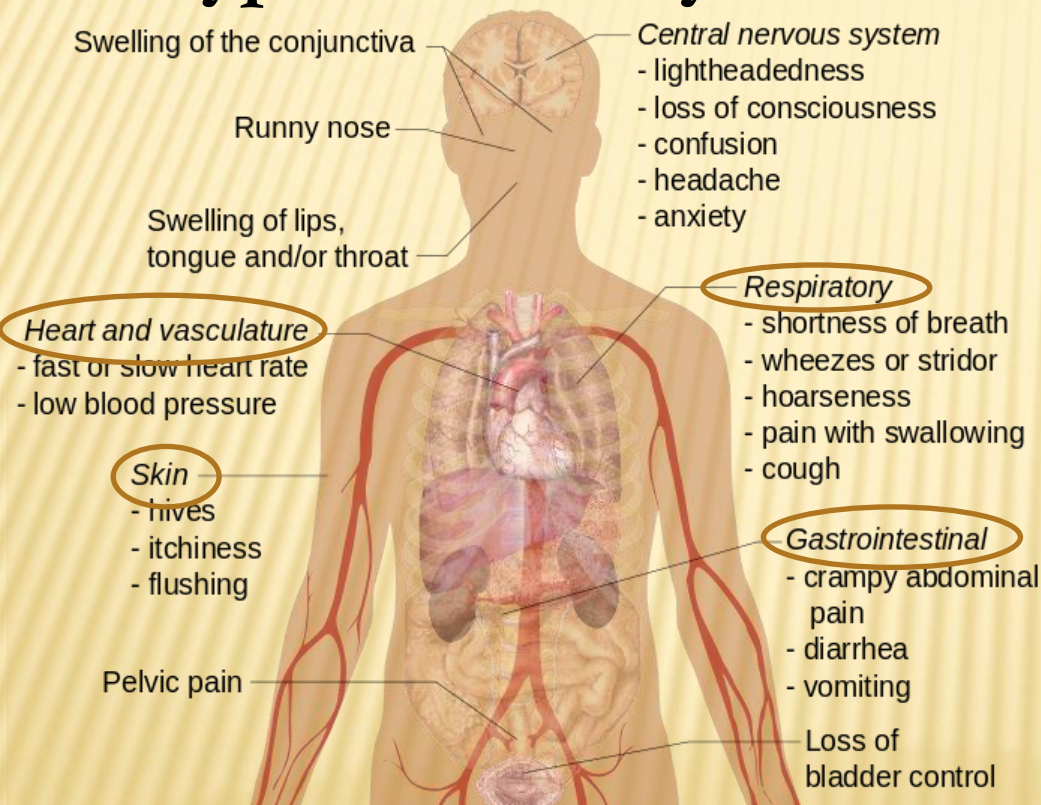
SPECIAL CONSIDERATIONS ON ANAPHYLAXIS IN LATIN AMERICA

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President-elect Sociedad Latinoamericana de Alergia Asma e Inmunología

ANAPHYLAXIS

✖ Severe life-threatening generalized or systemic hypersensitivity reaction



Circulatory collapse and complete airway blockage can be fatal

Sampson HA, et al. J Allergy Clin Immunol. 2006;117:391-397.

Simons et al. World Allergy Organization Journal 2014, 7:9

EPIDEMIIOLOGY

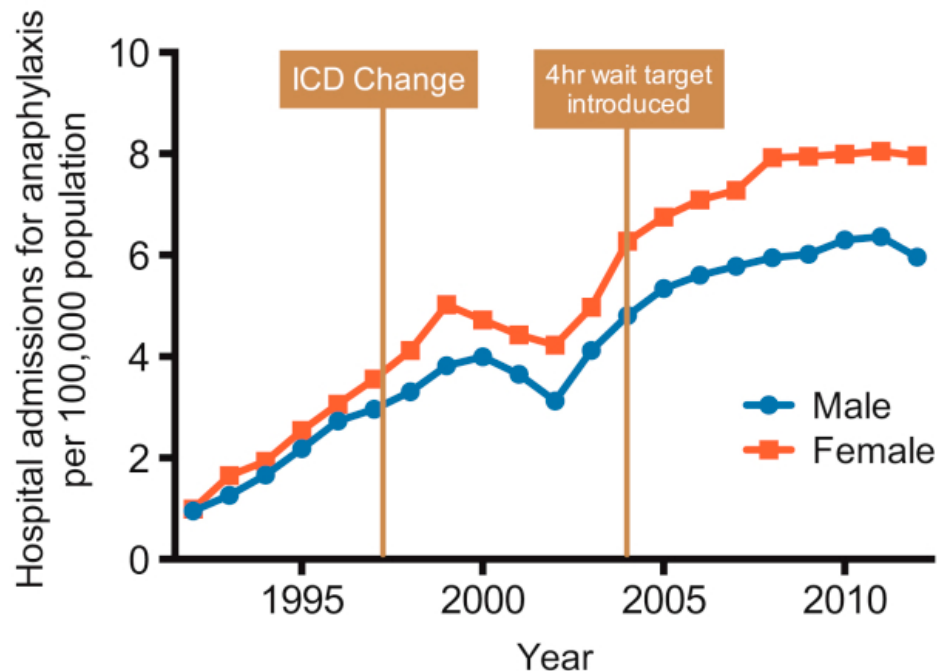
- ✗ Incidence: 3 to 300 per 100 000 person years
- ✗ Lifetime prevalence: 0.05-2%

Panesar SS, et al. Allergy 2013; 68: 1353–1361.

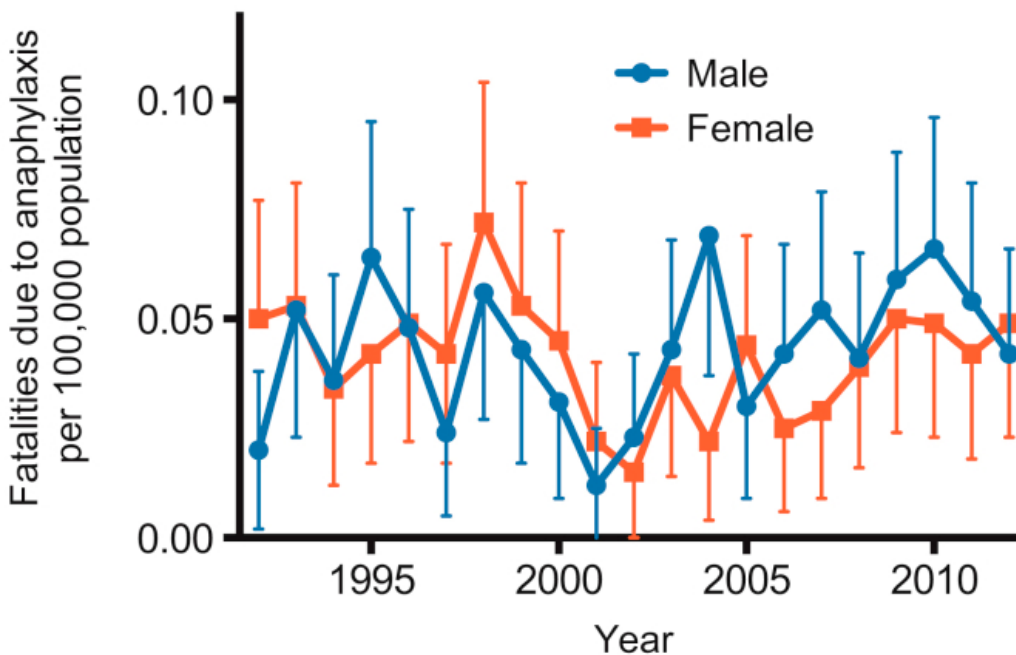
Lieberman P et al. Ann Allergy Asthma Immunol 2006;97:596–602.

Decker WW, et al. J Allergy Clin Immunol 2008;122:1161–1165.

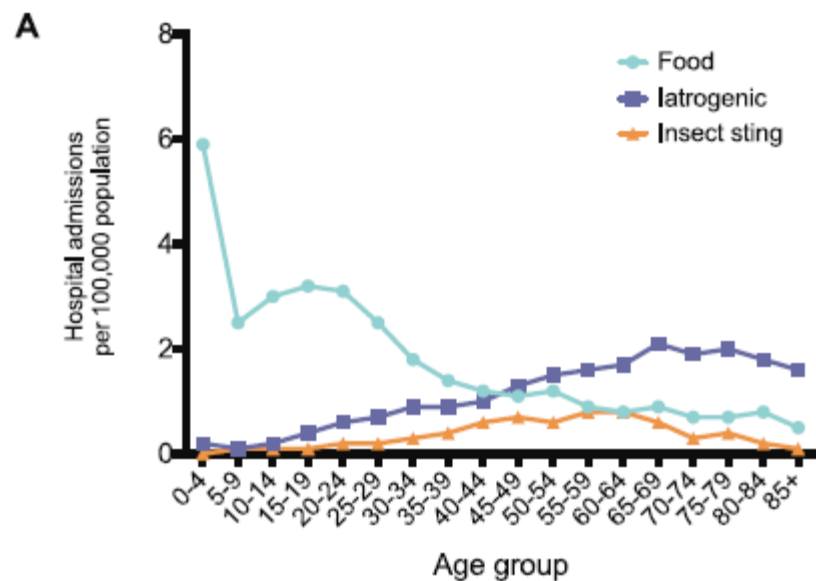
Gupta R et al, Thorax 2007

A

Hospital admissions from all-cause anaphylaxis increased by 615% over the time period studied, but annual fatality rates remained stable at 0.047 cases (95% CI, 0.042-0.052 cases) per 100,000 population.

B

Turner P et al. Increase in anaphylaxis-related hospitalizations but no increase in fatalities: An analysis of United Kingdom national anaphylaxis data, 1992-2012 J ALLERGY CLIN IMMUNOL APRIL 2015



Food-triggered anaphylaxis were most common in young people, with a marked peak in the incidence of fatal food reactions during the second and third decades of life.

