

REFERRAL TO CARE NELLE MALATTIE INFIAMMATORIE CRONICHE INTESTINALI

IL PATIENT JOURNEY del paziente con IBD

NAPOLI

HOLIDAY INN

Centro Direzionale - Isola E6,
Via Domenico Aulisio, Napoli

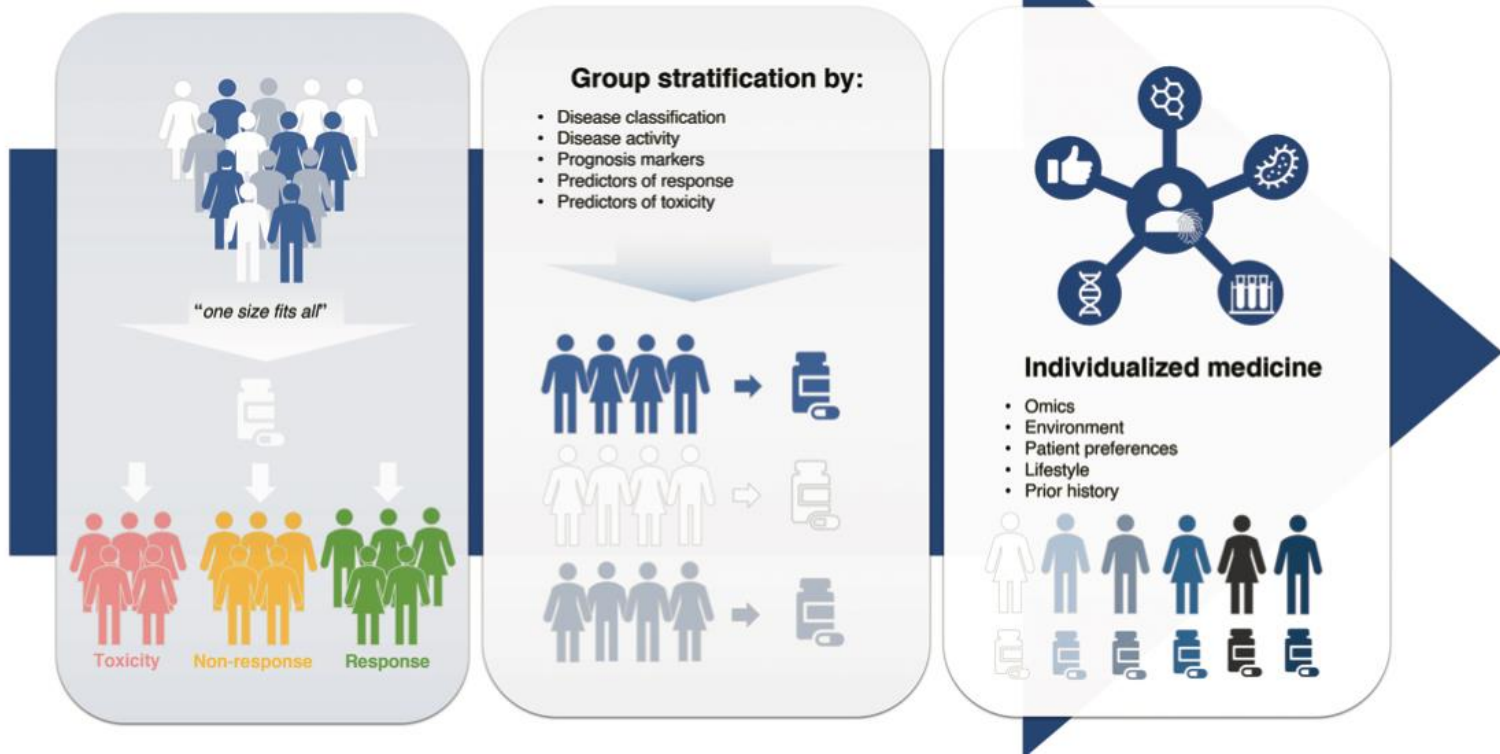
27 Marzo
2024



TITOLO:

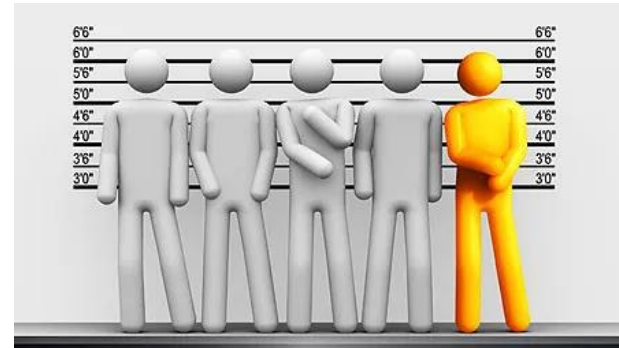
Ritardo Diagnostico: il ruolo della
diagnosi precoce nella gestione delle
MICI

RELATORE: Angela Sannino



Noor NM et al Early Diagnosis, Early Stratification, and Early Intervention to Deliver Precision Medicine in IBD. *Inflamm Bowel Dis.* 2022 Aug

Delayed diagnosis of IBD may potentially impact disease progression and subsequent clinical outcomes



Poor clinical outcomes may also negatively impact psychological well-being, quality of life, and work productivity, at a considerable cost to the individual and the economy

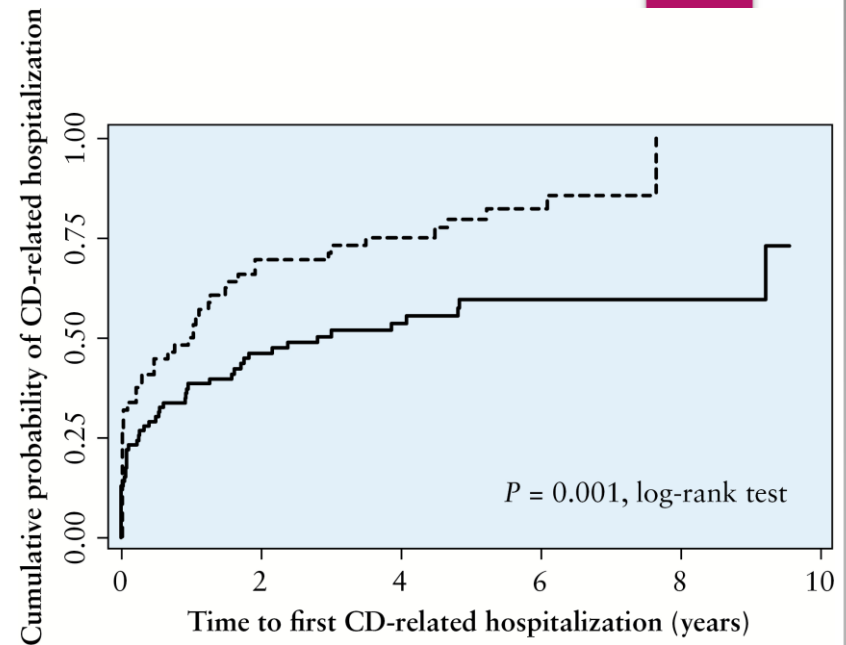
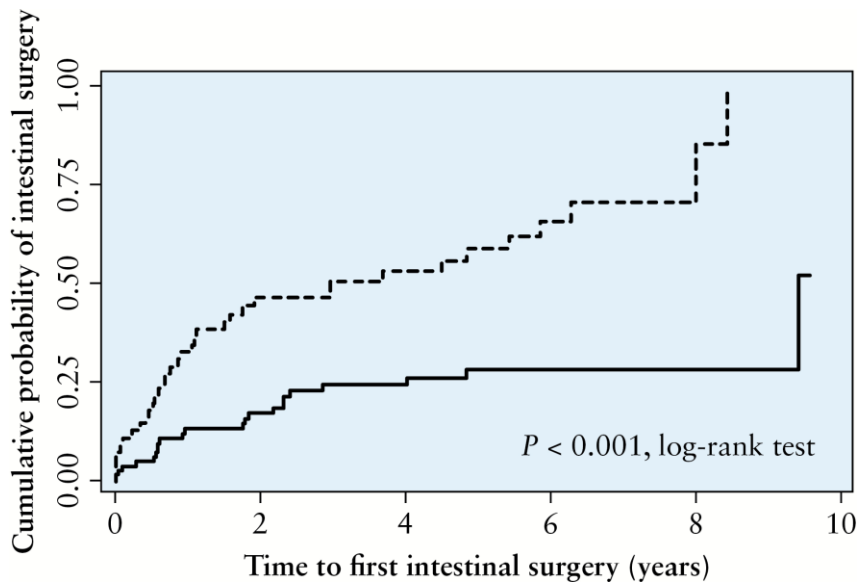


