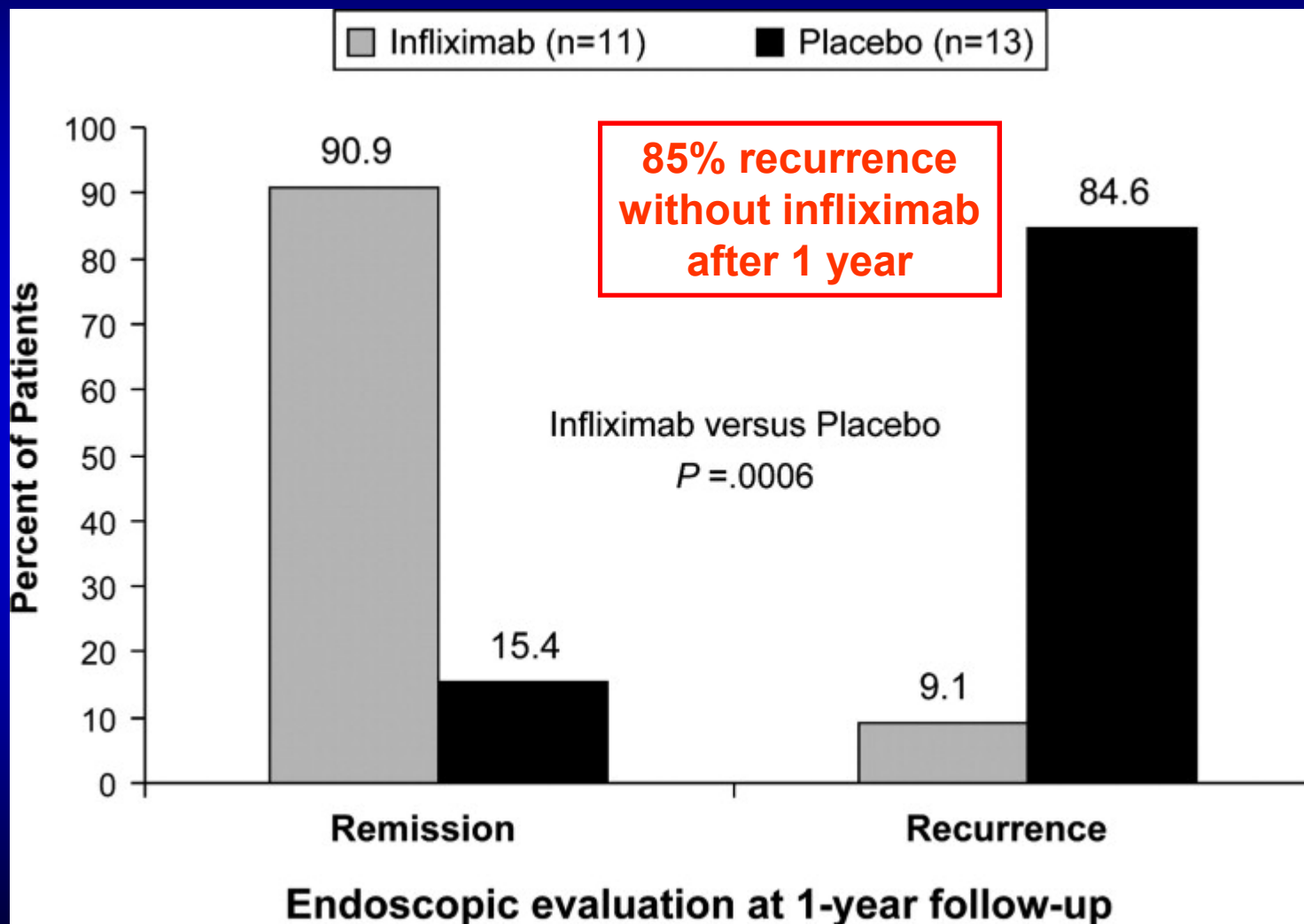
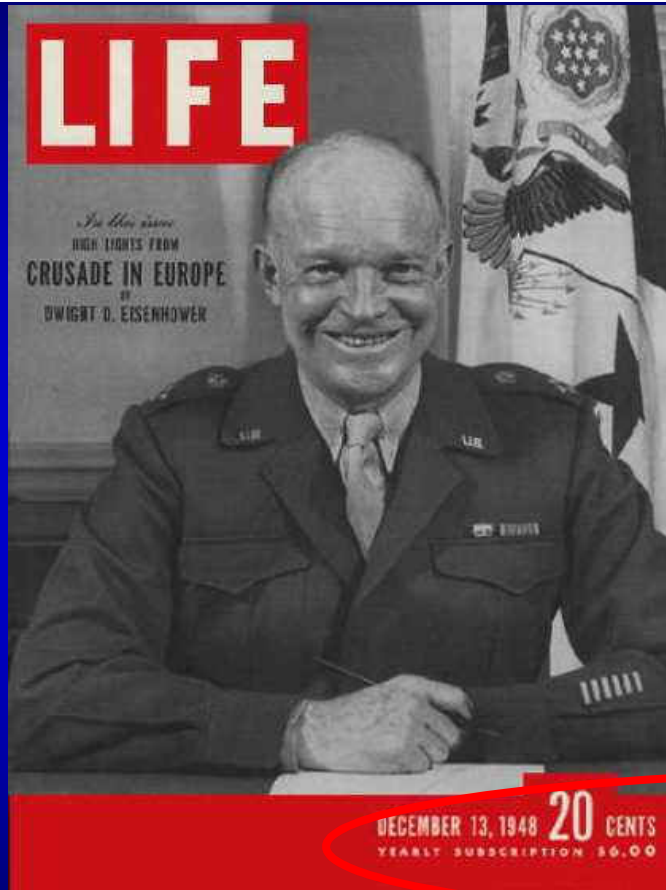


# Infliximab prevents recurrence of Crohn's disease after ileocecal resection



Regueiro M et al. *Gastroenterology* 2009;136:441-50.

# Ein amerikanischer Präsident mit M. Crohn Noch vor der Erstbeschreibung durch B. Crohn



Dwight D. Eisenhower  
34. Präsident der USA  
M. Crohn, ileale Stenose:  
1956 Ileotransversotomie

Eisenhower wrote in his 1967 book "At Ease: Stories I Tell to Friends":

*"Three decades would pass before I would learn the cause of my repeated distress, when doctors described it as 'a young man's disease' ileitis."*

**1923: Appendectomy**

**1949: Abdominal X-ray:**

*"irregularity of caliber of the small bowel."*

# Ein amerikanischer Präsident mit M. Crohn Noch vor der Erstbeschreibung durch B. Crohn



The man who beat Hitler and became U.S. president –  
*with Crohn's disease*

gettyimages®

117297614

# Stadien autoimmuner NNR-Insuffizienz

NNR-Funktion / Masse

Genetische  
Prädisposition



Eunice  
Kennedy  
(Schwester  
mit M. Addison)

