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Hungarian Pancreatic Study Group

13th November 2016
Budapest

Hungarian Pancreatic Study Group – Eastern and Central European Pancreatic Study Groups



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General Utilization of early energy Administration in Acute pancreatitis.



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AIM

Whether **energy restoration** in the early phase of acute pancreatitis is beneficial?



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What is the clinical current knowledge?

Meta-analysis

Data analysis from clinical registry

RCT



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What is the clinical current knowledge?



Meta-analysis

Data analysis from clinical registry

RCT



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META-ANALYSES

February 2016



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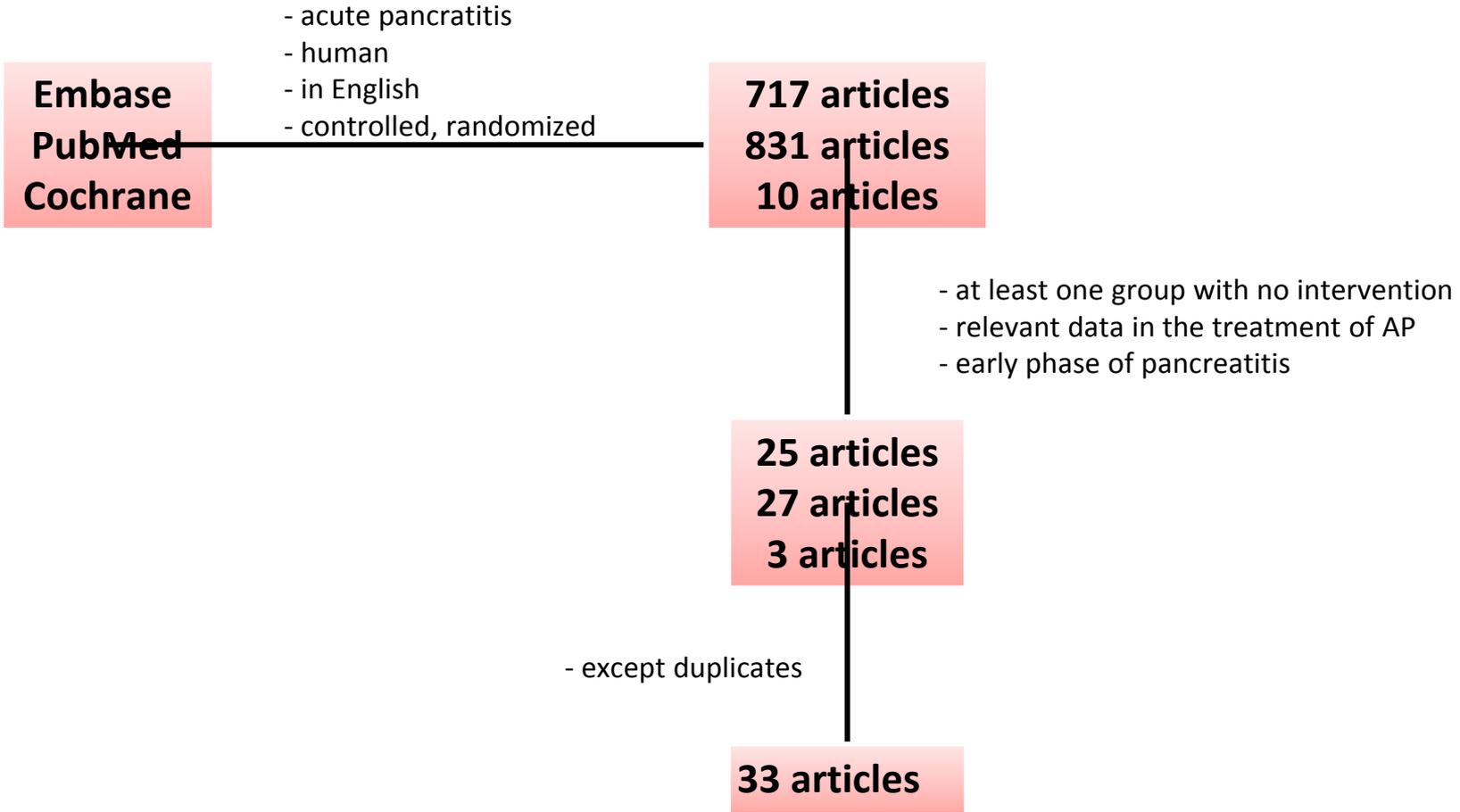
- acute pancreatitis
- human
- in English
- controlled, randomized

