

MATERA | 18-20
CASA CAVA | MAGGIO
2023



ALLERGIE E INTOLLERANZE NELLA FIBROMIALGIA

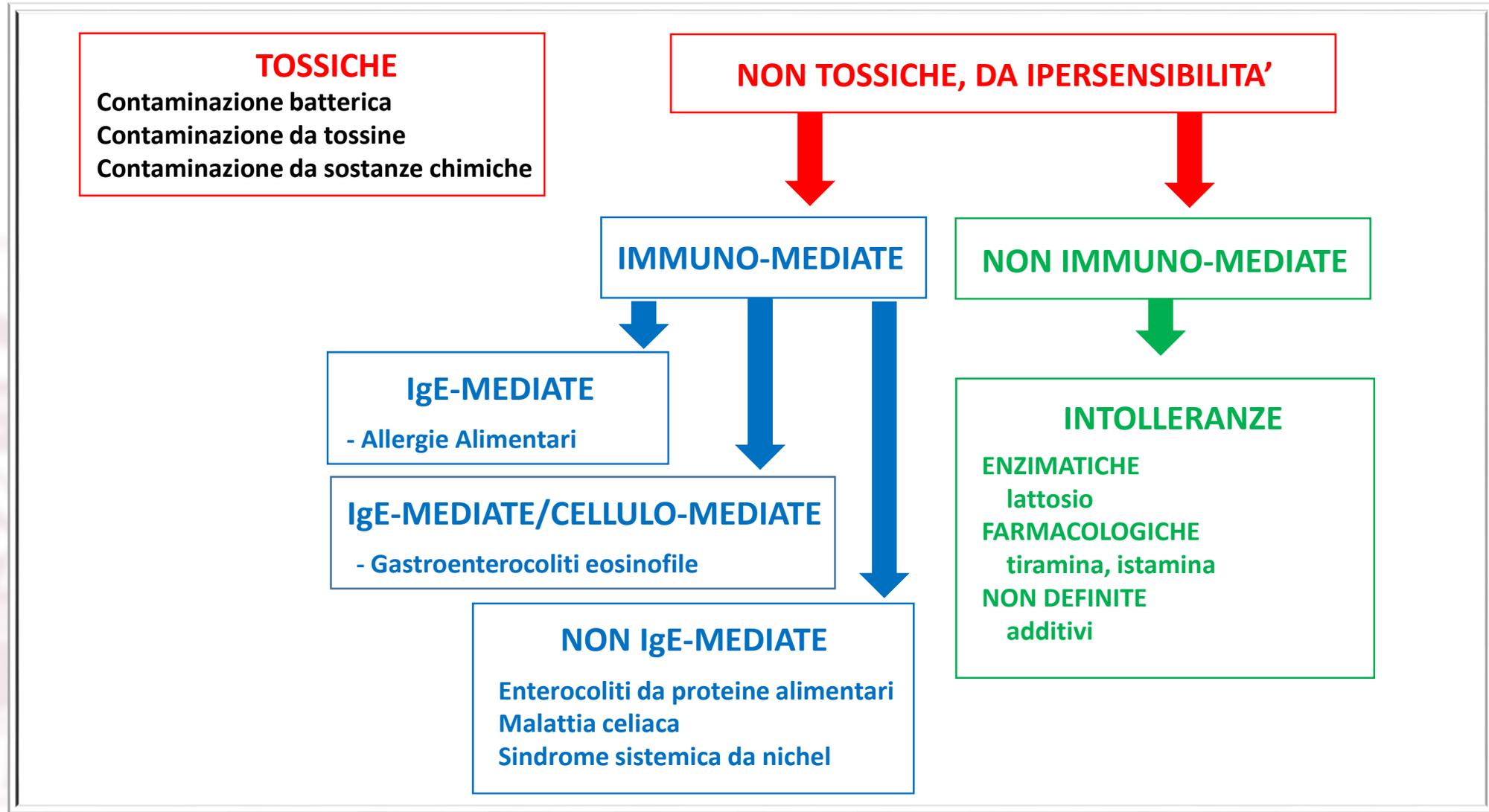
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Fondazione IRCCS Policlinico S.Matteo

Pavia

CLASSIFICAZIONE DELLE REAZIONI AVVERSE AL CIBO



DIFFERENZE TRA ALLERGIE E INTOLLERANZE ALIMENTARI

ALLERGIA ALIMENTARE

>> età pediatrica

Può ridursi con l'età

IgE-mediata

Pochi cibi

Reazioni immediate o precoci

Riproducibili

Diagnosi diretta

INTOLLERANZA ALIMENTARE

Qualsiasi età

Aumenta con l'età

Non immuno-mediata

Diversi cibi

Ritardata

Variabile

Diagnosi spesso difficile

PREVALENZA DELLE ALLERGIE IN RELAZIONE AL TEST DIAGNOSTICO

Arachidi, proteine del latte, uova, pesce, crostacei

Sintomi riferiti dai pazienti – età pediatrica	12%
Sintomi riferiti dai pazienti – adulti	13%
Sintomi + Skin Prick Test	3%
Food challenge	3%

Frutta, verdura/ortaggi/legumi, frutta secca, grano, soia

Sintomi riferiti dai pazienti	0.02-8.5%
Skin Prick Test	0.02-4.2%
Food challenge	0.1-4.3%

Rona RJ et al, *JACI* 2007
Zuidmeer L et al, *JACI* 2008

PREVALENZA DELLE REAZIONI AVVERSE AL CIBO

	2006	2014
PREVALENZA DI REAZIONI AVVERSE AL CIBO	Adulti 3-4% Bambini 6%	Adulti 5% Bambini 8%
INCIDENZA DI RICOVERI OSPEDALIERI CAUSATI DA REAZIONI AL CIBO	0.6/1000 pazienti	1.3/1000 pazienti

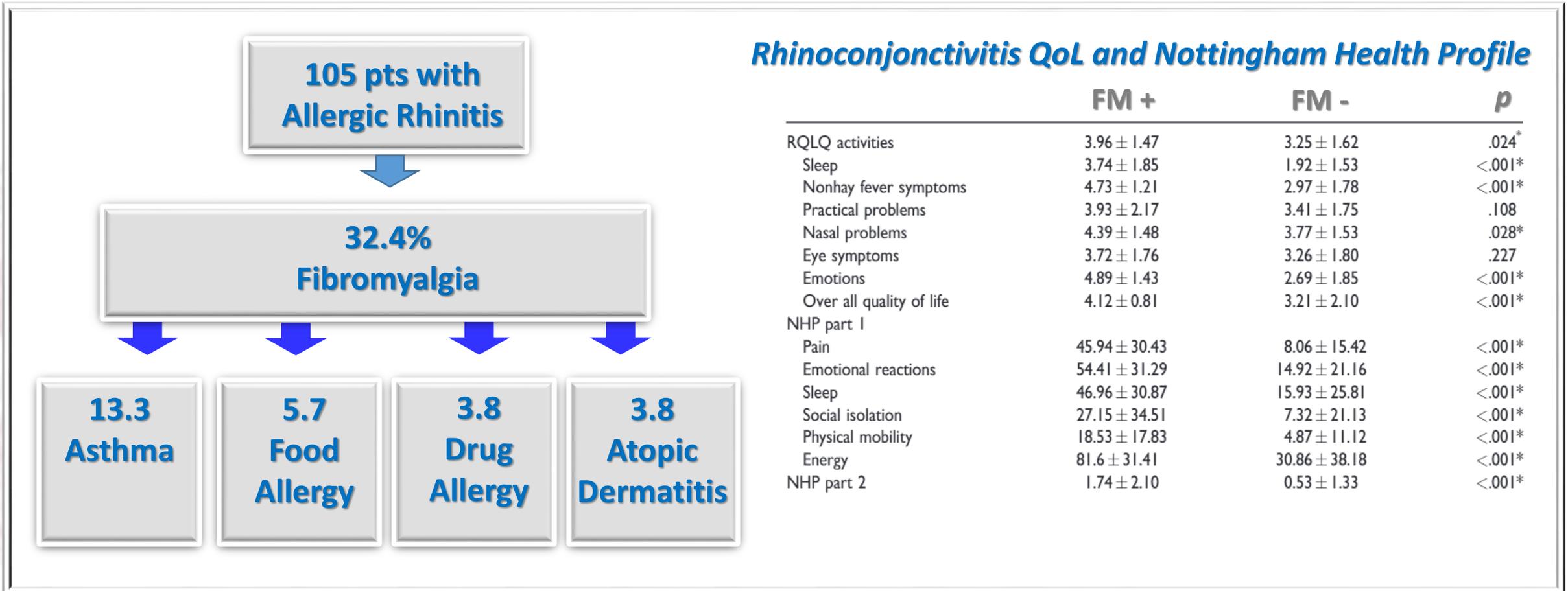
Sicherer SA et al, *JACI* 2006
Sicherer SH & Sampson HA, *JACI* 2014
Rudders SA et al, *JACI* 2014

FATTORI RITENUTI RESPONSABILI DEL PEGGIORAMENTO DEI SINTOMI DA PAZIENTI CON FM

Perceived stressor	Frequency
Emotional distress	83%
Weather changes	80%
Sleeping problems	79%
Strenuous activity	70%
Mental stress	68%
Worrying	60%
Car travel	57%
Family conflicts	52%
Physical injuries	50%
Physical inactivity	50%
Infections	43%
Allergies	37%
Low to moderate physical activity	36%
Lack of emotional support	36%
Time zone changes	34%
Airplane travel	34%
Perfectionism	32%
Work related conflicts	29%
Menses	27%
Medication side effects	27%
Chemical exposures	27%
Sexual intercourse	17%

Bennett RM et al, *BMC Muscoloskel Dis* 2007

PREVALENCE OF FIBROMYALGIA IN PATIENTS WITH ALLERGIC RHINITIS



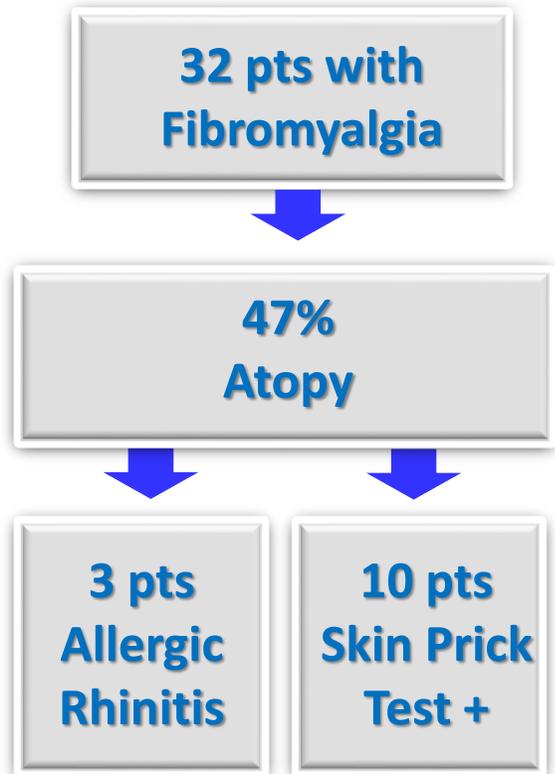
Rhinoconjunctivitis QoL and Nottingham Health Profile

	FM +	FM -	p
RQLQ activities	3.96 ± 1.47	3.25 ± 1.62	.024*
Sleep	3.74 ± 1.85	1.92 ± 1.53	<.001*
Nonhay fever symptoms	4.73 ± 1.21	2.97 ± 1.78	<.001*
Practical problems	3.93 ± 2.17	3.41 ± 1.75	.108
Nasal problems	4.39 ± 1.48	3.77 ± 1.53	.028*
Eye symptoms	3.72 ± 1.76	3.26 ± 1.80	.227
Emotions	4.89 ± 1.43	2.69 ± 1.85	<.001*
Over all quality of life	4.12 ± 0.81	3.21 ± 2.10	<.001*
NHP part 1			
Pain	45.94 ± 30.43	8.06 ± 15.42	<.001*
Emotional reactions	54.41 ± 31.29	14.92 ± 21.16	<.001*
Sleep	46.96 ± 30.87	15.93 ± 25.81	<.001*
Social isolation	27.15 ± 34.51	7.32 ± 21.13	<.001*
Physical mobility	18.53 ± 17.83	4.87 ± 11.12	<.001*
Energy	81.6 ± 31.41	30.86 ± 38.18	<.001*
NHP part 2	1.74 ± 2.10	0.53 ± 1.33	<.001*