1917

Asympto-  
matisch



1948

Symptomat.  
unter Streß



1961

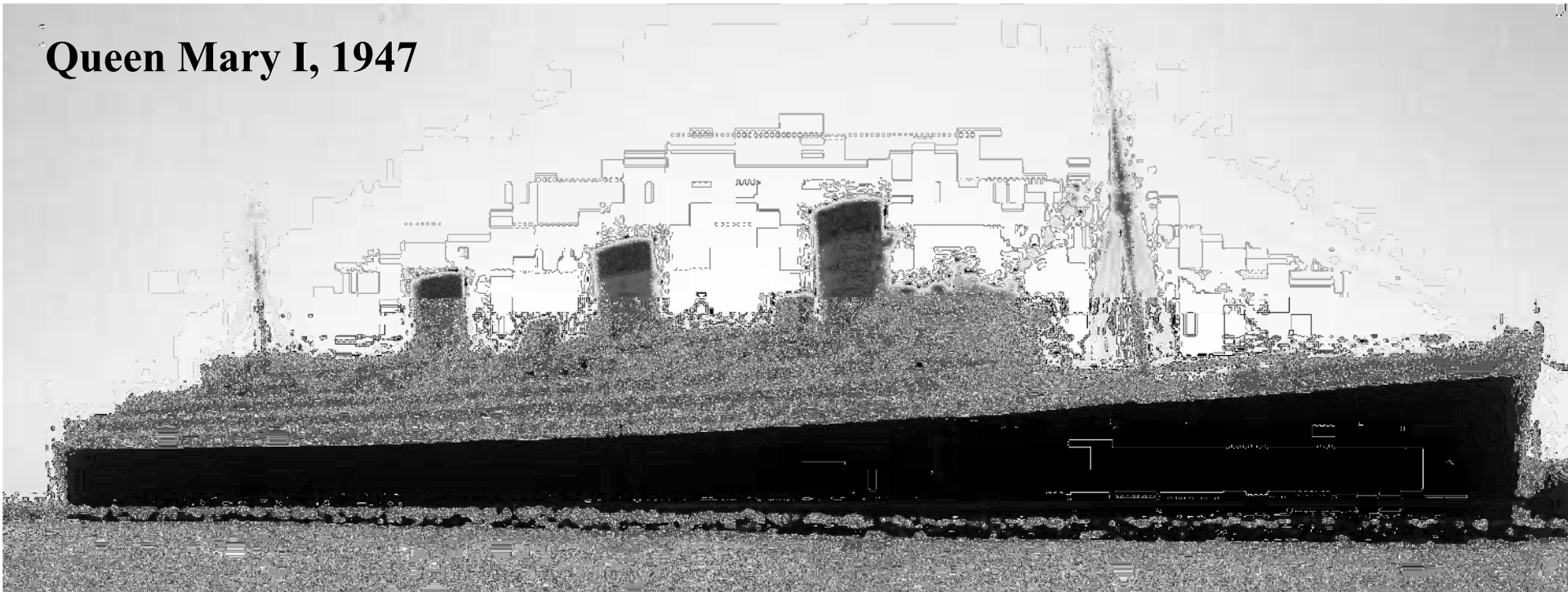
Symptomatisch



1963



# Queen Mary I, 1947



London Clinic 1947



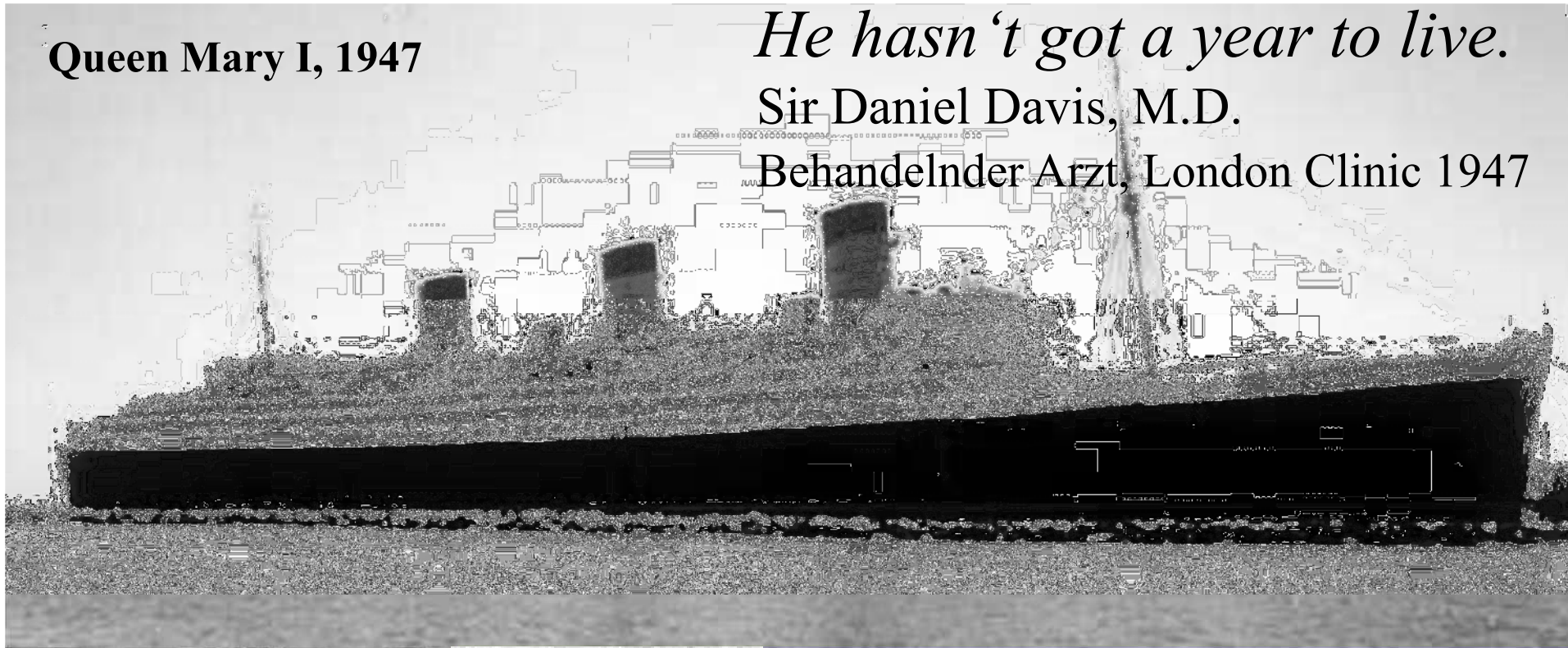
*He hasn't got a year to live.*  
Sir Daniel Davis, M.D.  
Behandelnder Arzt, London Clinic 1947

Queen Mary I, 1947

*He hasn't got a year to live.*

Sir Daniel Davis, M.D.

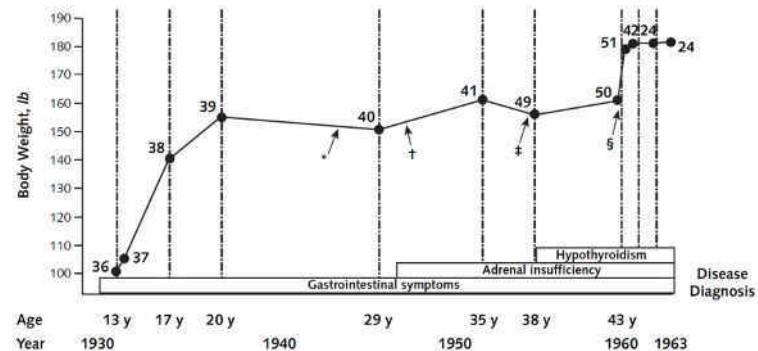
Behandelnder Arzt, London Clinic 1947



London Clinic 1947



Figure. John F. Kennedy's medical profile.



The time of diagnosis of gastrointestinal symptoms, adrenal insufficiency, and hypothyroidism are plotted against Kennedy's body weight at various ages. Arabic numbers at each solid circle are the references from which body weight information was obtained.

\* Sinking of PT-109, August 1943.

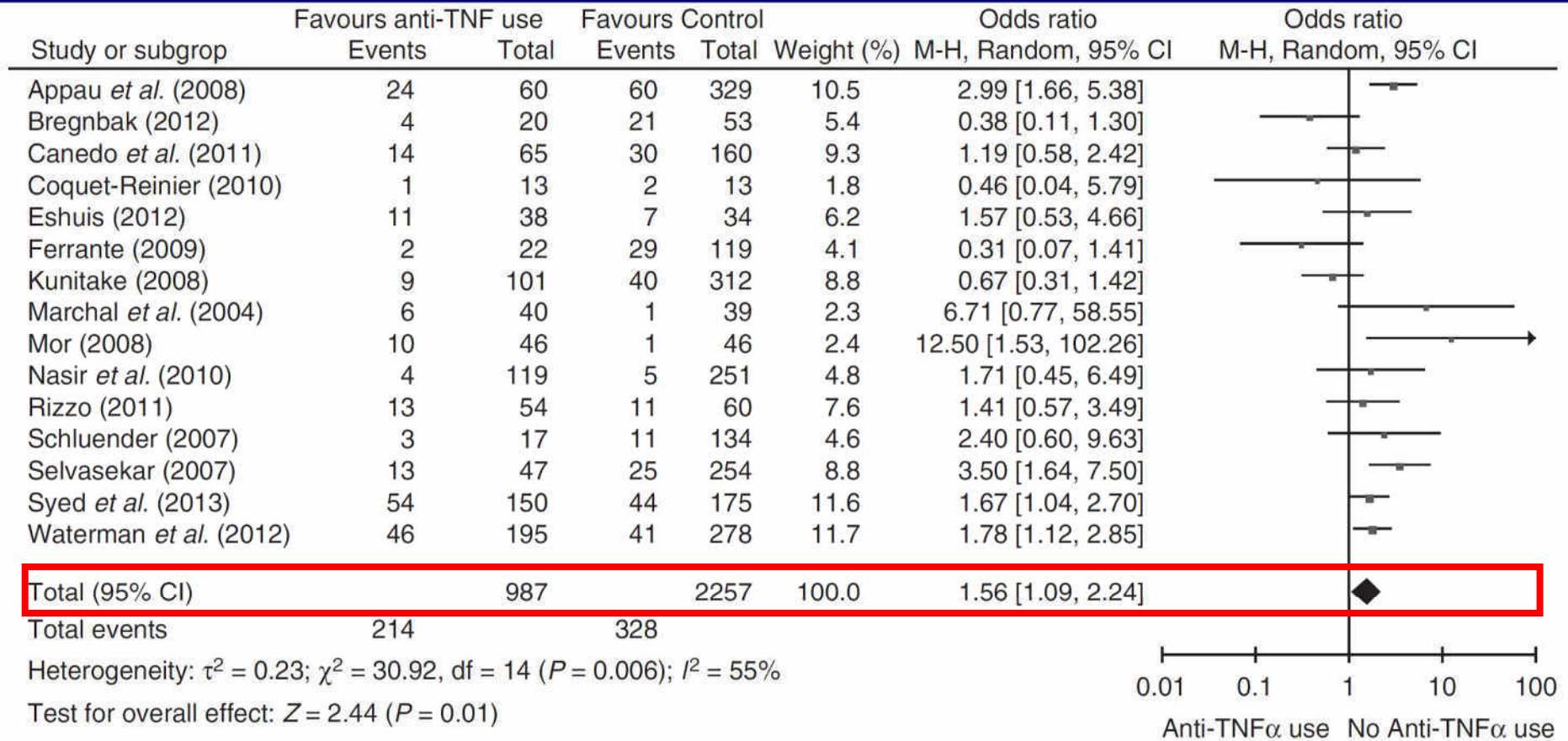
† Addison disease diagnosed, September 1947.

