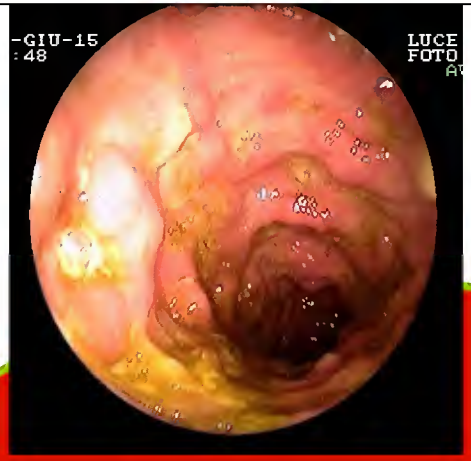
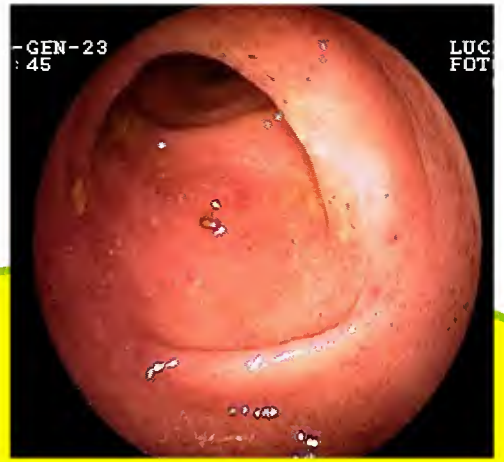

Pediatria On Line in Tour
Marsala
MICI
Pediatria On Line
29 - 31 maggio 2018
Centro
Villa
STEFANO MARTELOSSI

Malattie infiammatorie croniche intestinali

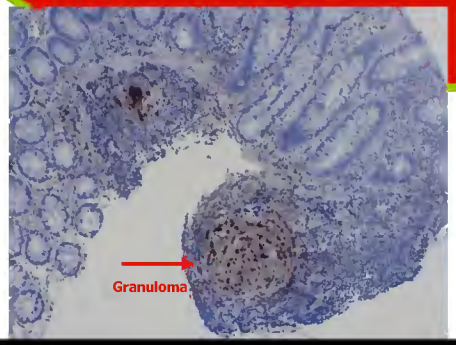


MORBO DI CROHN

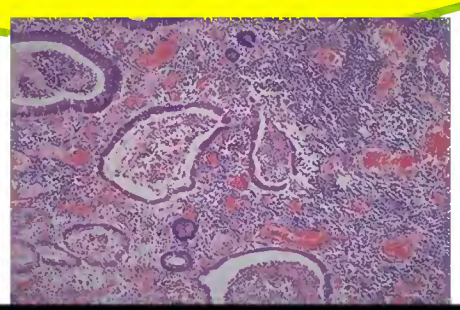
MICI
Non classificata



RETTOCOLITE ULCEROSA

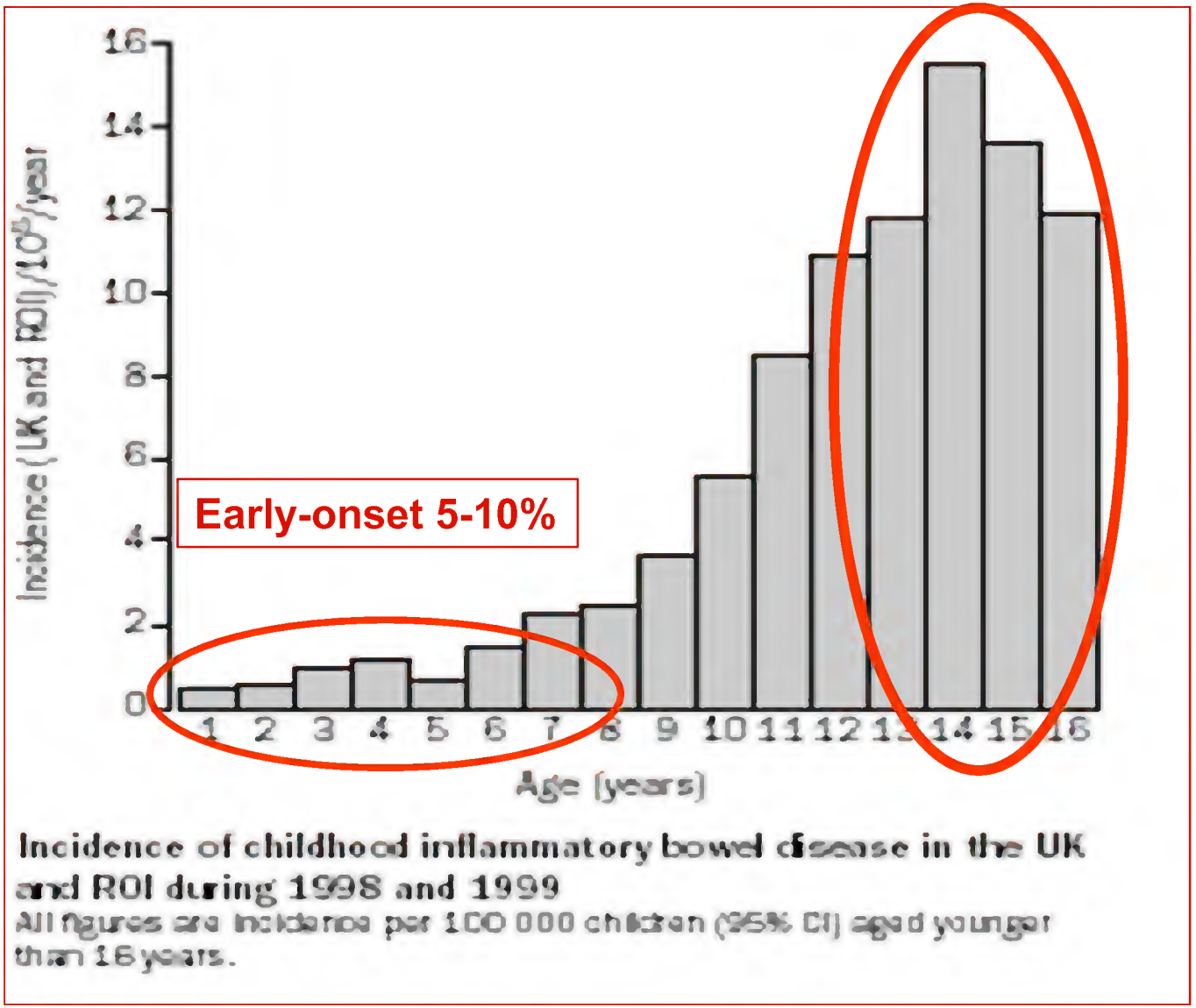


Tutto il tubo digerente
Flogosi transparietale
Chirurgia non risolutiva



Limitata al colon
Flogosi mucosale continua
Colectomia risolutiva

20% di tutti i casi esordio età pediatrica



Incidence of childhood inflammatory bowel disease in the UK and ROI during 1998 and 1999

All figures are incidence per 100 000 children (95% CI) aged younger than 16 years.

Epidemiology of Pediatric Inflammatory Bowel Disease: A Systematic Review of International Trends

Eric I. Benchimol, MD, PhD,[*,†,‡,§,‖] Kyle J. Fortinsky, BSc,*[*,†] Peter Gozdyra, MA,[‖] Meta Van den Heuvel, MD,[§] Johan Van Limbergen, MD, PhD,[‡,§] and Anne M. Griffiths, MD[‡,§]*

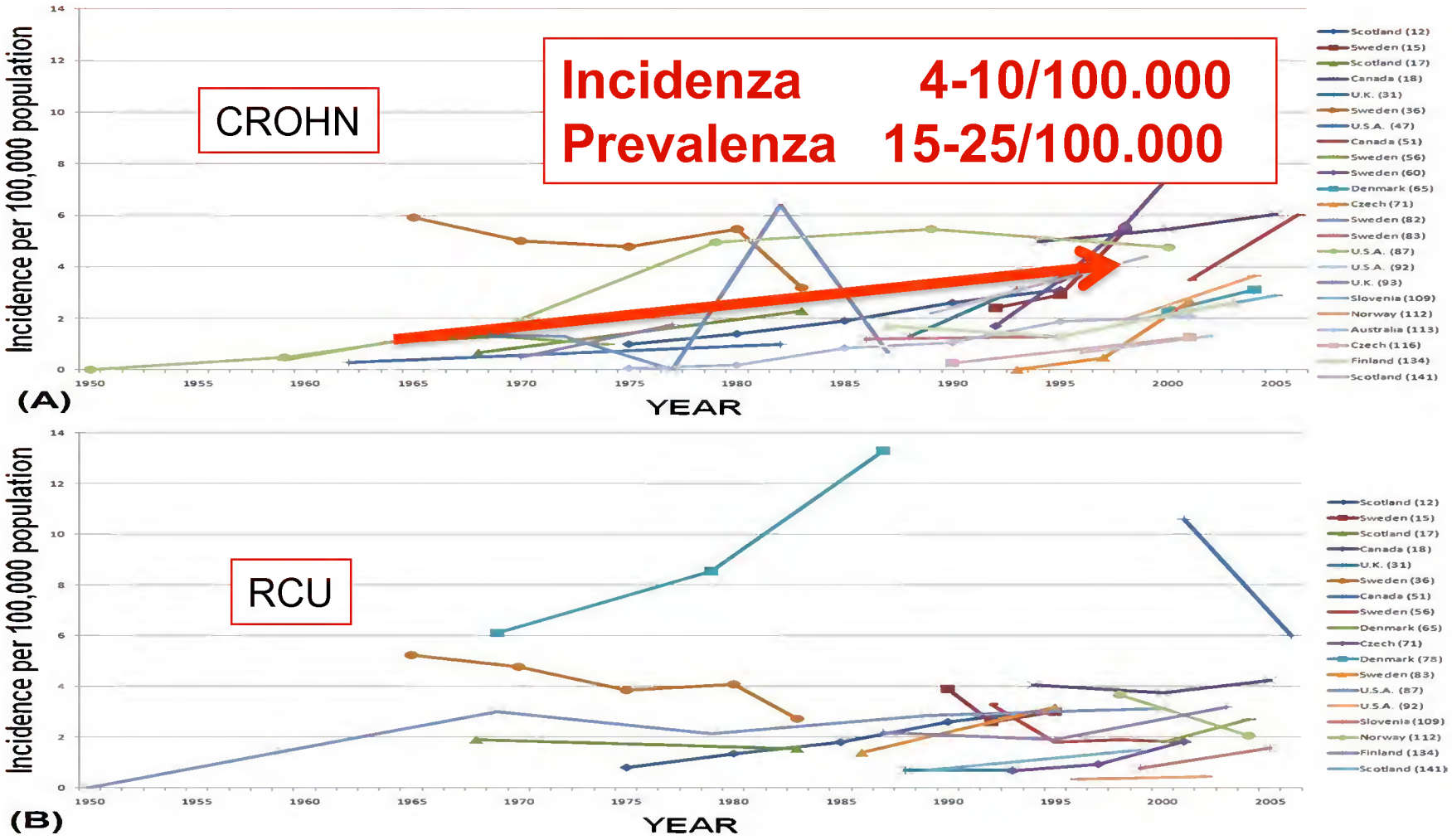


FIGURE 3. Temporal trends of incidence rates for (A) Crohn's disease and (B) ulcerative colitis in studies reporting incidence at multiple timepoints. Where a year range is reported, incidence rate is reported for the final year in the range (e.g., if incidence is reported for 1990–1999, rate is plotted as incidence for 1999).