Gultuna S et al, Am J Rhinol All 2019

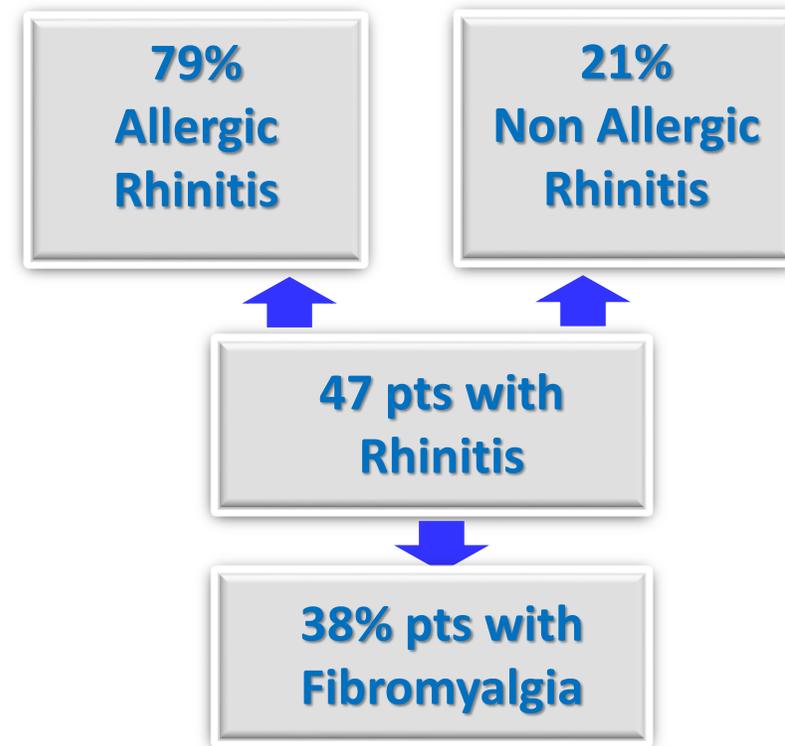
RELATIONSHIP BETWEEN FIBROMYALGIA, ALLERGY AND RHINITIS

Prevalence of Allergy in FM



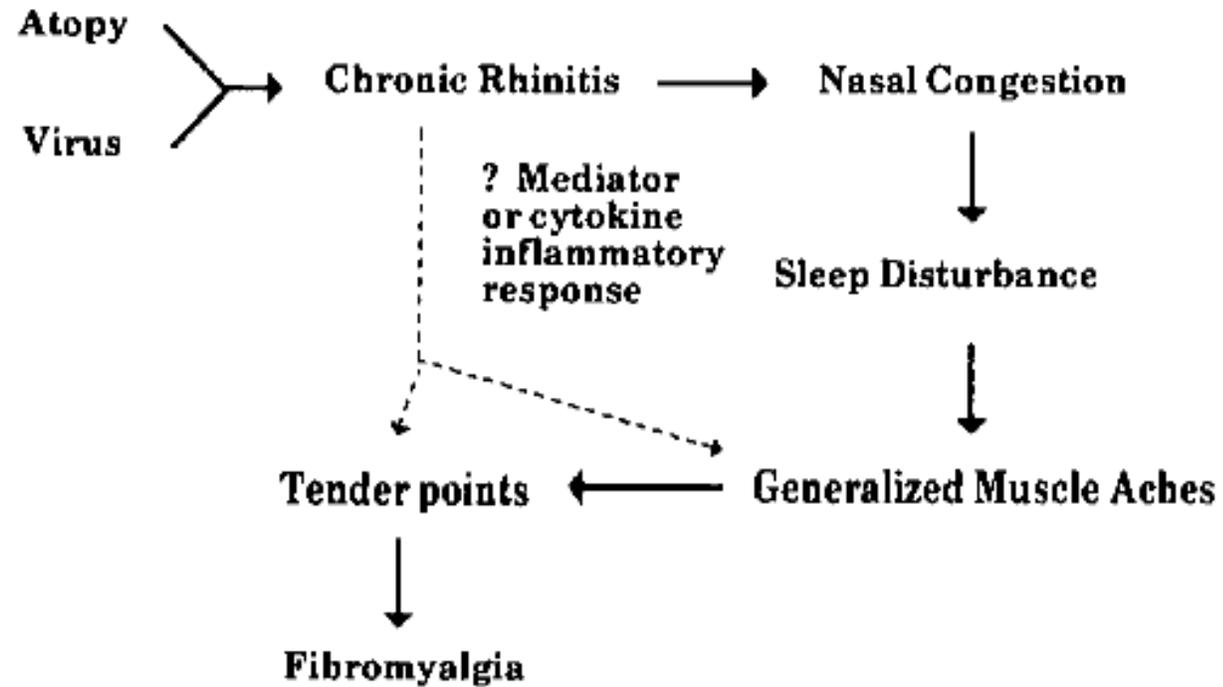
Tuncer T et al, *Clin Rheumatol* 1997

Prevalence of FM in Rhinitis



Cleveland CH Jr et al, *Allergy Proc* 1992

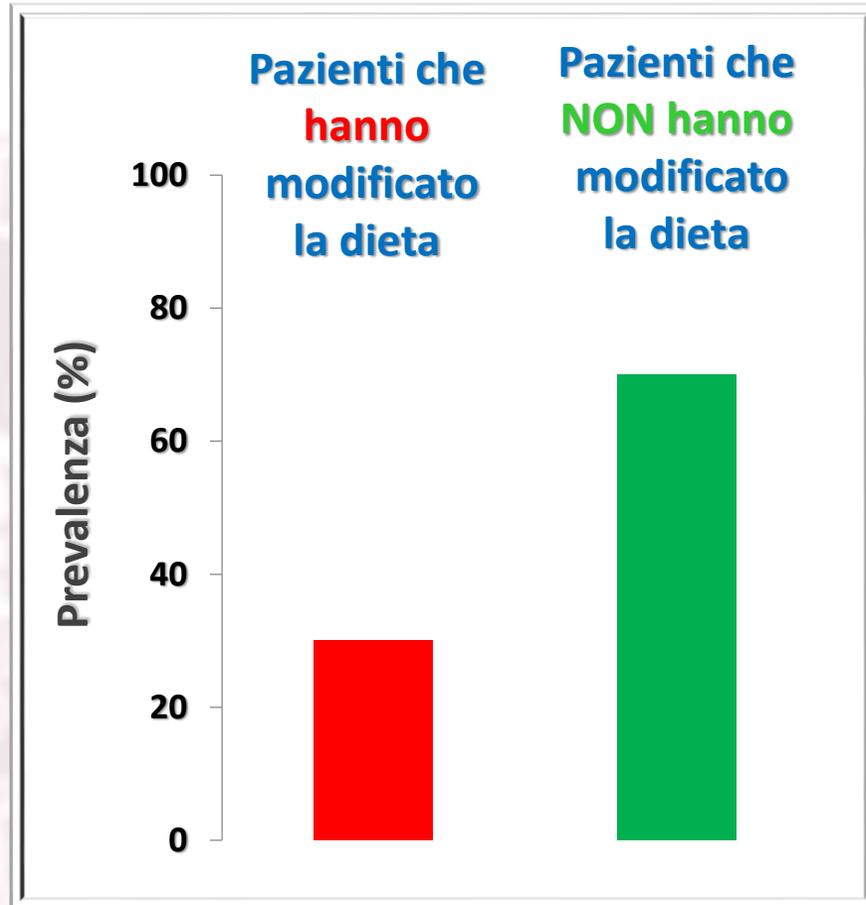
RELATIONSHIP BETWEEN FIBROMYALGIA, ALLERGY AND RHINITIS



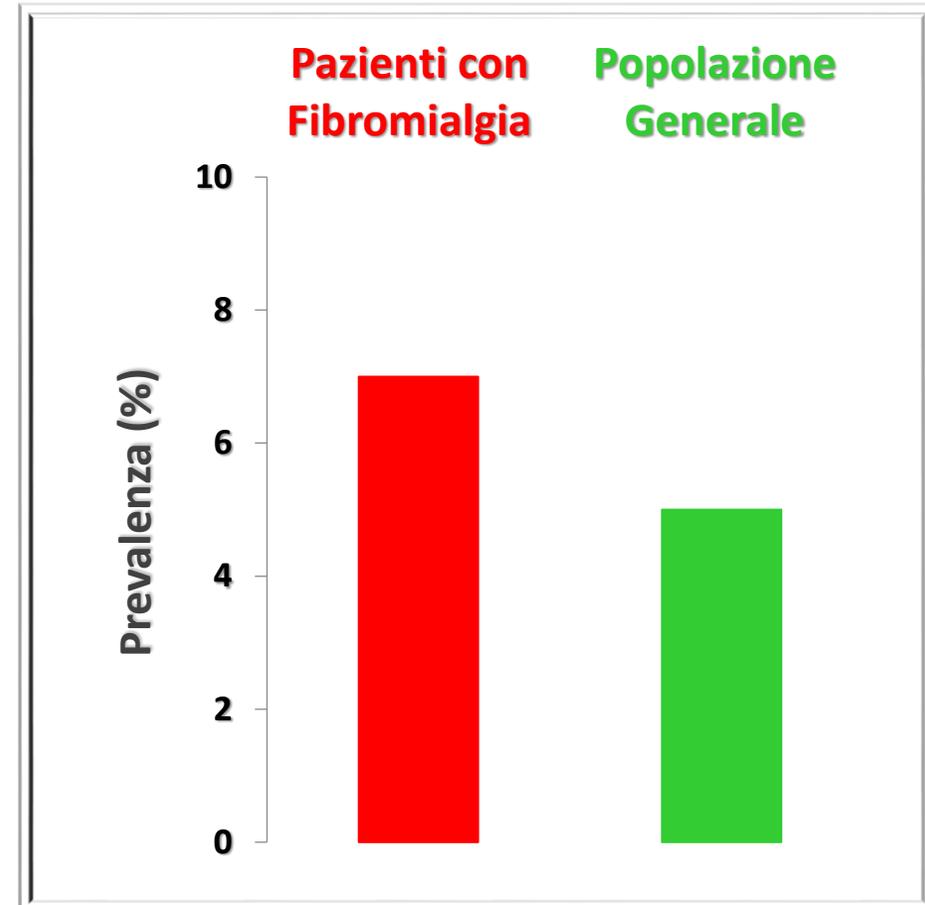
Cleveland CH Jr et al, *Allergy Proc* 1992

MODIFICAZIONE DELLA DIETA ALLA DIAGNOSI IN PAZIENTI CON FM

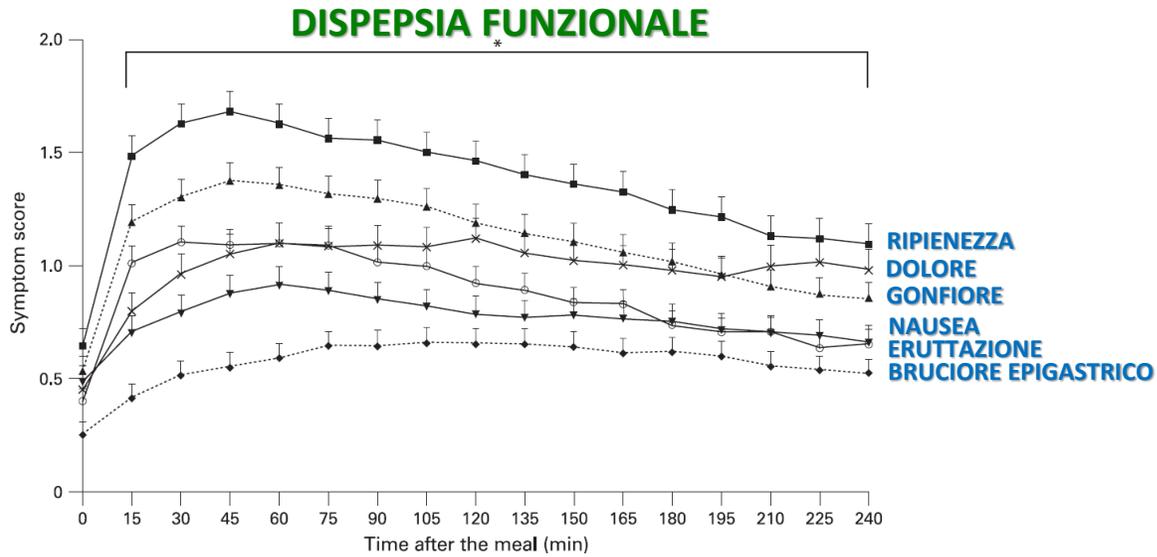
Prevalenza di modificazioni della dieta alla diagnosi di Fibromialgia



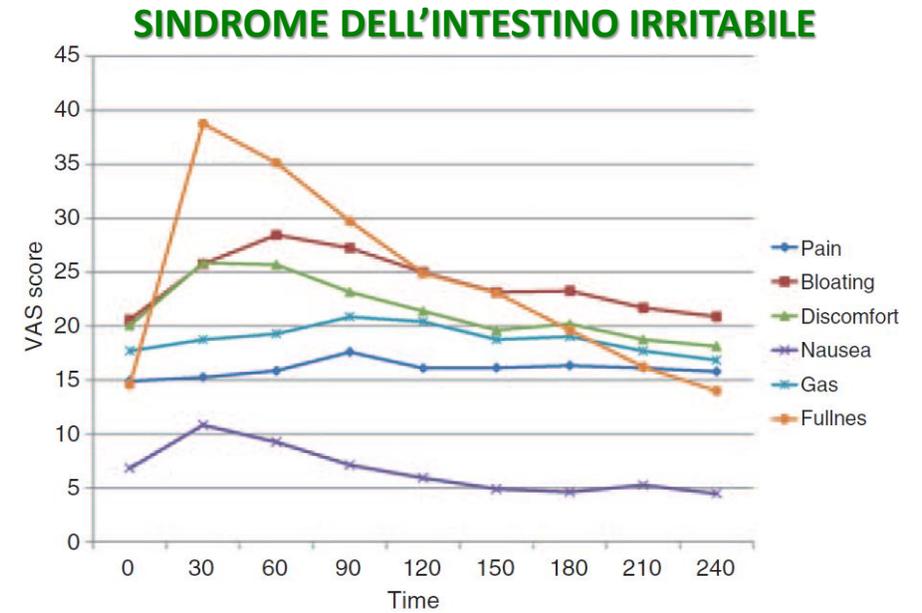
Prevalenza di reazioni avverse al cibo alla diagnosi di Fibromialgia



SINTOMI INDOTTI DAL PASTO IN PAZIENTI CON PATOLOGIA FUNZIONALE GASTROINTESTINALE

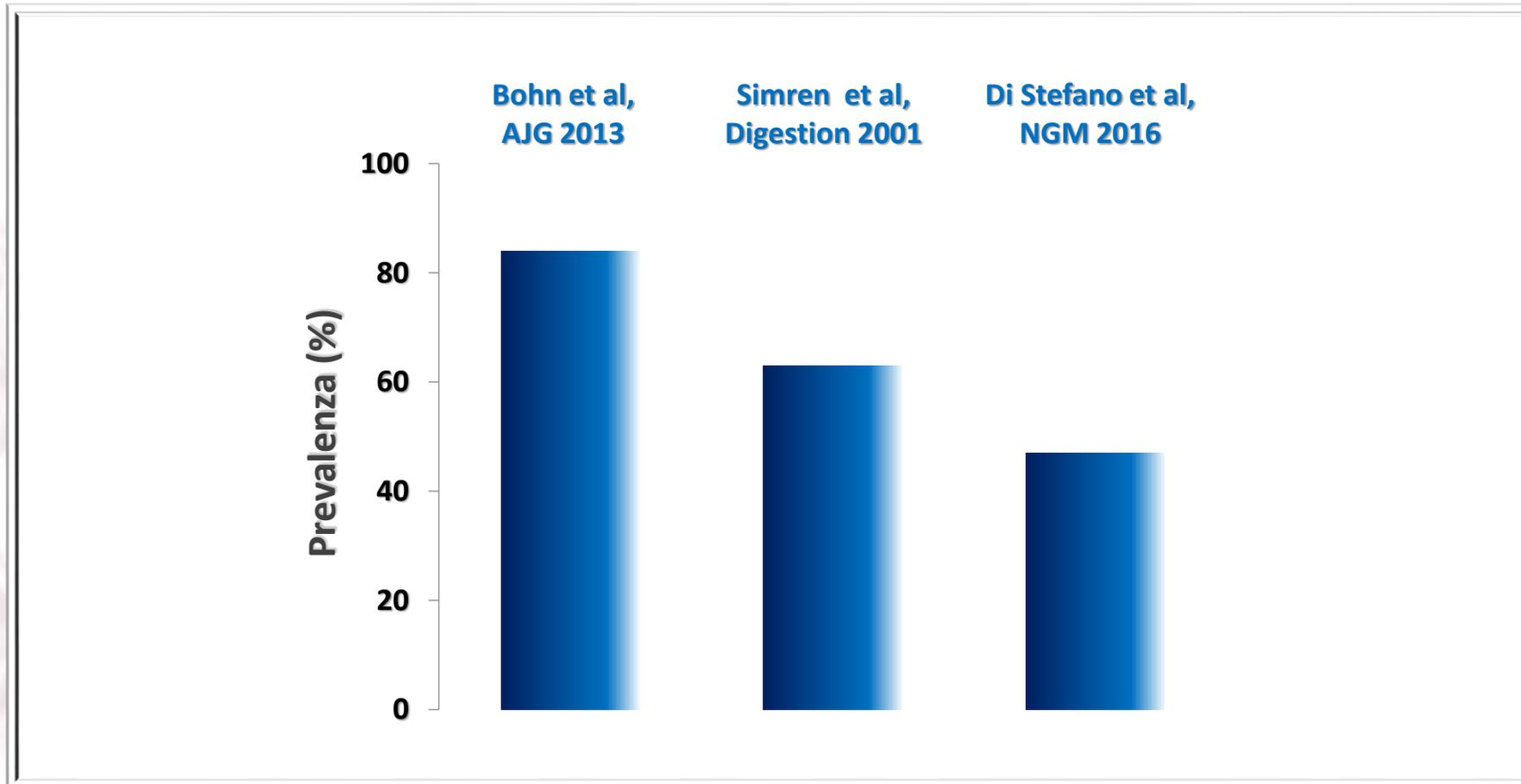


Bisshops R et al, *Gut* 2008



Posserud I et al, *UEGJ* 2013

PREVALENCE OF POST-PRANDIAL SYMPTOMS IN IRRITABLE BOWEL SYNDROME



FREQUENZA DI SINTOMI E COMORBIDITA' NELLA FIBROMIALGIA

La sindrome dell'intestino irritabile rappresenta il disordine gastrointestinale **più comunemente correlato** alla fibromialgia con tassi di prevalenza che variano dal **32% all'81%**, a seconda dei criteri diagnostici utilizzati

Sperber AD et al, *AJG* 1999
Kurland JE et al, *Dig Dis Sci* 2006
Sperber AD et al, *JNM* 2010

FREQUENZA DI SINTOMI E COMORBIDITA' NELLA FIBROMIALGIA

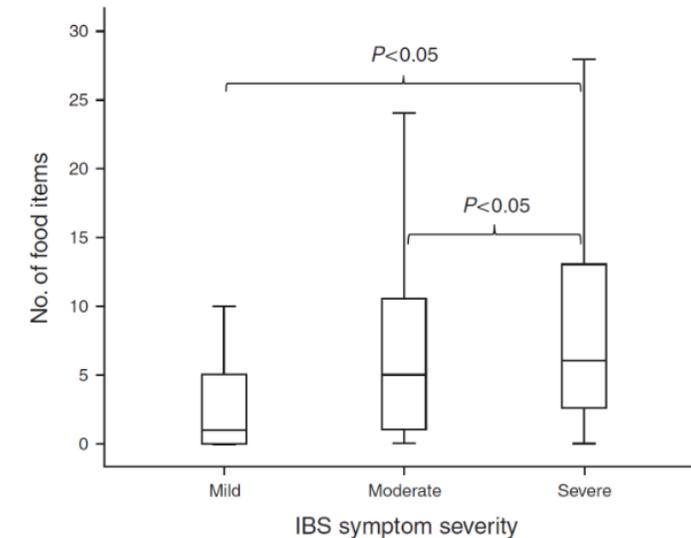
Current Symptom	Frequency
Low back pain	63%
Recurrent headaches	47%
Arthritis	46%
Muscle spasm	46%
Tingling	46%
Balance problems	45%
Irritable bowel syndrome	44%
Numbness	44%
Chronic fatigue	40%
Bloating	40%
Depression	40%
Anxiety	38%
Sinus problems	37%
Tooth disorders	32%
Restless legs	32%
Tinnitus	30%
Jaw pain	29%
Bladder problems	26%
Rashes	25%

Bennett RM et al, *BMC Musculoskel Dis* 2007

ALIMENTI RESPONSABILI DI SINTOMI MODERATO/SEVERI NELL'IBS

		Number of patients with			
		moderate symptoms	severe symptoms	very severe symptoms	total
Animal products	Pork	37 (11%)	10 (3%)	5 (2%)	52 (16%)
	Beef	35 (11%)	12 (4%)	4 (1%)	51 (15%)
	Egg	41 (12%)	23 (7%)	12 (4%)	76 (23%)
	Cheese	43 (13%)	16 (5%)	8 (2%)	67 (20%)
	Cream	56 (17%)	37 (11%)	30 (9%)	122 (37%)
	Milk	49 (15%)	28 (8%)	22 (7%)	99 (30%)
Cereal products	Pasta	34 (10%)	8 (2%)	2 (0.6%)	44 (13%)
	Wheat bran	26 (8%)	9 (3%)	9 (3%)	44 (13%)
	Breakfast cereals	27 (8%)	5 (2%)	1 (0.3%)	33 (10%)
	Crispbread	38 (12%)	8 (2%)	5 (2%)	51 (16%)
	Wholemeal bread	52 (16%)	21 (6%)	8 (2%)	81 (25%)
	White bread	39 (12%)	16 (5%)	8 (2%)	63 (19%)
Fruits and vegetables	Citrus fruits	43 (13%)	20 (6%)	12 (4%)	75 (23%)
	Bananas	30 (9%)	8 (2%)	9 (3%)	47 (14%)
	Pears	38 (12%)	20 (6%)	5 (2%)	63 (19%)
	Apples	52 (16%)	31 (9%)	13 (4%)	96 (29%)
	Tomatoes	26 (8%)	10 (3%)	3 (1%)	39 (12%)
	Red/green pepper	53 (16%)	37 (11%)	23 (7%)	113 (34%)
	Raw vegetables	65 (20%)	31 (9%)	15 (5%)	111 (34%)
	Cabbage	82 (25%)	63 (19%)	43 (13%)	188 (57%)
	Onion	82 (25%)	66 (20%)	38 (12%)	186 (56%)
	Peas/beans	86 (26%)	45 (14%)	22 (7%)	153 (46%)
	Maize	32 (10%)	10 (3%)	9 (3%)	51 (15%)
Potatoes	13 (4%)	5 (2%)	3 (1%)	21 (6%)	
Various products	Hot spices	72 (22%)	53 (16%)	24 (7%)	149 (45%)
	Chewing gums	43 (13%)	31 (9%)	10 (3%)	84 (26%)
	Chocolate	62 (19%)	21 (6%)	9 (3%)	92 (28%)
	Pastries	69 (21%)	26 (8%)	14 (4%)	109 (33%)
	Fried food	68 (21%)	33 (10%)	14 (2%)	115 (35%)
	Deep-fried food	62 (19%)	51 (15%)	33 (10%)	145 (44%)
	Smoked food	48 (15%)	51 (15%)	17 (5%)	116 (35%)
	Alcohol	68 (21%)	30 (9%)	12 (4%)	110 (33%)
	Tea	27 (8%)	14 (4%)	3 (1%)	44 (13%)
	Coffee	72 (22%)	29 (9%)	27 (8%)	128 (39%)
	Pizza	76 (23%)	42 (13%)	27 (8%)	144 (44%)