Admission and fatality rates for drug- and insect sting-induced anaphylaxis were highest in the group aged 60 years and older

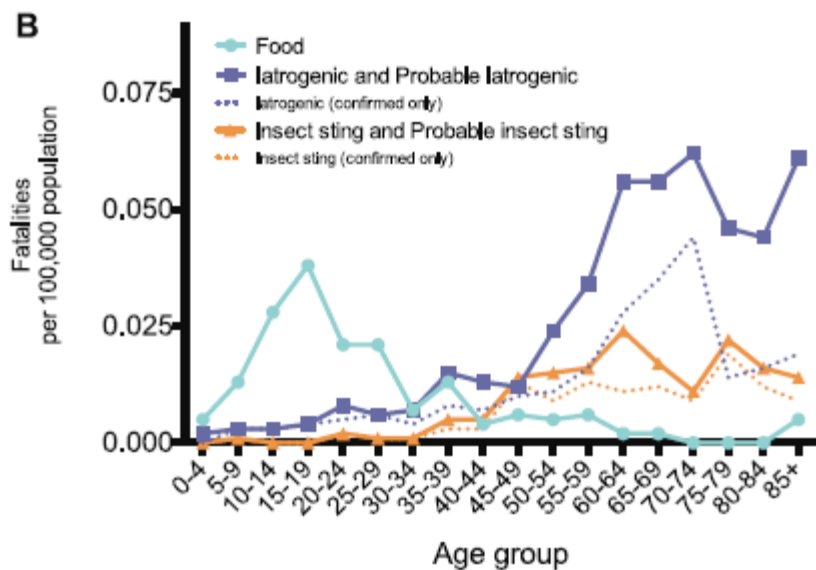


FIG 2. Age distribution of ASRs for admissions (1998-2012; **A**) and fatalities (1992-2012; **B**) caused by anaphylaxis by triggering agent (food, iatrogenic causes, and insect stings).

Turner P et al. Increase in anaphylaxis-related hospitalizations but no increase in fatalities: An analysis of United Kingdom national anaphylaxis data, 1992-2012 J ALLERGY CLIN IMMUNOL APRIL 2015

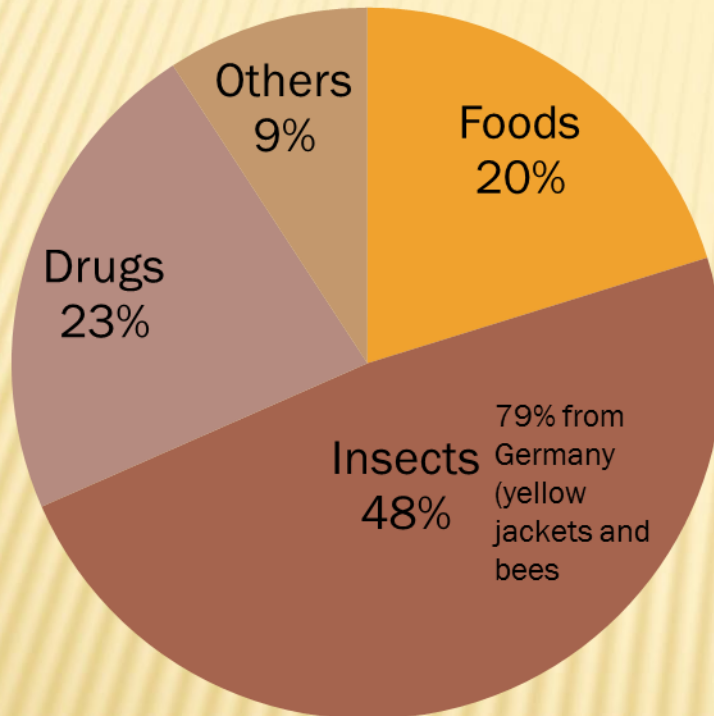
FIRST EUROPEAN ANAPHYLAXIS REGISTRY

- ✖ 10 European countries
- ✖ Online questionnaire
- ✖ Fifty-nine centers reported 3333 cases of anaphylaxis (2011-2014)
- ✖ Pilot study for European Registry

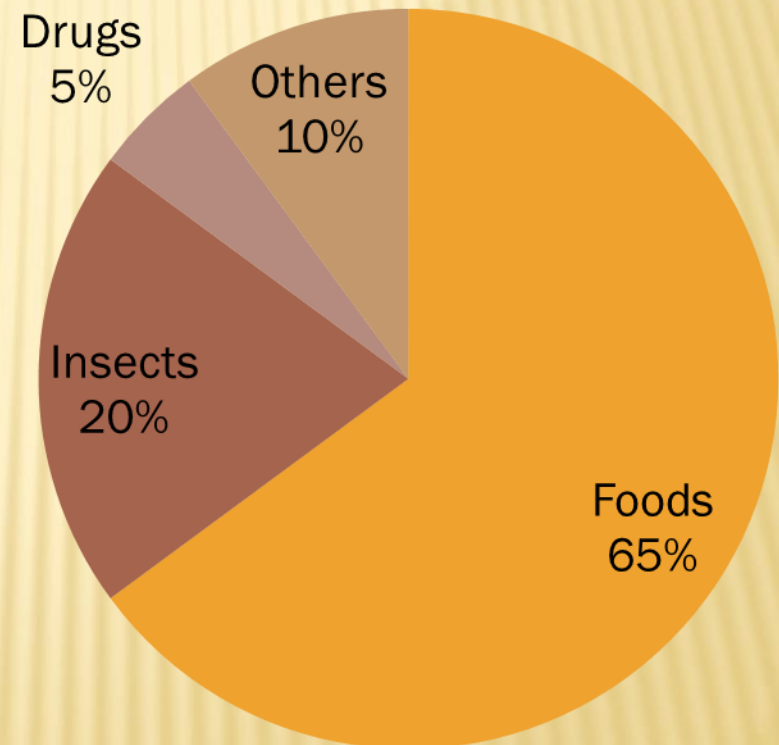
Worm M, et al. First European data from the network of severe allergic reactions (NORA). Allergy 2014; 69: 1397–1404.

EUROPE: MAIN INDUCERS

Adults



Children



34.2% previous, most frequently milder reaction to the same allergen

Worm M, et al. First European data from the network of severe allergic reactions (NORA). Allergy 2014; 69: 1397–1404.

First reaction

100%

Proportion of cases receiving drug

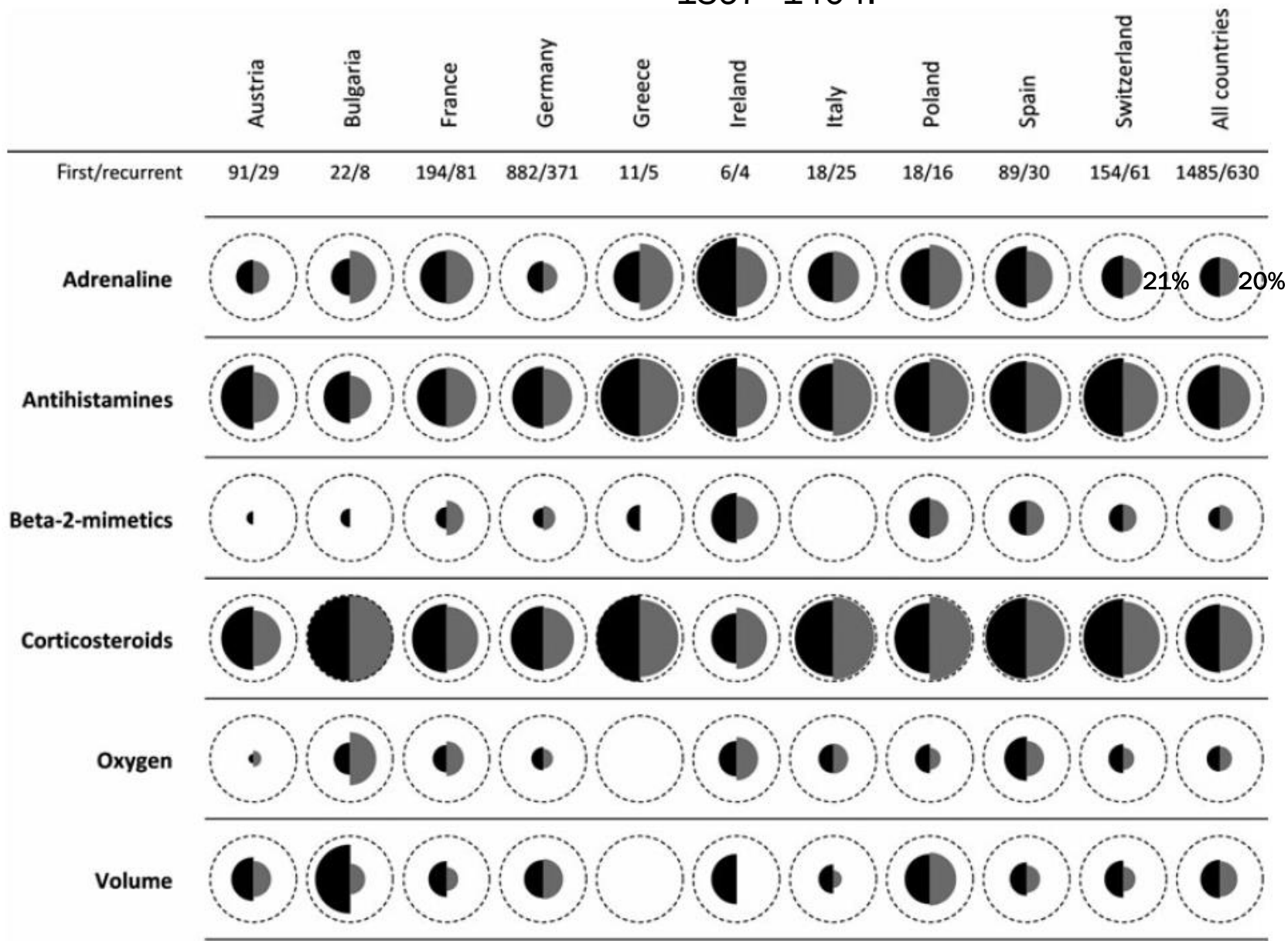


Recurrent reaction

100%

Proportion of cases receiving drug

Worm M, et al. First European data from the network of severe allergic reactions (NORA). Allergy 2014; 69: 1397–1404.