Embase
PubMed
Cochrane

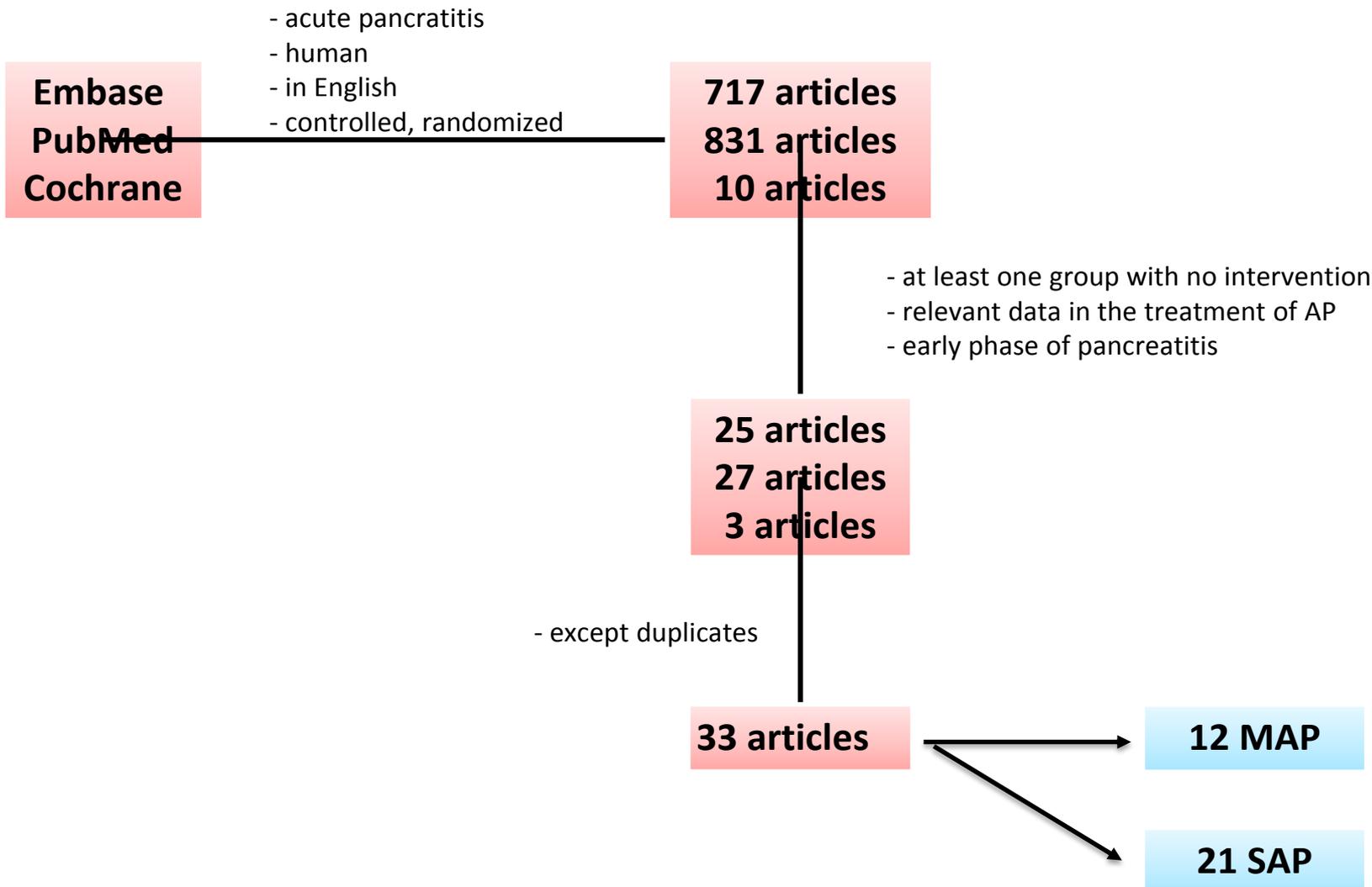
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831 articles
10 articles



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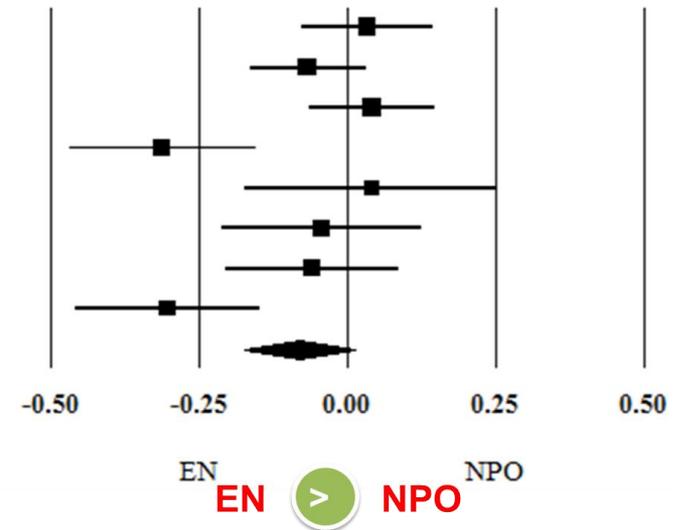
SAP MORTALITY