Numero di alimenti che causano sintomi e severità dell'IBS



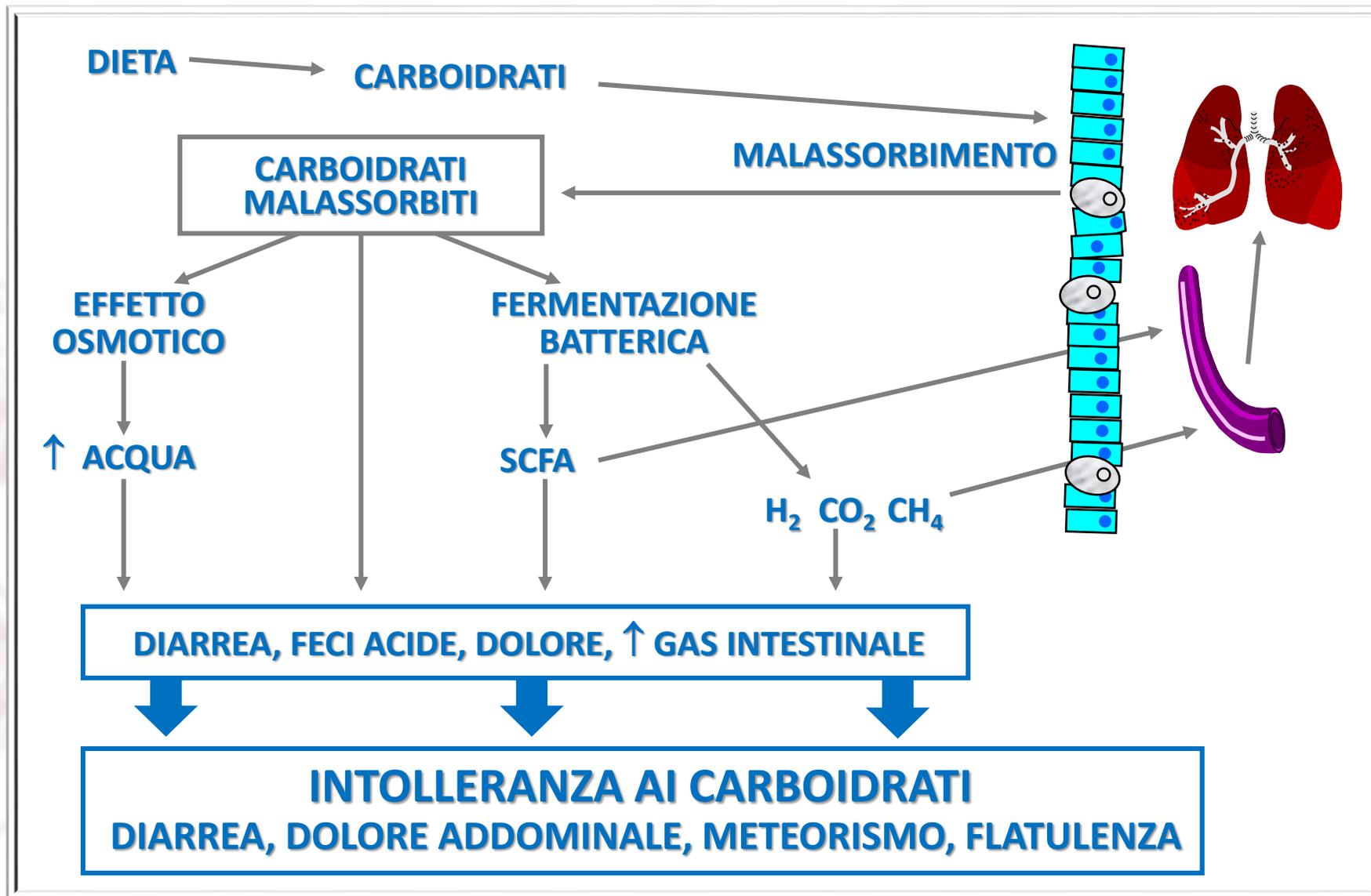
Bohn L et al, *AJG* 2013

EFFETTO DELLA FIBRA ALIMENTARE IN PAZIENTI CON IBS

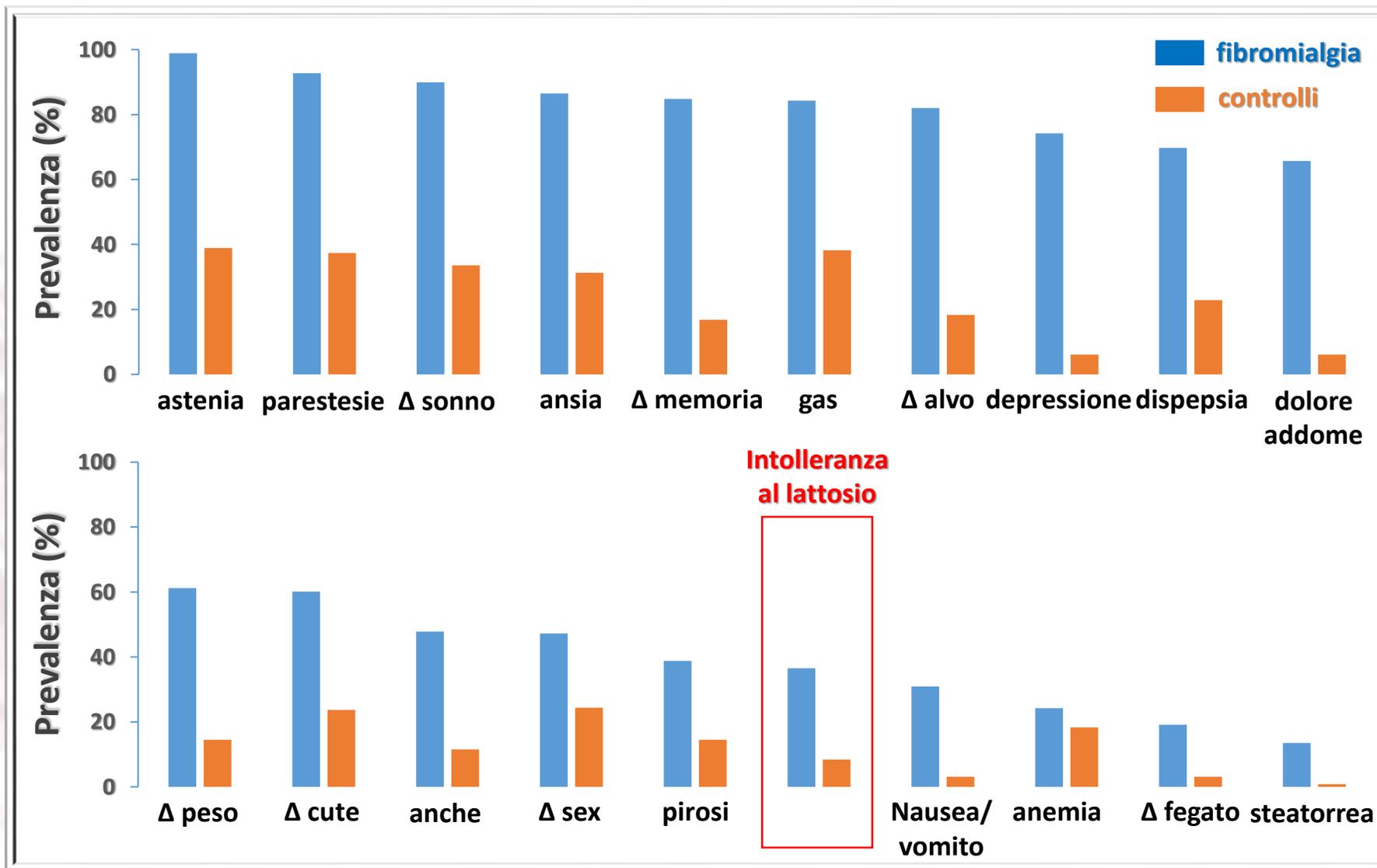
Alimento	Miglioramento (%)	Peggioramento (%)	Invariato (%)
Fibra alimentare	10	55	35
Cornflakes	0	0	100
Riso soffiato croccante	0	0	100
Porridge	0	12	88
Muesli	0	27	73
Ortaggi/Verdure	3	25	72
Frutta	5	45	50
Legumi	0	25	75
Frutta secca	0	27	73

Francis & Whorwell, *Lancet* 1994

FISIOPATOLOGIA DEL MALASSORBIMENTO DI CARBOIDRATI



FREQUENZA DI SINTOMI CELIAC-LIKE IN 178 PAZIENTI CON FIBROMIALGIA

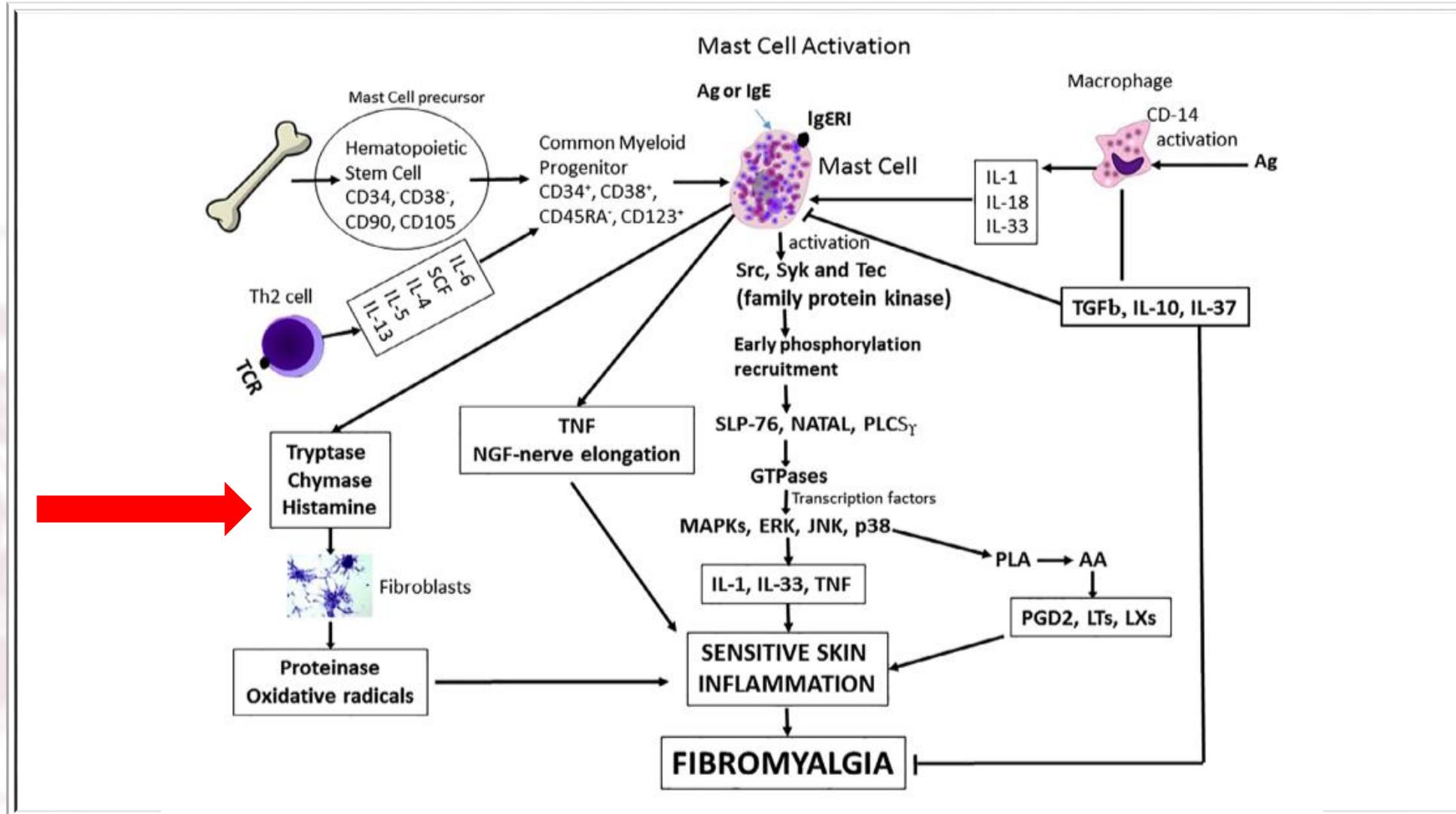


PRODOTTI CASEARI E SINTOMI DA INTOLLERANZA IN IBS

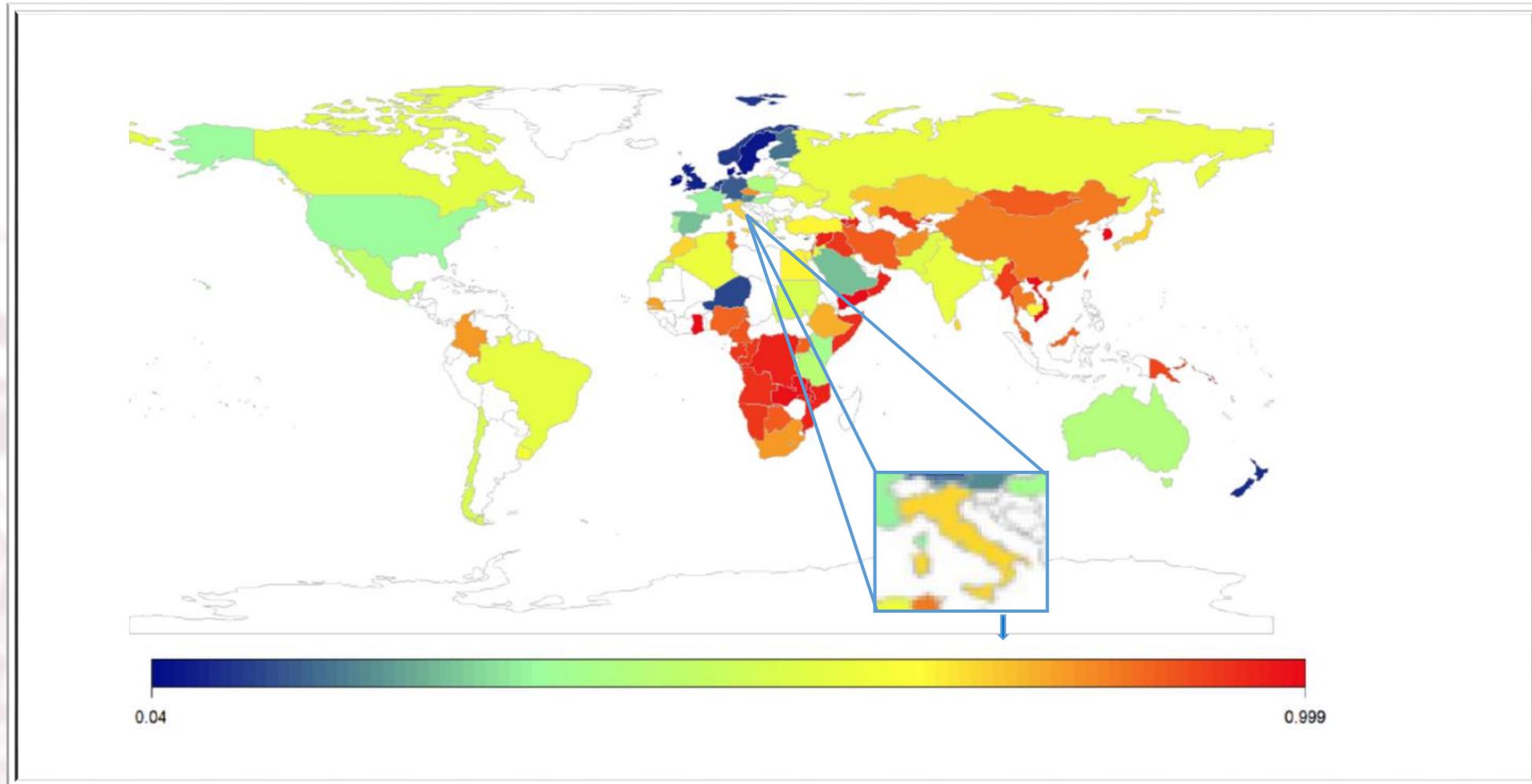
Food item/food group	Number of patients who reported GI symptoms with each food item/food group (n=197)
<i>Incompletely absorbed carbohydrates</i>	
Dairy products (milk, sour milk, yogurt, cheese)	97 (49.2%)
Beans/lentils	71 (36.0%)
Apple	55 (27.9%)
Flour (wheat and other)	48 (24.4%)
Plum	46 (23.4%)
Peas	38 (19.3%)
Chocolate	33 (16.8%)
Pear	31 (15.7%)
Bananas	25 (12.7%)
Dried fruit	25 (12.7%)
Nectarine	23 (11.7%)
Apricot	20 (10.2%)
Potato	20 (10.2%)
Cherries	19 (9.6%)
Peach	19 (9.6%)
Soy beans	11 (5.6%)
Melon	10 (5.1%)
Avocado	9 (4.6%)
Celery	8 (4.1%)
<i>Fatty/fried foods</i>	103 (52.3%)

Food item/food group	Number of patients who reported GI symptoms with each food item/food group (n=197)
<i>Histamine-releasing</i>	
Milk	85 (43.1%)
Wine/beer	61 (31.0%)
Pork	41 (20.8%)
Chocolate	33 (16.8%)
Orange	33 (16.8%)
Shellfish	25 (12.7%)
Strawberries	22 (11.2%)
Tomato	18 (9.1%)
Fish	10 (5.1%)
Egg	0