MICI in età pediatrica : localizzazione estesa

Definition of Phenotypic Characteristics of Childhood-Onset Inflammatory Bowel Disease

JOHAN VAN LIMBERGEN,*·†·# RICHARD K. RUSSELL,§ HAZEL E. DRUMMOND,* MARIAN C. ALDHOUS,* NICOLA K. ROUND,*·† ELAINE R. NIMMO,* LINDA SMITH,* PETER M. GI[illegible] PARAIC McGROGAN,§ LAWRENCE T. WEAVER,‖ W. MICHAEL BISSET,¶ GAMAL MAHDI,¶ IAN D[illegible] DAVID C. WILSON†·#

416 pediatric vs 1297 adults

Table 5. Comparison of Childhood-Onse Using the Mon

n	
CD phenotype: Location*	
L1	
L2	
L3	
L1 + L4	
L2 + L4	
L3 + L4	
L4	
p	
CD phenotype: Behavior	
B1 (–p)	
B2 (–p)	
B3 (–p)	
p	
UC phenotype	
E3	
E2	
E1	
p	

*Five children had oral (*n* adults had oral (*n* = 4)/ disease.

CD panenteric	**43% vs**	**3.2%**
CD ileo-cecal	**2,6% vs**	**31.5%**
CD upper GI	**47% vs**	**23%**
RCU pancolonic	**82% vs**	**47.6%**

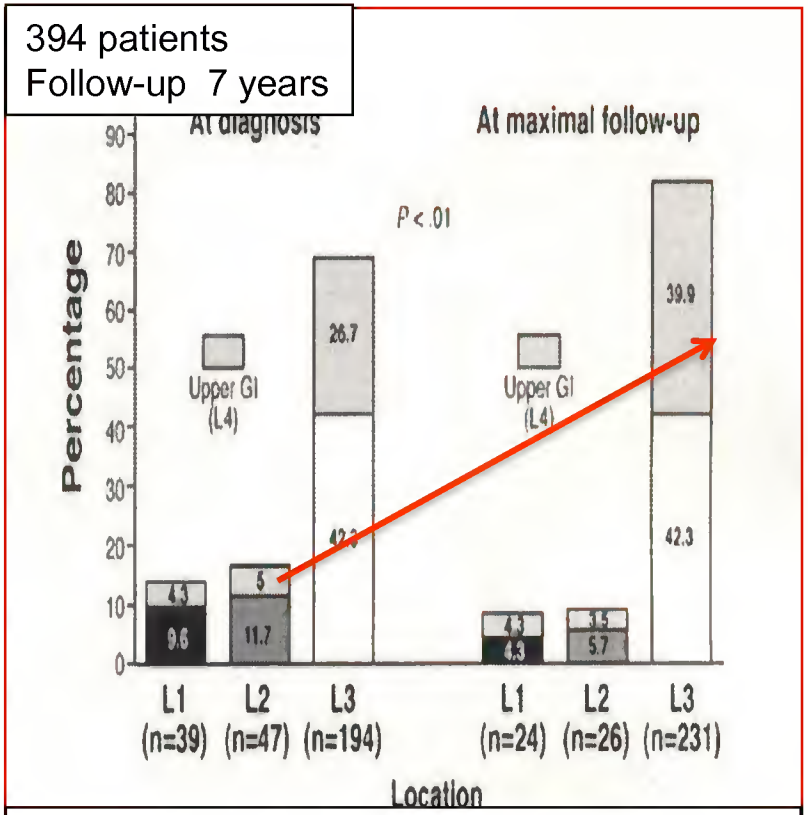
Progressione e decorso severo

Natural History of Pediatric Crohn's Disease: A Population-Based Cohort Study

GWENOLA VERNIER-MASSOUILLE,* MAMADOU BALDE,‡ JULIA SALLERON,* DOMINIQUE TUROCK,‡ JEAN LOUIS DUPAS,¶ OLIVIER MOUTERDE,** VERONIQUE MERLE,** JEAN LOUIS SALOMEZ,‡ JULIEN BRANCHU,‡ RAYMOND MARTI,‡ ERIC LEREBOURS,** ANTOINE CORTOT,* CORINNE GOWER-ROUSSEAU,‡ and JEAN FREDERIC COLOMBEL*

GASTROENTEROLOGY 2008;135:1106–1113

394 patients
Follow-up 7 years



Malattia panenterica
Progressione di malattia

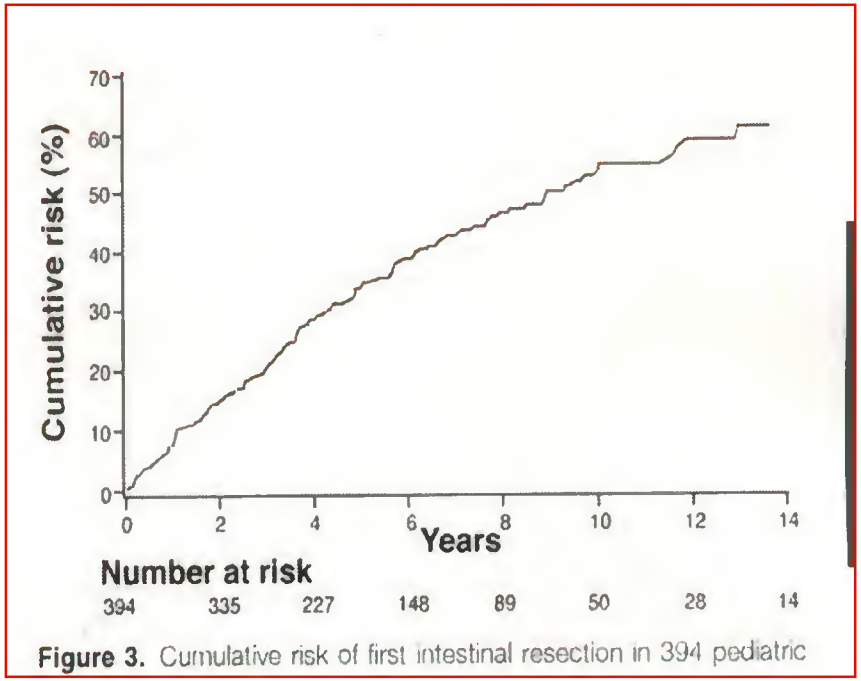


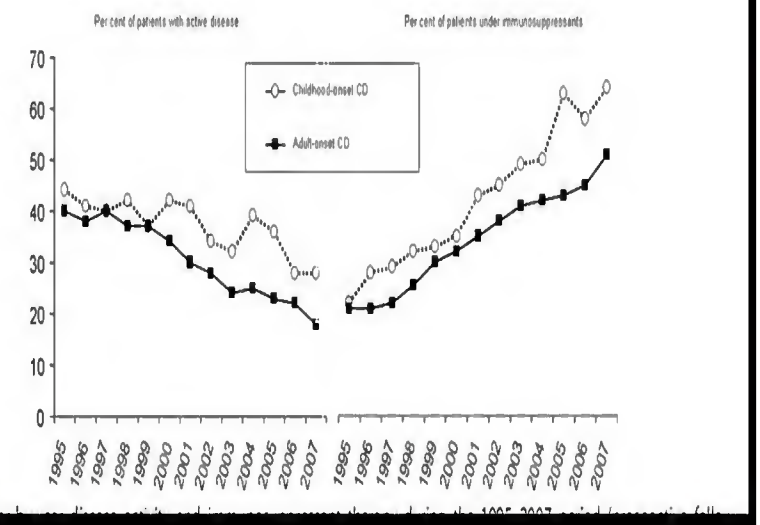
Figure 3. Cumulative risk of first intestinal resection in 394 pediatric

7 years : 44% need surgery

Resistenza alla terapia maggiore

Natural History of Crohn's Disease: Comparison Between Childhood- and Adult-Onset Disease

Bénédicte Pigneur, MD,* Philippe Seksik, MD, PhD,† Sheila Viola, MD,* Jérôme Viala, MD, PhD,‡ Laurent Beaugerie, MD, PhD,† Jean-Philippe Girardet, MD,* Frank M. Ruemmele, MD, PhD,§ and Jacques Cosnes, MD†



Active disease	37%	vs 31%
Immunomodulators	41%	vs 33%
Biologic agents	10.5%	vs 3.5%

Surgery :

1 every 16.6 ys ped
1 every 17.9 ys adult

At 30 years follow-up:

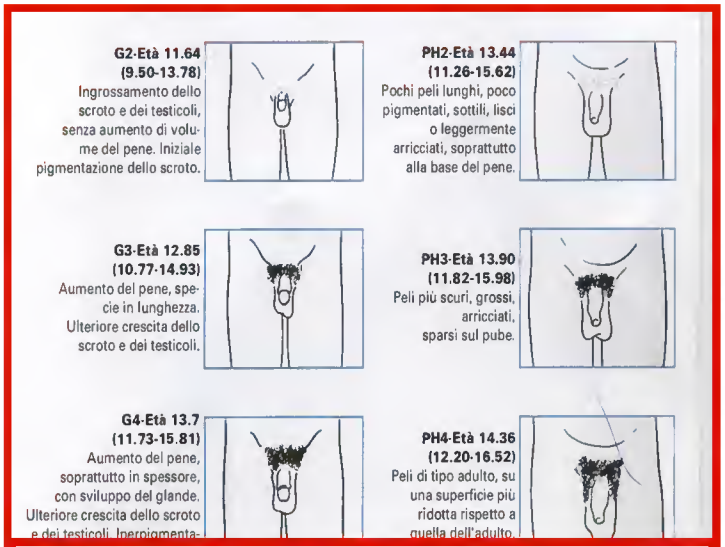
48% vs 14% estensive
12% vs 7% permanent stoma

La specificità pediatrica : il difetto di crescita

Difetto di crescita è presente alla diagnosi nel 30-50% di bambini con CD e persiste nell'età adulta nel 10-20%

PCDAI

GROWTH		
7. Weight	• Weight gain or voluntary weight stable/loss	= 0 p
	• Involuntary weight stable, weight loss 1-9%	= 5 p
	• Weight loss ≥ 10%	= 10 p
8. Height	At Diagnosis: (refer to percentile chart)	OR Follow-up: (refer to growth velocity chart)
	<1 channel decrease = 0 p	Height velocity ≥ -1SD = 0 p
	≥1, <2 channel decrease = 5 p	Height velocity < -1SD, > -2SD = 5 p
	≥2 channel decrease = 10 p	Height velocity ≤ -2SD = 10 p
		PARTIAL SCORE
		Pediatric Crohn's Disease Activity Index (PCDAI)