Study name

Statistics for each study

Risk difference and 95% CI

Study name	Risk difference	Lower limit	Upper limit	p-Value	EN	NPO
Sun et al., 2013	0.033	-0.077	0.143	0.552	2 / 30	1 / 30
Wang et al., 2013	-0.067	-0.165	0.030	0.176	3 / 61	7 / 60
Eckerwall et al., 2006	0.042	-0.064	0.148	0.441	1 / 24	0 / 26
Wu et al., 2010	-0.313	-0.470	-0.156	0.000	6 / 53	23 / 54
Doley et al., 2009	0.040	-0.173	0.253	0.712	5 / 25	4 / 25
Kalfarentzos et al., 1997	-0.044	-0.213	0.124	0.606	1 / 18	2 / 20
Sun et al., 2004	-0.060	-0.207	0.087	0.423	7 / 50	10 / 50
Modena et al., 2006	-0.303	-0.459	-0.148	0.000	2 / 44	15 / 43
	-0.081	-0.175	0.013	<u>0.091</u>		



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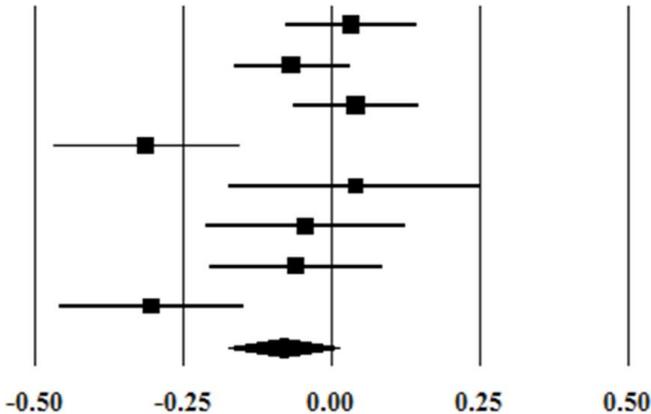
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EN > NPO

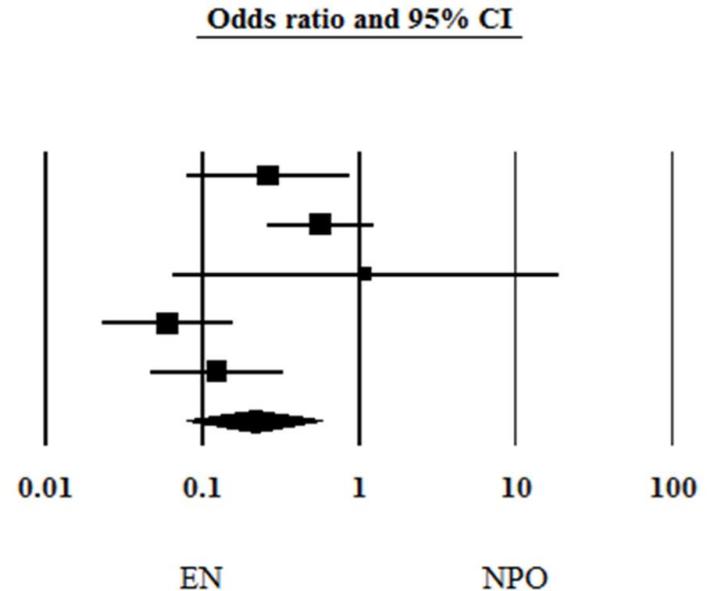
Tendency

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MOF

Study name	Statistics for each study				Events / Total	
	Odds ratio	Lower limit	Upper limit	p-Value	EN	NPO
Sun et al., 2013	0.262	0.079	0.870	0.029	5 / 30	13 / 30
Wang et al., 2013	0.563	0.257	1.234	0.151	15 / 61	22 / 60
Eckerwall et al., 2006	1.087	0.064	18.402	0.954	1 / 24	1 / 26
Wu et al., 2010	0.060	0.023	0.155	0.000	11 / 53	44 / 54
Modena et al., 2006	0.124	0.047	0.326	0.000	14 / 44	34 / 43
	0.214	0.080	0.576	<u>0.002</u>		



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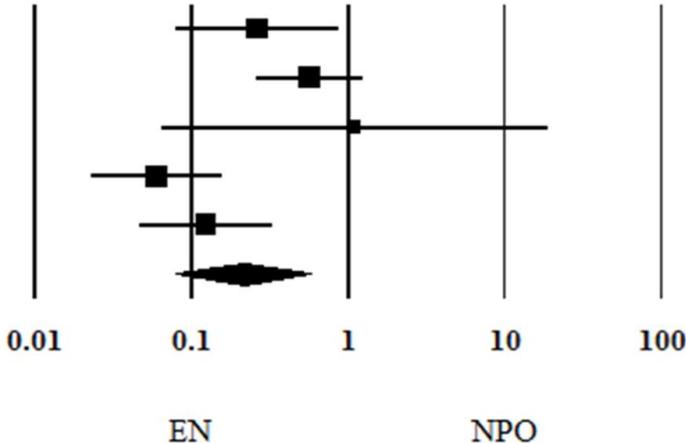
Study name