‡ Unsuccessful back surgery, October 1954.

§ Suspected initiation of testosterone therapy, July to August 1960.



# Anti-TNF therapy: Slight increase in postoperative complications



**Figure 1** | Forrest plot of studies that assessed post-operative infectious complications on peri-operative anti-TNF $\alpha$  therapies compared to controls.

# Lymphozyten-Migration

**Aktivierte Lymphozyten migrieren von Blutgefäßen in die Darmmukosa**





## Anti-TNF therapy and slight increase in postoperative complications is biased !

more likely to have severe disease. Notably, seven studies that reported increased risks of infectious complications also reported higher concurrent use of immunomodulators or corticosteroids in the group treated perioperatively with infliximab.<sup>31, 32, 37, 38, 45–47</sup> Accordingly, increases in the rate of complications may reflect differences in morbidity rather than an effect of anti-TNF $\alpha$  therapy.

# Anti-TNF therapy and slight increase in postoperative complications is biased !

## Conclusion

Anti-TNF $\alpha$  therapies appear to increase the risk of post-operative complications. The increase in risk is small, and may well reflect residual confounding rather than a true biological effect. Nevertheless, physicians should exercise caution when continuing biological therapies during the peri-operative period.





# Preoperative anti-TNF treatment

and surgeons. Patients with undetectable levels of anti-TNF can likely go on to surgery with little risk of adverse consequences related to treatment with anti-TNF, whereas those with higher anti-TNF- $\alpha$  levels (>3  $\mu\text{g}/\text{ml}$ ) have a higher risk for overall postoperative morbidity and infectious complications. In such patients, the decision to wait for the drug serum washout period may be wise in patients undergoing more elective surgery for CD.

# Risk factors for complications after ileocolonic resections in Crohn's disease

UNITED EUROPEAN  
GASTROENTEROLOGY  
**ueg journal**

*Original Article*

## Risk factors for complications after ileocolonic resection for Crohn's disease with a major focus on the impact of preoperative immunosuppressive and biologic therapy: A retrospective international multicentre study

Takayuki Yamamoto<sup>1</sup>, Antonino Spinelli<sup>2</sup>, Yasuo Suzuki<sup>3</sup>,  
Rogerio Saad-Hossne<sup>4</sup>, Fabio Vieira Teixeira<sup>5</sup>,  
Idblan Carvalho de Albuquerque<sup>6</sup>, Rodolff Nunes da Silva<sup>7</sup>,  
Ivan Folchini de Barcelos<sup>7</sup>, Ken Takeuchi<sup>3</sup>, Akihiro Yamada<sup>3</sup>,  
Takahiro Shimoyama<sup>1</sup>, Lorete Maria da Silva Kotze<sup>8</sup>, Matteo Sacchi<sup>9</sup>,  
Silvio Danese<sup>10</sup> and Paulo Gustavo Kotze<sup>7</sup>

United European Gastroenterology Journal

2016, Vol. 4(6) 784-793

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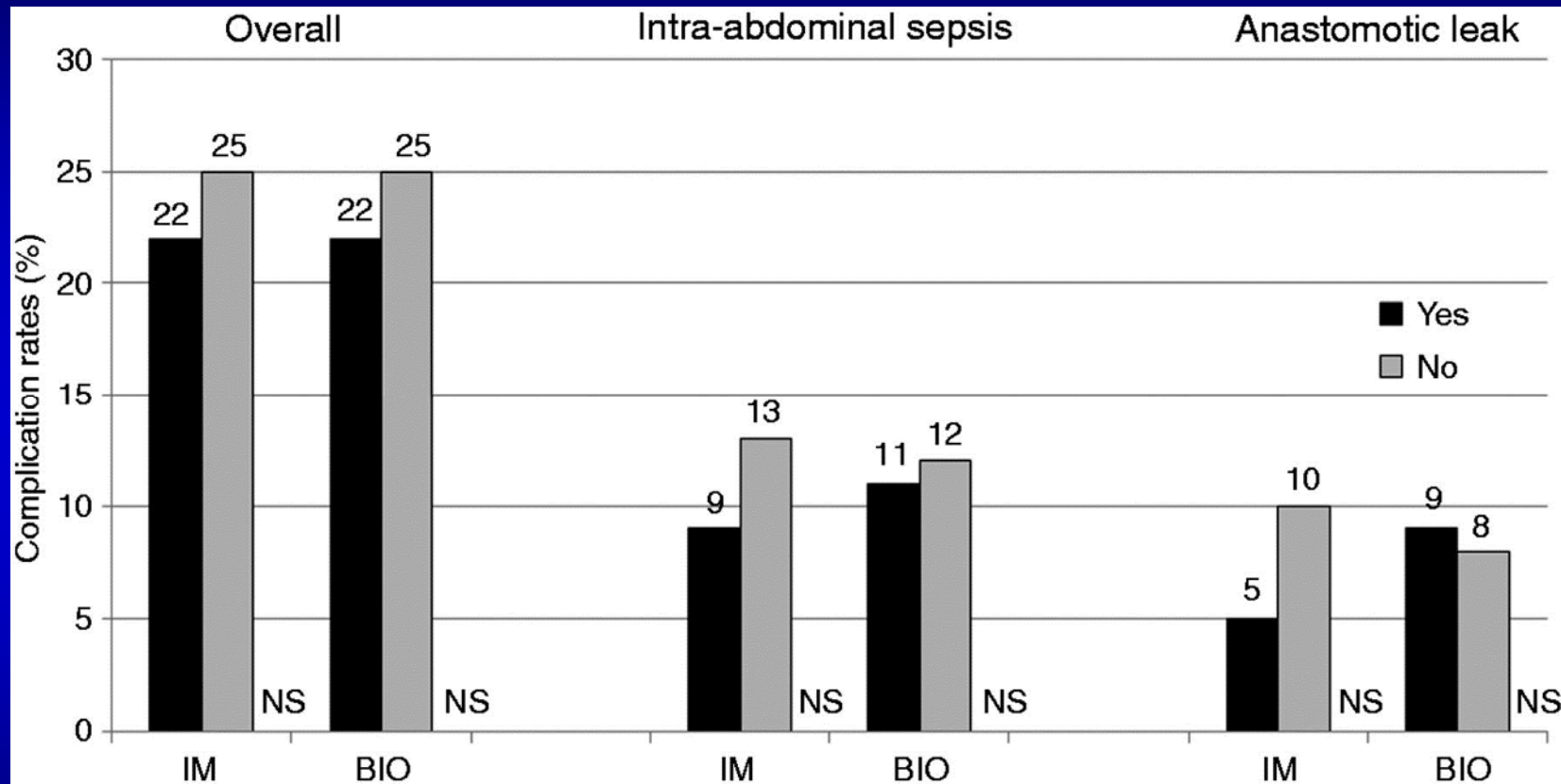
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DOI: 10.1177/2050640615600116

[ueg.sagepub.com](http://ueg.sagepub.com)



# Risk factors for complications after ileocolonic resections in Crohn's disease



Neither immunosuppressive nor biologic therapy prior to surgery was significantly associated with the incidence of overall complications, intra-abdominal sepsis or anastomotic leak.

