

# 'ON DEMAND' VERSUS PLANNED RELAPAROTOMY IN PATIENTS WITH SECONDARY PERITONITIS:

A RANDOMIZED CLINICAL MULTICENTER TRIAL

## RELAP Trial

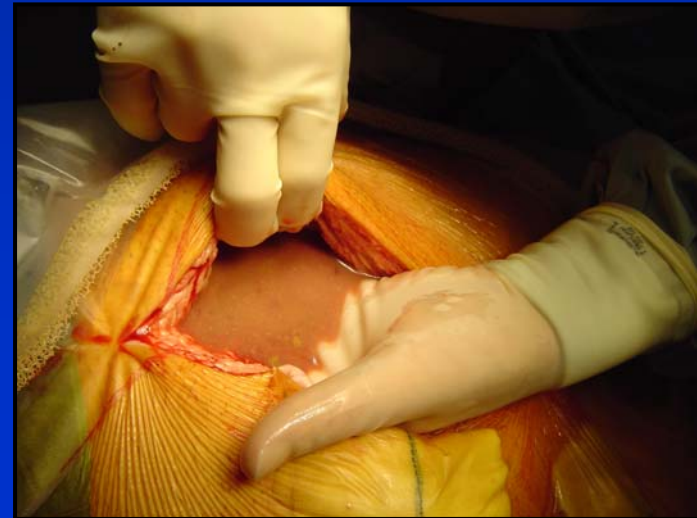
Dutch Peritonitis Study Group

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# Background

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- Both techniques applied world-wide
- **Planned:** more aggressive, more interventions in critically ill patient, leading to complications
- **On demand:** conservative, less interventions, if too late: point of no return
- No evidence on superiority
- Call for randomized trial 1990 by SIS-E



# Study Hypothesis

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Relaparotomy 'on demand' (OD) reduces the risk of 'bad outcome' within **1 year** after initial emergency laparotomy in patients with secondary peritonitis in comparison with a planned relaparotomy (PR)

# Study Design

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- prospective, randomized, multicenter (9)
- 111 patients per arm (222) + 5% dropout (234)
- block randomization per institute
- stratification for APACHE II score
  - APACHE II 11-20
  - APACHE II >20

# Inclusion Criteria

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- secondary peritonitis
- APACHE II-score  $> 10$
- informed consent