MAST CELL ACTIVATION IN SENSITIVE SKIN FROM FM PATIENTS



PREVALENCE OF LACTOSE MALABSORPTION



Misselwitz B et al, *Gut* 2019

CONSUMO PRO-CAPITE DI LATTE IN ITALIA

Indicatori		2012				2016			
	udm	LATTE tot.	UHT	FRESCO	ARRICCHITO	LATTE tot.	UHT	FRESCO	ARRICCHITO
<i>Indice di penetrazione</i>	(%)	96,8	86,2	54,5	35,8	96,4	86,3	51	34,3
<i>Acquirenti in promozione</i>	(%)	65,9	53,8	21,5	18,2	67,4	56,8	20,5	17
<i>Prezzo medio</i>	(€/Kg)	1,1	0,9	1,3	4,7	1,1	0,8	1,3	4,4
<i>Acquisto medio per famiglia/anno</i>									
- in volume	(Kg)	87,8	63,7	51,1	6	81,2	61,2	46,2	5,9
- in valore	(€)	97,7	55,3	67	28,6	87,3	51,6	60,3	26,1
<i>N. medio di atti d'acquisto/anno</i>	(n)	35,5	18,8	33,3	7,6	33,3	18,9	30,3	7,4
<i>Intervallo d'acquisto/anno</i>	(gg)	10,2	19,3	10,9	47,8	10,9	19,2	12	48,9
<i>Acquisto medio per atto</i>									
- in volume	(Kg)	2,5	3,4	1,5	0,8	2,4	3,2	1,5	0,8
- in valore	(€)	2,7	2,9	2	3,8	2,6	2,7	2	3,5

ISMEA su dati Nielsen Consumer Panel

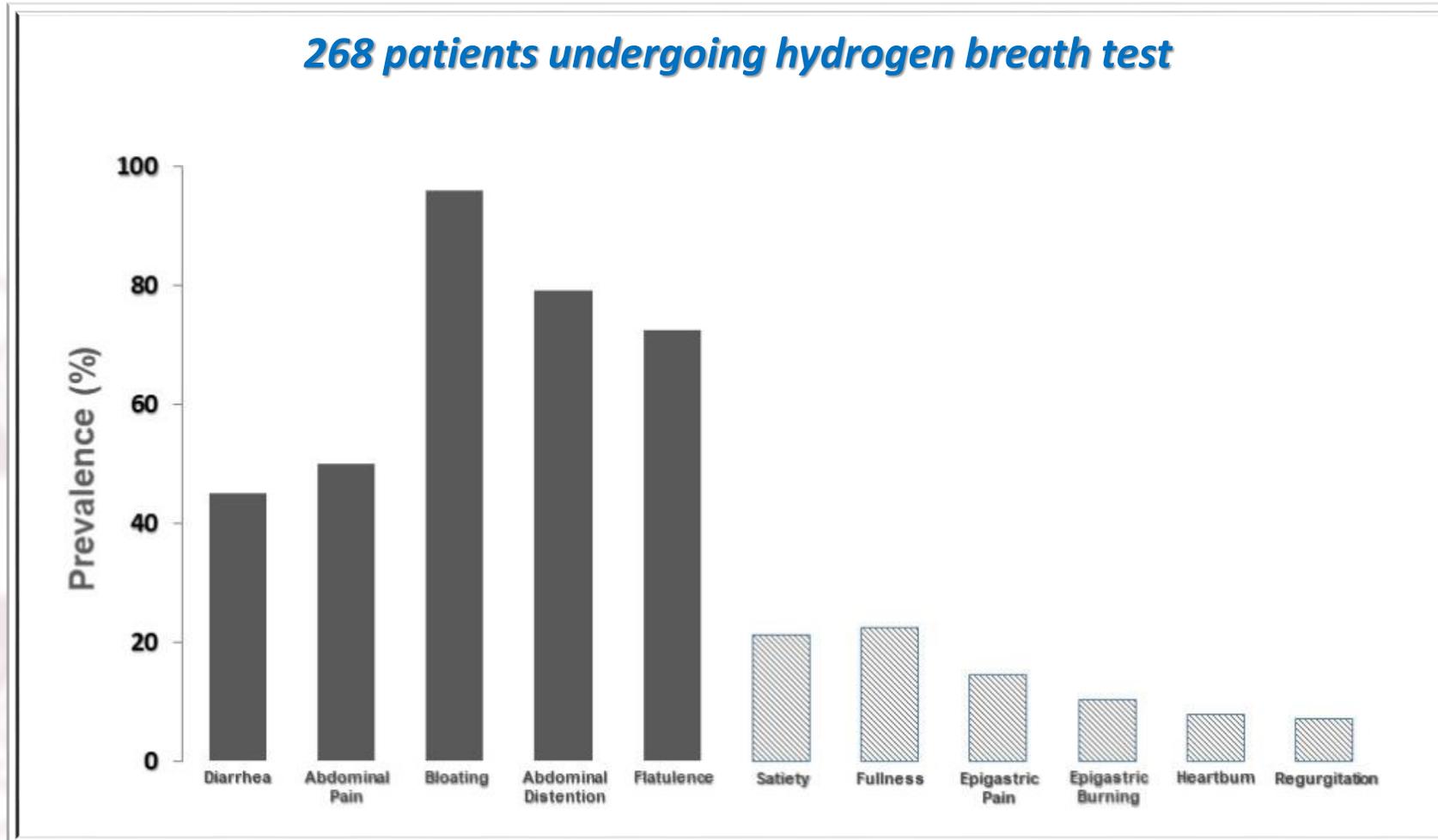
CONSUMO PRO-CAPITE DI LATTE NEL MONDO

Paese	2013 Kg	2014 Kg	2015 Kg	2016 Kg	2017 Kg	2018 Kg	± su 2017
Belarus	106,55	111,12	112,27	110,76	112,48	111,09	▼ -1,24%
Ukraine	117,83	123,39	120,58	117,94	113,02	110,48	▼ -2,25%
Australia	107,73	110,76	113,45	105,70	103,47	105,76	▲ +2,22%
New Zealand	99,82	108,39	107,69	106,63	105,61	105,26	▼ -0,33%
Canada	84,58	82,74	81,31	80,38	78,75	76,64	▼ -2,68%
United States *	77,42	74,66	73,07	72,07	70,02	68,00	▼ -2,89%
EU-28	66,91	67,16	66,47	65,86	65,61	65,38	▼ -0,34%
India	42,55	46,36	48,70	51,13	53,90	56,26	▲ +4,38%
Brazil	44,64	47,30	46,48	46,23	47,75	51,04	▲ +6,89%
Russia	70,68	68,58	66,02	62,24	59,41	50,83	▼ -14,44%
Argentina	48,75	47,76	48,25	39,18	37,97	39,63	▲ +4,37%
Mexico	33,95	33,65	33,24	32,80	32,32	31,99	▼ -1,01%
Japan	30,96	30,49	30,72	31,22	31,17	31,41	▲ +0,76%
South Korea	31,63	30,56	30,22	29,53	30,62	30,61	▼ -0,04%
Taiwan	15,25	15,76	16,35	16,85	17,27	17,73	▲ +2,65%
China	9,15	9,33	9,40	8,95	9,09	8,97	▼ -1,25%
Philippines	0,65	0,59	0,61	0,78	0,82	0,90	▲ +9,96%

5°

Ultimo aggiornamento: 12/02/2020

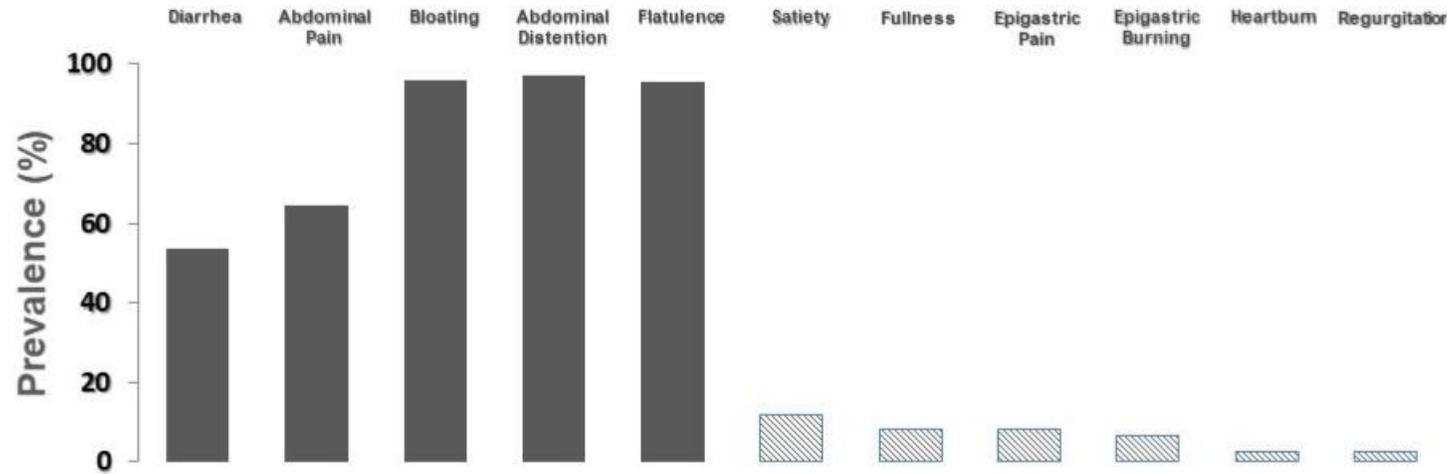
LACTOSE-RELATED SYMPTOMS REPORTED BY PATIENTS



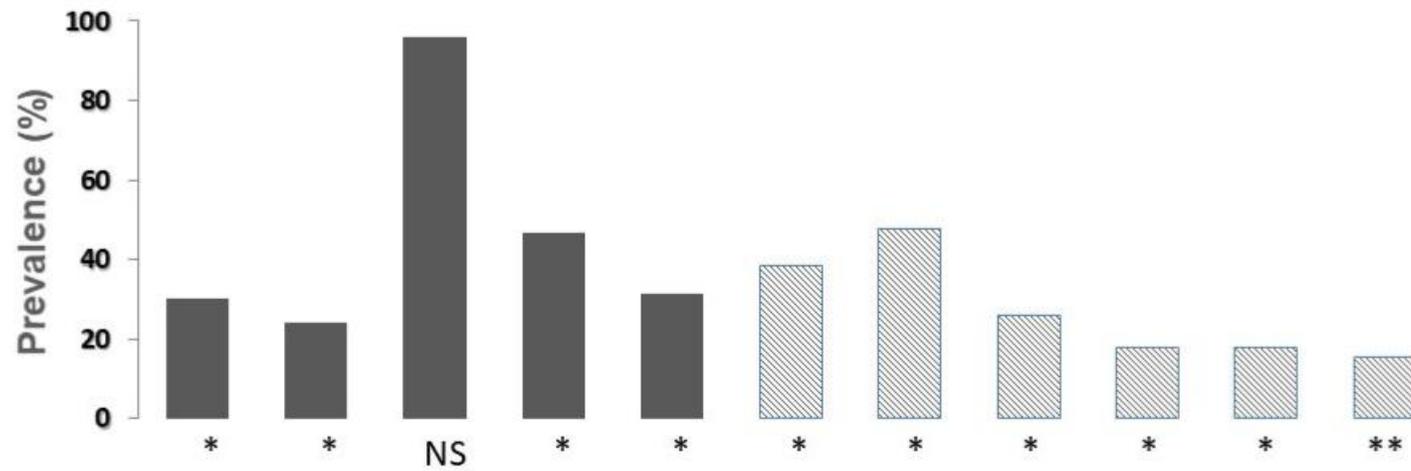
Di Stefano M et al, *Int J Environ Res Public Health* 2022