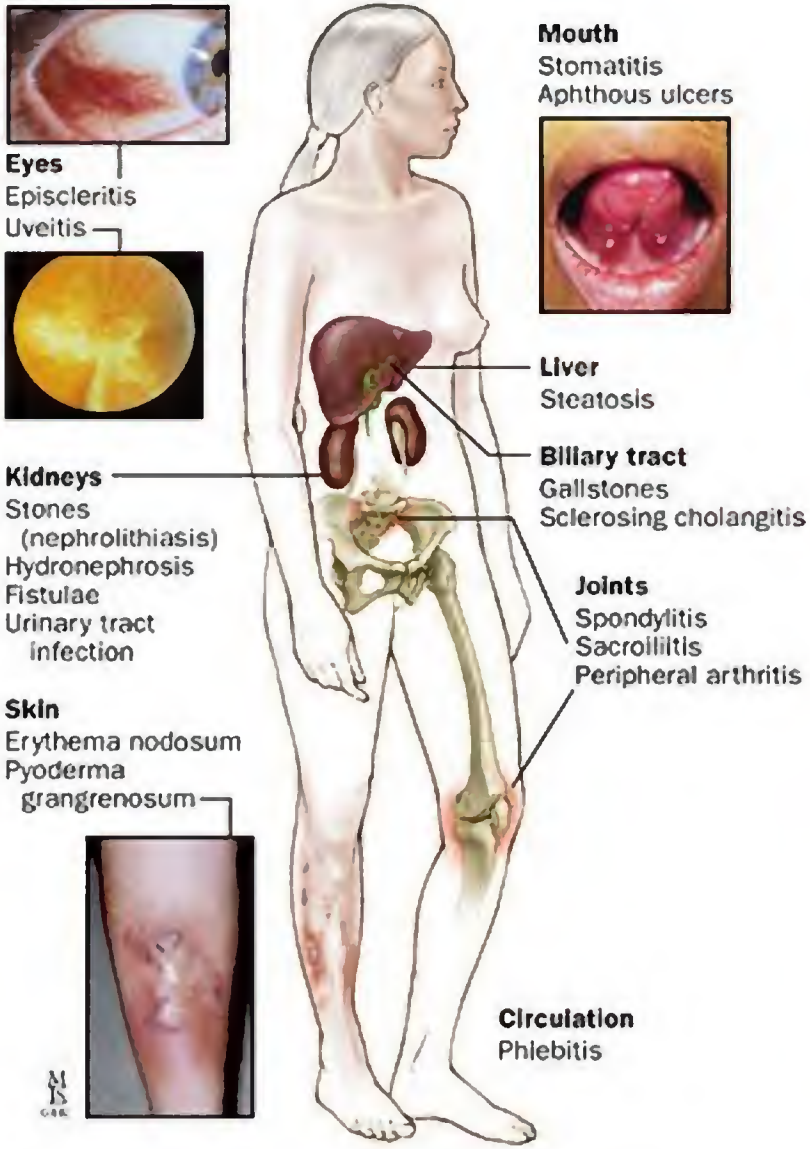


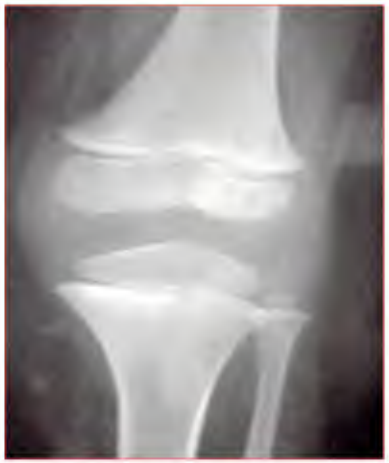
- Misurazioni accurate
- Velocità crescita 6 m
- Bersaglio genetico
- Età ossea
- Stadio pubere

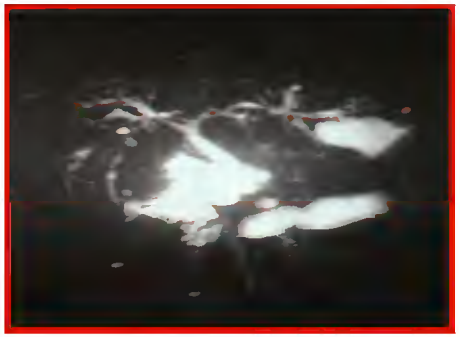
Table. Clinical Presentation of IBD in Children and Adolescents

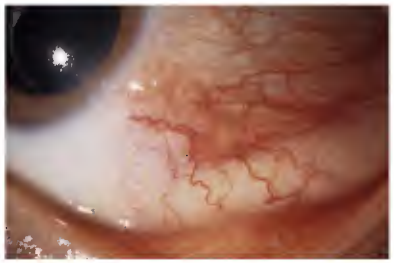
Presenting Symptom	Classification of IBD, % of Patients[a]	
	Crohn Disease	Ulcerative Colitis
General		
Weight loss	55-80	31-38
Fever	38	NA
Anorexia	2-25	6
Growth retardation	3-4	0
Lethargy	13-27	2-12
Gastrointestinal tract		
Abdominal pain	67-86	43-62
Diarrhea	30-78	74-98
Rectal bleeding	22-49	83-84
Nausea/vomiting	6	[illegible]
Constipation	1	0
Perianal disease	6-15	0
Mouth ulcers	5-28	13

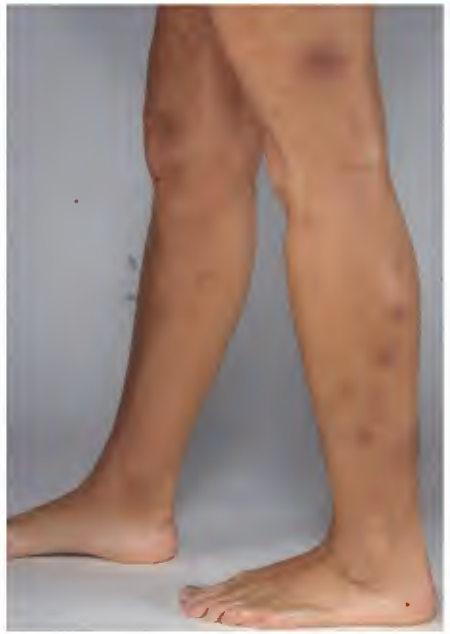
La presentazione clinica può essere extraintestinale