Yamamoto T et al. *United European Gastroenterology Journal* 2015;4:784-793.



# Risk factors for complications after ileocolonic resections in Crohn's disease

	Overall complications OR (95% CI)	Intra-abdominal sepsis OR (95% CI)	Anastomotic leak OR (95% CI)
Age at surgery: < 17 years vs. 17-40 years vs. > 40 years	<sup>a</sup> P=0.69, <sup>b</sup> P=0.55 1.23 (0.44-3.45) <sup>a</sup> 1.46 (0.42-5.04) <sup>b</sup>	<sup>c</sup> P=0.72, <sup>d</sup> P=0.96 1.28 (0.34-4.75) <sup>c</sup> 1.04 (0.21-5.08) <sup>d</sup>	<sup>e</sup> P=0.24, <sup>f</sup> P=0.29 2.56 (0.54-12.11) <sup>e</sup> 2.79 (0.42-18.04) <sup>f</sup>
Gender: male vs. female	P=0.79 1.10 (0.55-2.17)	P=0.91 0.95 (0.37-2.42)	P=0.66 1.27 (0.43-3.79)
<b>Behaviour of CD: perforating disease</b> vs. non-perforating disease	P=0.63 1.18 (0.60-2.30)	<b>P=0.04</b> <b>2.67 (1.04-6.86)</b>	P=0.47 0.67 (0.23-1.99)
Smoking: yes vs. no	P=0.38 1.45 (0.63-3.35)	P=0.19 2.02 (0.71-5.78)	P=0.11 2.76 (0.80-9.47)
Preoperative steroids: yes vs. no	P=0.75 1.12 (0.56-2.23)	P=0.52 1.34 (0.55-3.29)	P=0.10 2.33 (0.84-6.43)
Preoperative immunosuppressants: yes vs. no	P=0.41 0.73 (0.34-1.54)	P=0.47 0.68 (0.24-1.93)	P=0.13 0.35 (0.09-1.37)
Preoperative biologics: yes vs. no	P=0.50 0.79 (0.39-1.59)	P=0.84 1.10 (0.43-2.81)	P=0.70 1.23 (0.42-3.59)
<b>Previous resection: yes</b> vs. no	P=0.16 1.64 (0.82-3.30)	P=0.68 1.21 (0.48-3.03)	<b>P=0.048</b> <b>2.87 (1.01-8.18)</b>
<b>Blood transfusion: yes</b> vs. no	<b>P=0.02</b> <b>3.02 (1.21-7.52)</b>	P=0.36 1.72 (0.54-5.48)	P=0.52 1.61 (0.38-6.75)
Surgical procedure: open approach vs. laparoscopic approach	P=0.31 1.50 (0.68-3.32)	P=0.18 2.25 (0.68-7.40)	P=0.28 2.18 (0.54-8.82)
Type of anastomosis: side-to-side vs. end-to-end	P=0.53 0.80 (0.39-1.64)	P=0.12 0.48 (0.19-1.20)	P=0.13 0.43 (0.14-1.28)

OR: odds ratio; CI: confidence interval.

**Risk for postoperative complications: multivariate analysis.**

**Yamamoto T et al. *United European Gastroenterology Journal* 2015;4:784-793.**

# Risk factor for wound infection in Crohn's disease

ORIGINAL CONTRIBUTION

## Risk Factors for Surgical Site Infection and Association With Infliximab Administration During Surgery for Crohn's Disease

Motoi Uchino, M.D., Ph.D.<sup>1,2</sup> • Hiroki Ikeuchi, M.D., Ph.D.<sup>1,2</sup>  
Hiroki Matsuoka, M.D., Ph.D.<sup>1,2</sup> • Toshihiro Bando, M.D.<sup>1,2</sup> • Kaoru Ichiki, R.N.<sup>3</sup>  
Kazuhiko Nakajima, M.D., Ph.D.<sup>3</sup> • Naohiro Tomita, M.D., Ph.D.<sup>1</sup>  
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3 Infection Control and Prevention, Hyogo College of Medicine, Hyogo, Japan

*Takayuki Yamamoto et al. United European  
Gastroenterology Journal 2015;4:784-793*

**Uchino M et al. *Dis Colon Rectum* 2013;56:1156-65.**

# Risk factor for wound infection in Crohn's disease

**TABLE 5.** Multivariate logistic regression analysis for risk factors associated with SSI in patients with penetrating Crohn's disease

	<i>Risk factors</i>	<i>p</i>	<i>OR (95%CI)</i>
Overall SSI	COLN	0.40	0.68 (0.28–1.66)
	Clean-contaminated wound	<0.01	0.28 (0.12–0.67)
	Duration of surgery ≥167 min	<0.01	3.09 (1.40–6.79)
	Ostomy creation	0.07	2.29 (0.94–5.60)
	Frequencies of surgery ≥2 times	0.03	2.59 (1.11–6.06)
	5-ASA administration	0.09	0.47 (0.20–1.11)
	Infliximab administration	0.70	0.82 (0.29–2.33)
	Intraoperative blood loss >100 mL	0.88	0.92 (0.34–2.53)
	Proctectomy	<0.01	19.15 (7.52–48.79)
Incisional SSI	COLN	0.09	0.29 (0.11–1.24)
	Clean-contaminated wound	0.06	0.43 (0.18–1.05)
	Ostomy creation	<0.01	4.30 (1.71–10.79)
	Frequencies of surgery ≥2 times	0.24	1.73 (0.69–4.37)
	Age at surgery ≥37 y	0.08	2.05 (0.92–4.57)
	Serum albumin <2.9g/dL	0.19	0.58 (0.26–1.32)
	Infliximab administration	<0.01	0.06 (0.01–0.46)
	Proctectomy	0.02	3.15 (1.22–8.11)
Organ/space SSI	Immunomodulator administration	0.17	6.89 (0.45–105.49)
	Clean-contaminated wound	0.08	0.24 (0.05–1.16)
	Duration of surgery >167 min	0.07	3.27 (0.92–11.71)
	Ostomy creation	0.25	2.18 (0.58–8.19)
	Preoperative serum albumin <2.9g/dL	0.03	4.46 (1.17–17.06)
	Preoperative CRP level ≥2.4 mg/dL	0.12	2.35 (0.79–7.01)
	Postoperative blood sugar ≥200 mg/dL	0.06	3.65 (0.93–14.40)
	Proctectomy	0.04	3.30 (1.08–10.05)

SSI = surgical site infection; COLN = colonic surgery; CRP = C-reactive protein; 5-ASA = 5-aminosalicylic acid.



# Risk factor for wound infection in Crohn's disease

**TABLE 5.** Multivariate logistic regression analysis for risk factors associated with SSI in patients with penetrating Crohn's disease