# Exclusion Criteria

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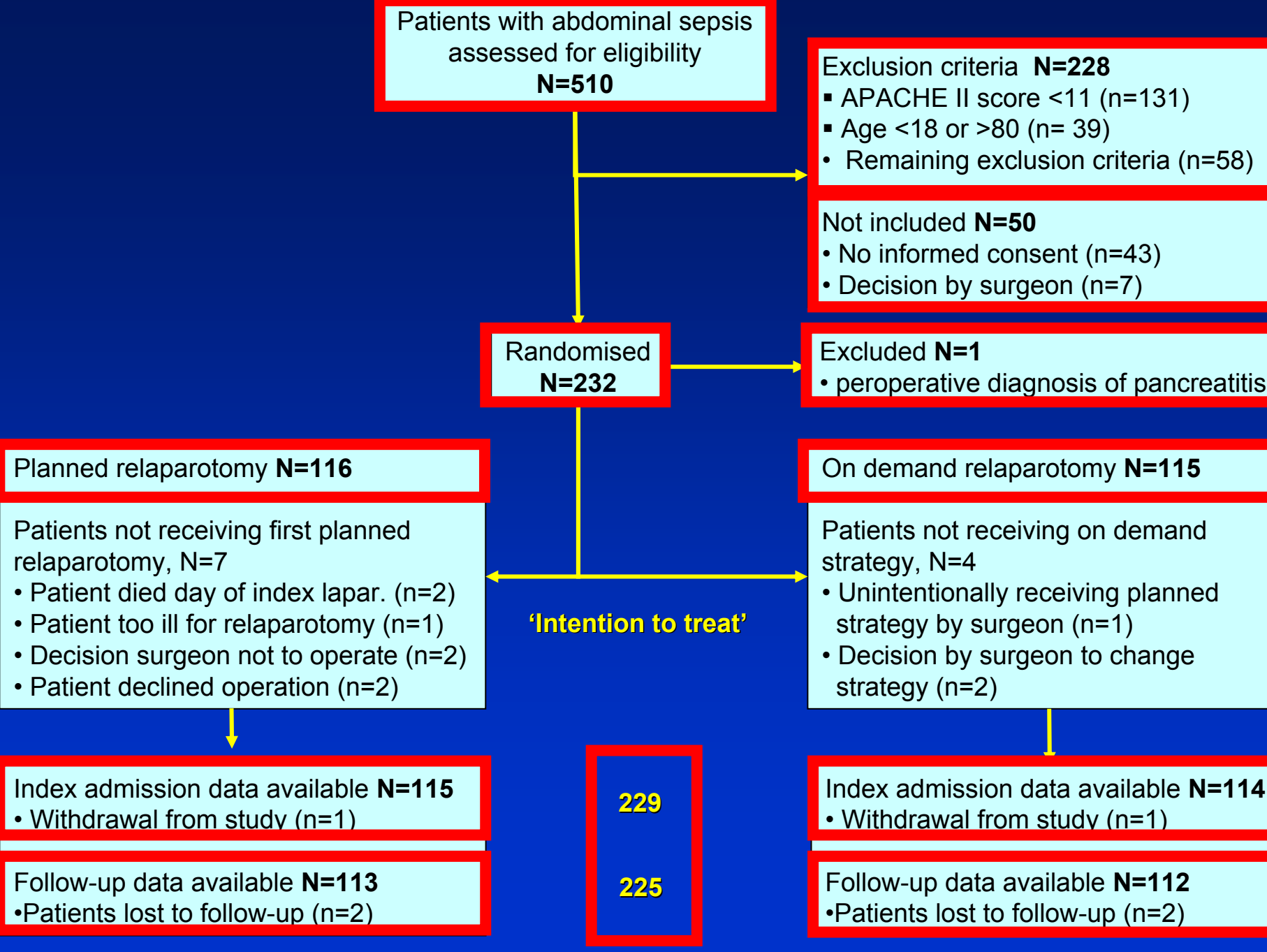
- age  $<18$  or  $> 80$
- abdominal infection due to iatrogenic perforation (24 hrs after endoscopy)
- CAPD-peritonitis
- acute pancreatitis
- expected survival of  $< 6$  months due to malignancy
- major cerebral damage by trauma or anoxia

# Primary Endpoint

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‘events’ leading to a primary endpoint:

1. death
- 2a. ‘survivors’: pre-specified disease-related morbidities during *first admission needing surgery*
- 2b. ‘survivors’: pre-specified disease-related morbidities during *follow-up needing readmission* for (non)-surgical treatment



# Demographic and Index Data

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- No differences between groups:
  - Mean age 65 yr
  - Mean APACHE II score 16 points
  - High incidence of major comorbidity (60%)
  - Empiric (initial) antibiotics all patients (protocol)
  - Perforation most frequent etiology
  - Colorectal localization focus (63%)
  - Diffuse contamination (60%)
  - Fecal contamination (40%)
  - Elimination focus possible (90% - index)
  - Primary closure at index laparotomy (85%)
  - Equal no. diagnostic imaging

# Results 1

	OD	PR	P
<b>No. relaparotomies</b>			0.0001
0	58%	6%	
1	24 %	51 %	
2	10 %	18 %	
3 or more	9 %	24 %	
<b>Negative findings at first relaparotomy</b>	32 %	66 %	0.0001