LACTOSE-RELATED SYMPTOMS REPORTED BY PATIENTS

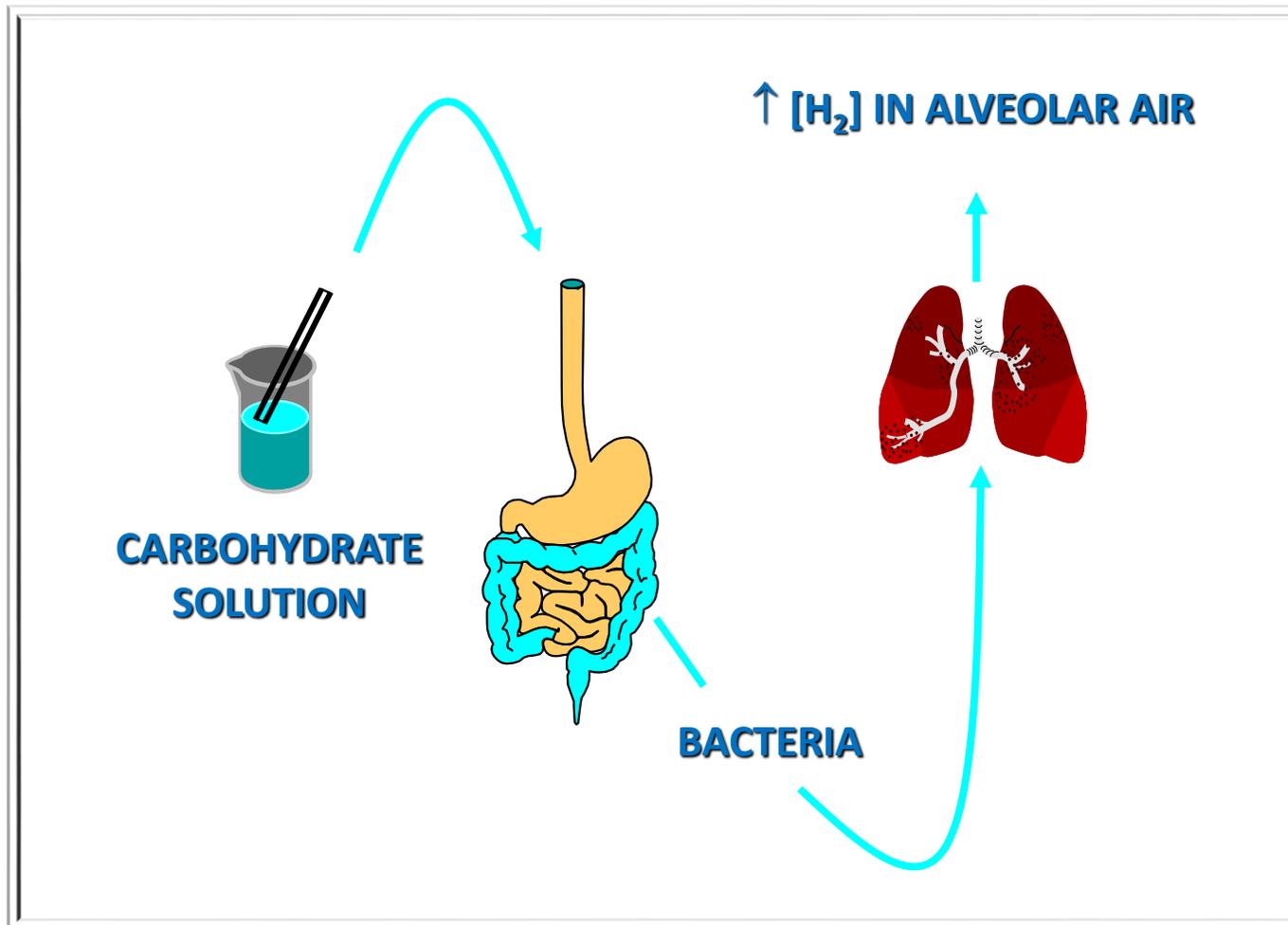
Patients with Lactose Malabsorption



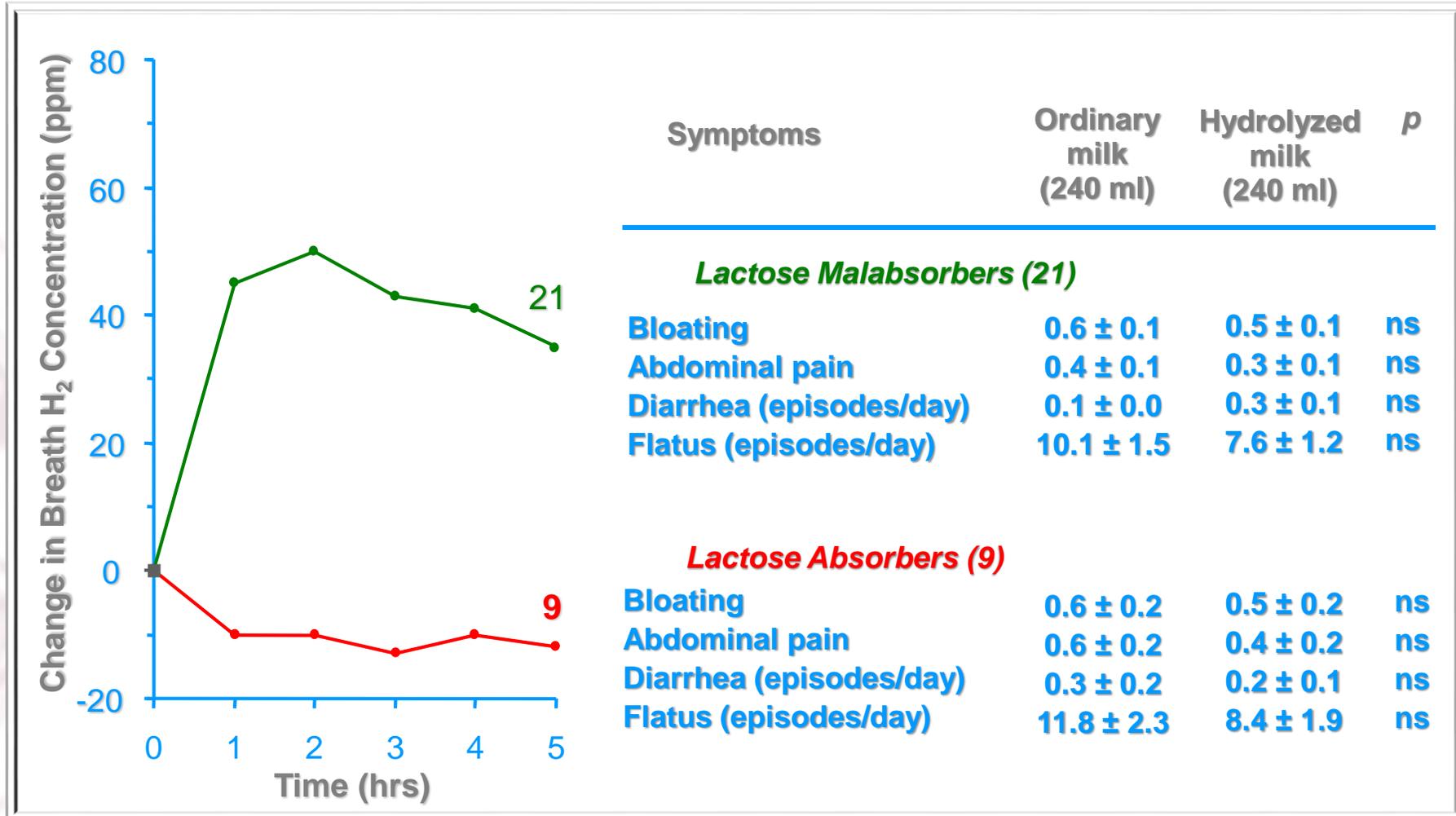
Patients with Normal Lactose Absorption



HYDROGEN BREATH TEST FOR CARBOHYDRATE MALABSORPTION

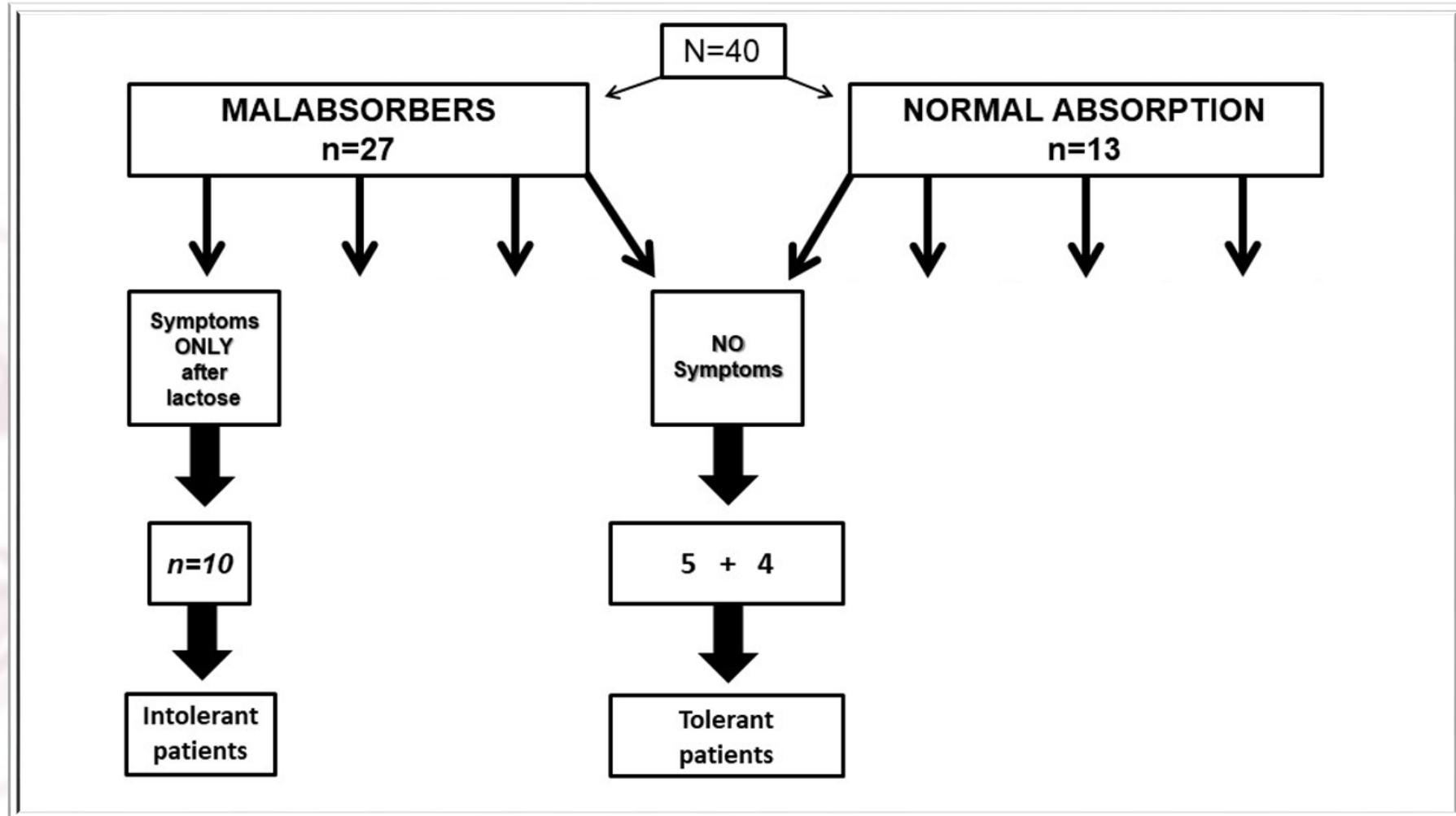


A RANDOMIZED, DOUBLE-BLIND, CROSSOVER TRIAL IN SELF-REPORTED SEVERE LACTOSE INTOLERANT PATIENTS



Suarez et al, *NEJM* 1995

SYMPTOM ONSET DURING BLINDED LACTOSE OR GLUCOSE BREATH TEST IN SELF-REPORTED LACTOSE INTOLERANCE

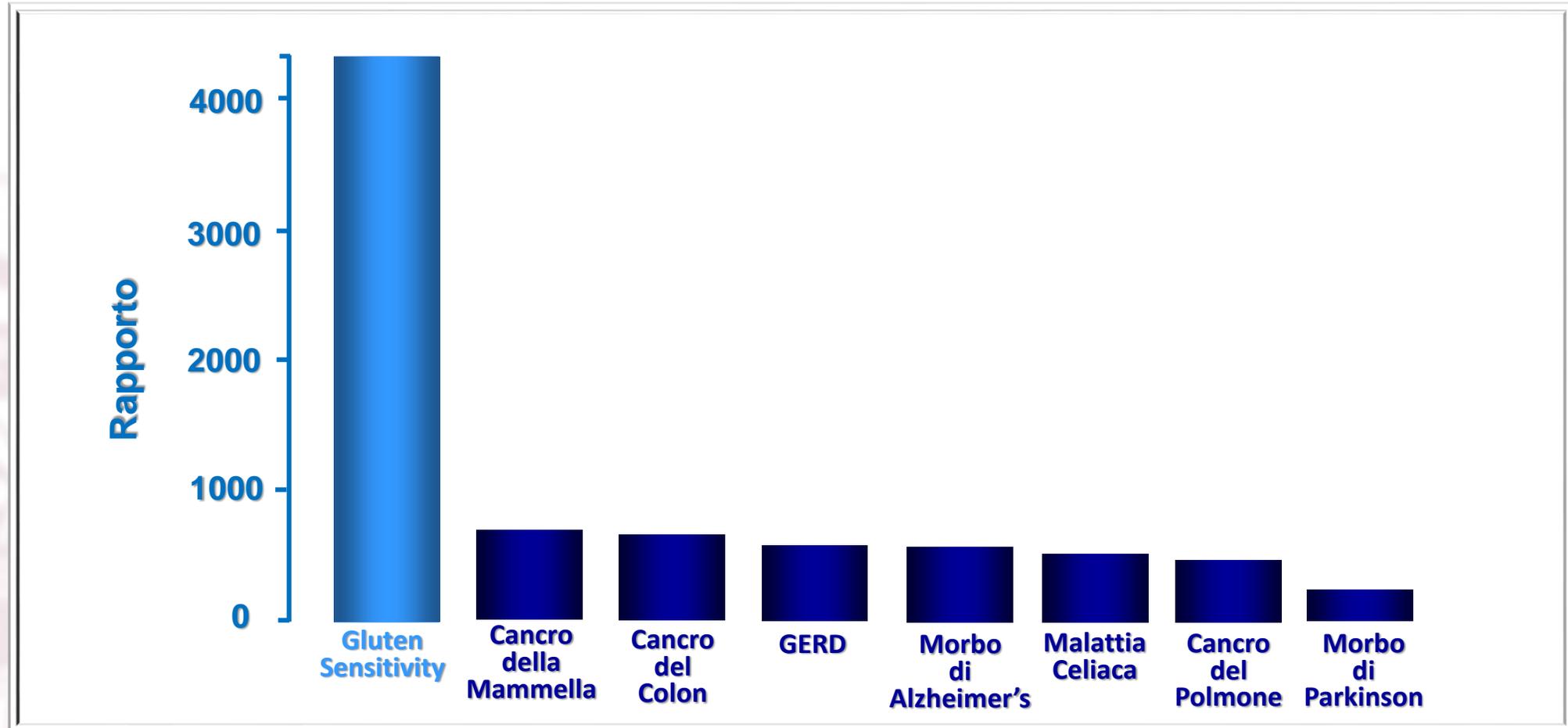


Di Stefano M et al, *Int J Environ Res Public Health* 2022

CARATTERISTICHE CLINICHE DELLA NON-CELIAC GLUTEN SENSITIVITY

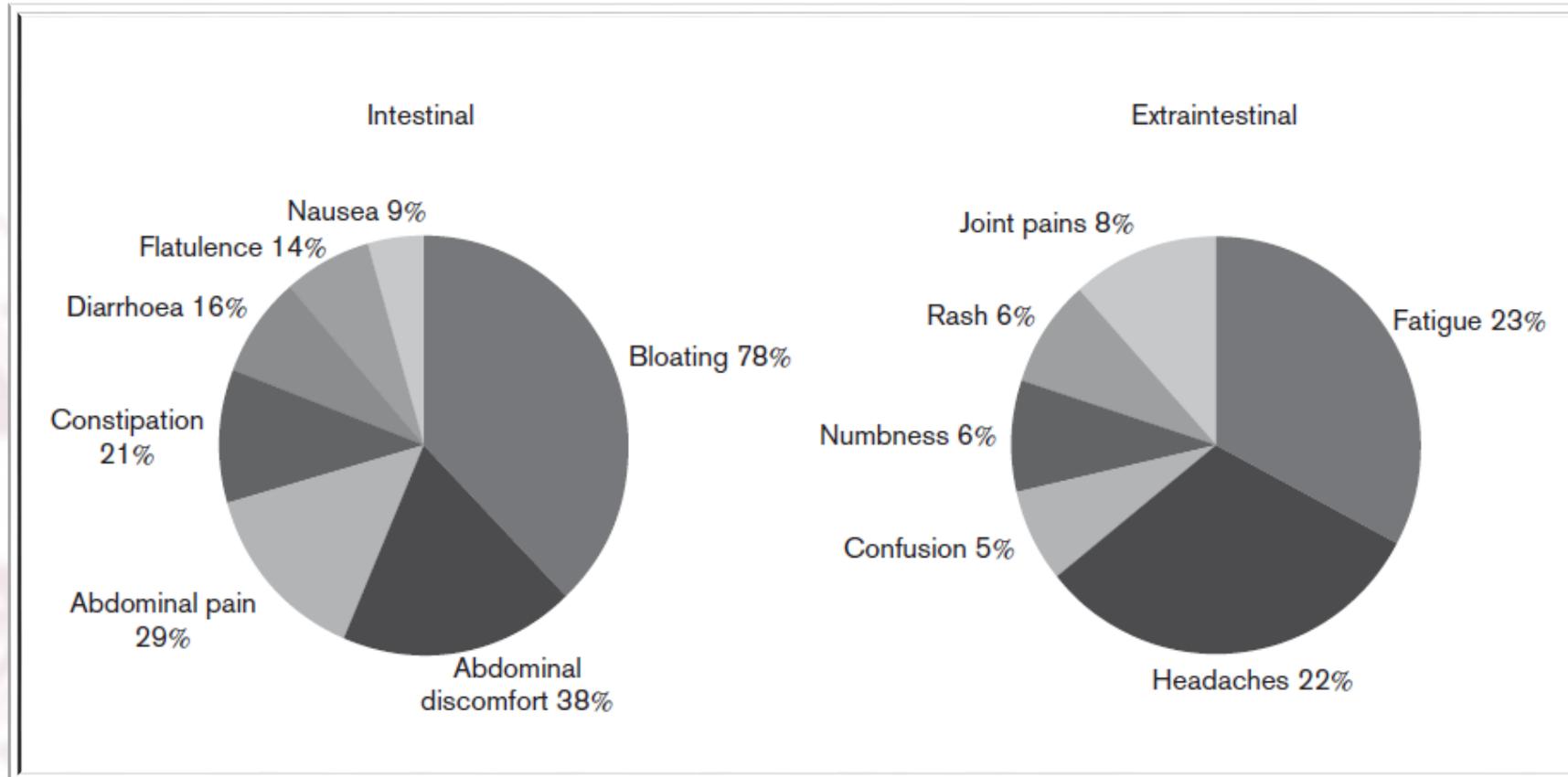
- Sintomi che **migliorano o scompaiono** dopo **abolizione del glutine** dalla dieta
- **Assenza** di lesioni intestinali
- **Negatività** degli anticorpi anti-transglutaminasi e anti-endomisio
- **Non associata** ad uno specifico pattern HLA
- Prevalenza **molto** elevata (6 volte > CD !)
- Standardized **mortality** ratio= 2.4 ?

NCGS – CITAZIONI SU GOOGLE / CITAZIONI SU PUBMED



Corazza GR, *Ann Intern Med* 2012

MANIFESTAZIONI CLINICHE DELLA NON-CELIAC GLUTEN SENSITIVITY

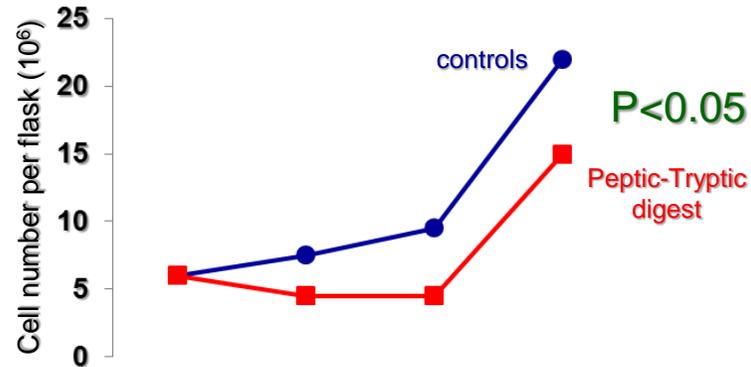


Aziz I, et al, *EJGH* 2013

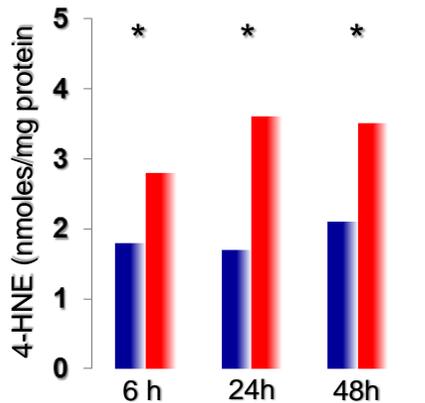
TOSSICITA' DEL GLUTINE *IN VITRO*

Incubazione con digesto peptico-triptico di comune pane di frumento

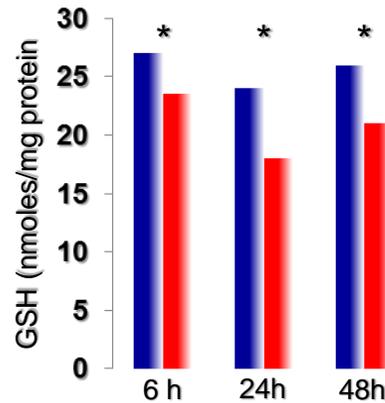
Replicazione di Cellule Intestinali Caco-2



Perossidazione lipidica

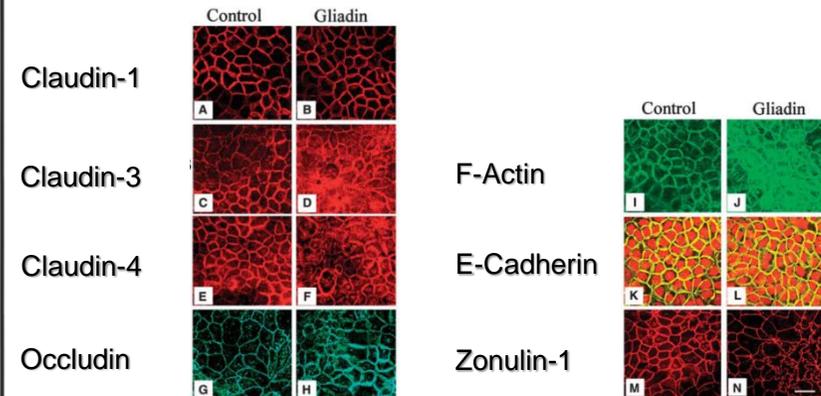
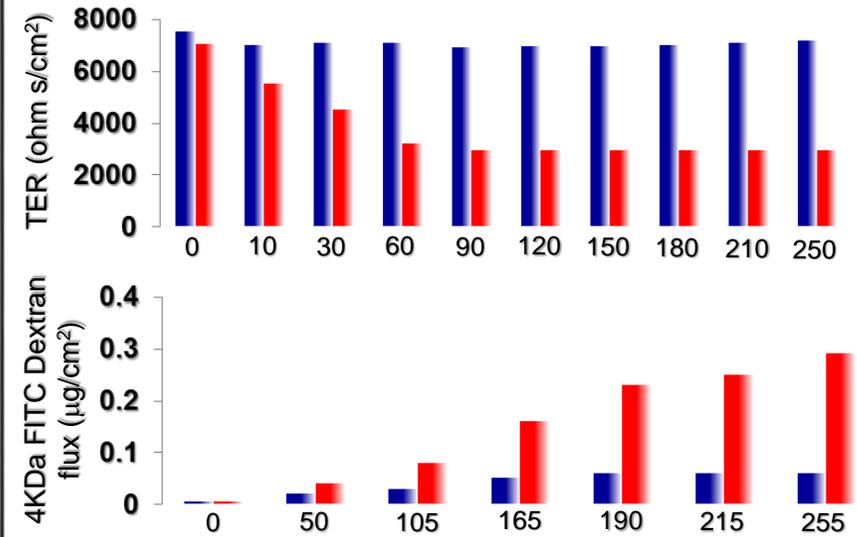