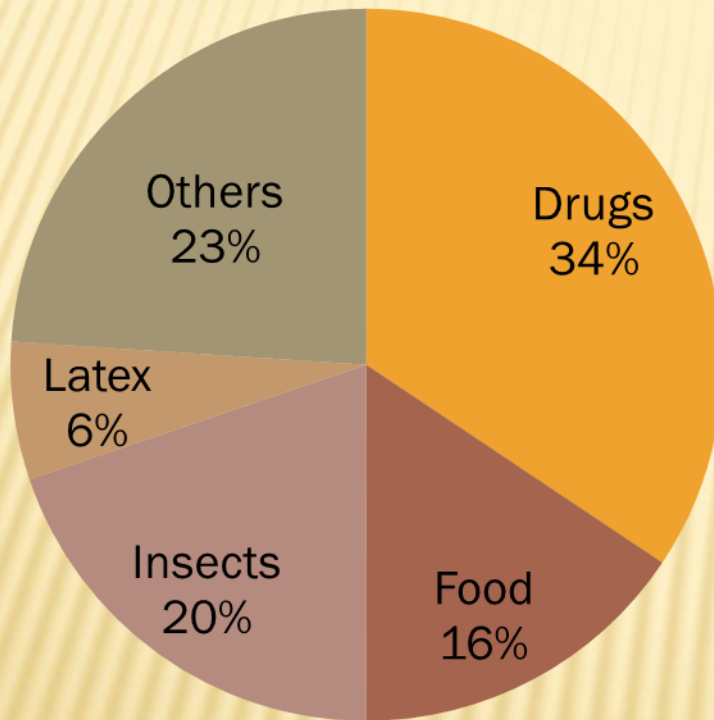


ANAPHYLAXIS IN AMERICA

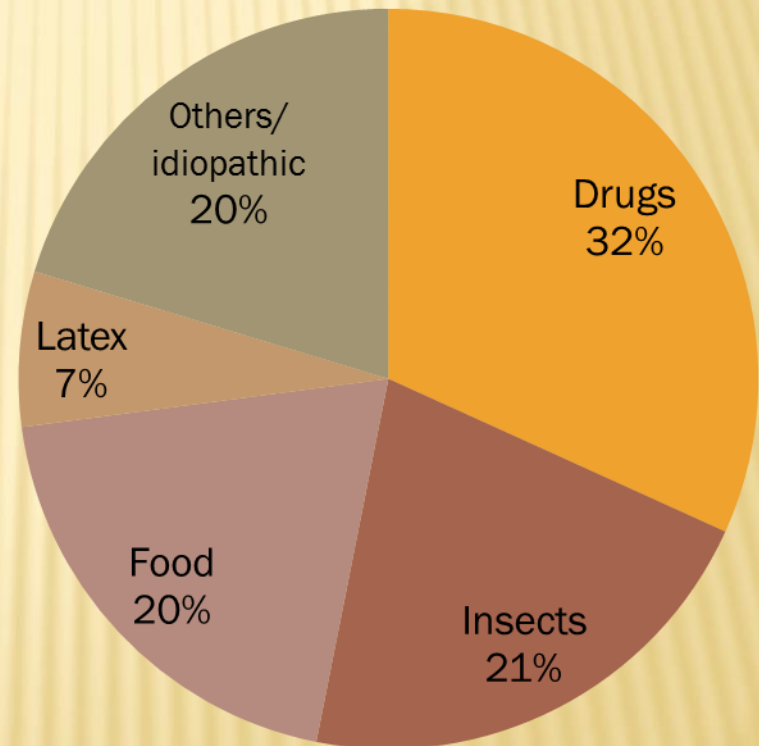
- ✖ Two nationwide, cross-sectional random-digit-dial surveys: patients and public
- ✖ Standardized questionnaires
- ✖ The public survey included 1,000 adults
 - + 5.1 and 1.6% probable and very likely anaphylaxis.
- ✖ The patient survey included 1,059 respondents: subjects who reported experiencing some type of generalized allergic reaction: 32.5% history of anaphylaxis

ANAPHYLAXIS IN AMERICA

Public Survey



Patients Survey



ANAPHYLAXIS IN LATIN AMERICA

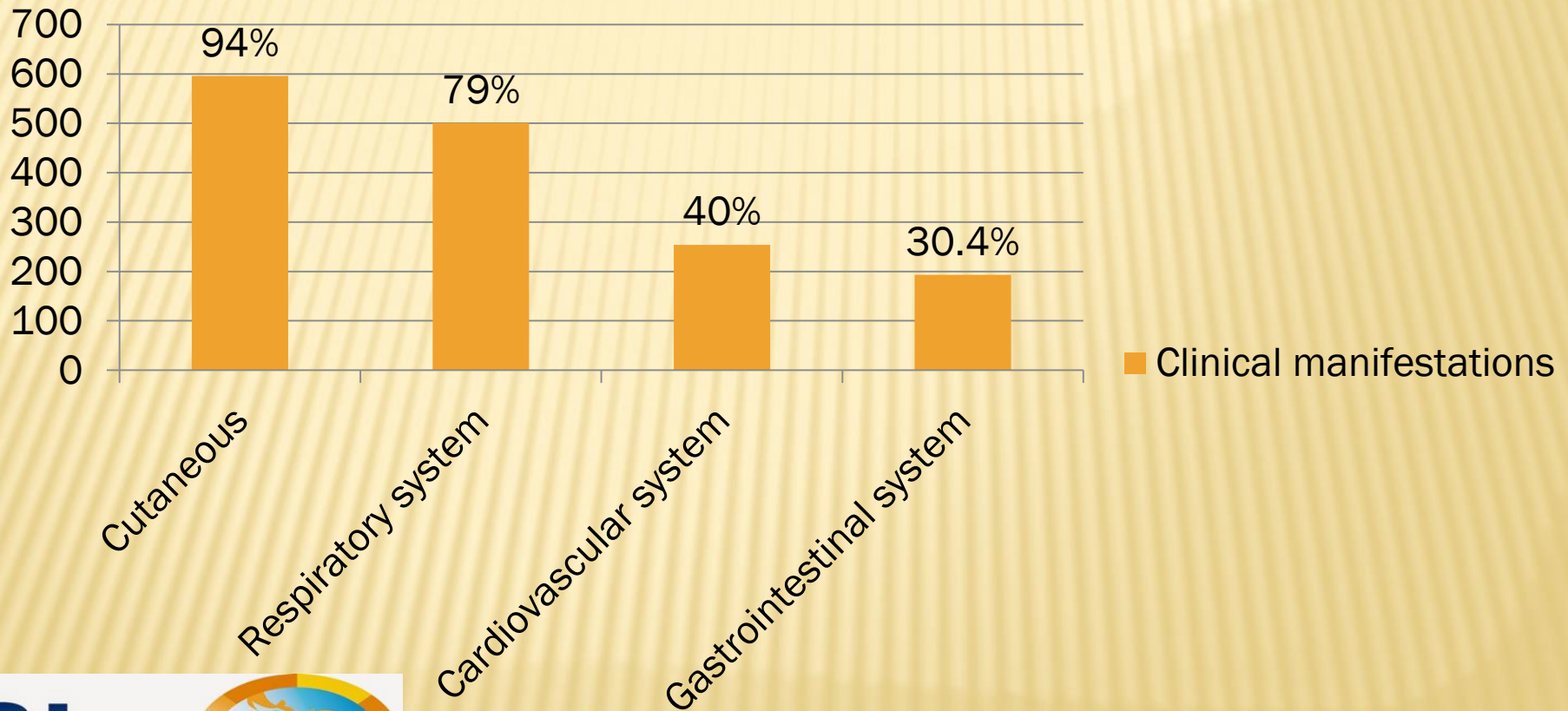
- ✖ Online Latin American Survey of Anaphylaxis (OLASA)
- ✖ Developed by Latin American Society of Allergy, Asthma and Immunology
- ✖ 634 patients from 15 countries were registered



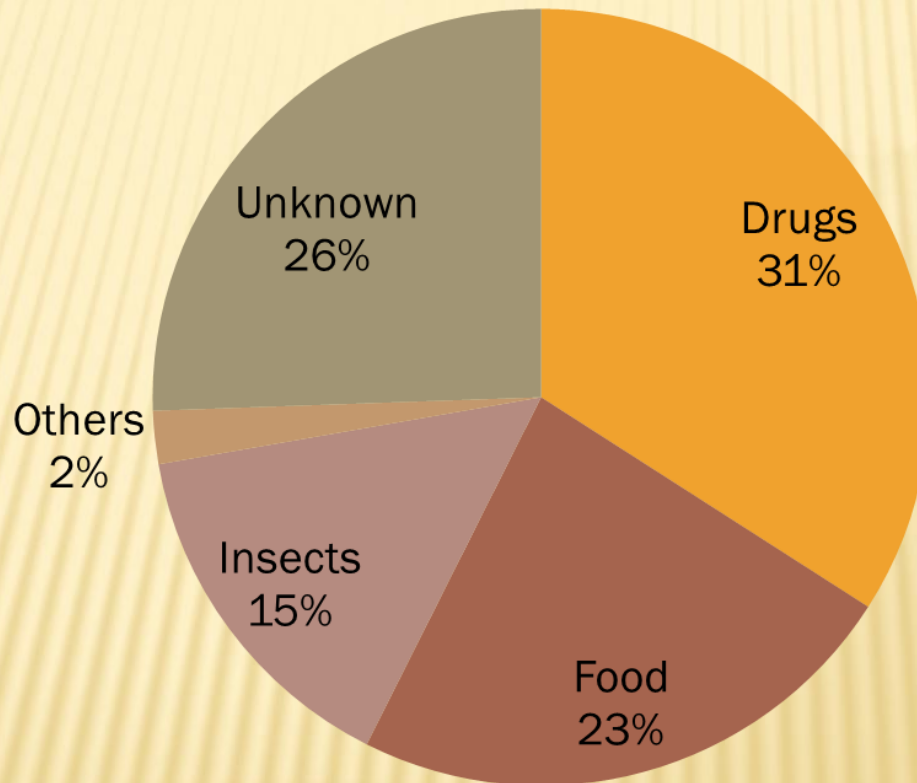
Anaphylaxis online survey in Latin America
Sole D et al. Clinics, 2011 66(6):943-947