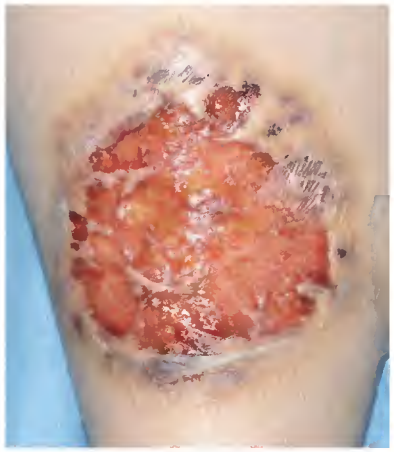








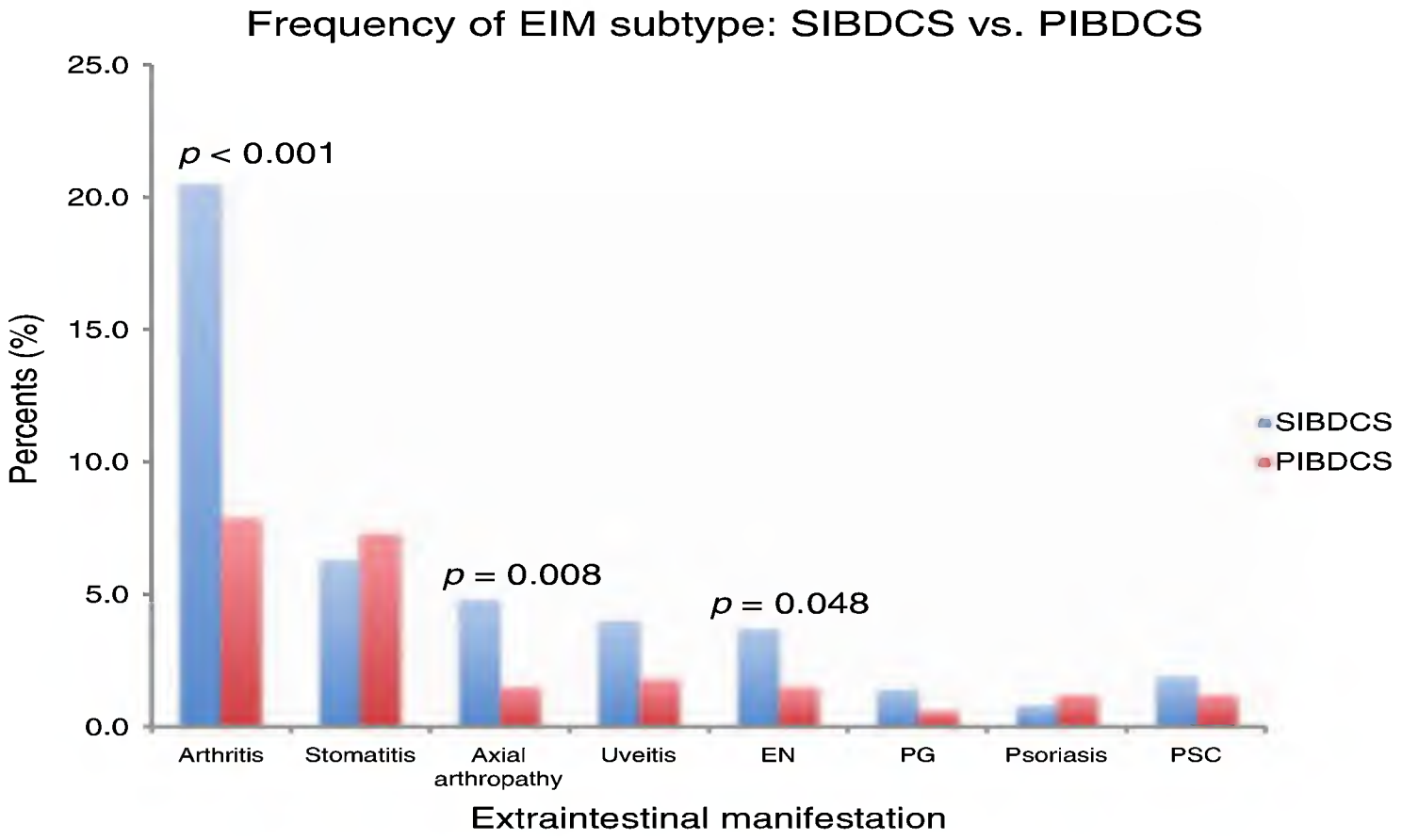




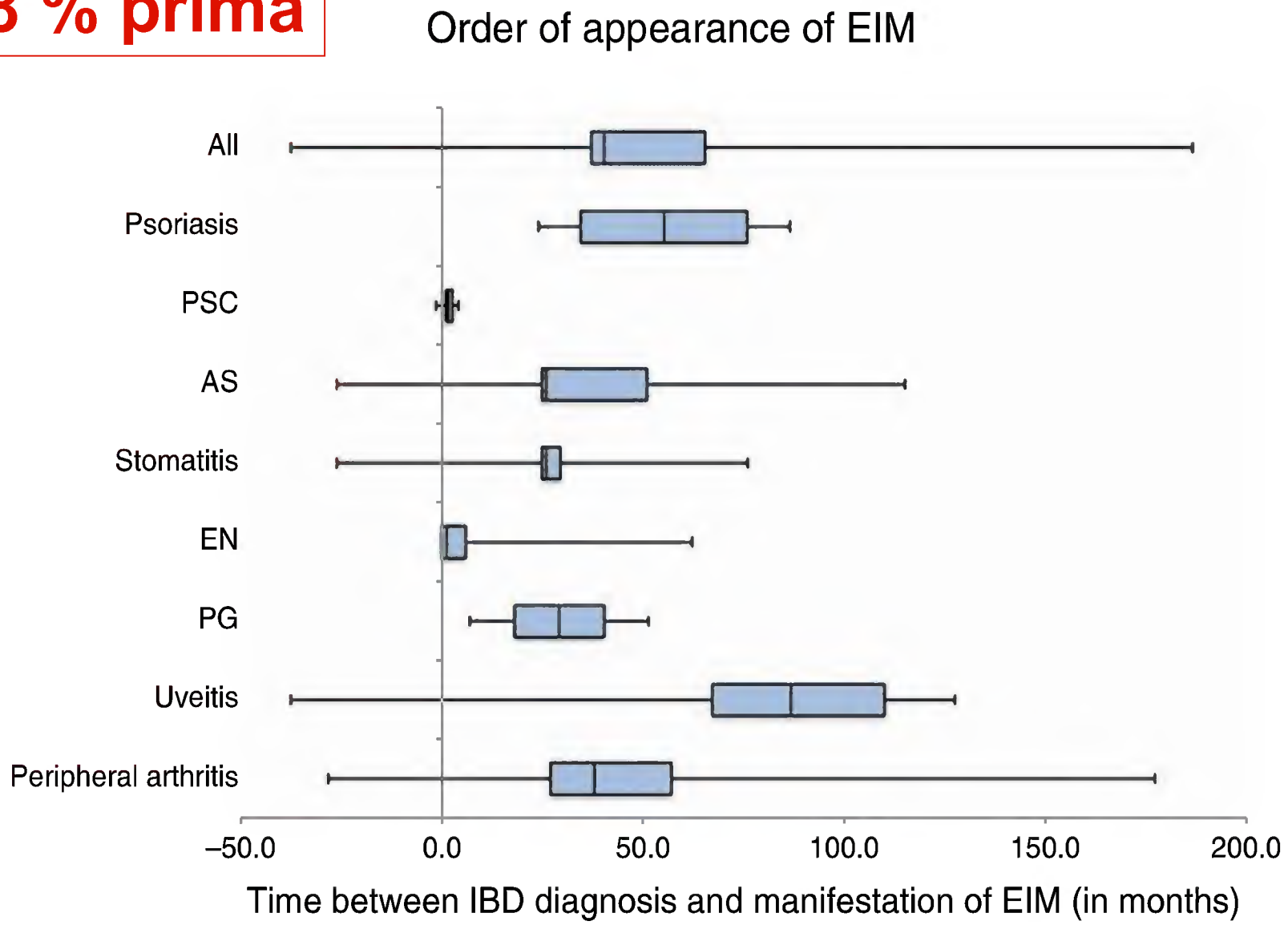
Extraintestinal Manifestations of Pediatric Inflammatory Bowel Disease: Prevalence, Presentation, and Anti-TNF Treatment

JPGN • Volume 65, Number 2, August 2017

329 pazienti da registro, 55 (16.7%) EIM **Crohn 22% RCU 10.3%**



28 % prima


Order of appearance of EIM
All
Psoriasis
PSC
AS
Stomatitis
EN
PG
Uveitis
Peripheral arthritis
–50.0
0.0
50.0
100.0
150.0
200.0
Time between IBD diagnosis and manifestation of EIM (in months)

LE MOLTE FACCE DELLE MICI

Sindrome Colitica (Diarrea muco ematica-dolore)	Sindrome infiammatoria (Febbre, anoressia, peso anemia , “ artralgie “)
RCU 90 %	RCU : Rara
CROHN 50%	CROHN : Frequente
PROBLEMA : Diagnosi differenziale delle Coliti	PROBLEMA : Pensare alla MICI in assenza di sintomi intestinali

MICI: la diagnosi

(Mack DR et al – Pediatrics 2007;119:1113-9)

- ✓ Analisi retrospettiva di 526 MICI pediatriche (134 RCU e 392 MC) – sensibilità di 4 test:

	MC lieve	MC grave	RCU lieve	RCU grave
4 test	79 %	98 %	46 %	100 %
VES	65 %	86 %	26 %	85 %
Hb	49 %	80 %	69 %	95 %
Piastrine	42 %	66 %	95 %	50 %
Albumina	18 %	69 %	13 %	90 %

1. Ileocolonoscopy
2. Upper GI endoscopy
3. Histology

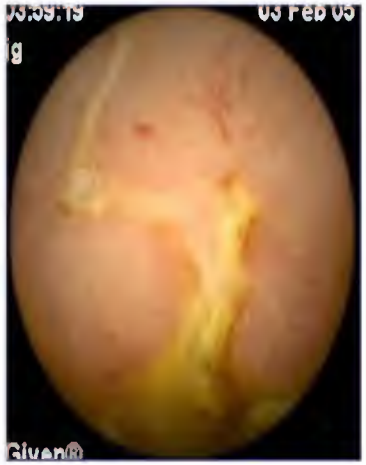
Crohn's disease
Colitis unclassified

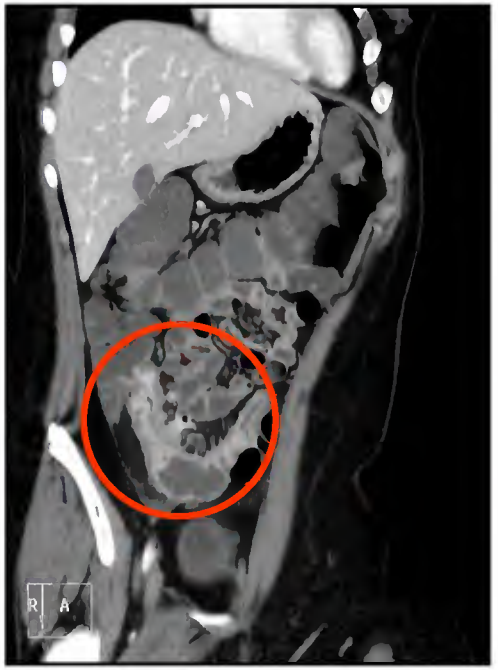
Ulcerative colitis

Radiology:
MRI

when diagnosis of UC is uncertain

Wireless capsule endoscopy (WCE) is a useful alternative

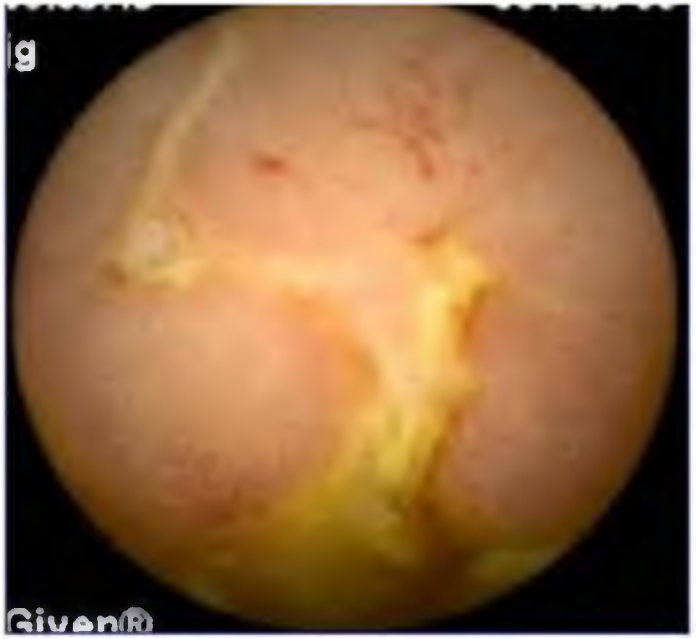




Marta 13 anni

Dolori addominali, nausea, astenia
Non calo ponderale
Padre con Crohn

VES 12, PCR 0,5
CP 1200

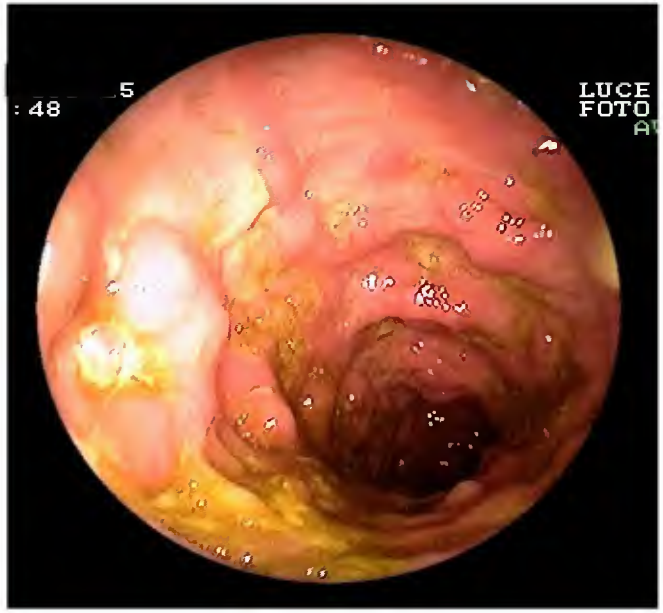


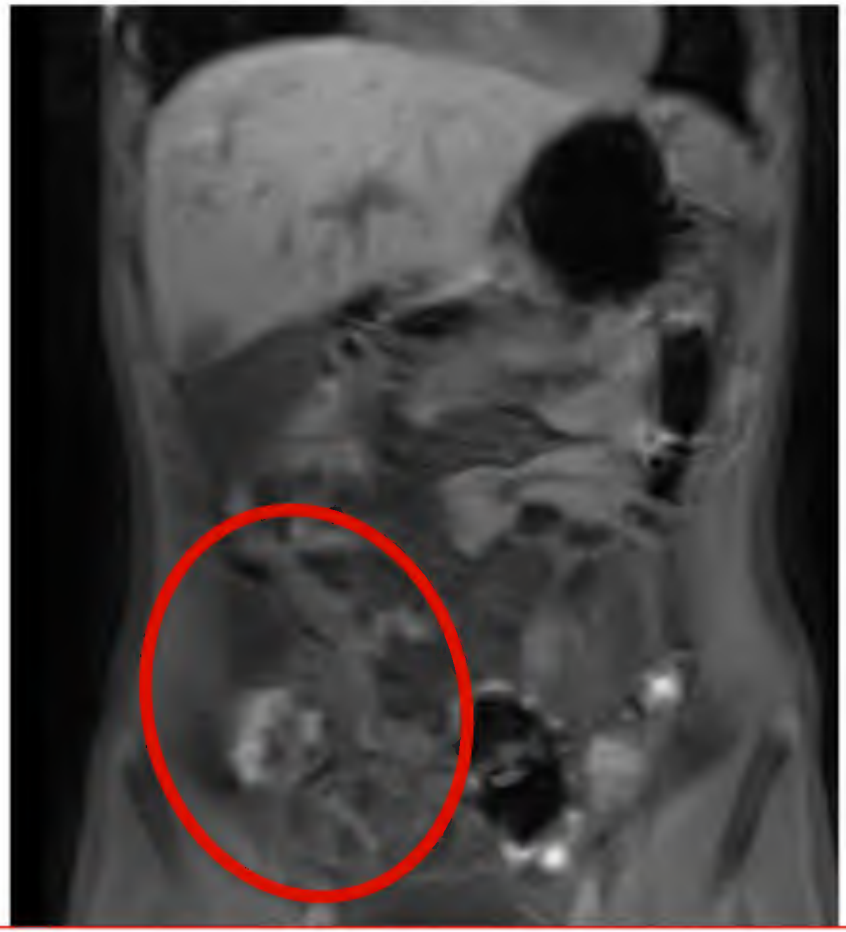
Nutrizione polimerica esclusiva per 8 settimane