GSH Intracellulare



Rivabene R et al, *BBA* 1999

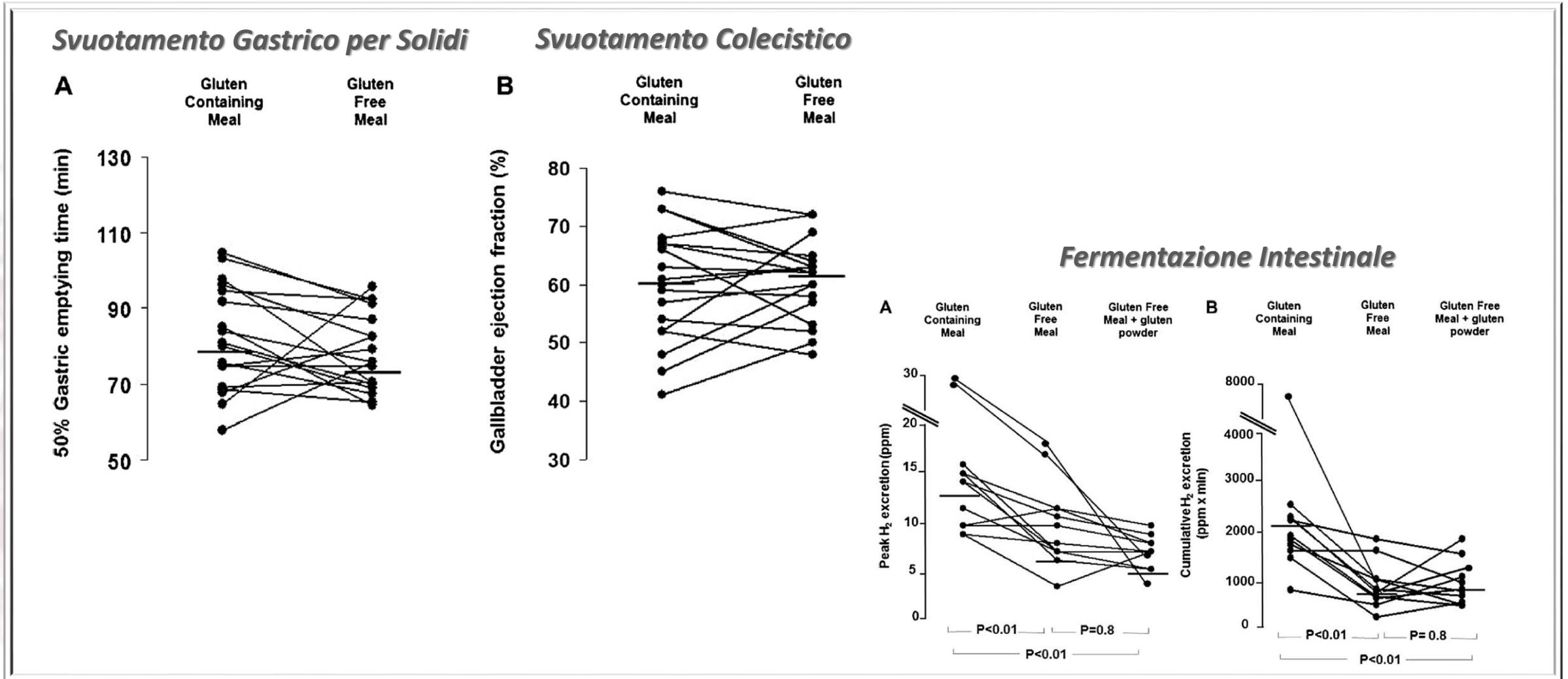
Permeabilità delle cellule Caco-2



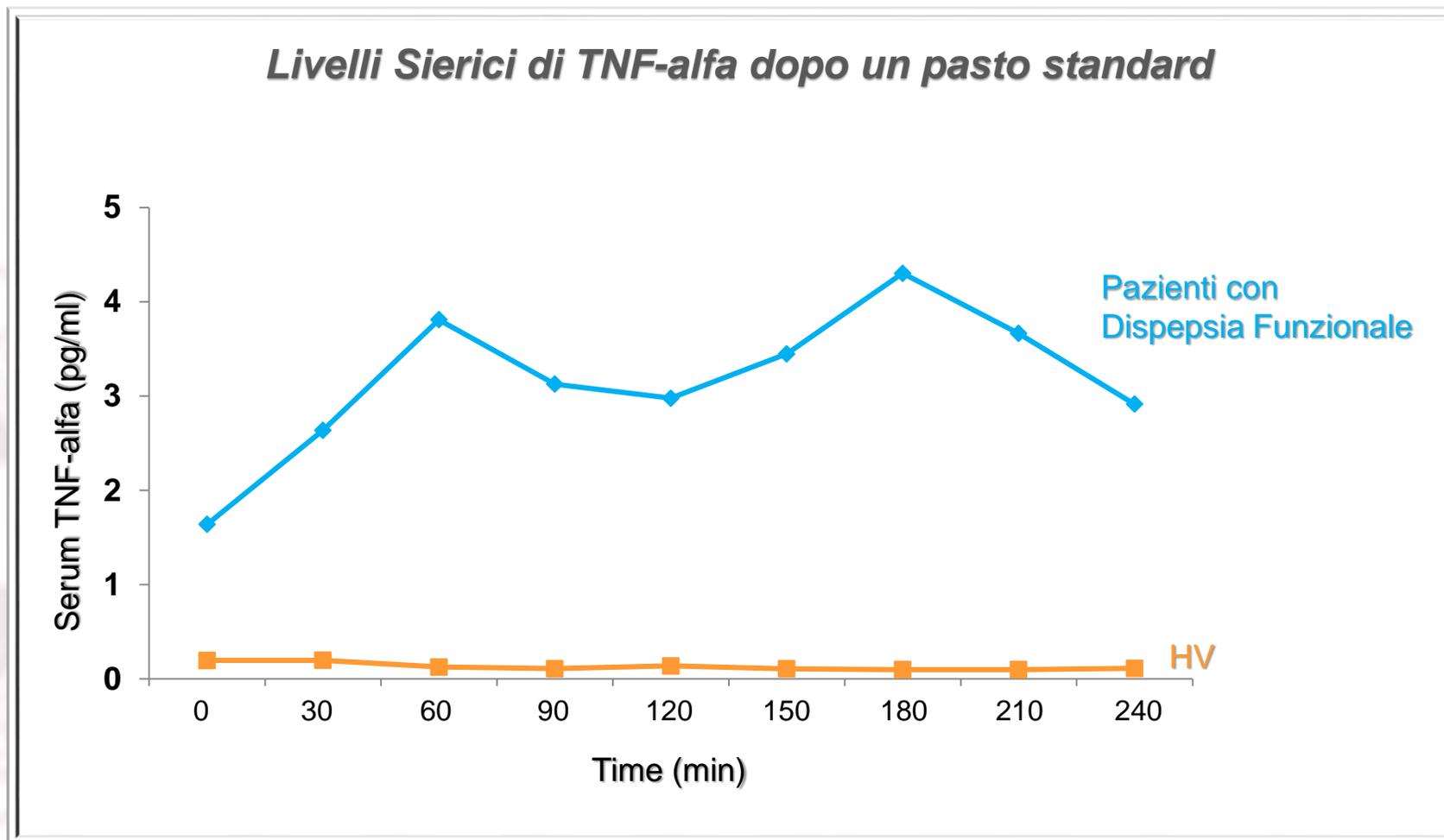
Sander GR et al, *FEBS Letters* 2005

TOSSICITA' DEL GLUTINE *IN VIVO*

Somministrazione di una porzione di pasta glutinata vs aglutinata in volontari sani

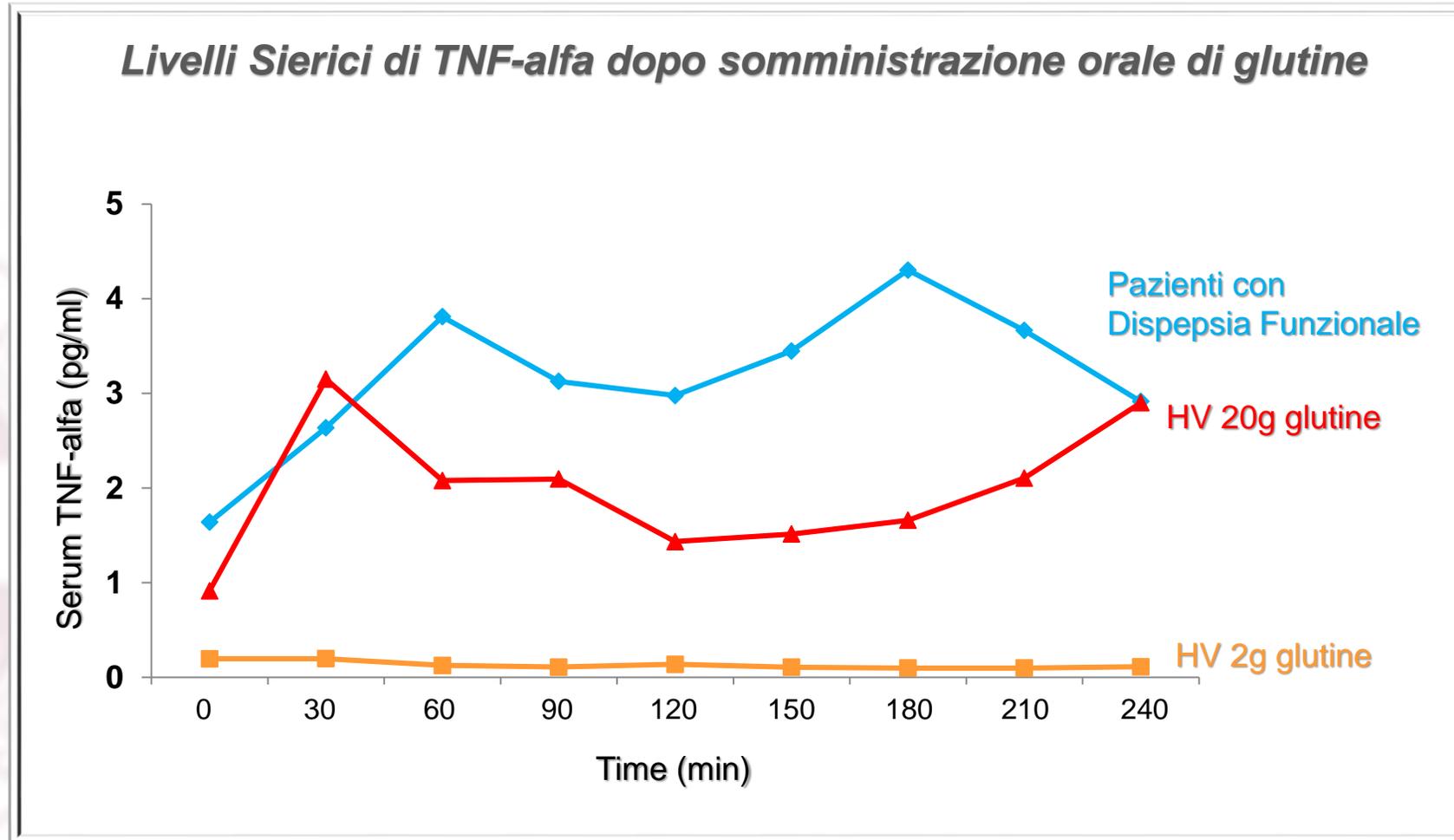


I SISTEMI PRO-INFIAMMATORI NEL POSTPRANDIUM



Di Stefano M, 2016

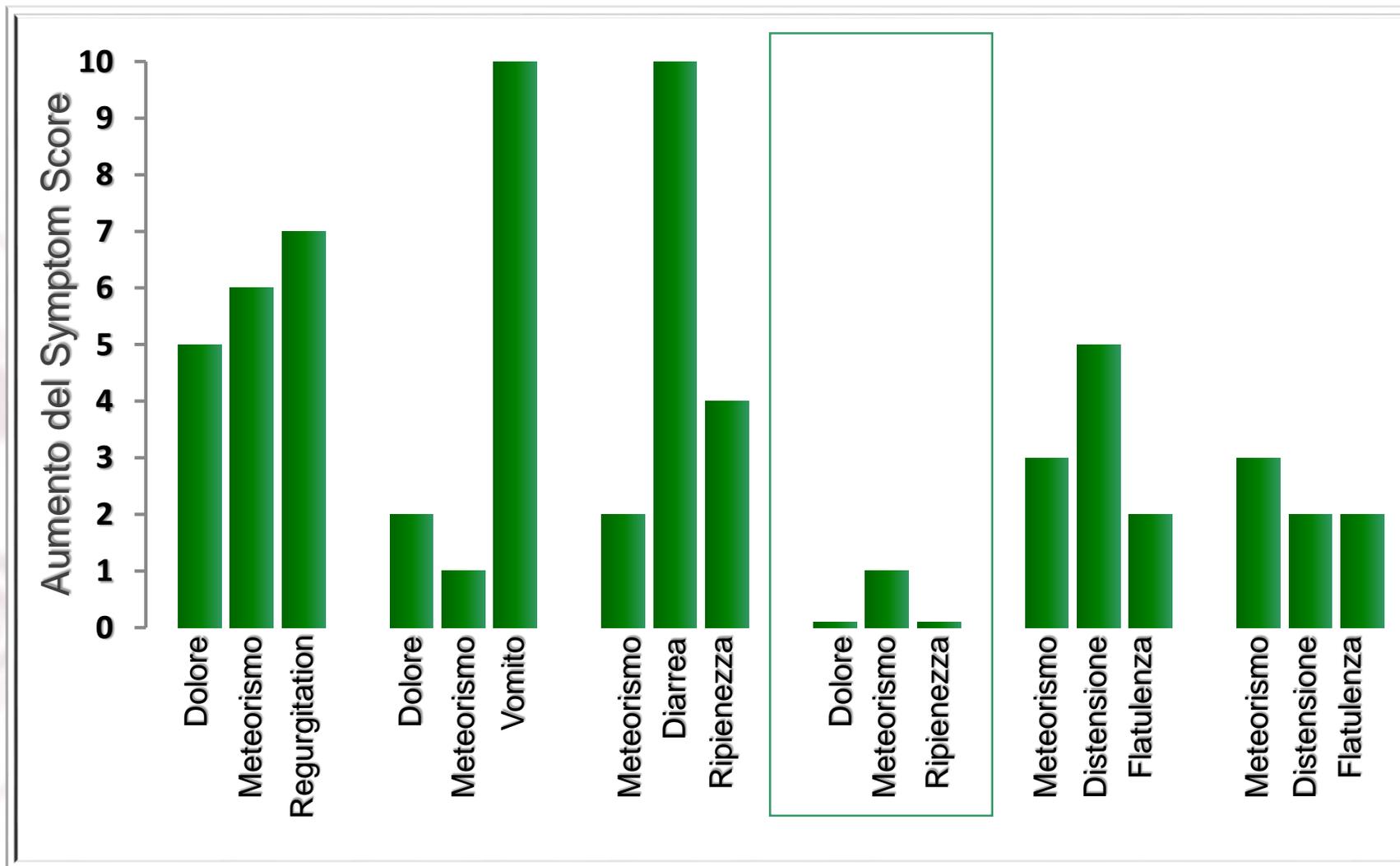
TOSSICITA' DEL GLUTINE *IN VIVO* IN VOLONTARI SANI