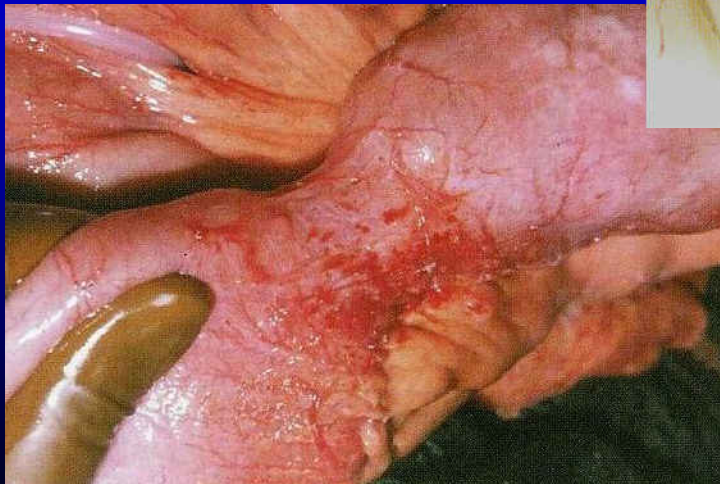
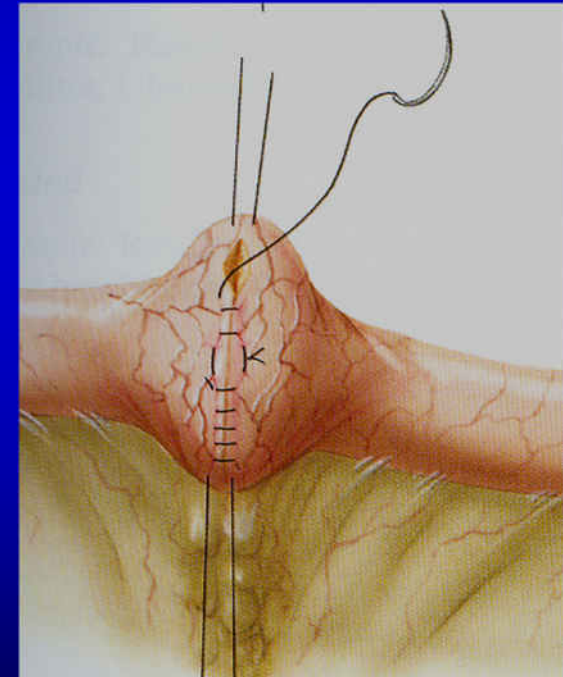
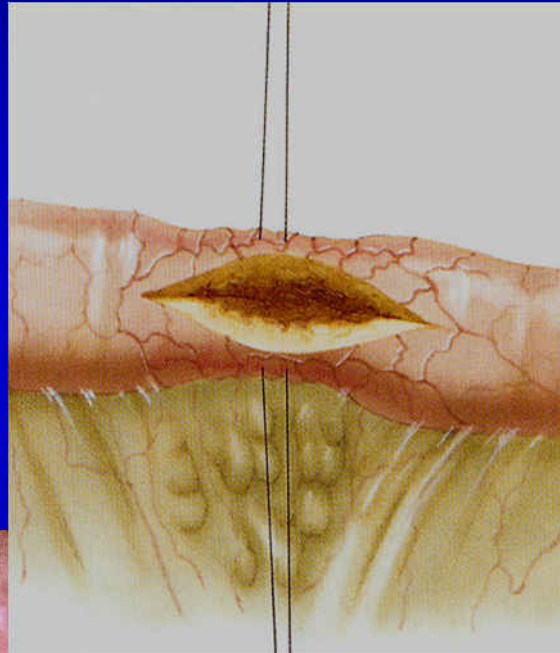
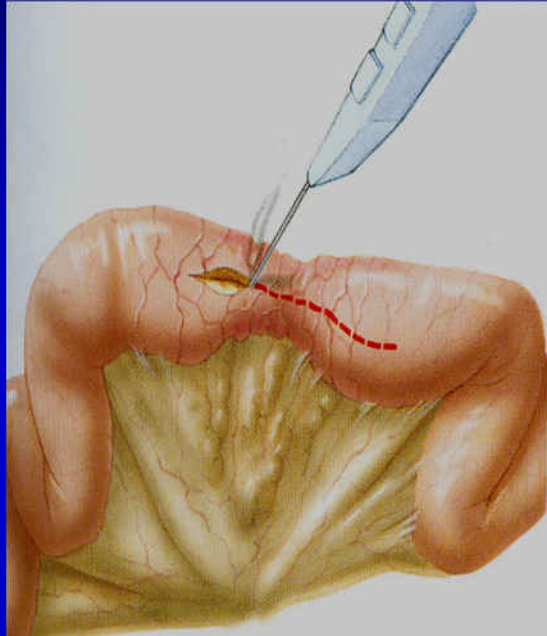
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Organ/space SSI	Immunomodulator administration	0.17	6.89 (0.45–105.49)
	Clean-contaminated wound	0.08	0.24 (0.05–1.16)
	Duration of surgery >167 min	0.07	3.27 (0.92–11.71)
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	Proctectomy	0.04	3.30 (1.08–10.05)

SSI = surgical site infection; COLN = colonic surgery; CRP = C-reactive protein; 5-ASA = 5-aminosalicylic acid.

# Surgery in Crohn's disease

## *Stricturoplasty for stenosis*

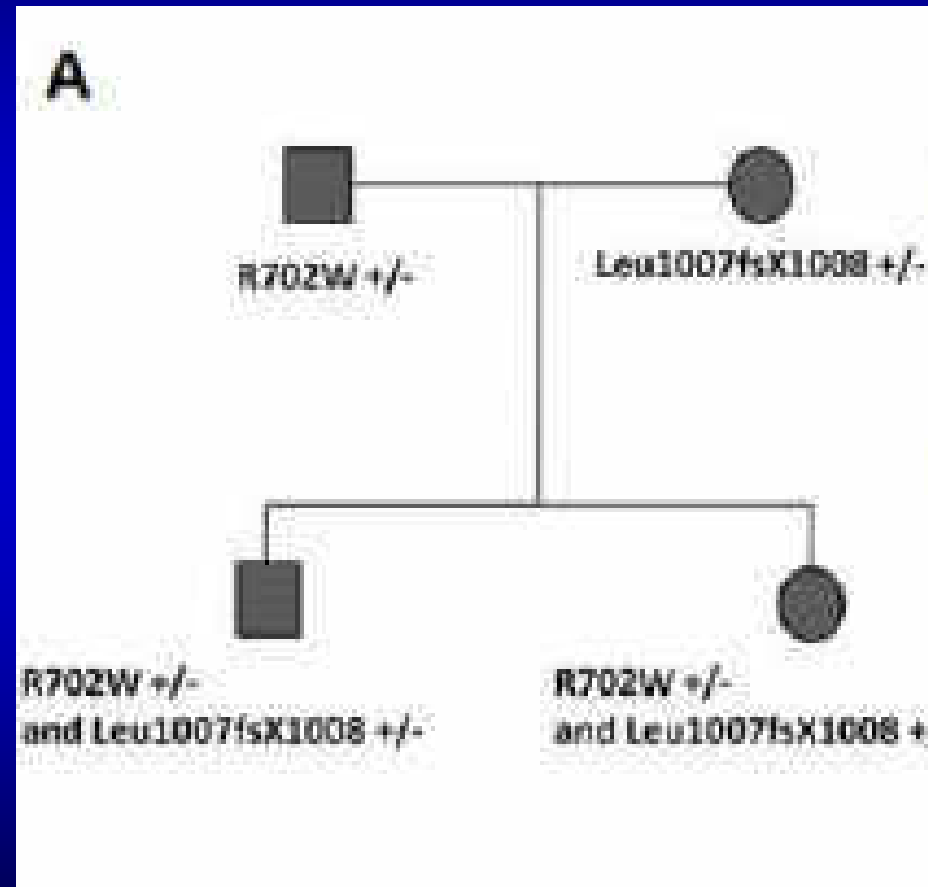
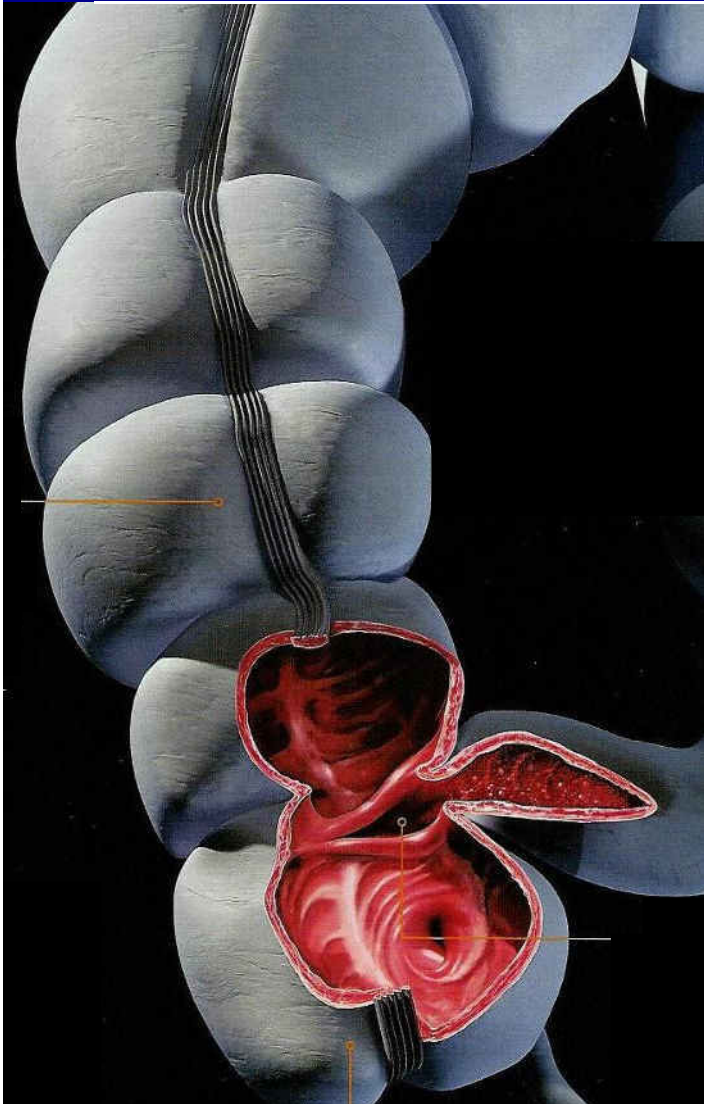
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# Which medication should be used for post-operative recurrence of Crohn's disease?