Matteo 10 anni

Febbre, dolori addominali, calo ponderale

VES 80, pcr 5,4
Hb 10 g/dl, albumina 3.2 g/dl

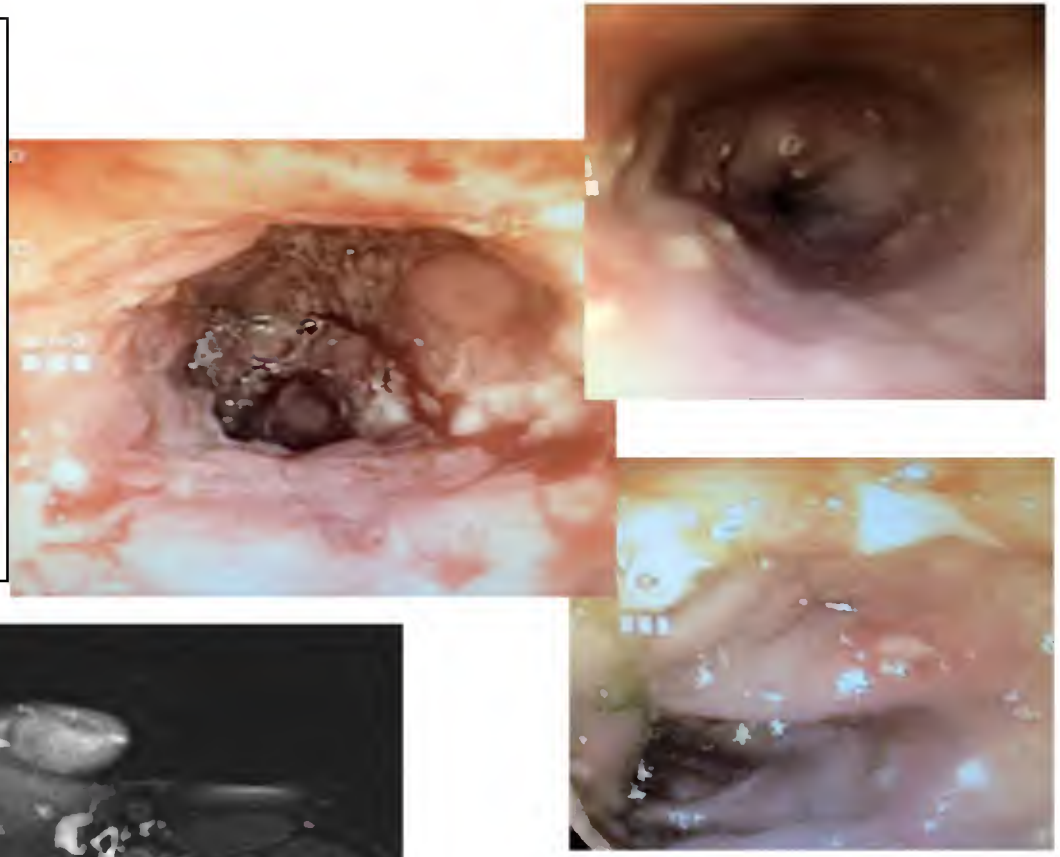


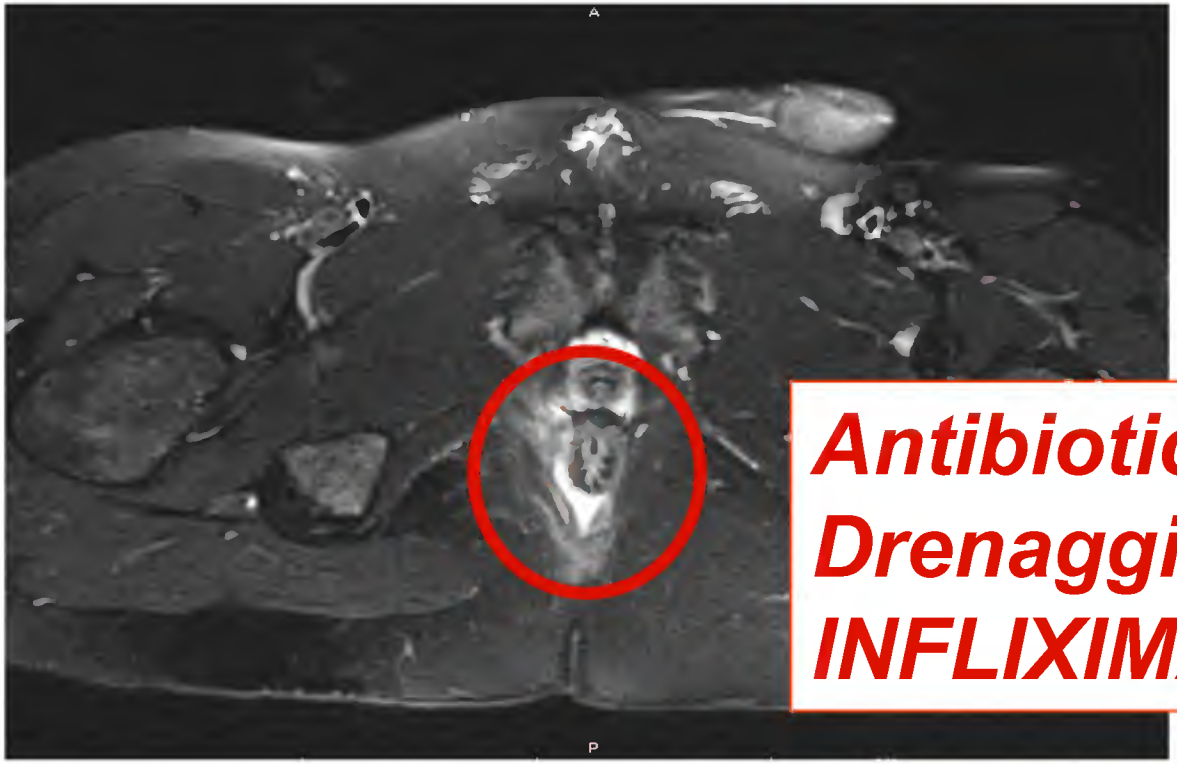


Nutrizione polimerica esclusiva + Azatioprina

Arturo 14 anni

Da 2 mesi 2-3 scariche febbricola,
calo ponderale (3 kg)
Ascesso perianale
VS 75, PCR 6.2, CP 2400





Antibiotici
Drenaggio + setone
INFLIXIMAB

I “moderni” obiettivi terapeutici del Crohn **pediatrico**

- Inducing clinical remission
- Maintaining clinical remission
- Allowing withdrawal of corticosteroids
- Promoting growth (pediatric specificity)
- Improving patients quality of live
- Minimizing drugs complication
- Prevent surgery
- Prevent disability

Sustained/deep remission

MUCOSAL HEALING : are associated with a significantly better clinical outcomes : more durable clinical response, optimize growth, restored quality of live, reduced resource utilisation and finally prevent bowel damage and surgery.

Enteral Nutrition and Corticosteroids in the Treatment of Acute Crohn's Disease in Children

Heuschkel, Robert B; Menache, Caroline C*; Megerian, J. Thomas*; Baird, Alison E*

JPGN 2000

Terapia nutrizionale (formula polimerica) prima scelta - No steroide, rapida crescita

Consensus guidelines of ECCO/ESPGHAN on the medical management of pediatric Crohn's disease

Journal of Crohn's and Colitis (2014) **8**, 1179–1207

benefit-risk analysis according to different clinical scenarios. In children and adolescents who did not have finished their growth, exclusive enteral nutrition (EEN) is the induction therapy of first choice due to its excellent safety profile, preferable over corticosteroids, which are