Table 1. Diagnostic delay and outcomes of Crohn's disease.

Author	Diagnostic Delay	Outcome	Ratio	p-Value
Schoepfer et al. [7]	4–9 months	Bowel stricture	OR 1.55	0.047
	≥25 months		OR 1.76	0.011
Pellino et al. [6]	>18 months	CD-related surgery	NA	0.02
Schoepfer et al. [21]	4–9 months	CD-related surgery	OR 1.527	0.056
Moon et al. [22]	10–24 months	Perianal fistula	OR 1.572	0.032
Li et al. [5]	≥25 months	CD-related surgery	OR 1.895	0.004

Ghosh, S. et al Impact of inflammatory bowel disease on quality of life: Results of the European Federation of Crohn's and Ulcerative Colitis Associations (EFCCA) patient survey. *J. Crohns Colitis* 2007

Cantoro L, et al The Earlier You Find, the Better You Treat: Red Flags for Early Diagnosis of Inflammatory Bowel Disease. *Diagnostics* (Basel). 2023 Oct.



Kaplan–Meier curves for the cumulative probability of intestinal surgery

‘complicated CD’ sub-cohort; dotted line

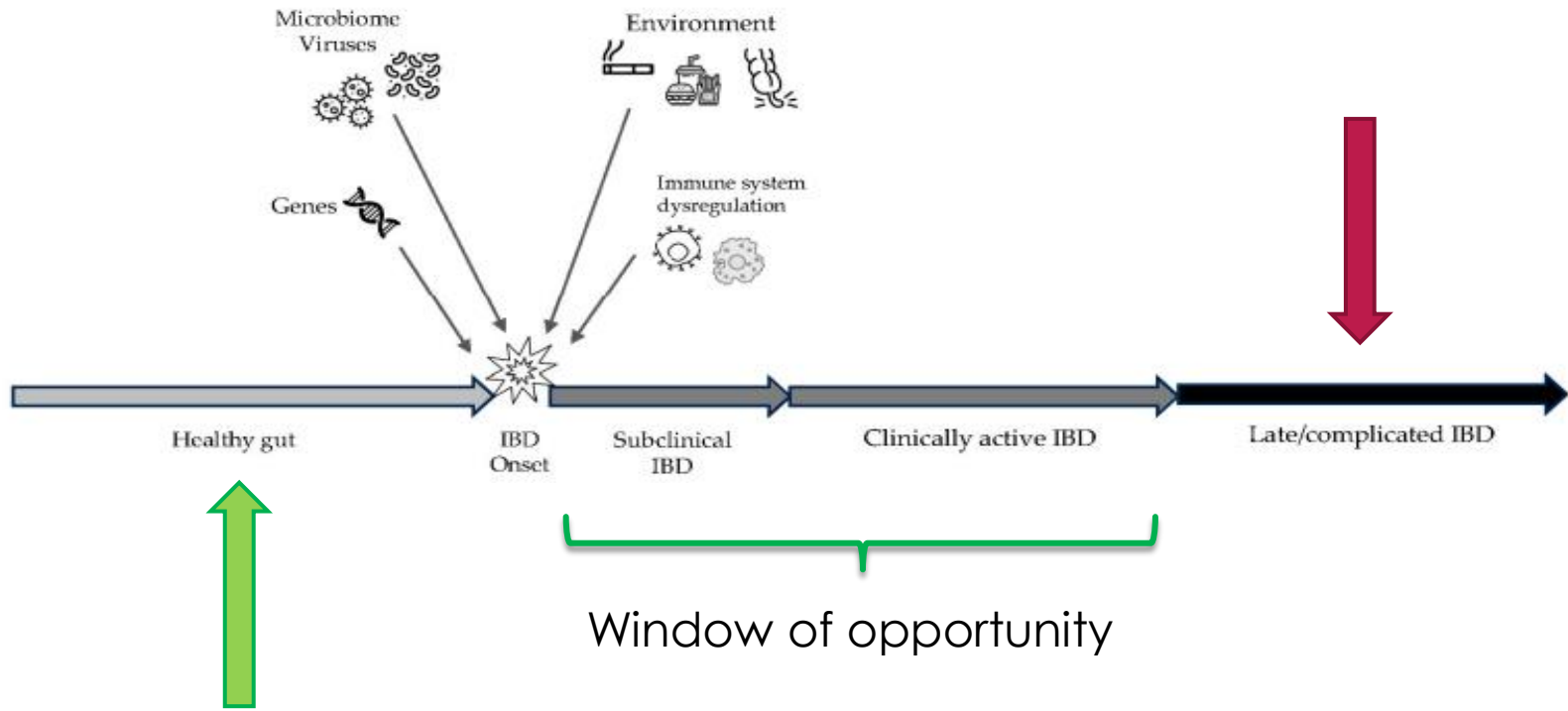
‘early CD’ sub-cohort; solid line

Kaplan–Meier curves for the cumulative probability of CD-related hospitalization

‘complicated CD’ sub-cohort; dotted line

‘early CD’ sub-cohort; solid line

Fiorino et al Prevalence of Bowel Damage Assessed by Cross-Sectional Imaging in Early Crohn’s Disease and its Impact on Disease Outcome, *Journal of Crohn’s and Colitis* March 2017



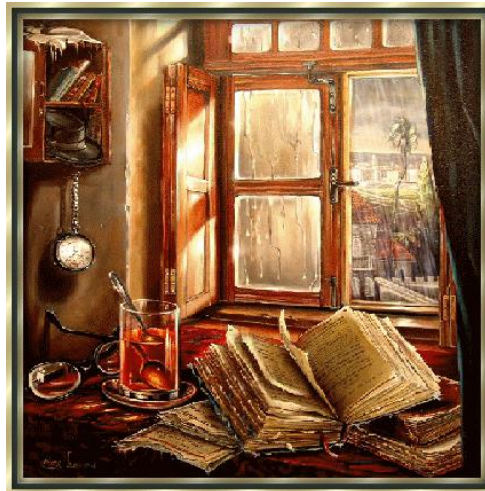