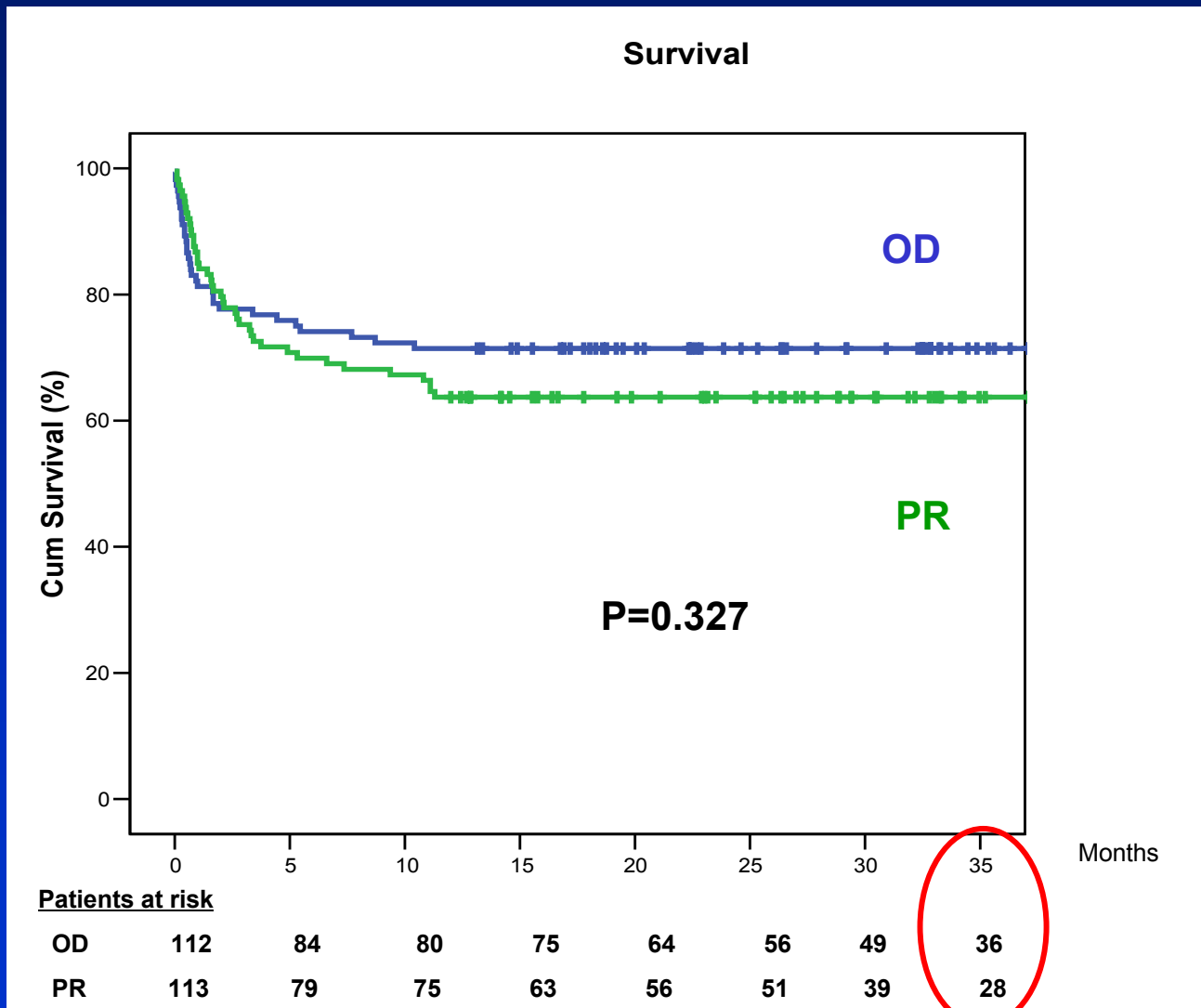
# Results 2

	OD	PR	P
<b>ICU admission (days)</b>			0.001
median (p25 – p75)	7 (3–13)	11 (6-24)	
<b>Mechanical ventilation (days)</b>			0.01
median (p25 – p75)	4 (1–9)	7 (3–17)	
<b>Hospital 1<sup>st</sup> admission (days)</b>			
median (p25 – p75)	27 (15–47)	35 (21–65)	0.008
<b>Percutaneous drainage</b>			
no. (%)	27%	39%	0.05

# Results 3

	OD	PR	P
<b>Mortality</b>	28.6%	36.3%	0.22
<b>Major morbidity in survivors</b>	40.0%	44.4%	0.58
<b>Combined primary endpoint</b>	56.3%	63.7%	0.25
<b>ARR (95% CI) for OD</b>	7.4% (-0.05 - 0.20)		
<b>NNT (95% CI) for OD</b>	13 (-19 - 5)		

# Survival



# High level ICU institute

ICU level 3	OD	PR	P
Mortality	23%	38%	0.044
Major morbidity in survivors	35%	37%	0.860
Combined primary endpoint	50%	60%	0.063

# Costs

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On demand generated less costs:

19% absolute reduction (15000 EUR per patient)

- fewer reoperations
- shorter ICU stay
- shorter in-hospital stay
- less percutaneous interventions