Statistics for each study

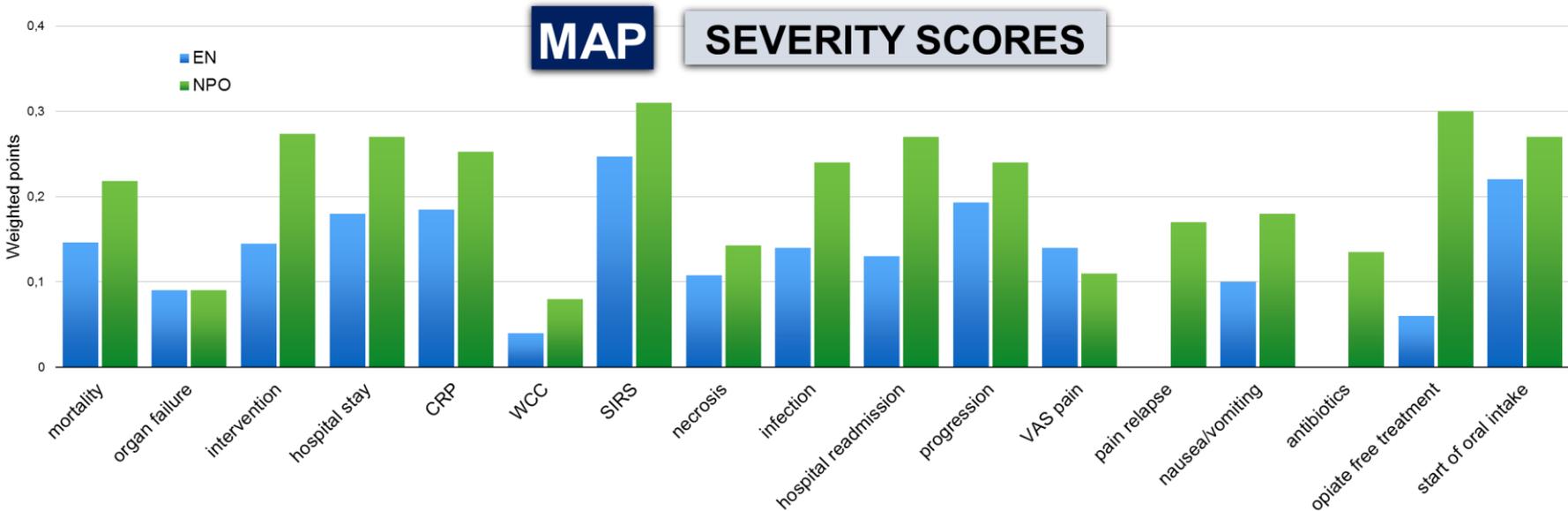
Events / Total

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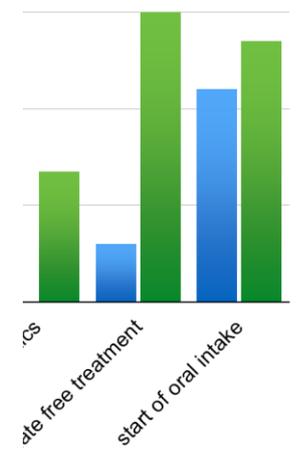
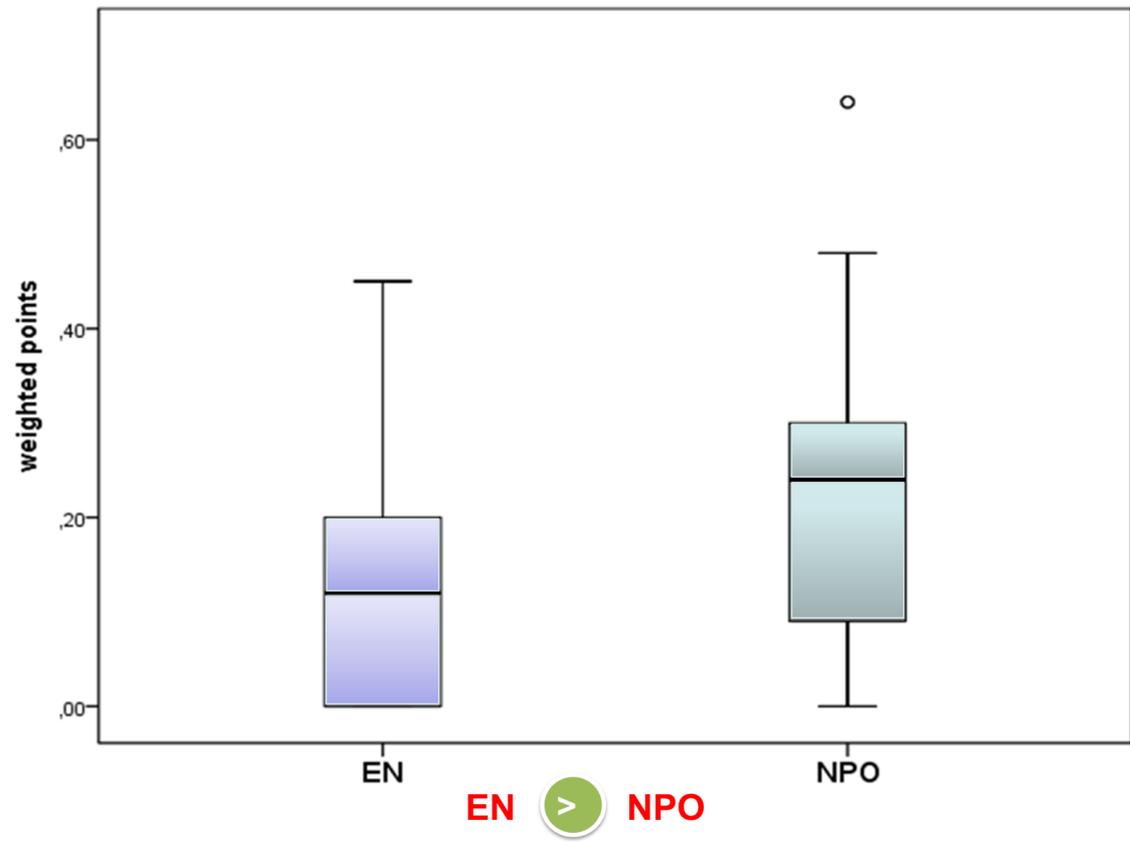
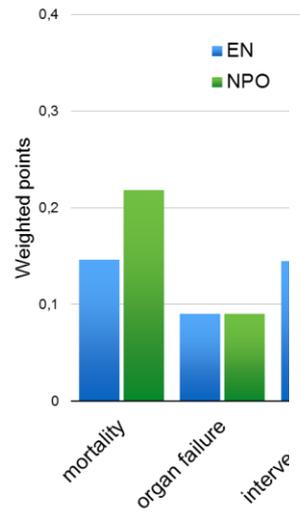


significant



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MAP SEVERITY SCORES





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Molecular Sciences

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Int. J. Mol. Sci. **2016**, *17*(10), 1691; doi:10.3390/ijms17101691

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Article

Meta-Analysis of Early Nutrition: The Benefits of Enteral Feeding Compared to a Nil Per Os Diet Not Only in Severe, but Also in Mild and Moderate Acute Pancreatitis

Katalin Márta ¹ ✉, Nelli Farkas ^{1,2} ✉, Imre Szabó ³ ✉, Anita Illés ³ ✉, Áron Vincze ³ ✉, Gabriella Pár ³ ✉, Patrícia Sarlós ^{1,3} ✉, Judit Bajor ^{1,3} ✉, Ákos Szűcs ^{1,4} ✉, József Czimmer ³ ✉, Dóra Mosztbacher ^{1,5} ✉, Andrea Párniczky ^{1,6} ✉, Kata Szemes ^{1,3} ✉, Dániel Pécsi ¹ ✉ and Péter Hegyi ^{1,7,8,*} ✉

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Academic Editors: Jaya Padmanabhan and Srikumar Chellappan

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Title / Keyword Journal

Author Section

Article Type Special Issue

Volume 17, Issue 10

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- Department of Gastroenterology, First Department of Medicine, University of Pécs, Pécs H-7624, Hungary
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Data analysis from clinical registry