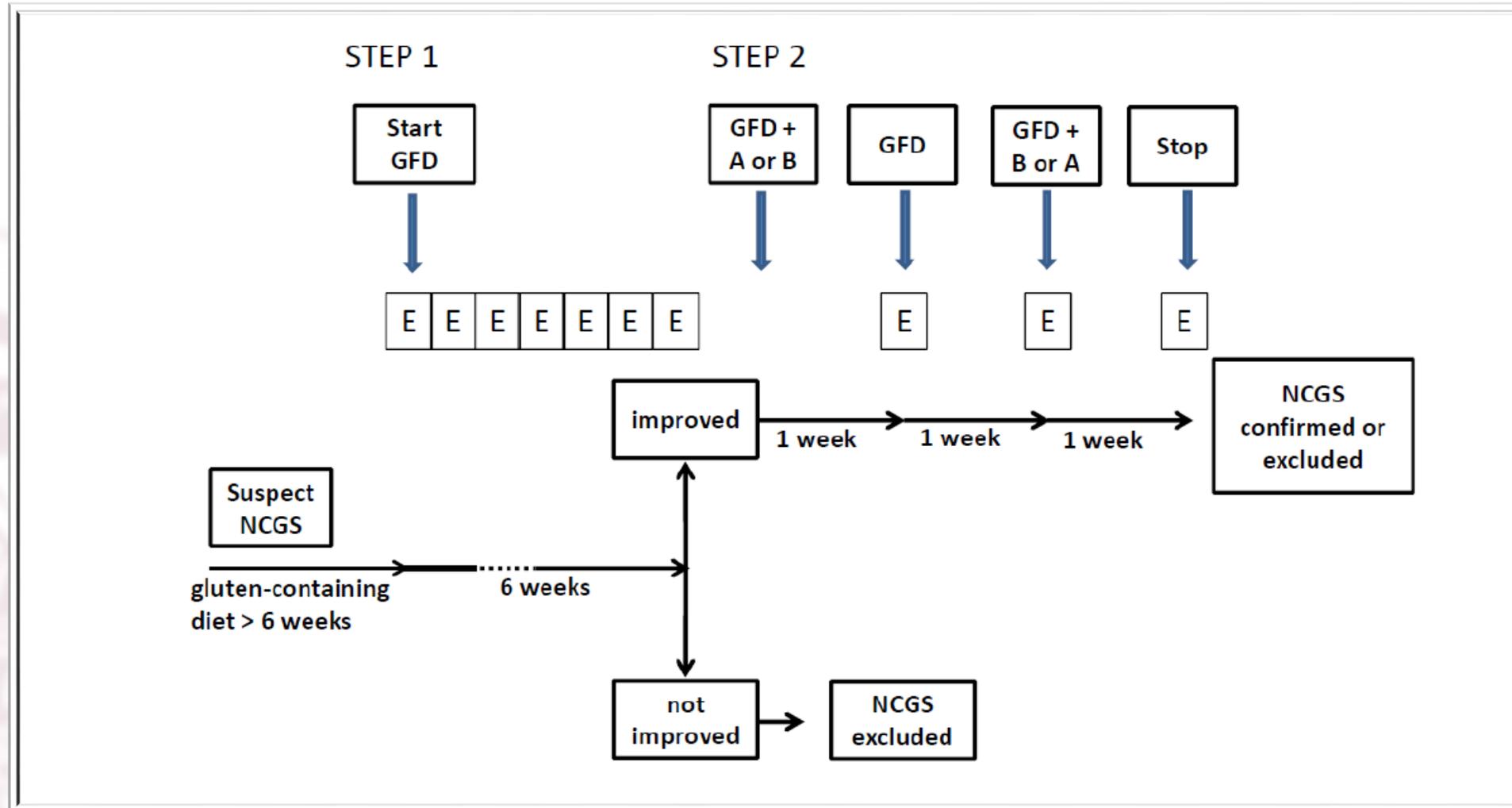
Di Stefano M, 2016

EFFETTO NOCEBO IN SELF-REPORTED NCGS

Peggioramento della severità dei sintomi dopo pasta gluten-free



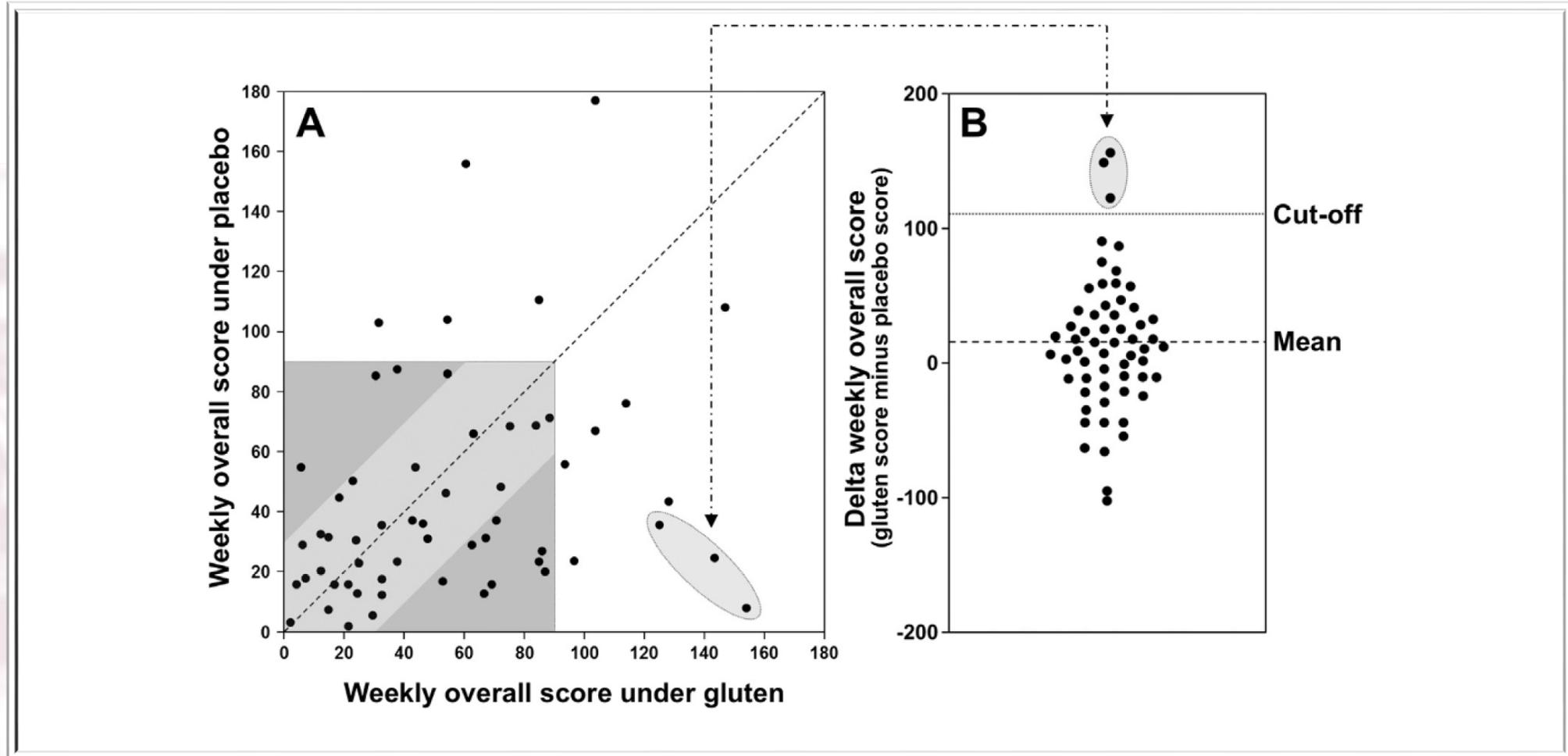
DOUBLE BLIND, PLACEBO CONTROLLED CHALLENGE GLUTEN vs PLACEBO IN NCGS



Catassi C et al, *Nutrients* 2015

BASSE DOSI DI GLUTINE IN PAZIENTI CON SOSPETTA NCGS

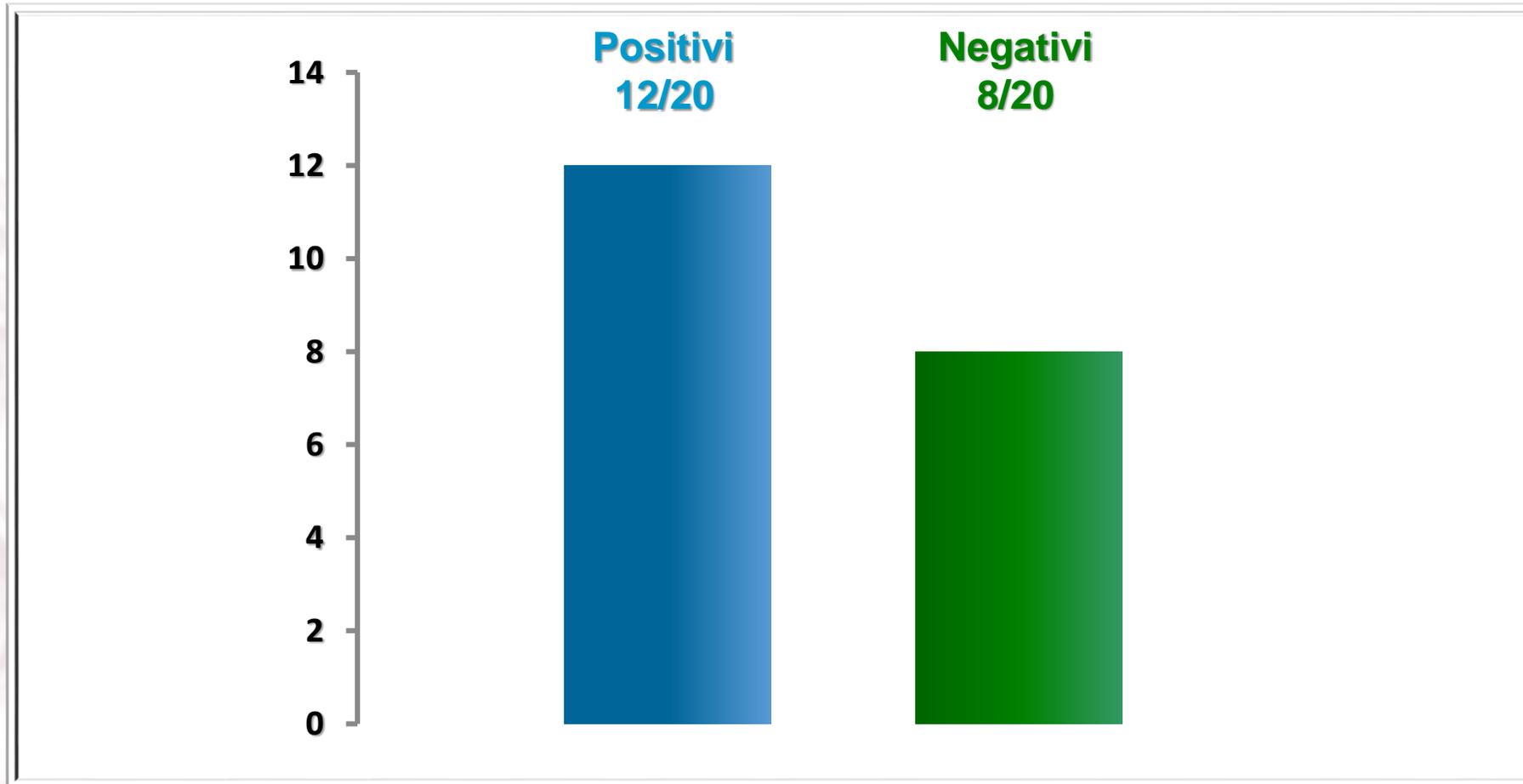
4.375 g glutine/die (10 capsule) per una settimana



Di Sabatino A et al, *CGH* 2015

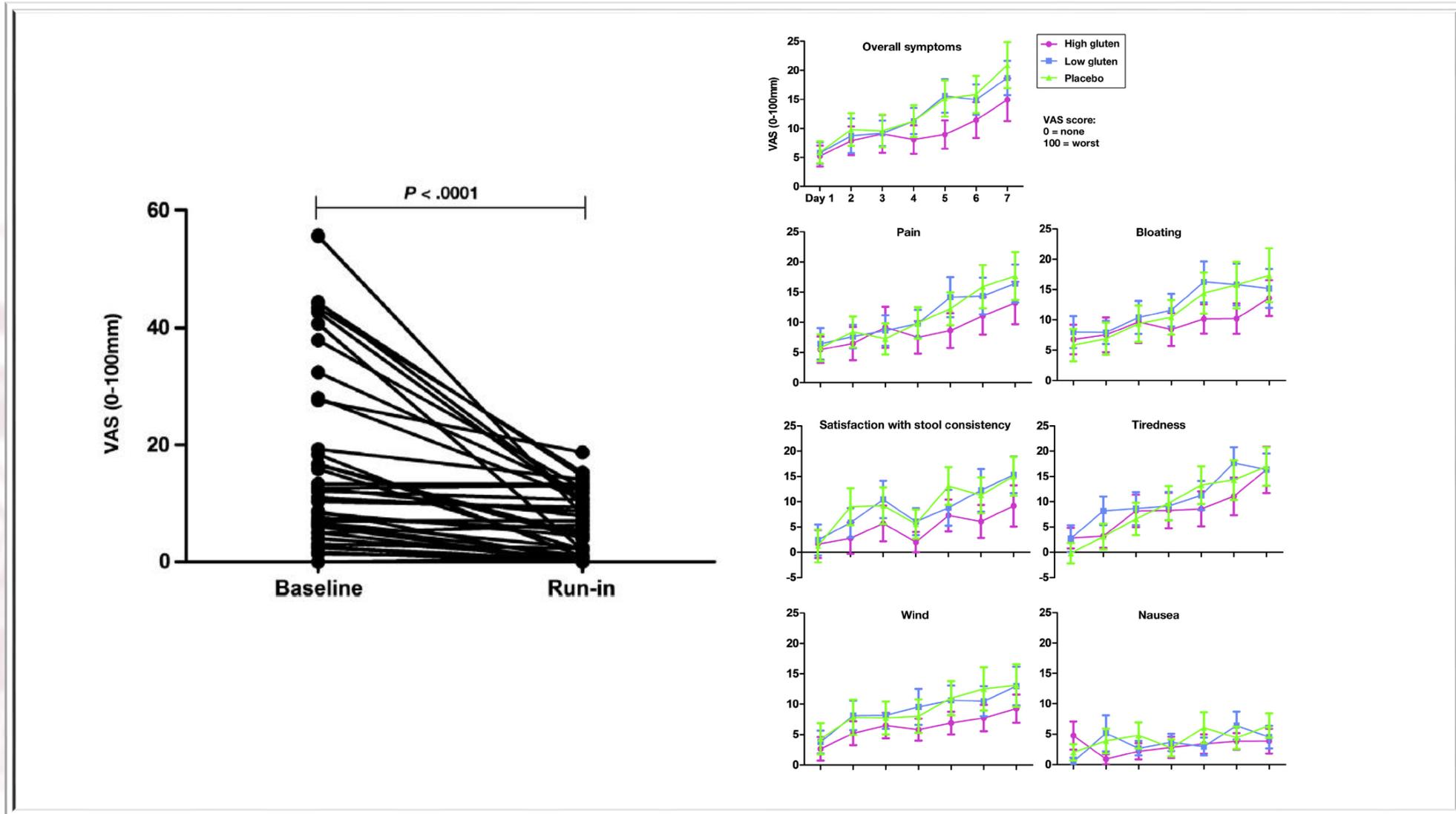
BASSE DOSI DI GLUTINE IN PAZIENTI CON METEORISMO FUNZIONALE

5 g glutine/die (10 capsule) per 1 settimana



Di Stefano M et al, 2016

RESTRIZIONE IN FODMAP IN IBS CON SELF-REPORTED NCGS



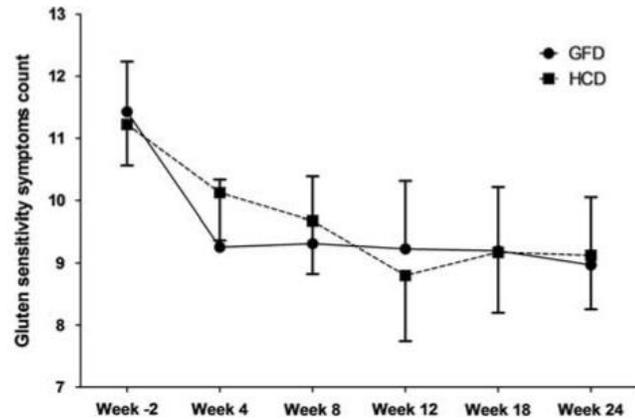
NON-CELIAC GLUTEN SENSITIVITY: UN PROBLEMA TRASVERSALE?

- Sempre più frequentemente viene **referita** una sensibilizzazione al glutine a viene **introdotta** una dieta priva di glutine in **assenza** di diagnosi di malattia celiaca o allergia al frumento
- E' caratterizzata da sintomi **intestinali** ed **extraintestinali**
- Componenti del frumento **diverse** dal glutine possono essere responsabili dello scatenamento dei sintomi in pazienti con NCGS
- **Non** esistono **biomarkers** accurati per diagnosticare tale condizione
- I pazienti con NCGS sono un gruppo **eterogeneo** e dovrebbero essere messi al corrente delle **difficoltà diagnostiche** di tale condizione

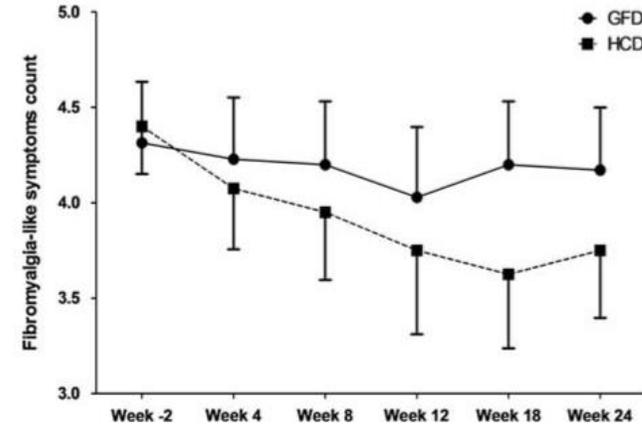
GFD vs DIETA IPOCALORICA IN PAZIENTI CON FIBROMIALGIA

75 pazienti con fibromialgia: 35 trattati con GFD, 40 trattati con dieta ipocalorica