# In summary

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- Selective re-operation is valid
- OD:
  - > 50% no relaparotomy and
  - negative relaparotomies reduced by 50%
  - less relaparotomies do not lead to an increase in no. of percutaneous interventions, complications or death
  - sign. less days mechanically ventilated
  - sign. less days admitted to the hospital

# Conclusion

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- On demand, non-significant but evident reduction in mortality en morbidity in particular in hospitals with high-level ICU
- at 19% lower costs



Although the study hypothesis is rejected

**OD = at least as effective  
at less costs**

# Dutch Peritonitis Study Group

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# Morbidity

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## Surgical Intervention 1<sup>st</sup> admission or readmission

- incisional hernia with indication for correction
- bowel obstruction / herniation due to adhesions
- burst abdomen
- 'abdominal compartment syndrome'
- fistulae
- intra-abdominal bleeding
- intra-abdominal haematoma (evacuation)
- perforation
- anastomotic leakage
- ischemia of necrosis visceral organ
- stoma dysfunction
- gastric or duodenal ulcer bleeding

# Morbidity

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## Non-surgical interventions and readmission

- fistulae
- wounddehiscence / obstruction due to hernia
- abcsess needing percutaneous drainage
- renal failure needing replacement therapy
- myocardial infarction / longembolus / CVA
- gastric or duodenal bleeding (coiling)
- respiratoiry insufficiency
- urosepsis

# Morbidity (180)

During admission period Surgical Interventions	Survivors			
	PR (n= 76)	(%)	OD (n= 84)	(%)
Incisional hernia	1	(1)	0	(0)
Bowel obstruction /herniation	1	(1)	0	(0)
Burst abdomen	3	(4)	6	(7)
Abd Compartment Syndrome	0	(0)	0	(0)
Fistula	0	(0)	1	(1)
Intra-abdominal bleeding	2	(3)	2	(2)
Intra-abdominal haematoma	2	(3)	1	(1)
Perforation	4	(5)	8	(10)
Anastomotic leakage	5	(7)	4	(5)
Ischemia / necrosis	0	(0)	1	(1)
Stoma dysfunction	4	(5)	1	(1)
Ulcer bleed	1	(1)	0	(0)

# Morbidity (180)

<b>During readmission Surgical Interventions</b>	<b>PR (n= 76)</b>	<b>(%)</b>	<b>OD (n= 84)</b>	<b>(%)</b>
Incisional hernia	14	(18)	13	(16)
Bowel obstruction /herniation	0	(0)	1	(1)
Burst abdomen	0	(0)	0	(0)
Abd Compartment Syndrome	0	(0)	0	(0)
Fistula	0	(0)	3	3.4
Intra-abdominal bleeding	0	(0)	0	(0)
Intra-abdominal haematoma	0	(0)	0	(0)
Perforation	0	(0)	1	(1)
Anastomotic Leakage	1	(1)	0	(0)
Ischemia / necrosis	0	(0)	0	(0)
Enterostomy dysfunction	1	(1)	1	1.2
Ulcer bleed	0	(0)	0	(0)
<b>Conservative treatment</b>				
Fistula	0	(0)	1	(1)
Incisional hernia	1	(1)	2	(2)
Abscess (PCD)	2	(3)	6	(7)
Renal failure	0	(0)	0	(0)
MI / Embolus / CVA	1	(1)	1	(1)
Gastric / duodenal bleeding	1	(1)	2	(2)
Respiratory failure	1	(1)	1	(1)
Urinary tract infection	1	(1)	1	(1)

# Power (1)

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- 16% verschil in *gecombineerd eindpunt* op 180 dagen (6 maanden) voor  
ROD

44% → 28%

- Aannamen:
  - Absolute reductie in mortaliteit van 10%
    - (30% → 20%)
  - Absolute reductie in ziekte-gerelateerde morbiditeit waarvoor heropname met of zonder chirurgische interventie bij overlevers van 10%
    - (20% → 10%)

# Power (2)

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44% ( $0.3 + (0.7 \times 0.2)$ ) to 28% ( $0.2 + (0.8 \times 0.1)$ )

- 111 patients ( $\alpha=0.05$ , power 80%, OR 0.495)
- in 2 strategy arms ( $n=222$ )
- expected 5% dropout in each arm ( $2 \times 6 = 12$ )
- total of **234** patients to be randomized