Cantoro L, et al The Earlier You Find, the Better You Treat: Red Flags for Early Diagnosis of Inflammatory Bowel Disease. Diagnostics (Basel). 2023 Oct.

Windows of opportunity: ADVANTAGES

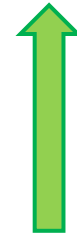


Risk of complications

Disease progression



Time in remission



Dose
Long term ADR
Healthcare costs





Timely access to IBD units to diagnose and manage patients with suspected IBD



IBD diagnosis and referral centre performed in IBD



Fiorino et al Prevalence of Bowel Damage Assessed by Cross-Sectional Imaging in Early Crohn's Disease and its Impact on Disease Outcome, *Journal of Crohn's and Colitis* March 2017

IOIBD (International Organization for the Study of Inflammatory Bowel Diseases) developed a **red flag index** for the early diagnosis of CD in patients presenting with GI symptoms

Parameter	Multiplier
Non-healing or complex perianal fistula or abscess or perianal lesions	5
First-degree relative with confirmed inflammatory bowel disease	4
Weight loss (5% of usual body weight) in the last 3 months	3
Chronic abdominal pain (>3 months)	3
Nocturnal diarrhea	3
Mild fever in the last 3 months	2
No abdominal pain 30–45 min after meals	2
No rectal urgency	2

Every parameter is scored 0 if absent or 1 if present, and then it is multiplied by the relevant multiplier. The sum of each sub-score results in the final score. A score of ≥ 8 identifies a subject with a high probability of having underlying Crohn's disease.