ANAPHYLAXIS IN LATIN AMERICA

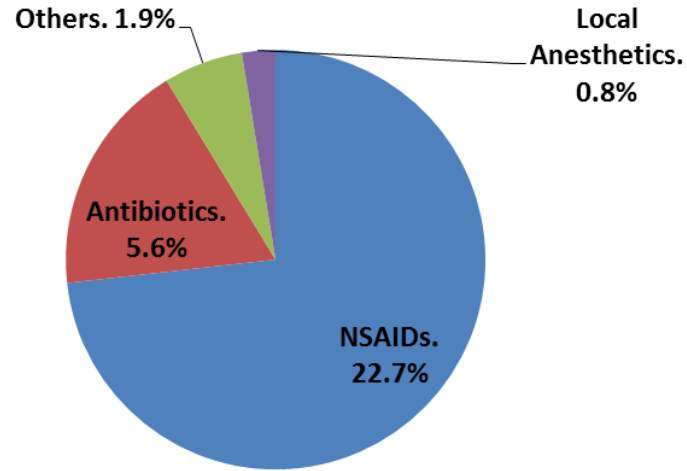
Clinical manifestations



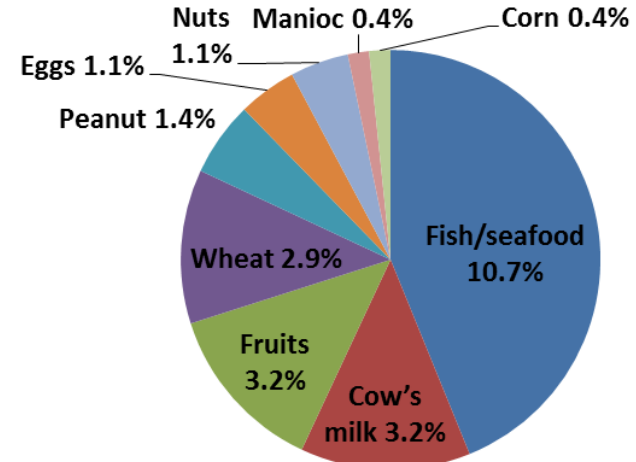
ANAPHYLAXIS IN LATIN AMERICA



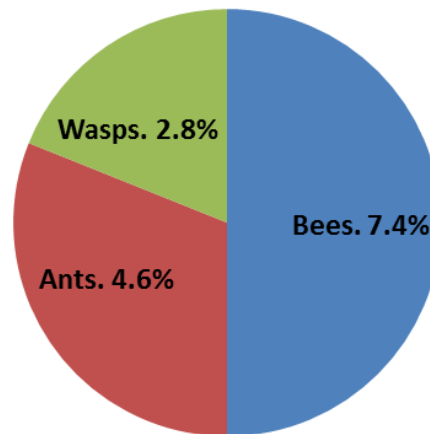
ANAPHYLAXIS IN LATIN AMERICA



Drugs: 31.2%

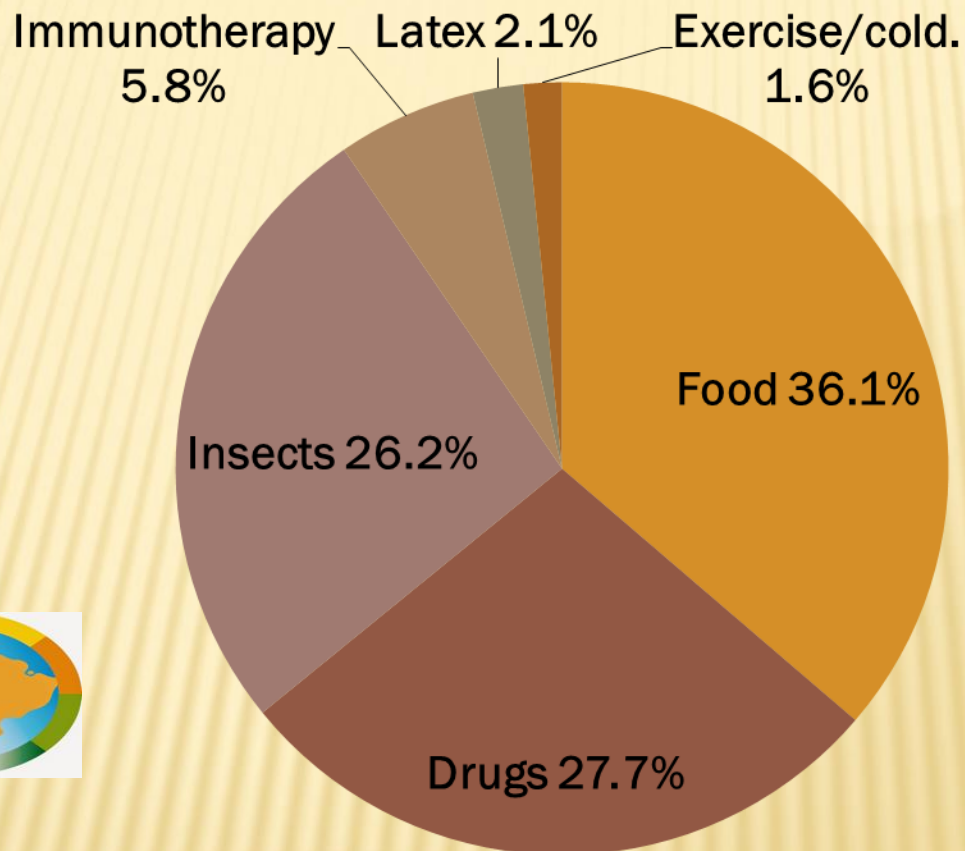


Food: 23.3%



Insects: 14.8%

MAIN INDUCERS IN 191 CHILDREN



MAIN INDUCERS IN 191 CHILDREN

Table 1 Main triggering agents for severe allergic reactions according to the age of patients registered in the Online Latin American Survey on Anaphylaxis.

Agents	Age (years)				
	<2 31 (16.3%)	2-5 28 (14.7%)	6-11 57 (29.9%)	12-18 75 (39.2%)	Total N= 191 (%)
<i>Food – total</i>	16 (53.3)	16 (56.5)	17 (30.5)	20 (26.2)	69 (36.1)
Cow's milk	7 (22.6)	7 (25.0)	4 (7.0)	–	18 (9.4)
Egg	8 (25.8)	5 (17.9)	–	1 (1.3)	14 (7.3)
Fish/seafood	–	1 (3.6)	4 (7.0)	9 (12.0)	14 (7.3)
Peanuts	–	1 (3.6)	2 (3.5)	2 (26.7)	5 (2.6)
Nuts	–	–	2 (3.5)	2 (26.7)	4 (2.1)
Manioc	–	–	1 (1.8)	–	1 (0.5)
Corn	–	–	–	1 (1.3)	1 (0.5)
Fruits	1 (3.2)	2 (7.1)	2 (3.5)	2 (26.7)	7 (3.7)
Wheat ^a	–	–	2 (3.5)	2 (26.7)	4 (2.1)
Soy	–	–	–	1 (1.3)	1 (0.5)
<i>Insects – total</i>	8 (26.7)	11 (39.1)	17 (30.5)	15 (19.7)	51 (26.2)
Bee	–	1 (3.6)	10 (17.5)	8 (10.7)	19 (10.0)
Ants	7 (22.6)	9 (32.1)	4 (7.0)	3 (4.0)	23 (12.0)
Wasp	1 (3.2)	1 (3.6)	3 (5.3)	4 (5.3)	9 (4.7)