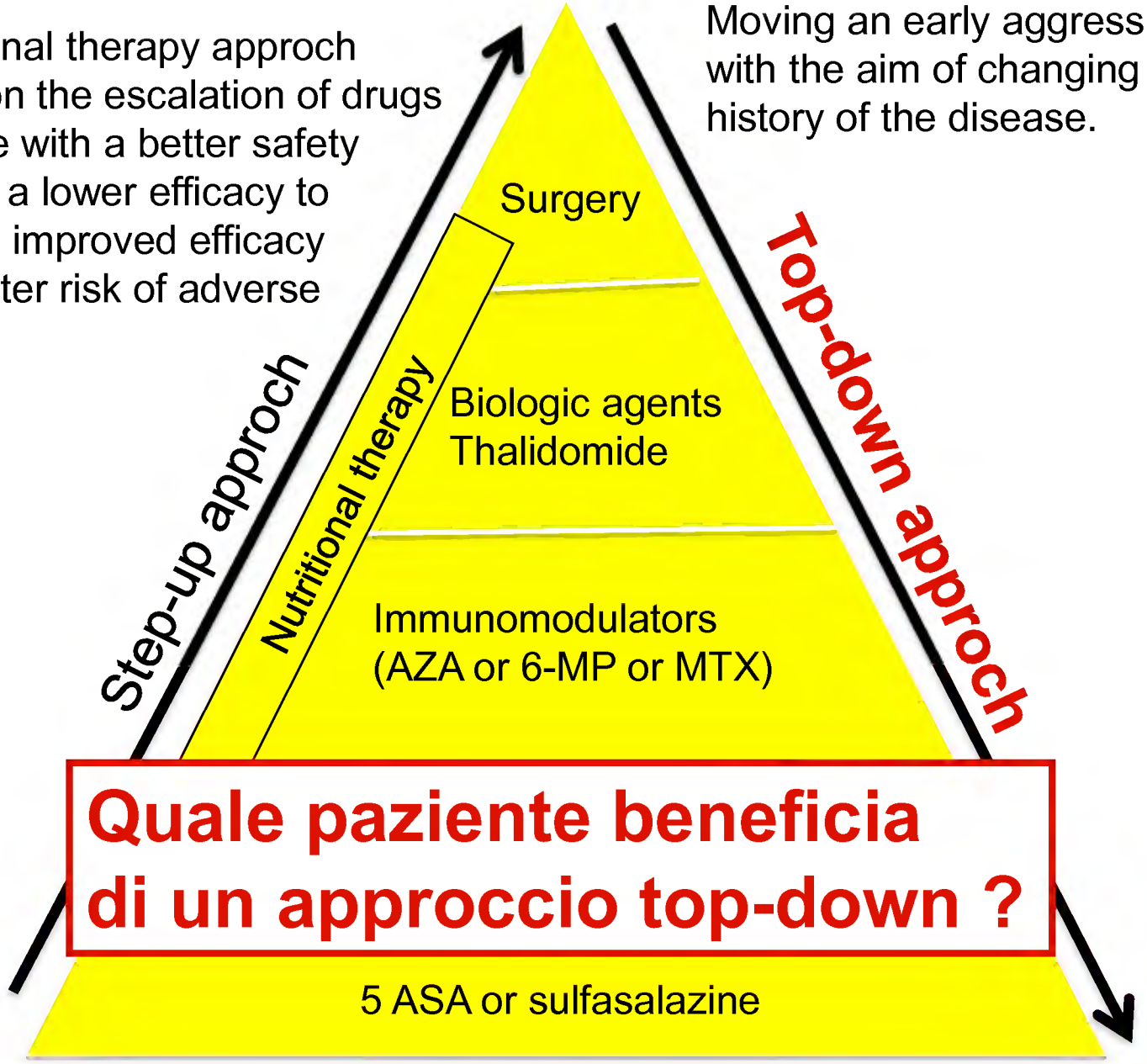
ORIGINAL ARTICLE

Exclusive enteral nutrition continues to be first line therapy for pediatric Crohn's disease in the era of biologics☆

An Pediatr (Barc). 2015;83(1):47–54

Conventional therapy approch is based on the escalation of drugs from those with a better safety profile but a lower efficacy to those with improved efficacy but a greater risk of adverse effects

Moving an early aggressive approach with the aim of changing the natural history of the disease.



Quale paziente beneficia di un approccio top-down ?

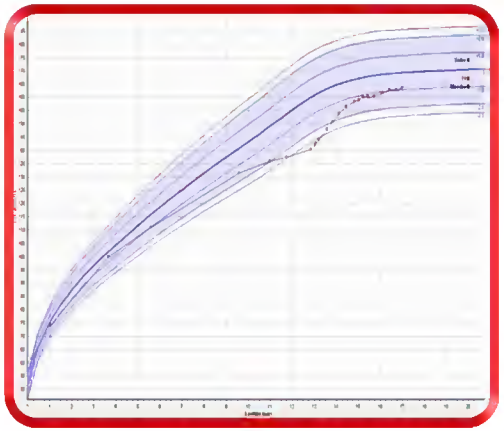
But not all patients are alike!

Assessing prognosis at an early stage is essential for the development of an appropriate management plan

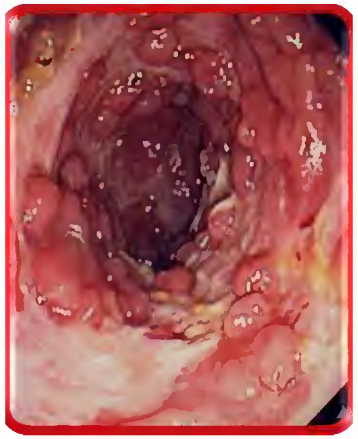
Indolent → Aggressive

Avoid intensive therapy, immunosuppression, adverse events

Assure early intensive therapy to avoid complications

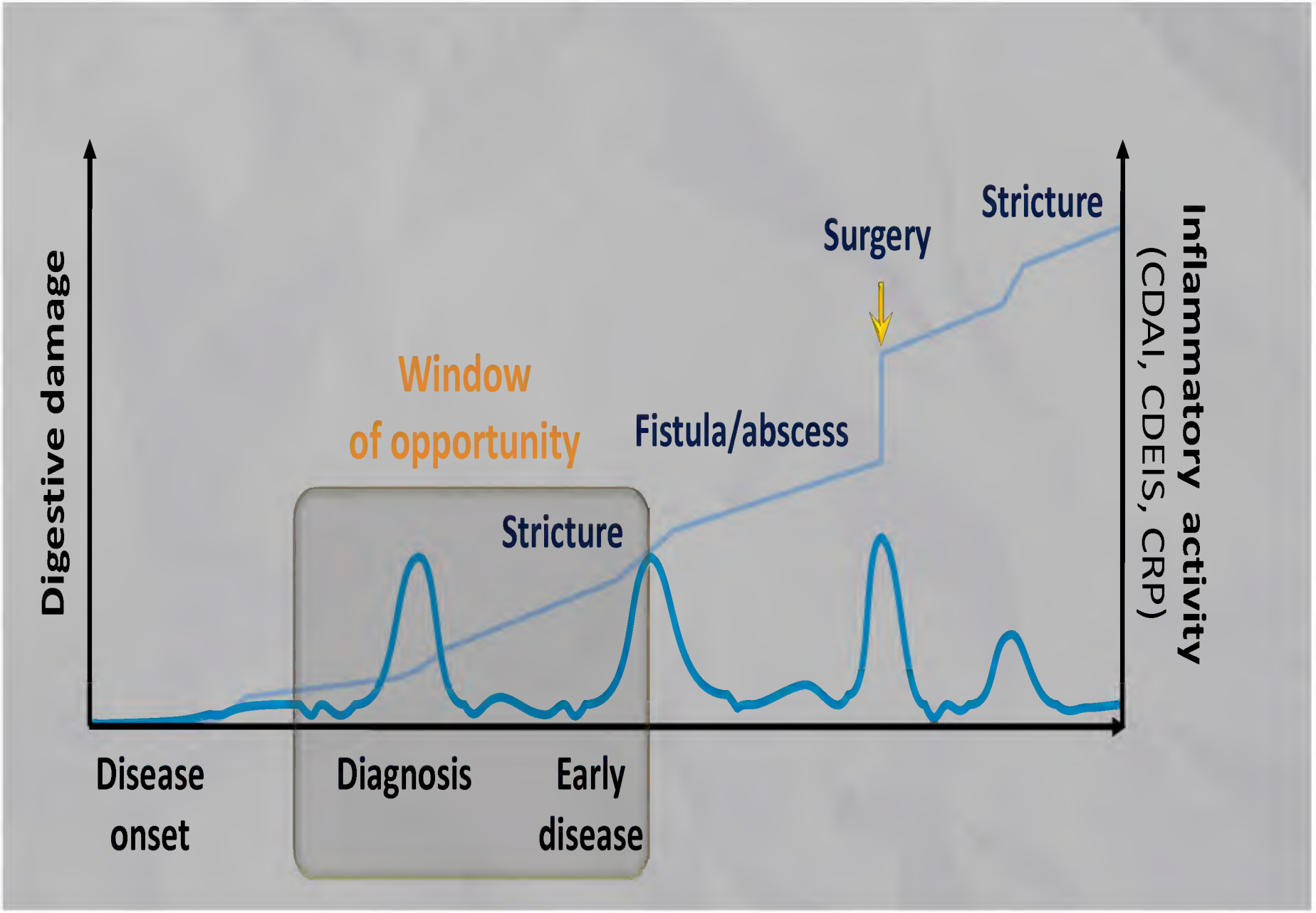


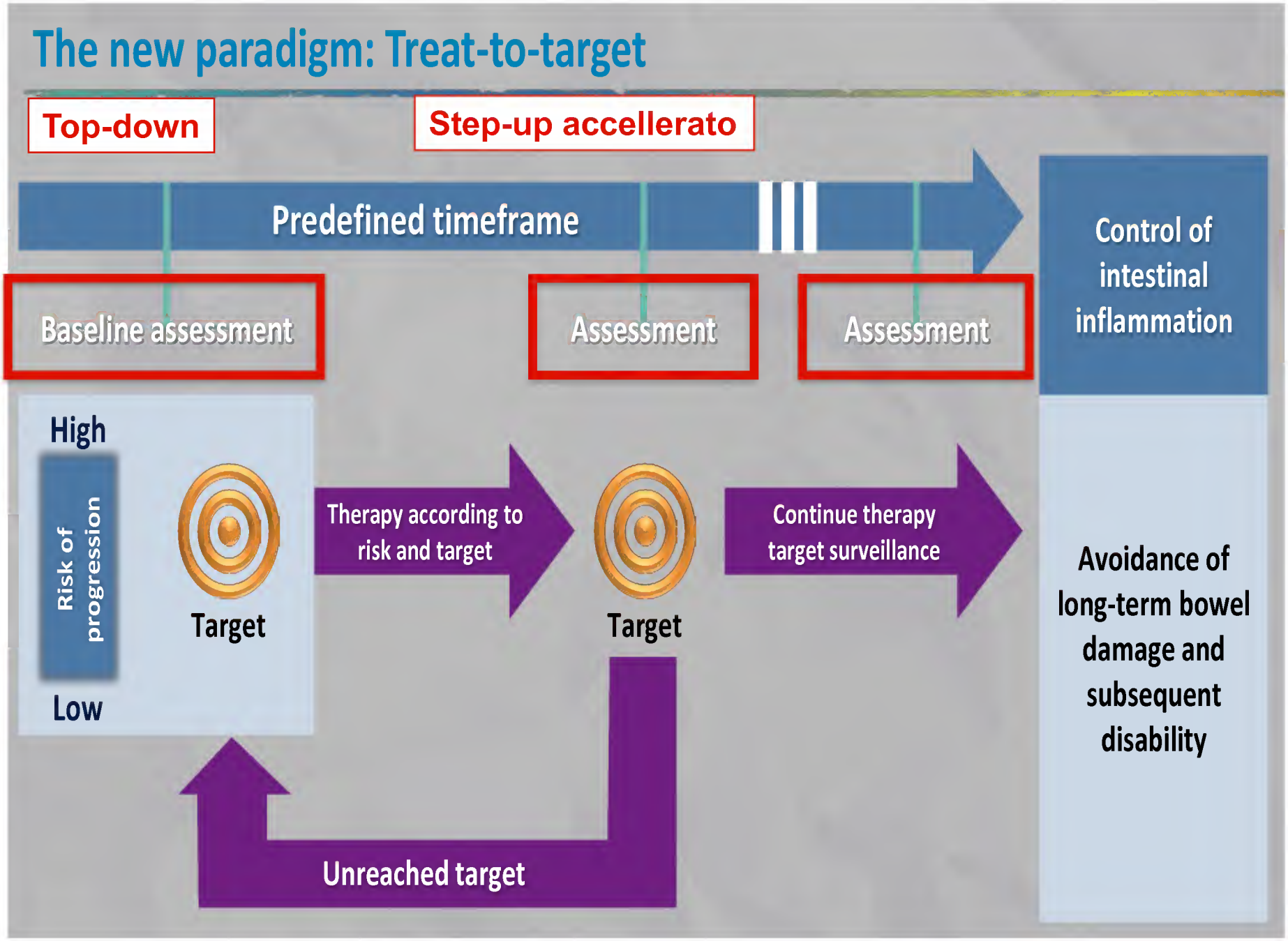
Fattori di rischio per cattivo outcome



be considered as potentially predictive for poor outcome:

- deep colonic ulcerations on endoscopy
- persistent severe disease despite adequate induction therapy
- extensive (pan-enteric) disease
- marked growth retardation >−2.5 (minus 2.5) height Z scores),
- severe osteoporosis
- stricturing and penetrating disease (B2 and/or B3 disease behavior[25,26]) at onset
- severe perianal disease


Digestive damage
Inflammatory activity
(CDAI, CDEIS, CRP)
Stricture
Surgery
Window
of opportunity
Fistula/abscess
Stricture
Disease
onset
Diagnosis
Early
disease


The new paradigm: Treat-to-target
Top-down
Step-up accellerato
Predefined timeframe
Baseline assessment
Assessment
Assessment
Control of intestinal inflammation
High
Risk of progression
Low
Target
Therapy according to risk and target
Target
Continue therapy target surveillance
Avoidance of long-term bowel damage and subsequent disability
Unreached target

Step-care algorithm :

treatment escalation solely on the basis of symptoms

Patient-tailored algorithm :

- **Phenotype of IBD**
- **Age-related IBD**
- **Genetic and serum markers** (not clinical role)
- **Personalization of therapy**

The new concept of "deep remission"

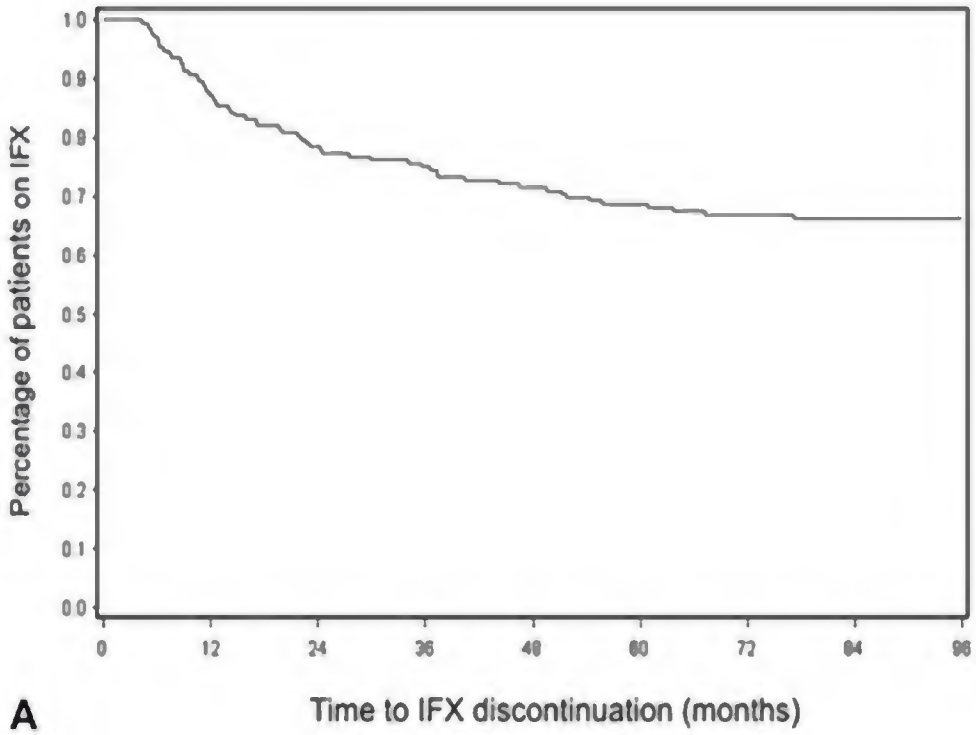
Aim of personalization of therapy :

- Appropiate drugs
- Dose regimen
- Reduce the risk of adverse events
- Maximize the treatment response
- Reduced the risk of overtreating

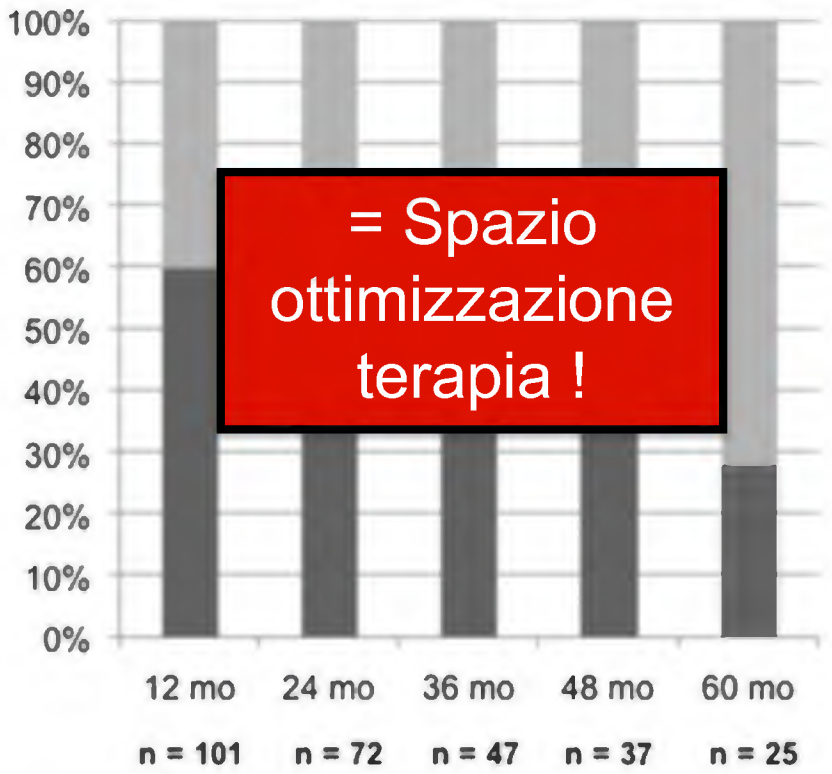
- Genetic markers for response
- Mucosal markers for response
- Genetic markers for adverse events
- **Drug monitoring**

NON RISPOSTA alla TERAPIA CON ANTI-TNF

- **Primary non responders (pochi, 10-15%)**
- **<u>Secondary loss of response</u>**