Cantoro L, et al The Earlier You Find, the Better You Treat: Red Flags for Early Diagnosis of Inflammatory Bowel Disease. Diagnostics (Basel). 2023 Oct.

EARLY IDENTIFICATION

Red flag index

EARLY DIAGNOSIS and STAGES

Blood Assessment - CRP

Faecal calprotectin

Bowel damage evaluation



EARLY INTERVENTION

Endoscopic or cross-sectional Imaging within
6 or 9 months from the starts of therapy

SELECTION OF THERAPEUTIC APPROACH

Stratification based on risk factors

HIGH RISK

Early combination therapy

LOW RISK

Step-up Therapy

KEY
FINDINGS
TO DATE

KEY
ONGOING
STUDIES

EARLY DIAGNOSIS

GEM

- **UC:** faecal proteolytic activity precedes diagnosis



- **CD:** increased intestinal permeability associated with HR 3.03 (95% CI 1.64-5.63) of CD

PREDICTS

- Panel of serum antibodies and proteins

- AUROC 0.76 in predicting CD development within 5 years



Red Flags Index

- Early symptoms and signs index has high predictive value for the diagnosis of CD

- Sensitivity and Specificity of 0.94



IBD-Character

- Multi-omic analyses being performed on blood, stool and biopsy samples obtained from 678 patients with IBD



Asca
pANCA
Anti E.Coli outer membran
porin

Noor NM et al Early Diagnosis, Early Stratification, and Early Intervention to Deliver Precision Medicine in IBD. Inflamm Bowel Dis. 2022 Aug

EARLY STRATIFICATION

PROGNOSIS	<p>GWAS</p> <ul style="list-style-type: none"> • Distinct genes associated with worse disease outcome <i>but low odds ratios</i> ✘ • Polygenic risk scores? 	RESPONSE and NON-RESPONSE	<p>Fluorescent targeting</p> <ul style="list-style-type: none"> • Anti-TNF response – cells with membrane bound TNF <ul style="list-style-type: none"> ◦ Clinical response at week 12: 92% vs 15%, p<0.01
	<p>RISK</p> <ul style="list-style-type: none"> • Gene signature of ileal genes controlling extracellular matrix production <ul style="list-style-type: none"> ◦ HR 1.70 (95% CI 1.12-2.57) of stricturing behaviour 		<p>HLA-DQA1*05 (PANTS)</p> <ul style="list-style-type: none"> • Associated with greater likelihood of immunogenicity to infliximab and adalimumab <ul style="list-style-type: none"> ◦ HR of 1.90 (95% CI 1.60-2.25)
SAFETY	<p>TPMT and NUDT15</p> <ul style="list-style-type: none"> • Risk of thiopurine-induced myelosuppression 		<p>OSM</p> <ul style="list-style-type: none"> • High pre-treatment OSM expression strongly associated with anti-TNF non-response <ul style="list-style-type: none"> ◦ RR 5.00 (95% CI 1.4-17.9)
	<p>HLA-DQA1 and HLA-DRB1</p> <ul style="list-style-type: none"> • Risk of thiopurine-induced pancreatitis 		<p>TREM-1</p> <ul style="list-style-type: none"> • Colonic biopsies predicting clinical non-response <ul style="list-style-type: none"> ◦ AUC 0.82
			<p>GIMATS</p> <ul style="list-style-type: none"> • Unique cellular module associated with anti-TNF non-response

PROFILE

- 1st precision medicine RCT in IBD. Comparing relative efficacy of top-down vs accelerated step-up treatment between biomarker defined subgroups of 400 patients with CD

Noor NM et al Early Diagnosis, Early Stratification, and Early Intervention to Deliver Precision Medicine in IBD. Inflamm Bowel Dis. 2022 Aug