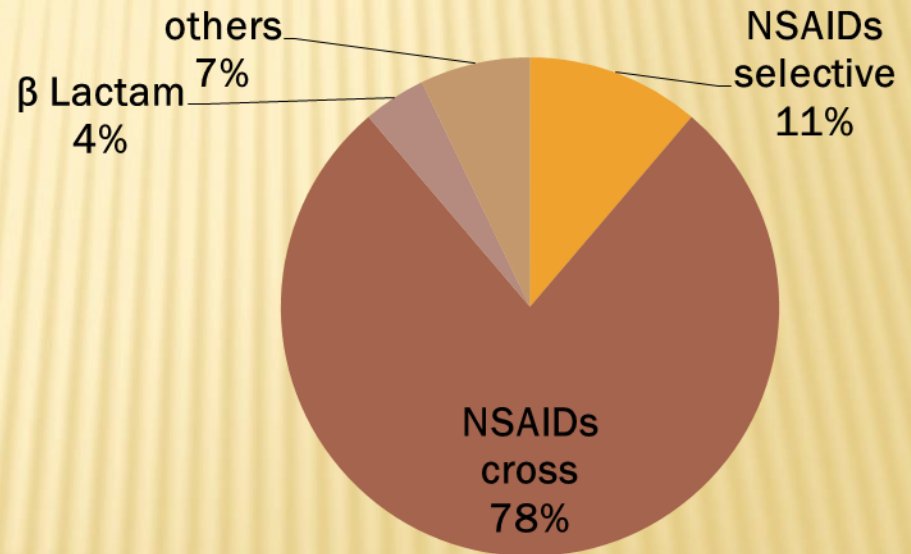
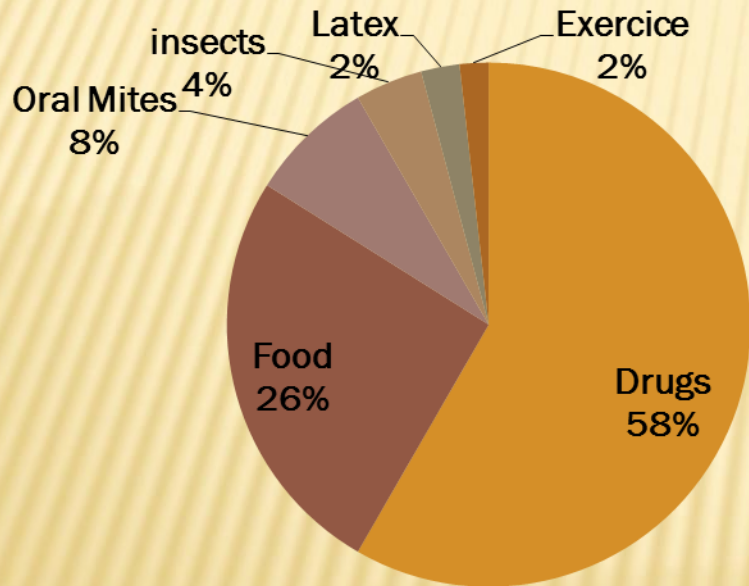
Sole D et al. Anaphylaxis in Latin American children and adolescents
Allergol Immunopathol (Madr). 2012;40(6):331---335

179 ANAPHYLACTIC REACTIONS

Female 70.4% Children 6.7%

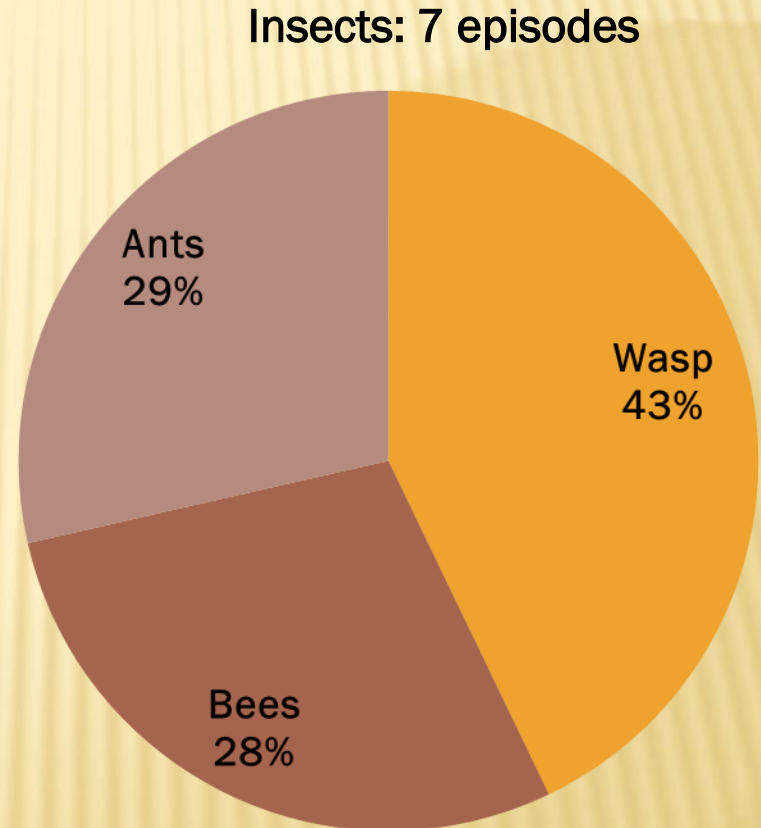
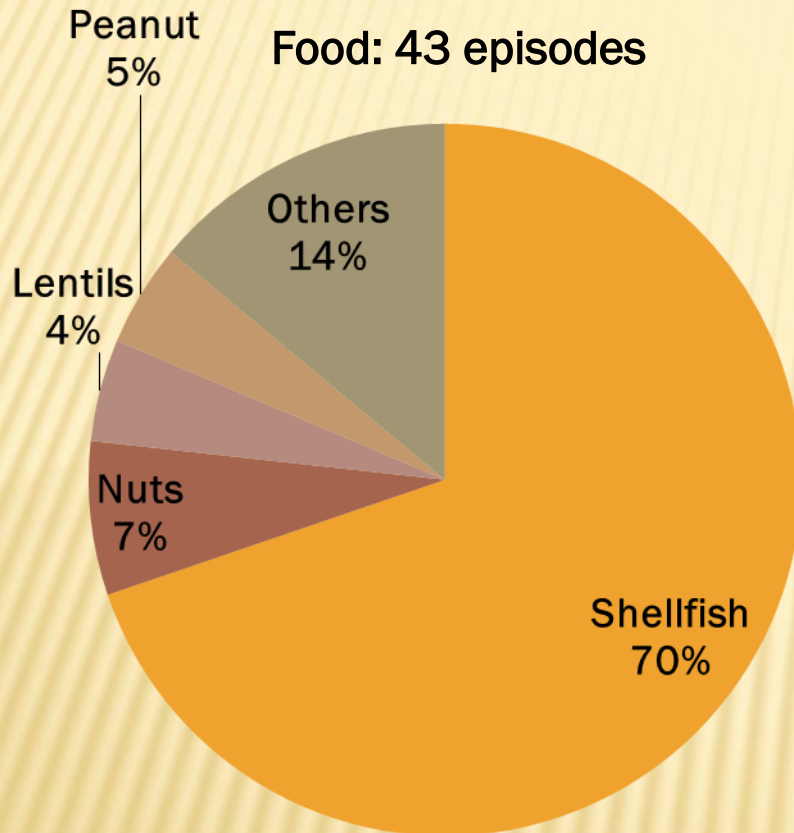
- ✖ The most commonly involved sites were the skin, oropharynx, and upper respiratory tract.

Drugs: 98 episodes



179 ANAPHYLACTIC REACTIONS

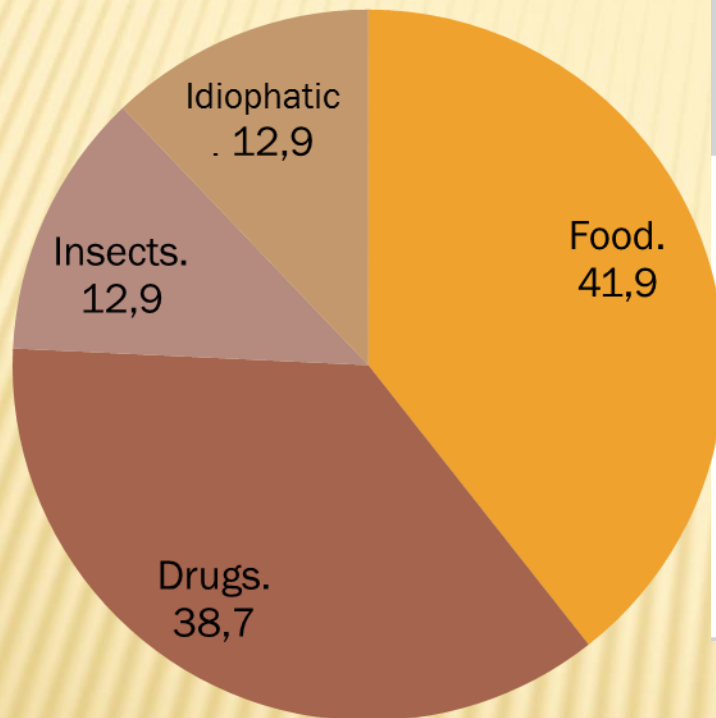
Female 70.4% Children 6.7%



ANAPHYLAXIS AND ACUTE ALLERGIC REACTIONS IN ED BETWEEN 2007-2009

- ✖ Six patients (4.4%) anaphylaxis
- ✖ 129 patients (95.6%) allergic reactions.
- ✖ Among the patients diagnosed with allergic reactions, 25 (23%) met the diagnostic criteria for anaphylaxis but were not recognized.