Medication	Preventing endoscopic postop. recurrence	Key Reference
Probiotika	-	Marteau P et al. <i>Gut</i> 2006;55:842-7.
Budenosid	-	Hellers G et al. <i>Gastroenterology</i> 1999;116:294-300.
Mesalazin	- / (+)	Lochs H et al. <i>Gastroenterology</i> 2000;118:264-73.
Metronidazol	+	Rutgeerts P et al. <i>Gastroenterology</i> 1995;108:1617-21.
Thiopurine	+	Peyrin-Biroulet L et al. <i>Am J Gastroenterol</i> 2009;104:2089-96.
Infliximab	++	Regueiro M et al. <i>Gastroenterology</i> 2009;136:441-50.
Adalimumab		

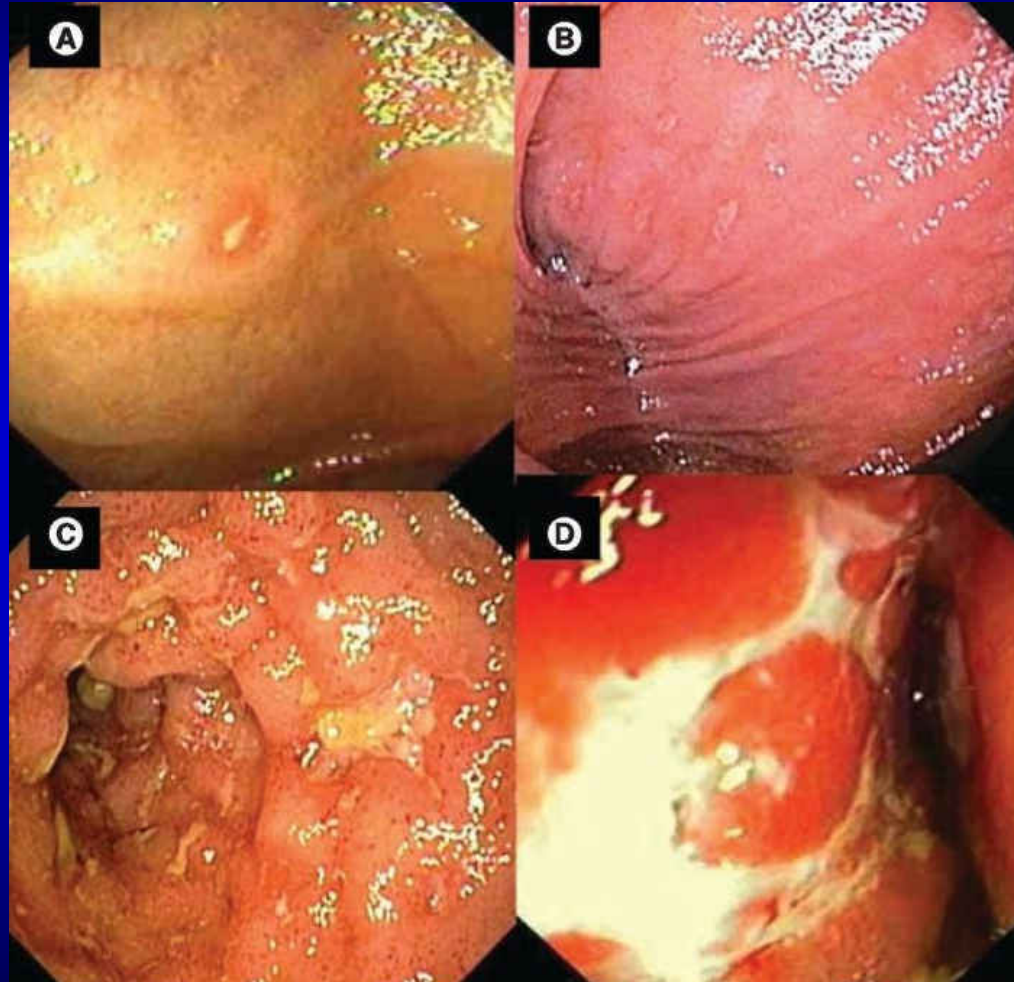
# Ileal Crohn's disease in all four family members due to *NOD2* mutations



Schnitzler F ... Brand S.  
*Inflamm Bowel Dis* 2012;18:395-6.