EARLY TREATMENT



EARLY MONITORING

REACT-1



- Early combined immunosuppression (ECI) not better than conventional management (CM) in treating CD symptoms
 - Clinical remission 66% vs 62%, $p=0.52$
- *BUT* lower 24 month rates of surgery, hospital admission and serious disease related complications in ECI practices vs CM practices
 - Adverse outcomes 28% vs 35%, $p<0.01$

CALM



- Timely treatment escalation based on clinical symptoms and biomarkers results in better clinical and endoscopic outcomes than decisions driven by symptoms alone in CD
 - Endoscopic remission 46% vs 30%, $p=0.01$
- Deep remission associated with lower risk of major adverse outcome
 - HR 0.19 (95% CI 0.07-0.31)

POCER



- In postoperative CD, active control with early colonoscopy and treatment escalation for recurrence is better than standard treatment alone for prevention of recurrence
 - Endoscopic recurrence 49% vs 67%, $p=0.03$

STARDUST



- In CD patients treated with ustekinumab, tight monitoring and standard of care strategies had similar rates of steroid-free clinical remission and endoscopic response at week 48.
 - Clinical remission 56% vs 63%, NS
 - Endoscopic response 34% vs 29%, NS

REACT-2

- Cluster RCT comparing endoscopy-based treatment escalation vs clinical symptom-based treatment escalation in 1100 patients with CD



VERDICT

- 1st tight control RCT in UC to determine the optimal treatment targets in 660 patients with UC



Noor NM et al Early Diagnosis, Early Stratification, and Early Intervention to Deliver Precision Medicine in IBD. Inflamm Bowel Dis. 2022 Aug

Take Home Message

Diagnostic delay is a very important challenge in IBD management

It's associated with a higher risk of complications and major surgery

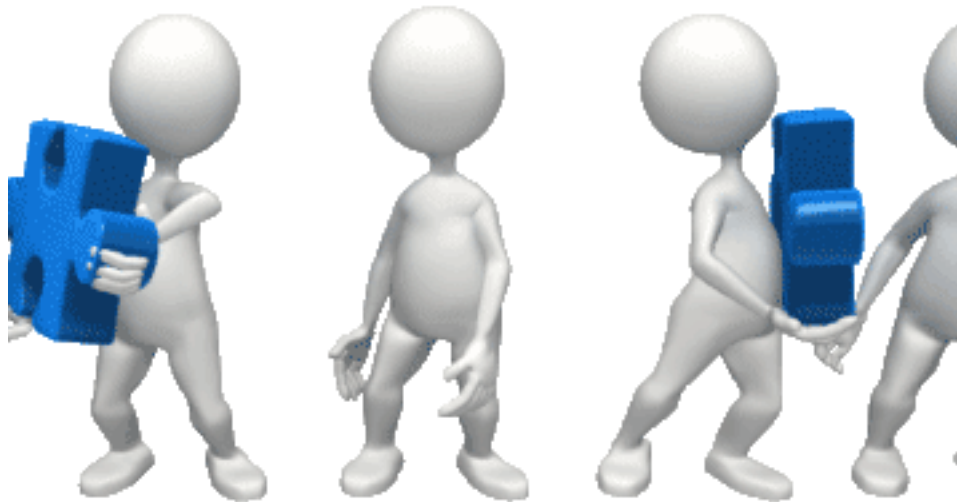
Early diagnosis is likely to allow timely early treatment with effective treatments

IBD shows a window of opportunity where patients can have the highest chance to respond to therapies and limit the risk of disease evolution to complications, organ damage, and surgery

The Red Flags Index and non-invasive first-line diagnostic tools such as fecal calprotectin might help in identifying patients with early-onset IBD

Take Home Message

Healthcare professionals who are not specialists in IBD or not gastroenterologists should be aware of the initial symptoms and signs of IBD and have a close connection with specialists in order to start the proper diagnostic workup as quickly as possible



Grazie per l'attenzione

**REFERRAL TO CARE NELLE MALATTIE
INFIAMMATORIE
CRONICHE INTESTINALI**
IL PATIENT JOURNEY del paziente con IBD

NAPOLI
HOLIDAY INN
Centro Direzionale - Isola E6,
Via Domenico Aulisis, Napoli

27 Marzo
2024