UNRECOGNIZED ANAPHYLAXIS (25) RECEIVED EPINEPHRINE IN ONLY 8% CASES



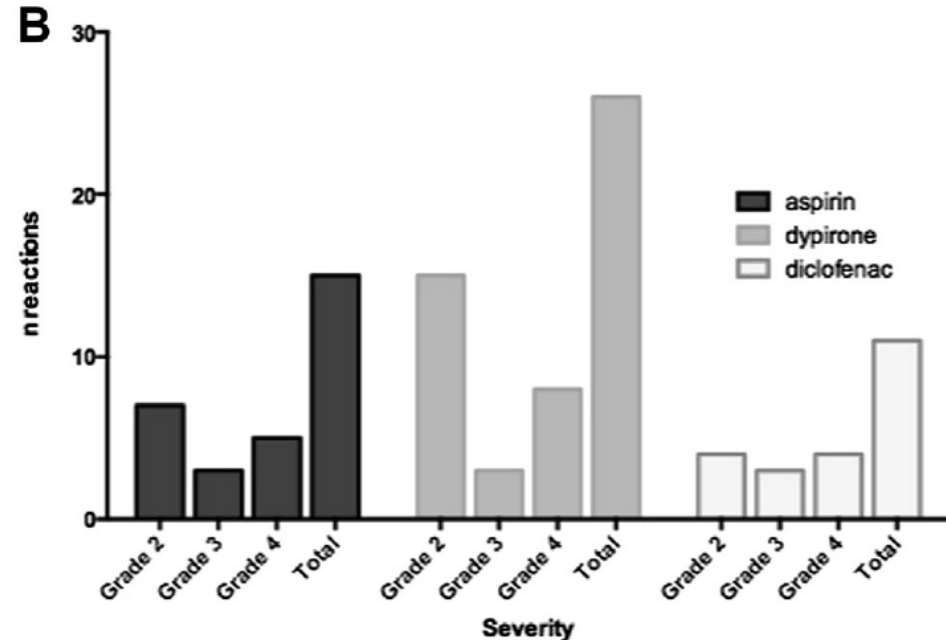
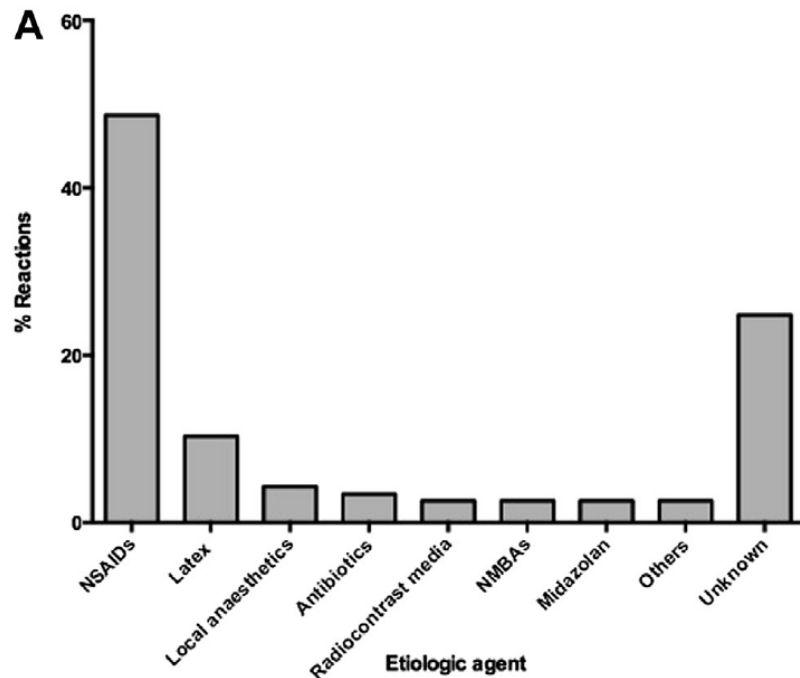
	Anaphylaxis (%)	Unrecognized anaphylaxis (%)	Allergy (%)	p-value
Epinephrine at ED	4/6 (66%)	2/25 (8%)	0/104 (0%)	<0.001
Epinephrine upon arrival	4/6 (66%)	0/25 (0%)	0/104 (0%)	<0.001
Steroids at ED	6/6 (100%)	22/25 (88%)	59/104 (57%)	0.002
Steroids at discharge	3/6 (50%)	12/25 (48%)	39/104 (37%)	0.552
Allergist referral	0/6 (0%)	7/25 (28%)	11/104 (11%)	0.044
Admission to hospital	3/6 (50%)	2/25 (8%)	5/104 (5%)	<0.001

KNOWLEDGE OF ANAPHYLAXIS AMONG IBERO-AMERICAN PHYSICIANS: 510 CASES

Table. Summary of Survey Results According to Physician Specialty (Allergy and Immunology) and Work in Emergency Care (EC)

	Allergy and Immunology Specialist						Significant differences
	Yes			No			
	EC ^a n=51 (%)	Not EC ^b n=299 (%)	Total ^c n=350 (%)	EC ^a n=77 (%)	Not EC ^b n=83 (%)	Total ^c n=160 (%)	
Which laboratory test supports the clinical diagnosis of anaphylaxis?							
Total serum tryptase	41 (80.4)	213 (71.2)	254 (72.6)	14 (18.2)	14 (16.9)	28 (17.5)	a>b; c>f; a>d; d>e
What is the treatment of choice for anaphylaxis?							
IM epinephrine	40 (78.4)	209 (69.9)	249 (71.1)	20 (26.0)	18 (21.7)	38 (23.8)	d>e; c>f; a>d;
SC epinephrine	6 (11.7)	64 (21.4)	70 (20.0)	38 (49.4)	36 (43.4)	74 (46.3)	c<f; a<d; b<e
When should epinephrine be administered in anaphylaxis?							
Patient in shock	7 (13.7)	36 (12.0)	43 (12.3)	26 (33.8)	23 (27.7)	49 (30.6)	c<f; a<d; b
When anaphylaxis is suspected	44 (86.3)	263 (88.0)	307 (87.7)	51 (66.2)	60 (72.3)	111 (69.4)	c>f; a>d; b

NONSTEROIDAL ANTI-INFLAMMATORY DRUGS ARE MAJOR CAUSES OF DRUG-INDUCED ANAPHYLAXIS

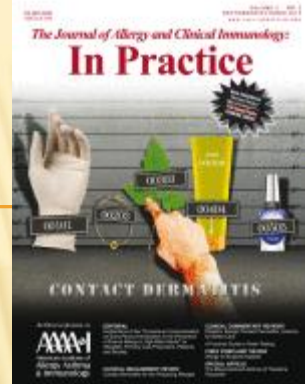


Seventy-eight patients (66.7%) reported previous reactions to the drug involved in the current reaction or to a drug from the same class and/or group.

NONSTEROIDAL ANTI-INFLAMMATORY DRUGS ARE MAJOR CAUSES OF DRUG-INDUCED ANAPHYLAXIS

- ✗ Epinephrine use: 34%, and less than 50% of patients with cardiovascular involvement

DRUG-INDUCED ANAPHYLAXIS IN LATIN AMERICA



- ✖ Patients presenting anaphylaxis were selected in a descriptive cross-sectional study using ENDA questionnaire
- ✖ Implemented in 22 allergy units from 11 Latin American countries
- ✖ U/A+ R-GI and/or CV Symptoms
- ✖ Or 2 of the following symptoms:
 - + Respiratory, persistent GI or CV symptoms
- ✖ From 1005 HDR, 264 presented anaphylaxis

DRUG-INDUCED ANAPHYLAXIS IN LATIN AMERICA

STRIKING FINDINGS

- ✖ Severe reactions were present in 43% of atopic patients and 59% of non-atopic patients ($p < 0.01$)
- ✖ Asthma patients has less severe reactions (38.6%) than non-asthmatic patients (54.6%) ($p < 0.05$)



ASTHMA, ALLERGY AND ANAPHYLAXIS

- + González Pérez et al (UK) found a 2 fold and 3.3 fold greater risk of anaphylaxis in non-severe and severe asthmatics respectively
- + Greenberger PA and Simmons FE:
 - × Severe and uncontrolled asthma → risk factor for more severe anaphylaxis

Gonzalez Pérez et al. J Allergy Clin Immunol 2010;125:1098-1104
Greenberger PA et al. Annals Allergy, Asthma Immunol, 2007
Simmons FE, J Allergy Clin Immunol 2009

DRUG-INDUCED ANAPHYLAXIS TREATED IN THE EMERGENCY DEPARTMENT OR HOSPITAL

- ✗ 716 patients with an ED visit and/or hospitalization for DIA
- ✗ Patients with DIA and atopy or asthma did not differ with respect to severity, site of treatment or management compared with patients without any concomitant allergic condition
- ✗ Aun M, and Faria E presented similar findings
- ✗ Park H et al did not find difference in atopy/asthma in anaphylaxis with or without shock

Banerji A et al. J Allergy Clin Immunol Pract 2014;2:46-51

Aun M et al J Allergy Clin Immunol Pract 2014;2:414-20

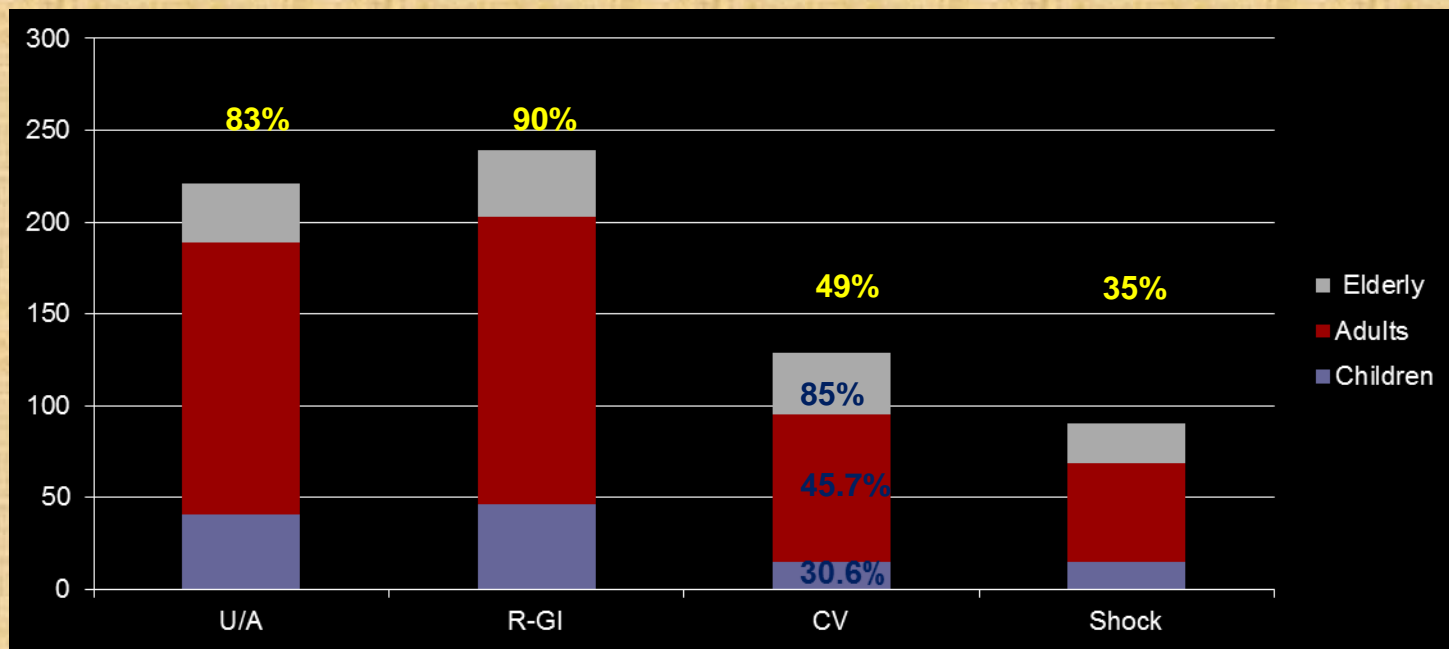
Faria E et al. J Investig Allergol Clin Immunol 2014; Vol. 24(1): 40-48