RCT



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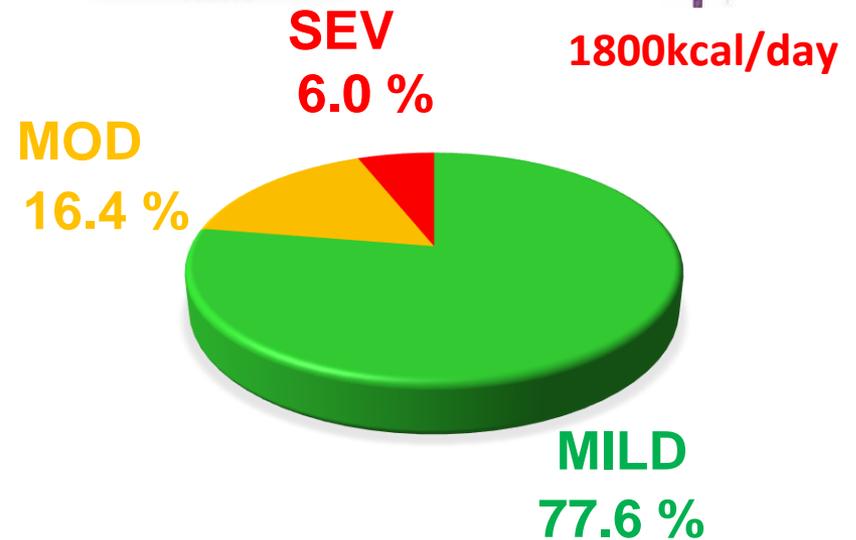
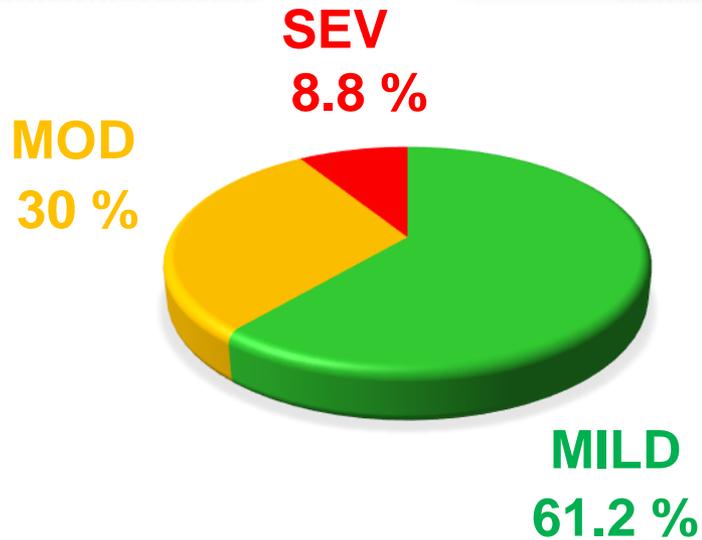
DATA ANALYSIS

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Prospective
Controlled Trial

HUNGARIAN COHORT
n=600