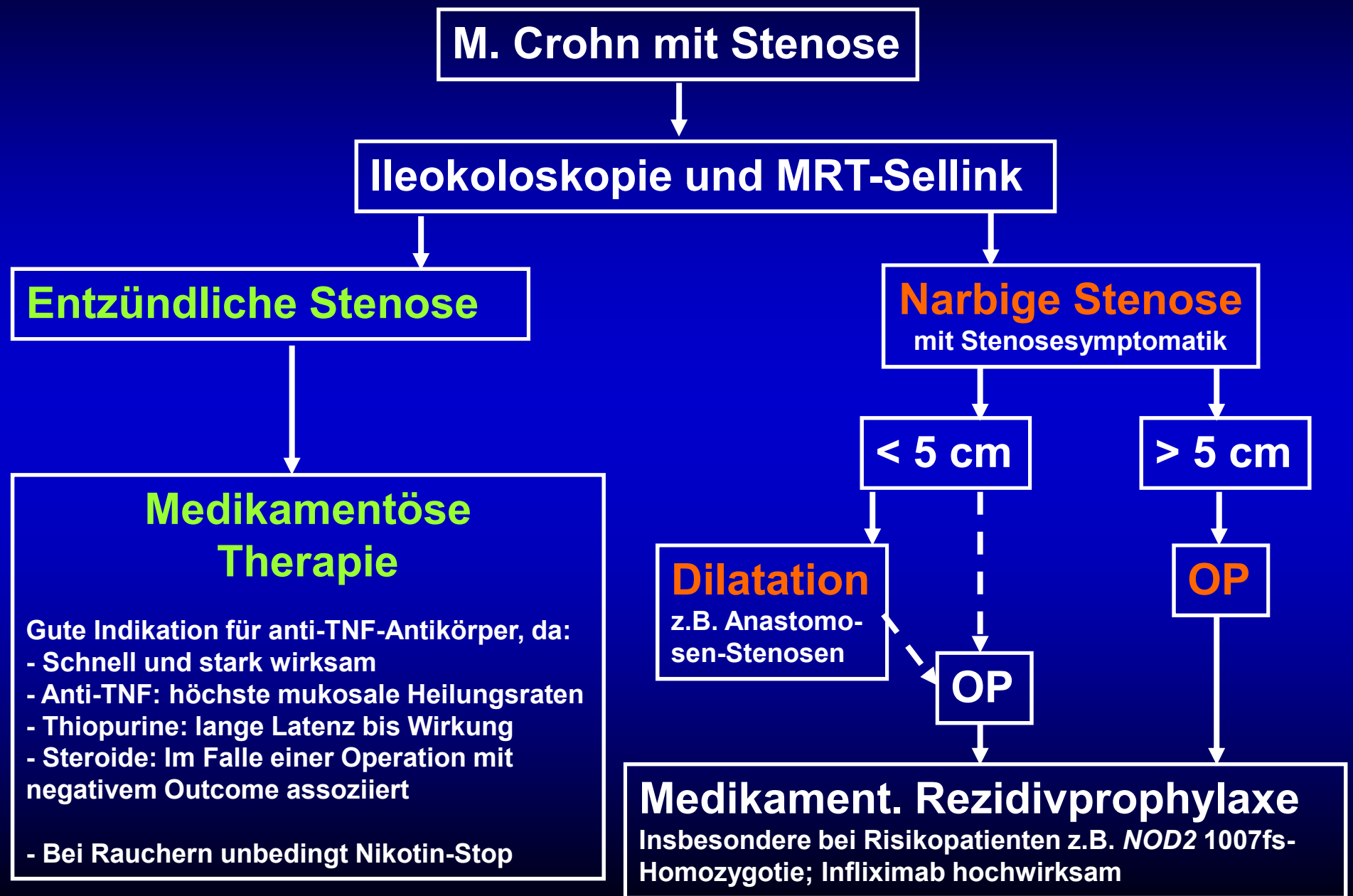
# Rutgeerts Score

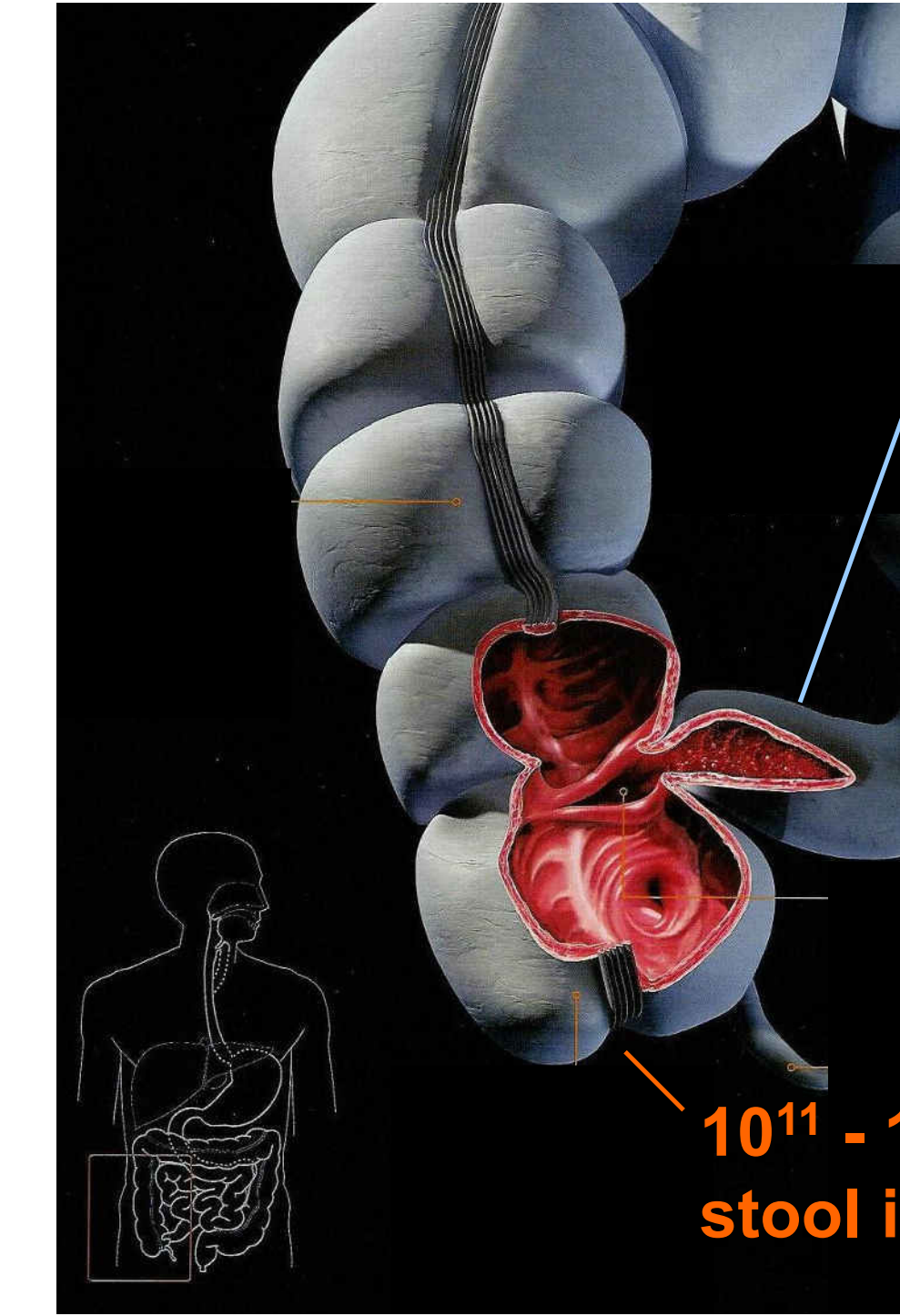


*Takayuki Yamamoto et al. United European*  
**Neoterminal ilea in the different Rutgeerts scores. (A) i1, (B) i2, (C) i3 and (D) i4.**

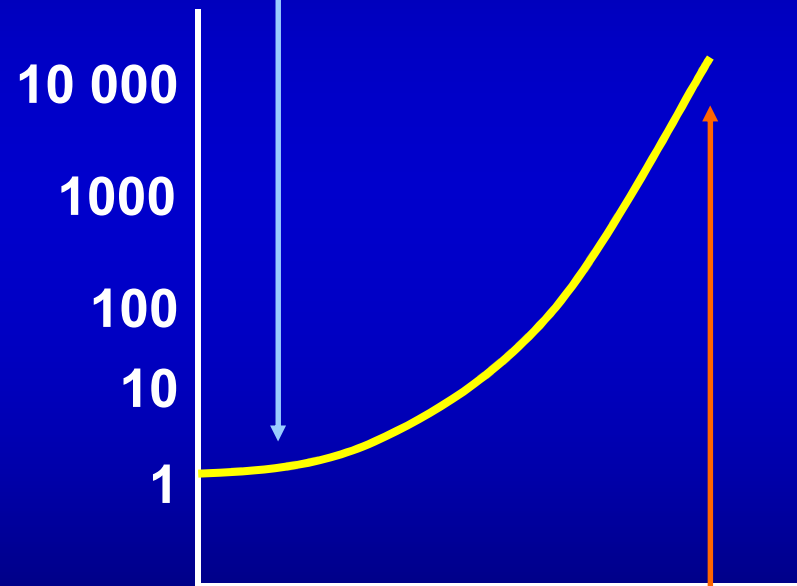
# Role of Calprotectin in postoperative CD

# Surgery and Immunosuppression in Stenosis





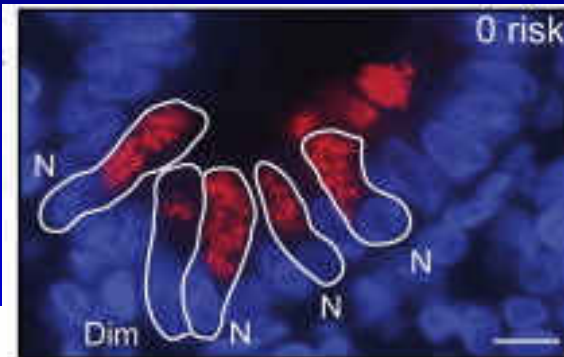
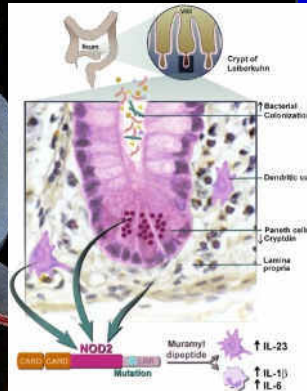
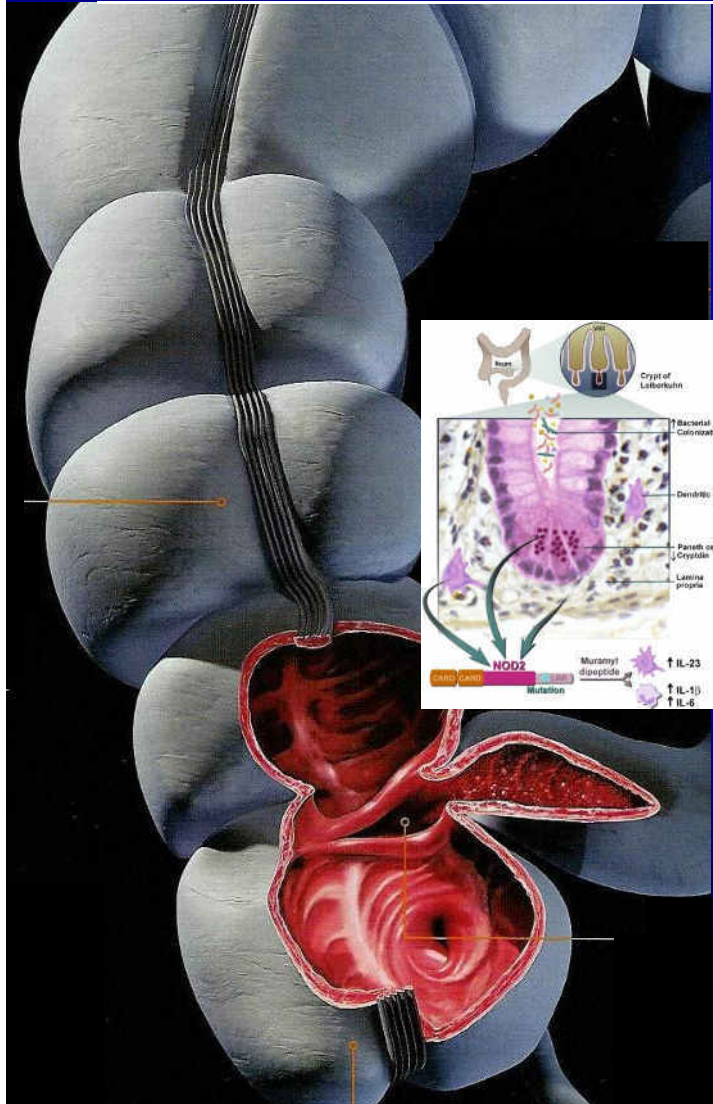
**$10^8$  Bacteria per gramm  
stool in the small intestine**