Park H. Am J Emerg Med. 2012 Nov;30(9):1674-8

-
- ✗ The presumption that atopic predisposition contributes to a more severe allergic reaction to drugs, as stated in many publications, requires further investigation

DRUG INDUCED ANAPHYLAXIS IN LATIN AMERICA

- ✗ U/A y R-GI: most frequent symptoms
- ✗ More than 45%: CV involvement

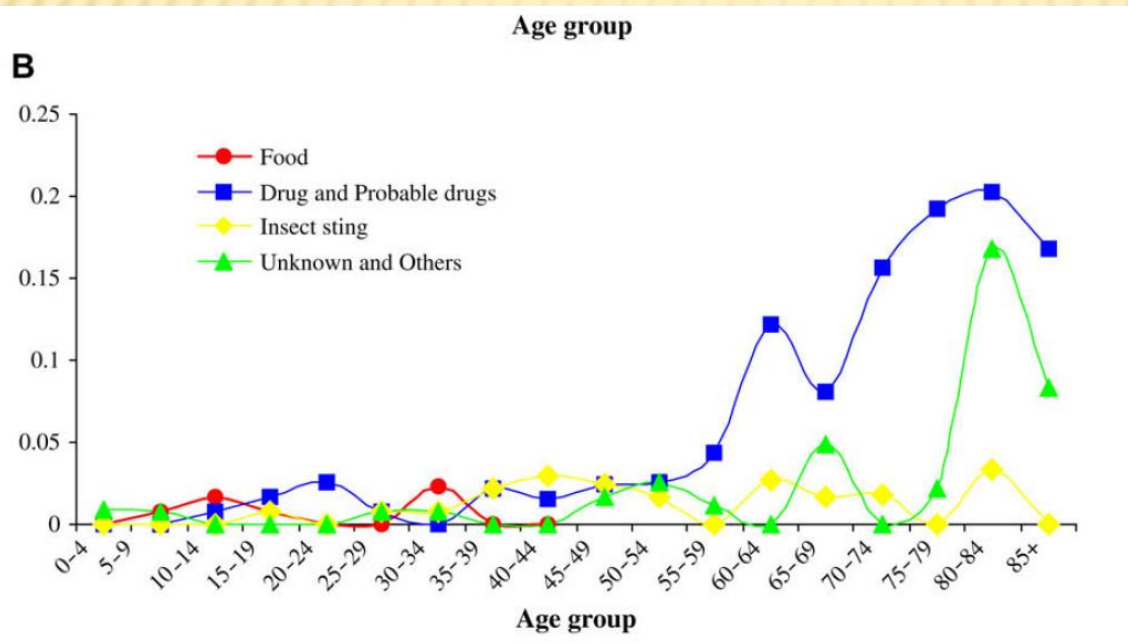


- ✗ CV symptoms were more frequent in elderly patients (85%) than in adults (45.7%) and children (30.6%; $p < 0.00001$)

Jares E et al, JACI in practice 2015

IN OUR STUDY, SHOCK AND SEVERE ANAPHYLAXIS WERE MORE FREQUENT IN ELDERLY PATIENTS

- ✘ In an Australian study of death in anaphylaxis most drug-induced anaphylaxis deaths occurred between 55 and 85 years old patients



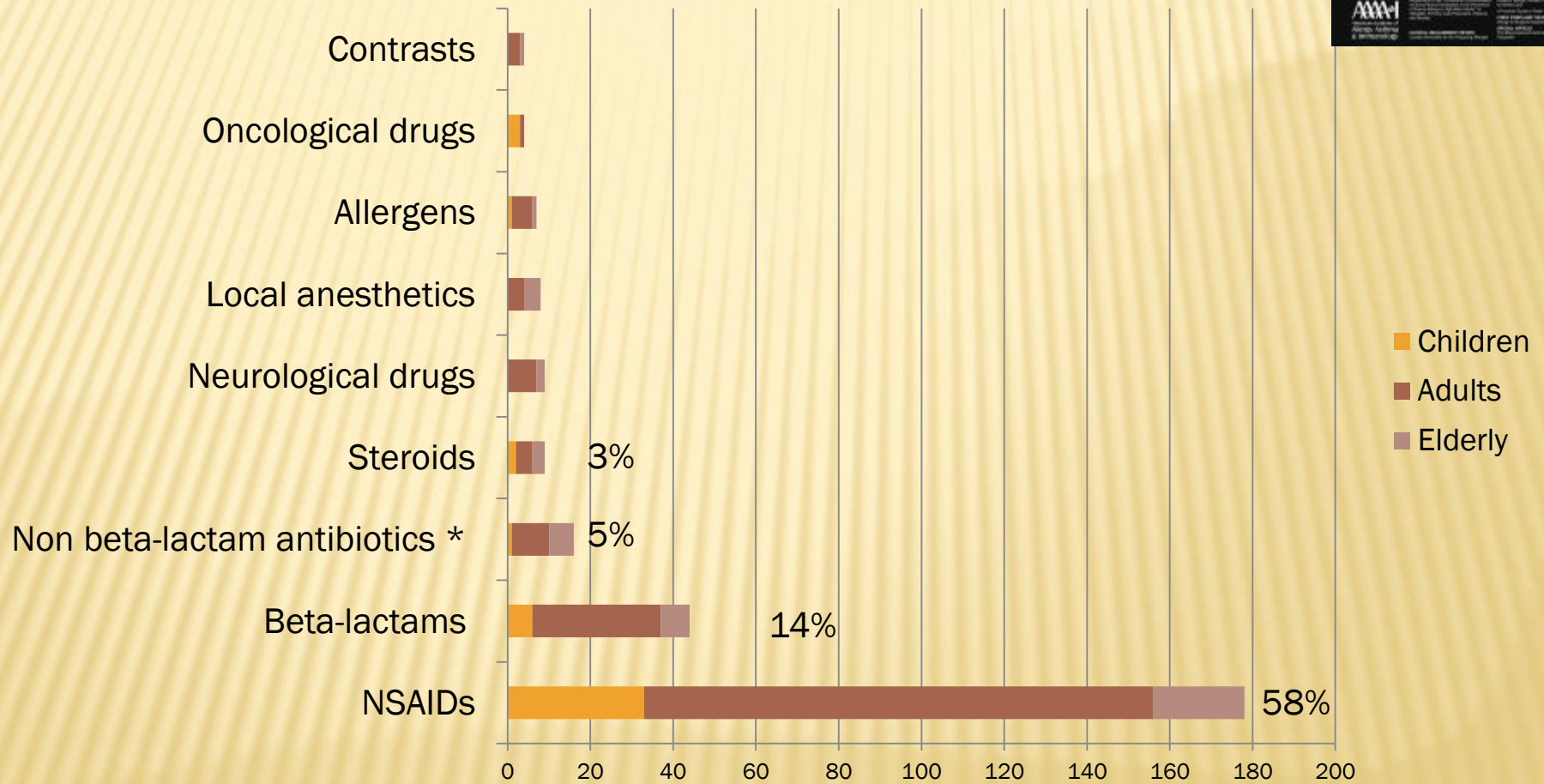
Liew WK, Williamson E, Tang ML. Anaphylaxis fatalities and admissions in Australia. J Allergy Clin Immunol 2009;123:434-42.

IN OUR STUDY, SHOCK AND SEVERE ANAPHYLAXIS WERE MORE FREQUENT IN ELDERLY PATIENTS

- ✘ Park et al found that elderly patients with anaphylaxis were at increased risk for the development of shock

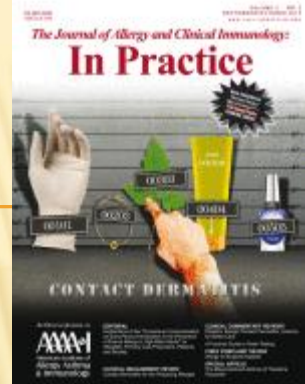
Park H, Kim S. Factors associated with shock in anaphylaxis. American Journal of Emergency Medicine (2012) 30, 1674–1678

MAIN IMPLICATED DRUGS (CERTAIN AND PROBABLE)