NG FEEDING
n=67



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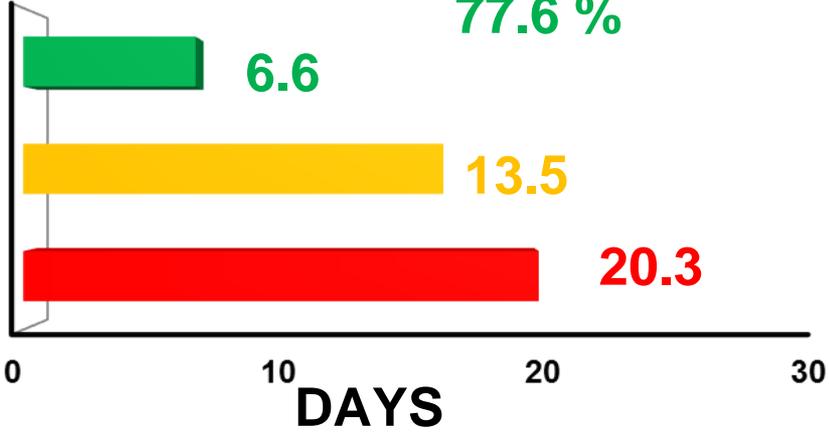
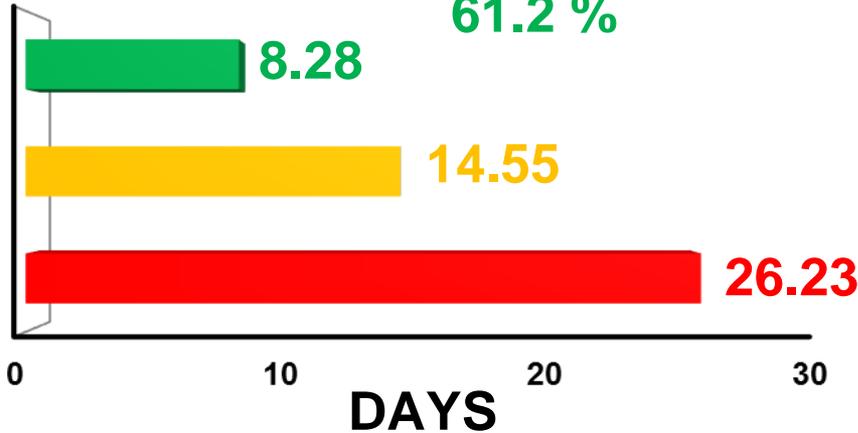
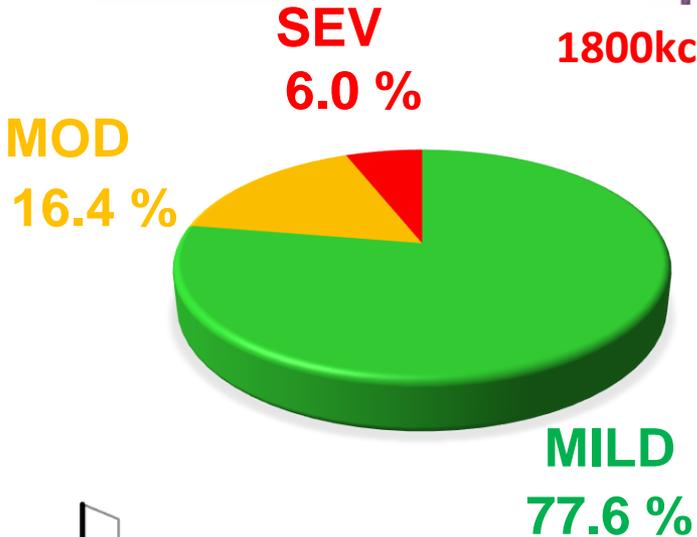
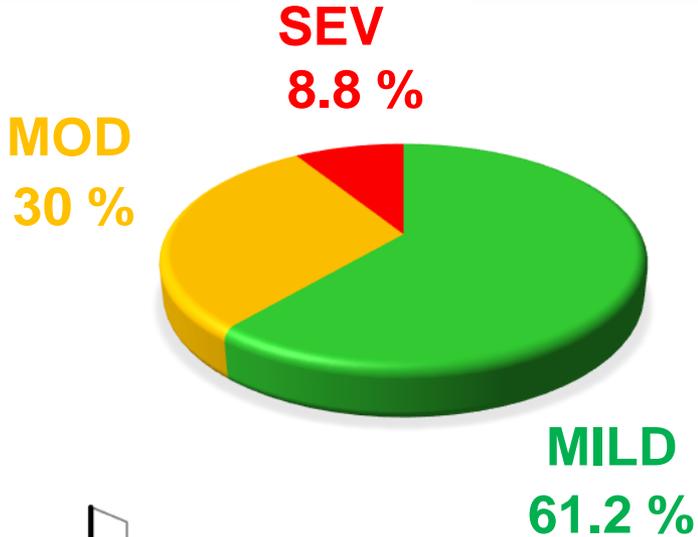
Prospective
Controlled Trial