**$10^{11} - 10^{12}$  Bacteria per gramm  
stool in the large intestine**



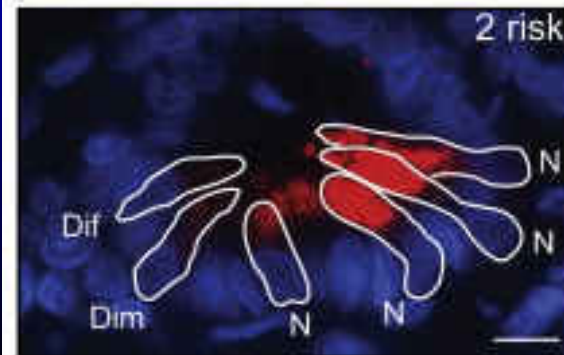
# ***NOD2 mutations modulate Paneth cell secretions***



***NOD2 Wildtype:  
Normal Paneth cells***



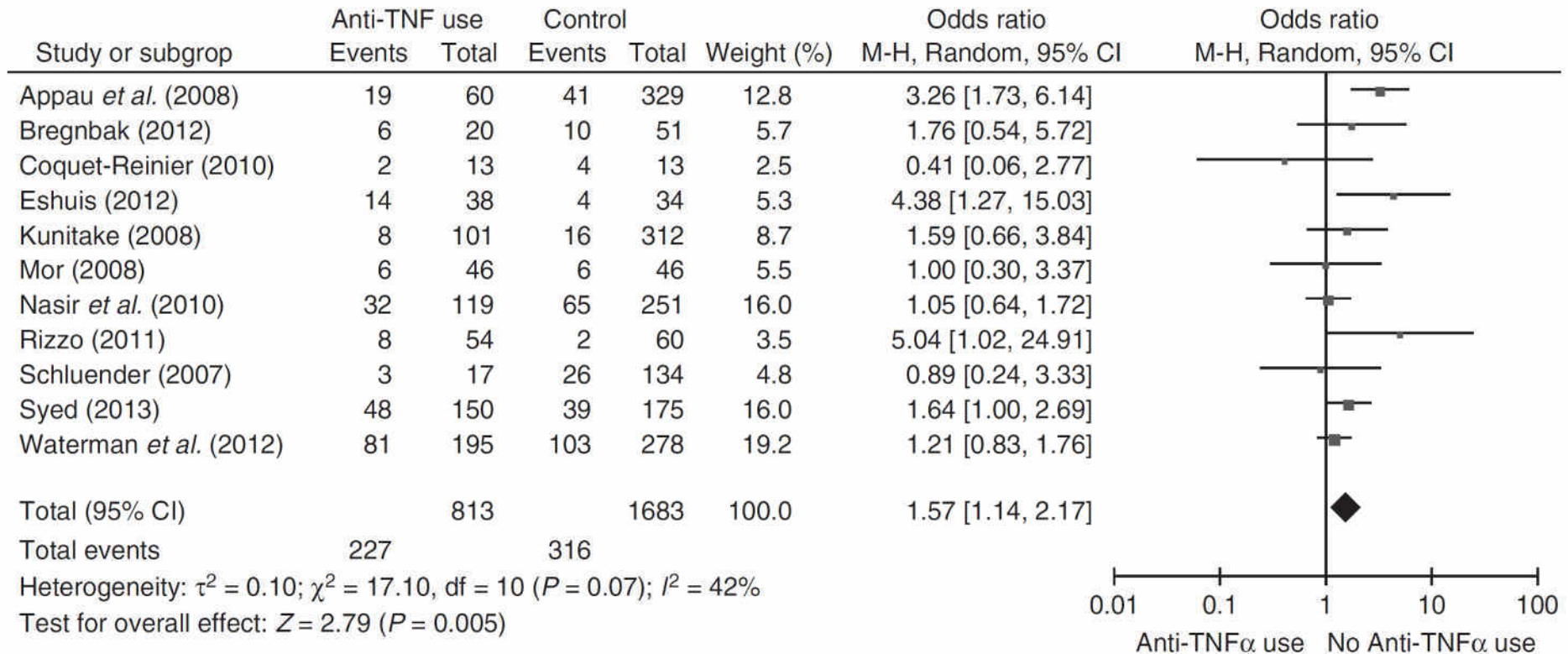
***NOD2 Heterozygotes:  
Disturbed Paneth cell  
secretion***



***NOD2 Homozygotes:  
Severely disturbed  
Paneth cell secretion***

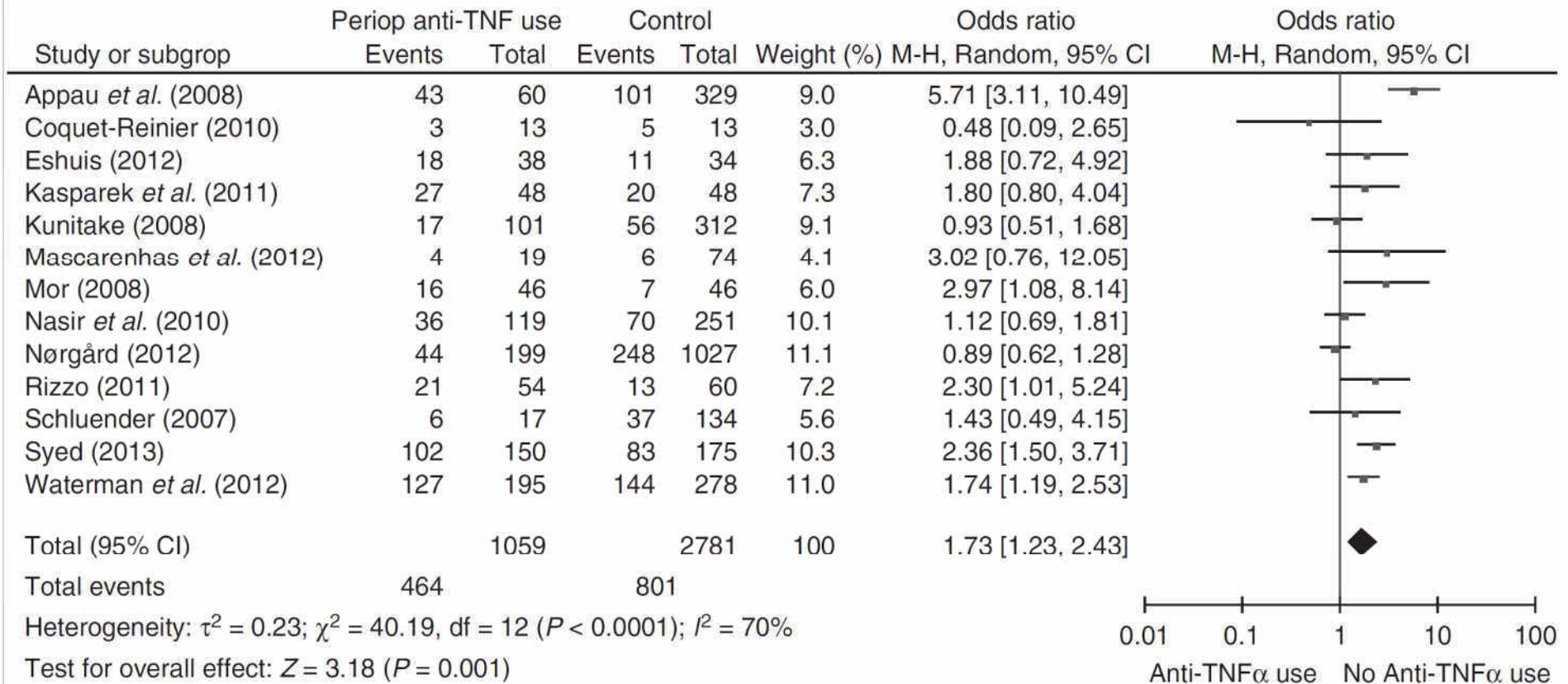
***Vandussen KL et al.  
Gastroenterology 2014;146:200-9.***

# Anti-TNF therapy and postoperative complications



**Figure 2 |** Forrest plot of studies that assessed post-operative non-infectious complications on peri-operative anti-TNF $\alpha$  therapies compared to controls.

# Anti-TNF therapy and postoperative complications



**Figure 3 |** Forrest plot of studies that assessed post-operative total complications on peri-operative anti-TNF $\alpha$  therapies compared to controls.