More than 15% of the patients had suffered a previous DHR with the same drug

Jares E et al, JACI in practice 2015



NSAIDS PREDOMINANCE

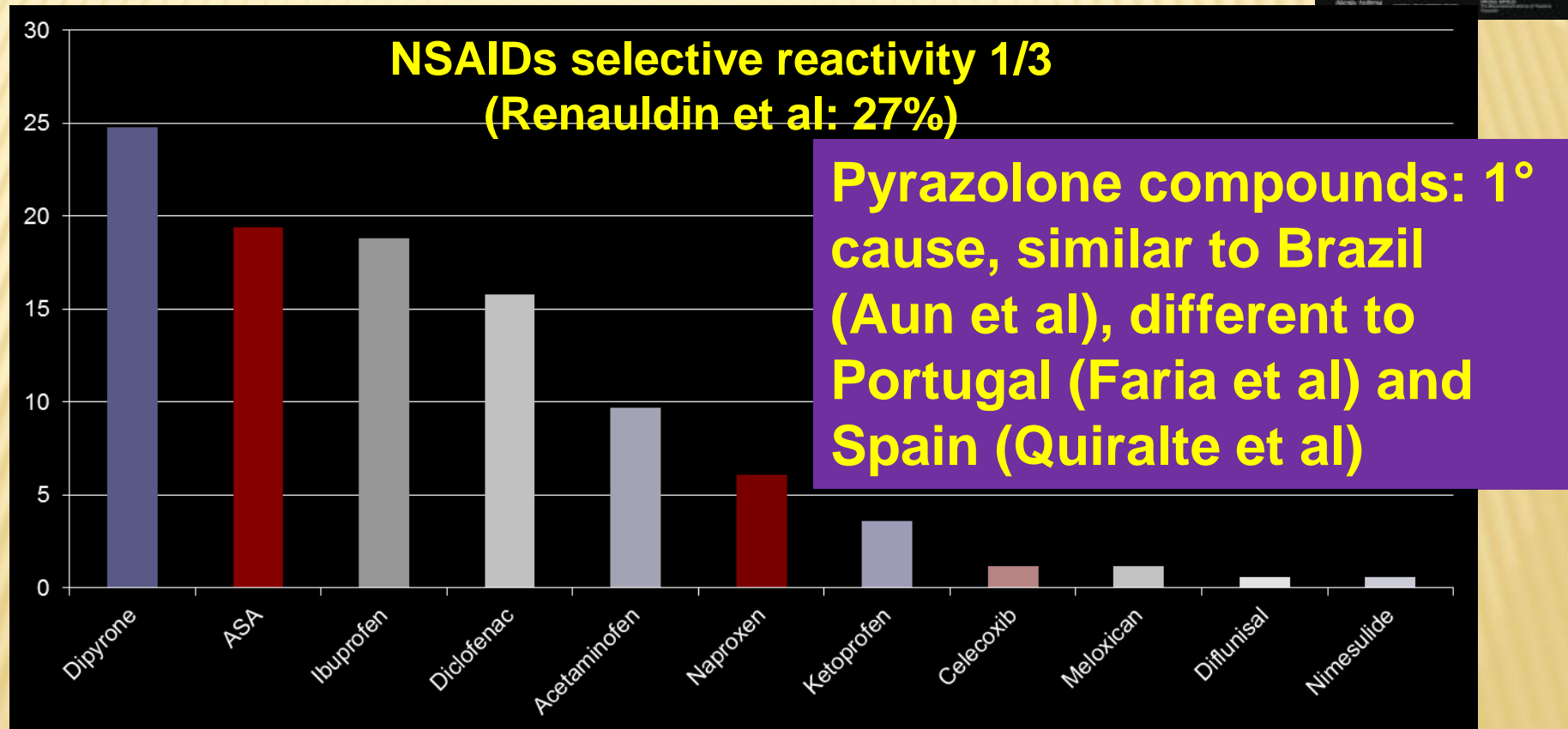
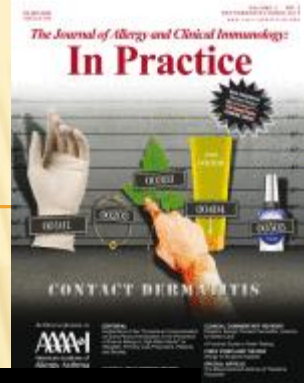
- ✖ Latin-America
 - + Sole D et al. Clinics (Sao Paulo). 2011;66(6):943-7
 - + Aun M et al. J Allergy Clin Immunol Pract. 2014 Jul-Aug;2(4):414-20.
- ✖ Other regions
 - + Çelik GE, Allergol Immunopathol (Madr). 2013. (Turkey)
 - + Messaad D et al, Ann Intern Med. 2004;140:1001-1006 (France)
 - + Doña I et al, J Investig Allergol Clin Immunol. 2012;22:363-371(Spain)
 - + Faria E et al. J Investig Allergol Clin Immunol 2014; Vol. 24(1): 40-48 (Portugal)
 - + Park H. Am J Emerg Med. 2012 Nov;30(9):1674-8 (Korea)

BETA LACTAMS PREDOMINANCE

- ✖ Gonzalez-Perez A, et al. J Allergy Clin Immunol 2010;125:1098-1104. (UK)
- ✖ Liew WK, et. J Allergy Clin Immunol 2009;123:434-42. (Australia)
- ✖ Cianferoni A et al. Ann Allergy Asthma Immunol. 2001;87:27-32. (Italy)
- ✖ Ribeiro-Vaz I et al. Eur J Clin Pharmacol. 2013 Mar;69(3):673-81 (Portugal)
- ✖ Renaudin J-M et al. Allergy 2013; 68: 929–937. (France)
- ✖ Worm M, et al. Allergy 2014; 69: 1397–1404. (Europe)

ANAPHYLAXIS INDUCERS

DRUG INDUCED ANAPHYLAXIS IN LATIN AMERICA

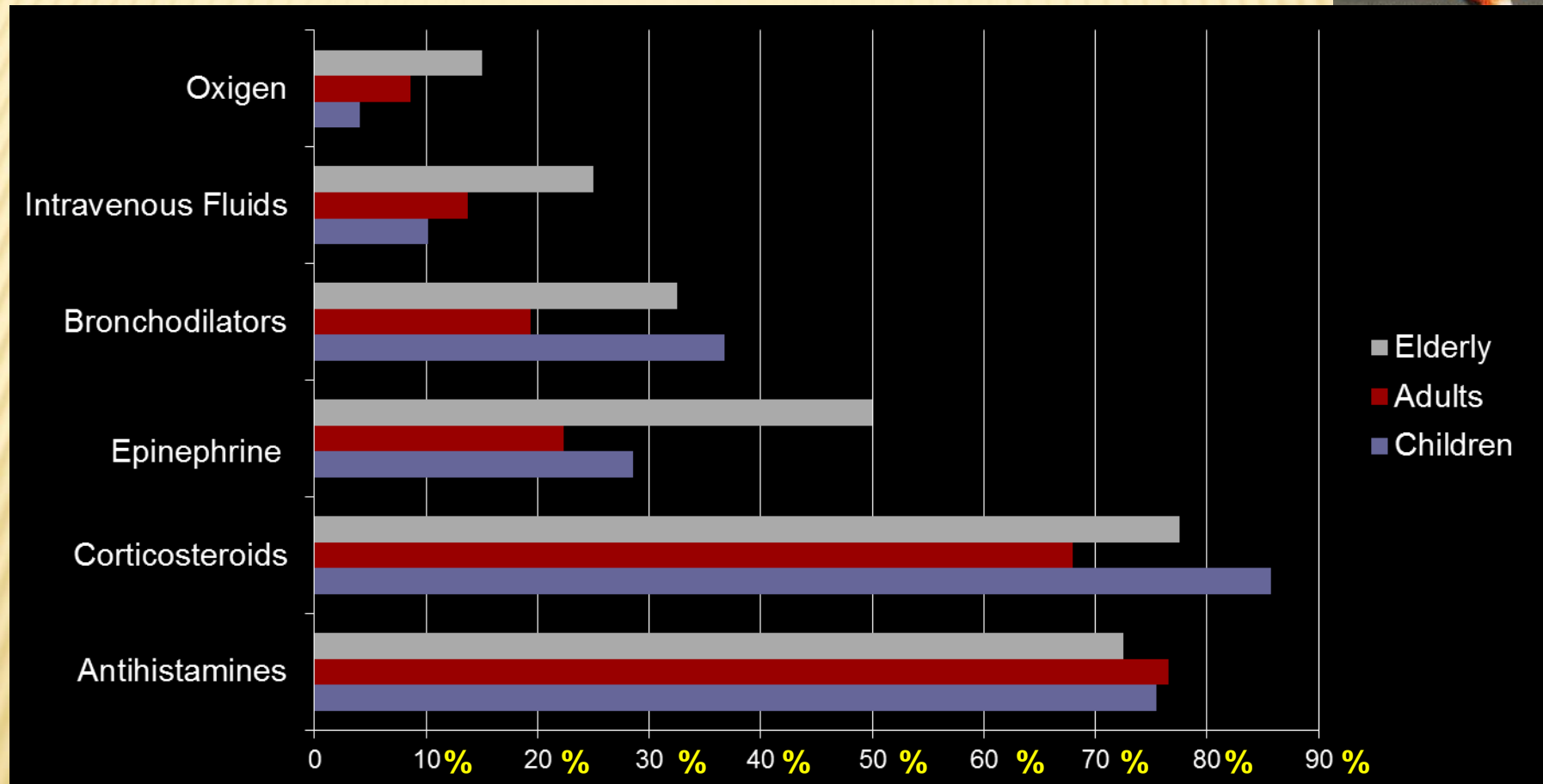


Aun MV, et al. J Allergy Clin Immunol Pract. 2014
Faria E et al, . J Investig Allergol Clin Immunol 2014
Quiralte J et al. J Investig Allergol Clin Immunol 2007
Renauldin et al, Allergy 2013

Jares E et al, JACI in practice 2015



TREATMENT: 78% WERE TREATED IN THE EMERGENCY DEPARTMENT, AND 8.7% HOSPITALIZED



Only 27% of anaphylaxis patients received epinephrine, 39.2% when CV symptoms were present

Jares E et al, JACI in practice 2015

EPINEPHRINE USE

- ✗ The low epinephrine use in anaphylaxis treatment is common in studies from Latin America and other regions

EPINEPHRINE USE

- ✖ Banerji et al: only 8% of patients with drug-induced anaphylaxis treated in the ED received epinephrine

Banerji A, Rudders S, Clark S, Wei W, Long A, Camargo C. Retrospective study of drug-induced anaphylaxis treated in the emergency department or hospital: patient characteristics, management, and 1-year follow-up. J Allergy Clin Immunol Pract. 2014;2:46-51.

CONCLUSIONS

- ✗ The relationship between atopic predisposition/asthma and anaphylaxis requires further investigation
- ✗ NSAIDs are the most frequent anaphylaxis inducers in Latin-America
- ✗ Epinephrine is underuse in anaphylaxis treatment in Latin America and other regions
- ✗ Medical education of ED physicians in Latin America should focus on this topic