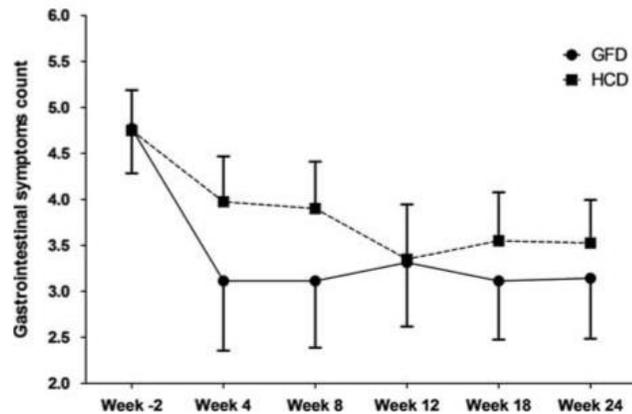
Sintomi da Gluten sensitivity



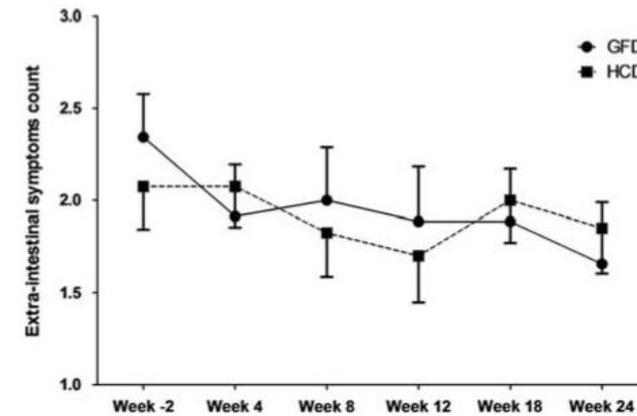
Sintomi da Fibromialgia



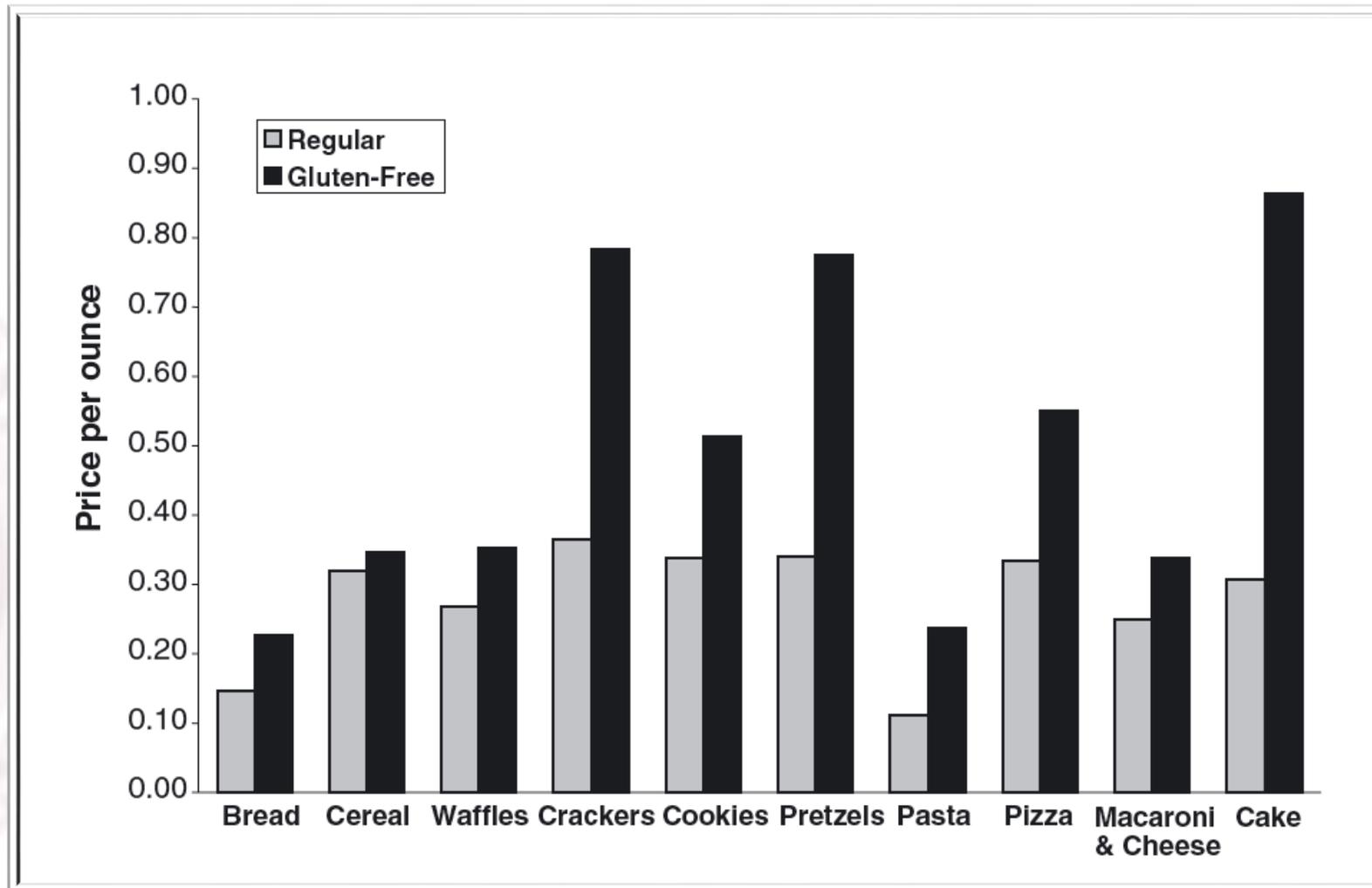
Sintomi Gastrointestinali



Sintomi Extraintestinali



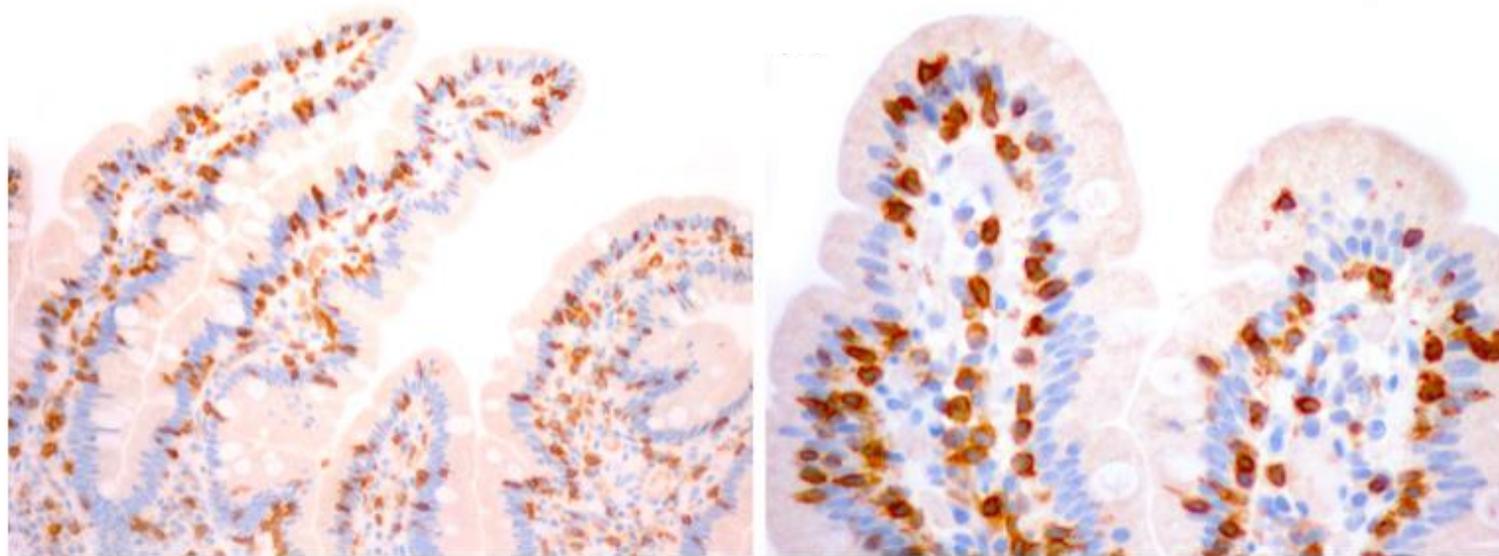
PESO ECONOMICO DELLA DIETA PRIVA DI GLUTINE



Lee AR et al, *J Hum Nutr Diet* 2007

NON-CELIAC GLUTEN SENSITIVITY E LINFOCITI INTRAEPITELIALI

Incremento dei linfociti intraepiteliali nei villi duodenali di pazienti con NCGS

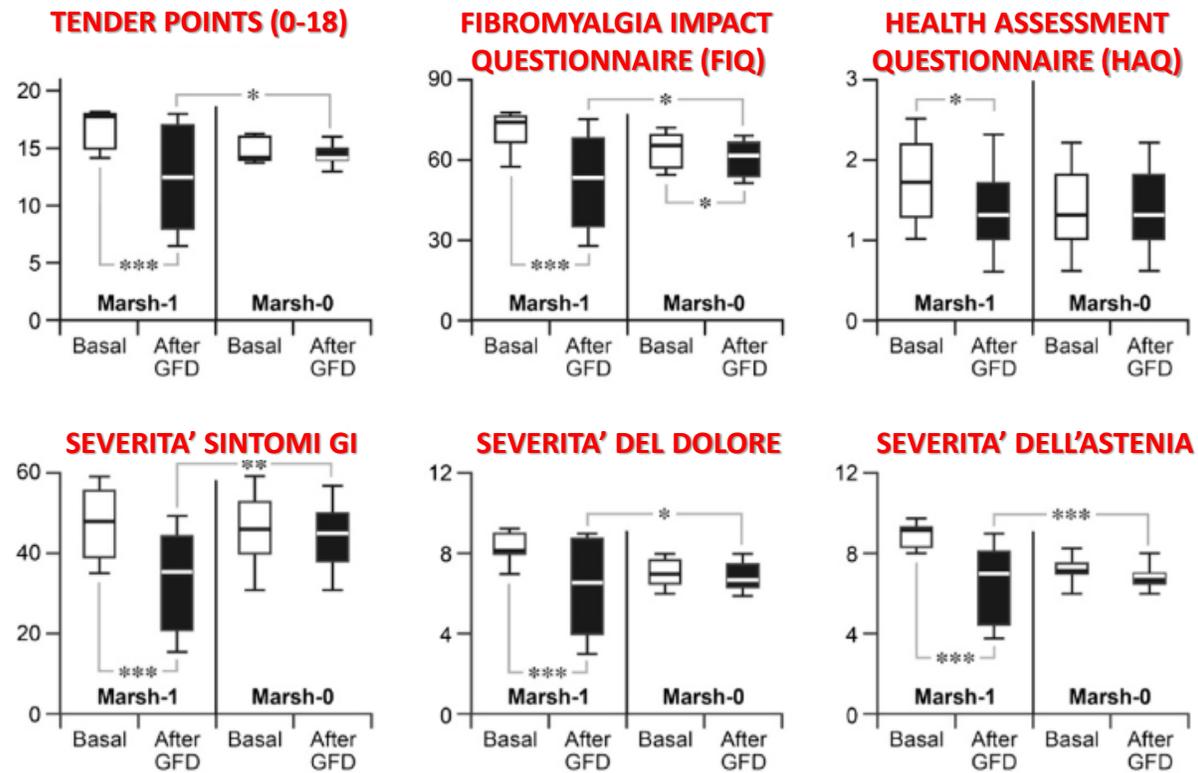


Isasi C et al, *Rheumatol Int* 2014

DIETA PRIVA DI GLUTINE IN FIBROMIALGIA E LINFOCITOSI DUODENALE

Pt no.	Età	Durata Malattia	Durata GFD	Remissione FM	Rientro a lavoro/ Vita attiva
1	49	20	31	+	+
2	35	7	30	+	
3	41	15	8	+	+
4	61	10	6	+	
5	46	10	24	+	+
6	57	20	17	+	+
7	73	5	7	+	+
8	61	10	5	+	
9	42	10	22	+	+
10	42	8	18		+
11	49	20	24		+
12	50	20	5		+
13	37	7	24	+	+
14	49	12	6	+	+
15	25	5	24	+	+
16	37	15	16		
17	33	3	8	+	+
18	43	15	6	+	+
19	42	20	24	+	
20	61	6	24		+

DIETA PRIVA DI GLUTINE IN FM + IBS + LINFOCITOSI DUODENALE



Effetto di un anno di dieta priva di glutine in pazienti con IBS e FM in rapporto alla presenza o assenza di linfocitosi duodenale

**Controllare la familiarità per malattia celiaca e FM in pazienti con linfocitosi duodenale!
Sono necessari ulteriori studi!**

PREVALENZA DELLA MALATTIA CELIACA IN PAZIENTI CON FM

MC in IBS con e senza FM

Cohorts	IBS (N = 125)	IBS/FMS (N = 104)
Gastroduodenal biopsy		
IEL count per 100 epithelial cells	15 (10)	27 (26)
Marsh stage 0	105 (84)	39 (37)
Marsh stage 1	20 (16)	58 (56)
Marsh stage 3	2 (2)	7 (7)

Rodrigo L et al, *Arthritis Res Ther* 2013

MC in pazienti reumatologici

100 pts con LES 1 Positivo
100 pts con AR 3 positivi
100 pts con FM 0 positivi

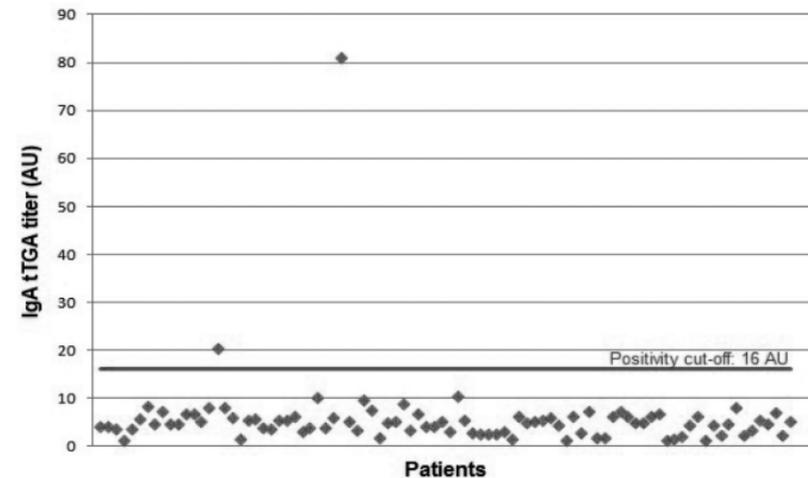
Elhami E et al, *Gastr Hep Bed Bench* 2018

MC in pazienti Fibromialgia

94 pts con FM 0 positivi

Nisihara R et al, *Rev Esp Enferm Dig* 2016

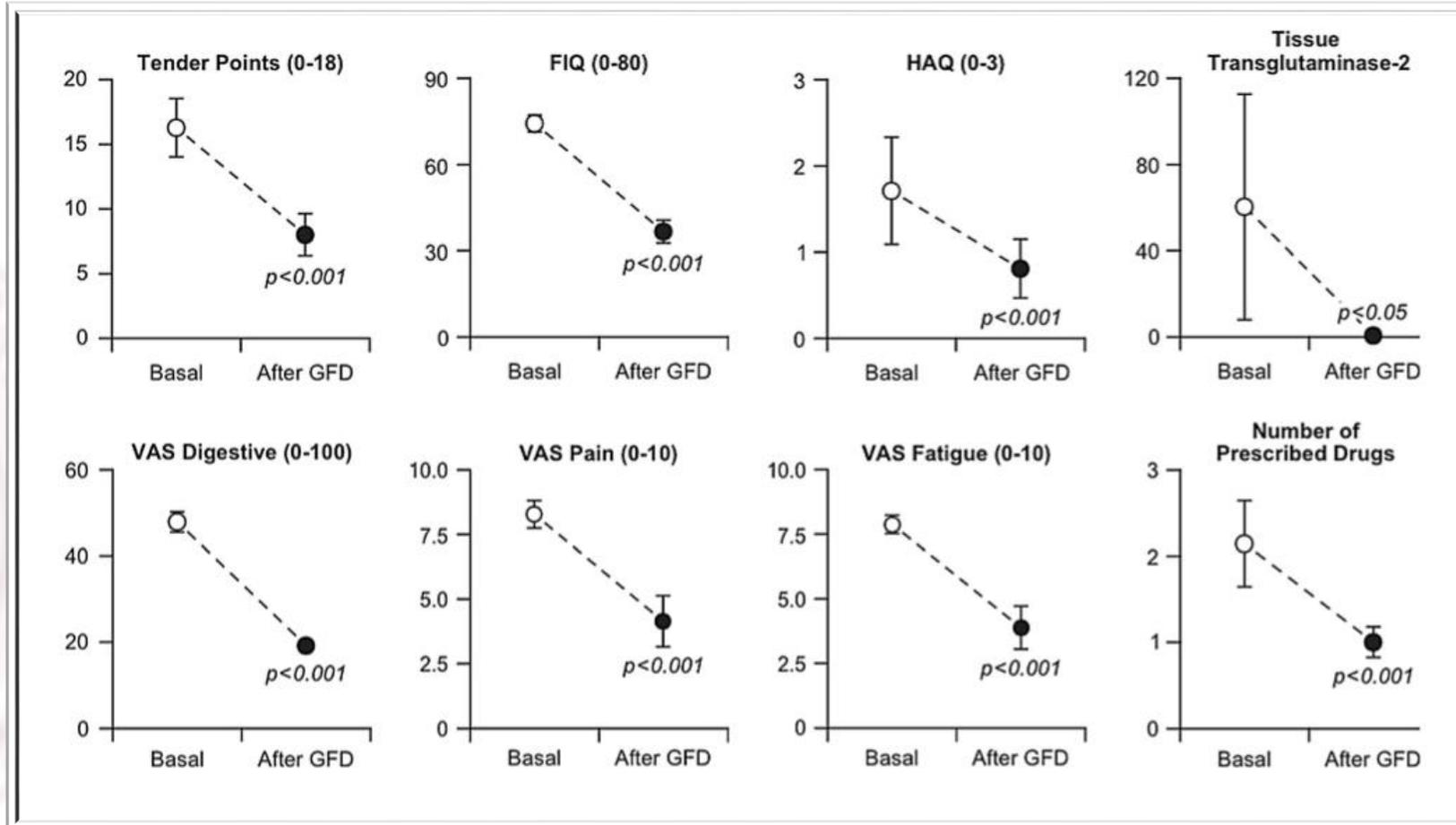
MC in pazienti con fibromialgia



Tovoli F et al, *Clin Exp Rheumatol* 2013

EFFETTO DELLA GFD IN FIBROMIALGICI CON MALATTIA CELIACA

GFD per un anno in 7 pazienti con fibromialgia e malattia celiaca



Rodrigo L et al, *BMG Gastroenterology* 2013

TAKE HOME MESSAGES

- La **reale** prevalenza di **allergie** ed **intolleranze** alimentari nella fibromialgia **non** è a tutt'oggi ben **definita**
- La stretta **associazione** tra fibromialgia e patologie funzionali gastrointestinali rende spesso **difficile** la definizione dell'origine della sintomatologia nel singolo paziente
- La **dieta priva di glutine** potrebbe essere utile in **sottogruppi** specifici di pazienti
- **Ulteriori studi** sono necessari per definire i **rapporti** tra alimentazione e fibromialgia



GRAZIE PER LA VOSTRA ATTENZIONE !!!