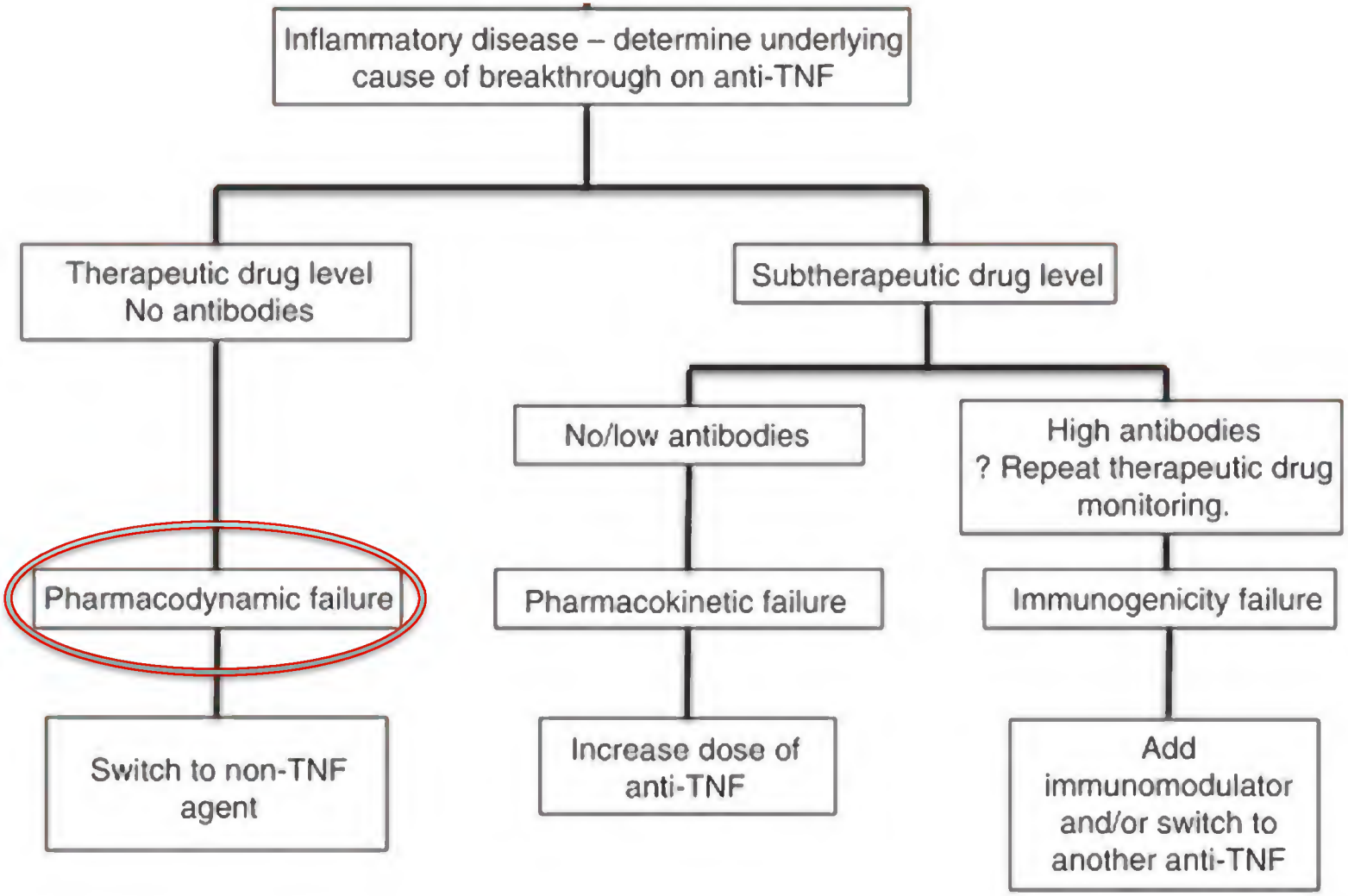


Tempo per discontinuare la terapia con IFX

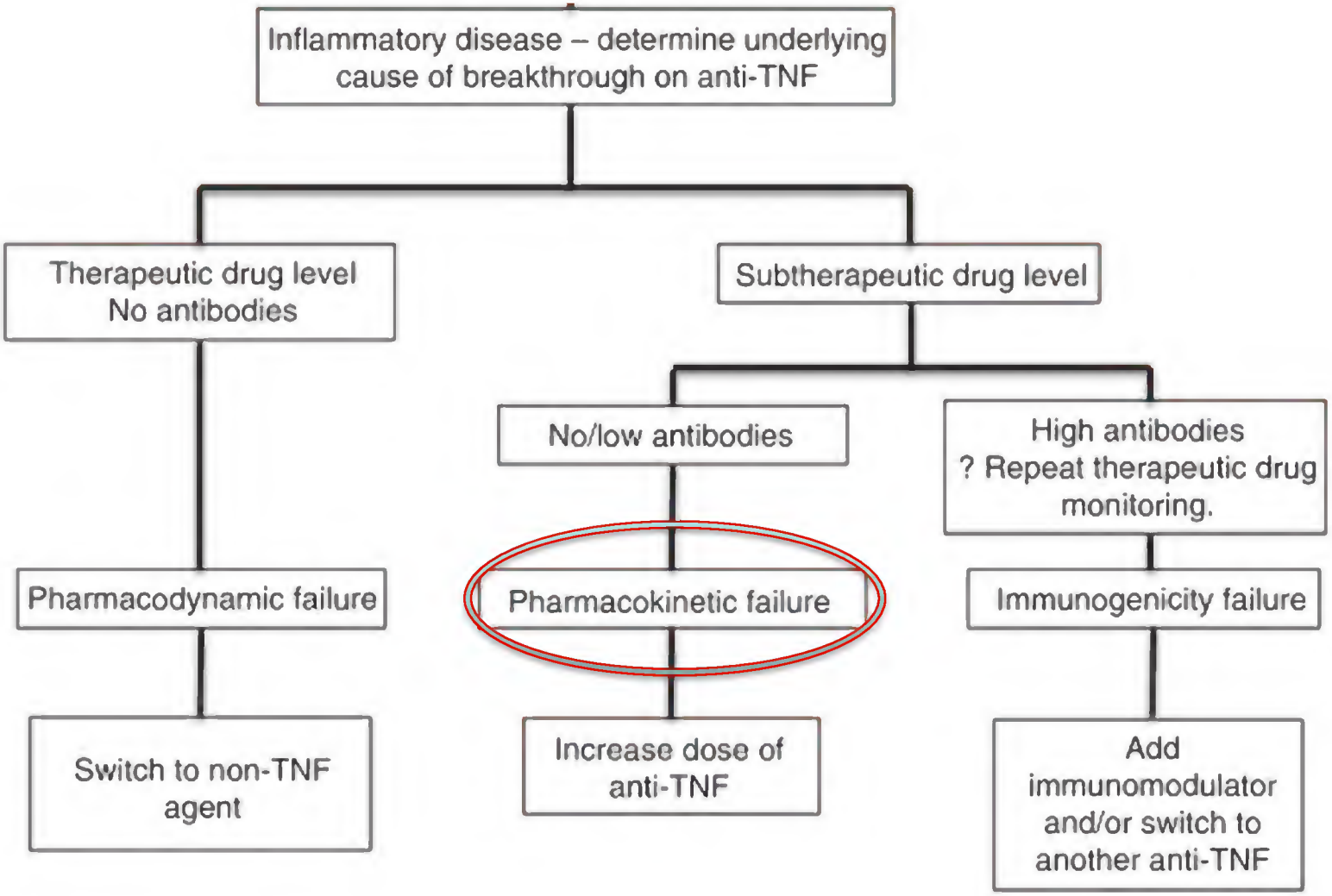


Pz che hanno necessitato di aggiustamento della terapia con IFX

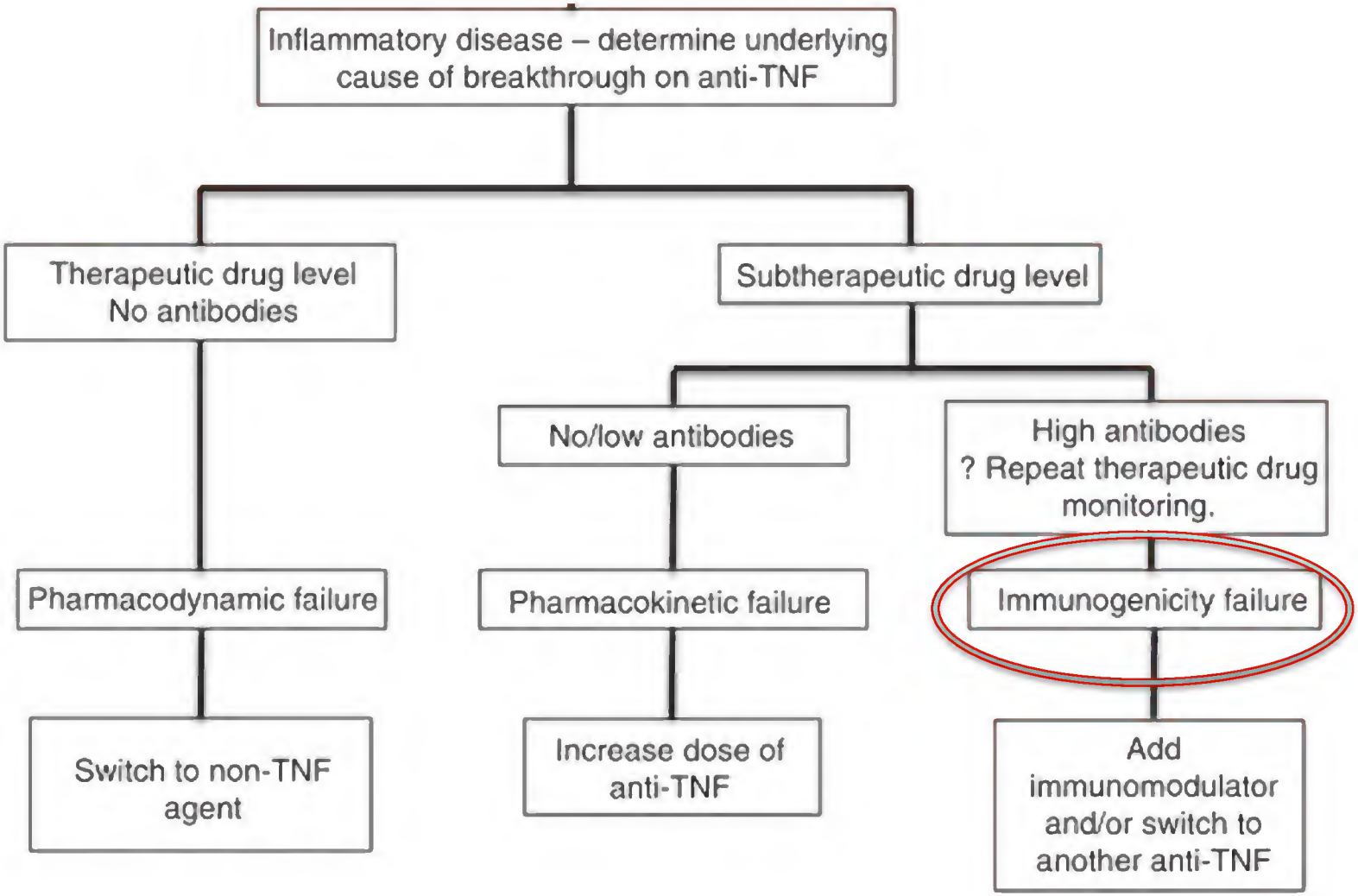
Perdita risposta anti-TNF



Perdita risposta anti-TNF



Perdita risposta anti-TNF



Malattia refrattaria anti-TNF

Assenza o perdita risposta o Aes a anti-TNF

30-50 %

Ottimizzare i biologici
"Altri" biologici

-Ustekinumab
-Vedolizumab

Chirurgia

Trapianto cellule staminali

Talidomide

Anti IL 12 e 23

Anti-integrina alfa 4-beta 7

Effect of Thalidomide on Clinical Remission in Children and Adolescents With Refractory Crohn Disease
A Randomized Clinical Trial

Risk of Infection and Prevention in Pediatric Patients With IBD: ESPGHAN IBD Porto Group Commentary

Reach study (IFX) : infezioni severe con ospedalizzazione 6%

Aumentato rischio infezioni in malattie prevenibili :

- Varicella
- Pneumococco
- Influenza
- Papillomavirus (Pap test ++) ?

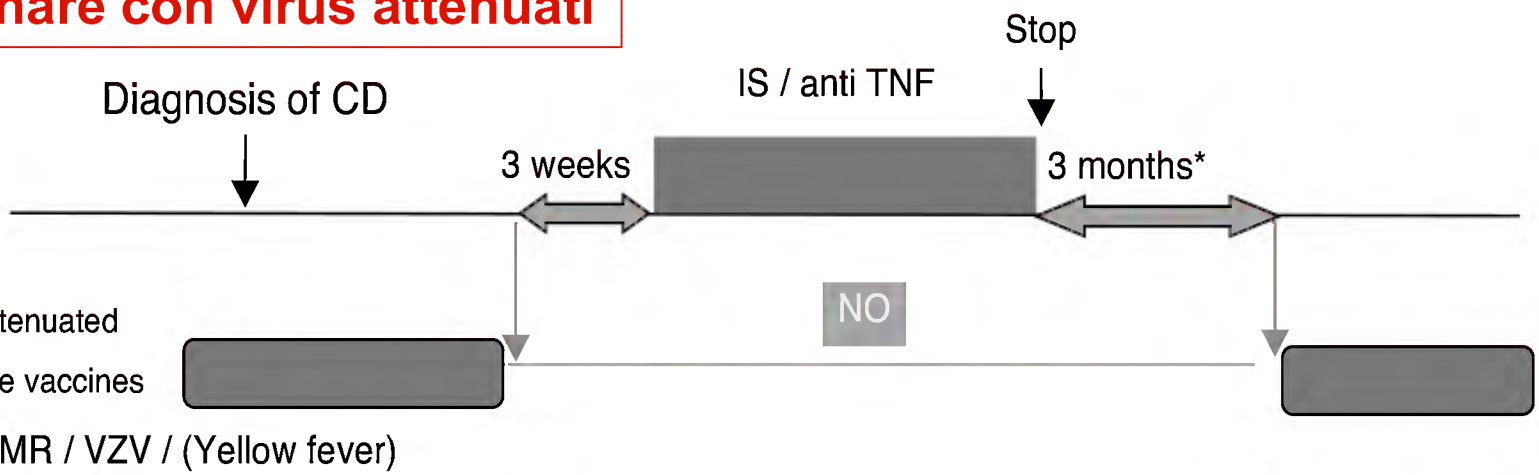
An australian audit of vaccination status in children and adolescents with inflammatory bowel disease

101 IBD età media 12.1 aa 50% immunosoppressiva

5% pneumococco 10% antiinfluenzale

Risk of Infection and Prevention in Pediatric Patients With IBD: ESPGHAN IBD Porto Group Commentary

Valutare stato vaccinale
Anamnesi per varicella
Vaccinare con virus attenuati



Vaccinare per influenza, pneumococco e HPV

DTP / Recombinant hepatitis B vaccines / Influenza yearly / Pneumococcal polysaccharide/ HPV girls under 18 / Hepatitis A

grazie