HUNGARIAN COHORT
n=600

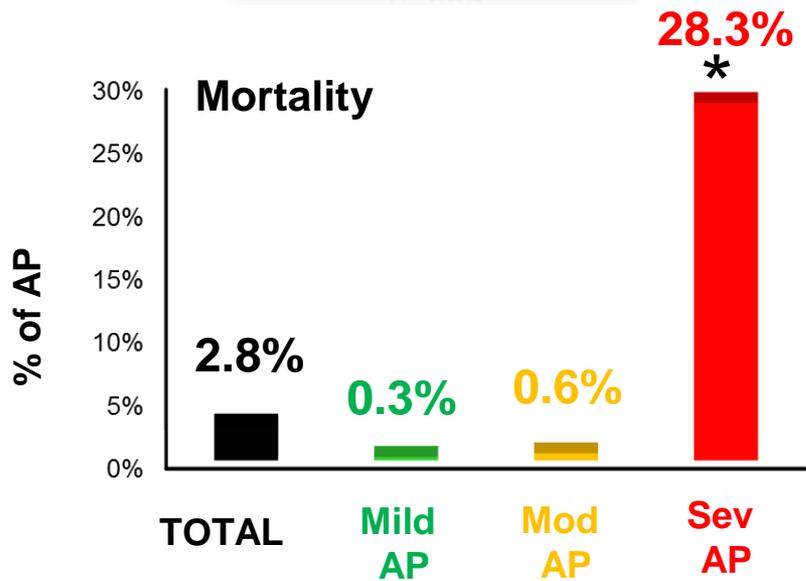
NG FEEDING
n=67



1800kcal/day



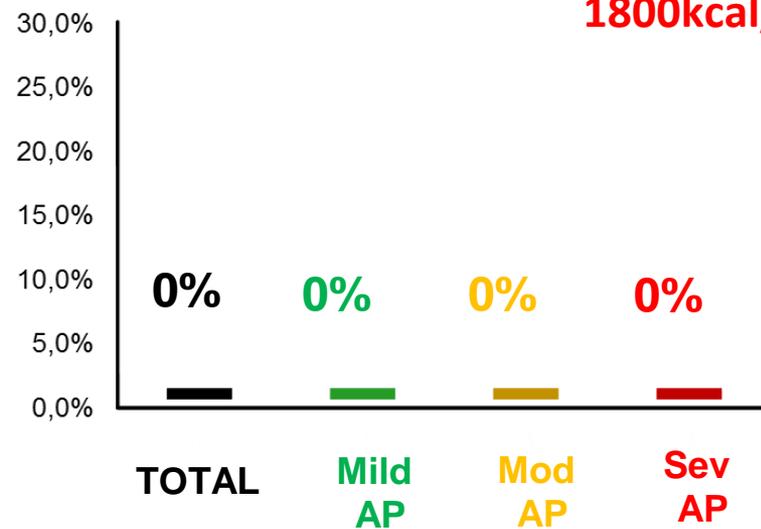
HUNGARIAN COHORT
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NG FEEDING
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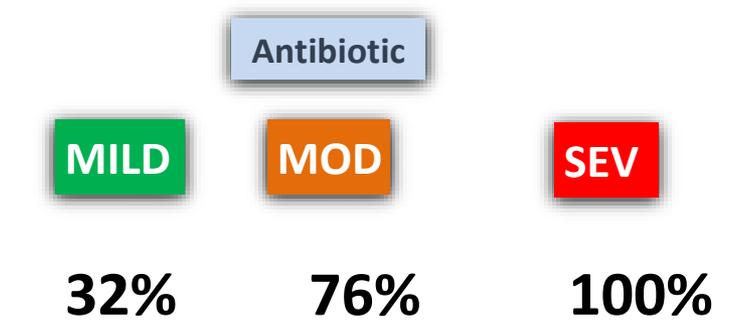
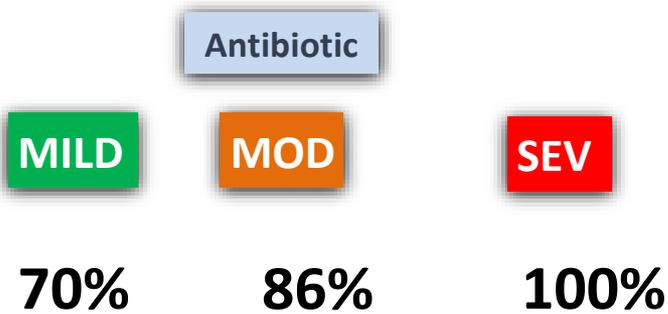
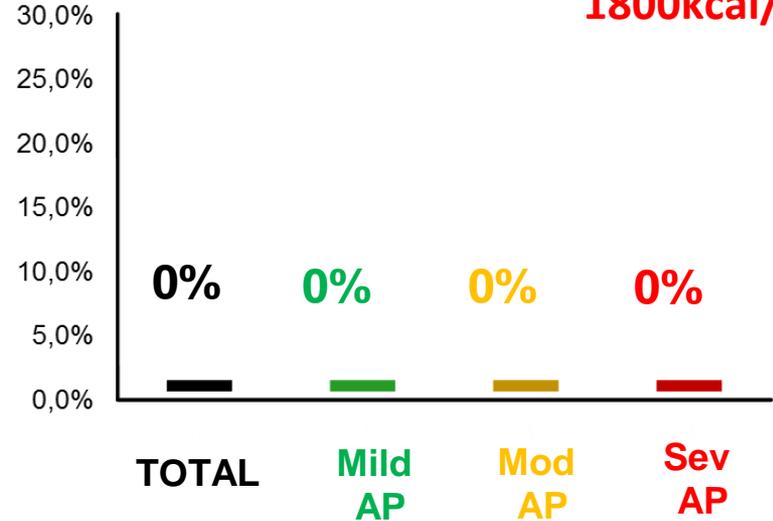
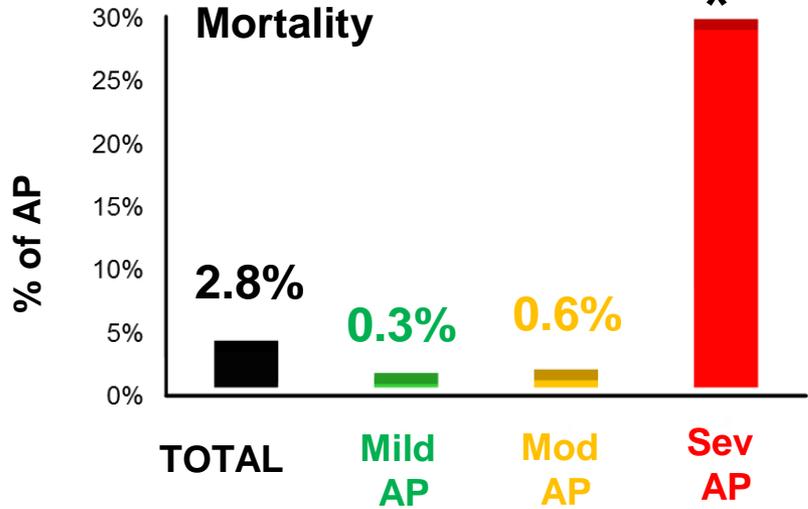


HUNGARIAN COHORT
n=600

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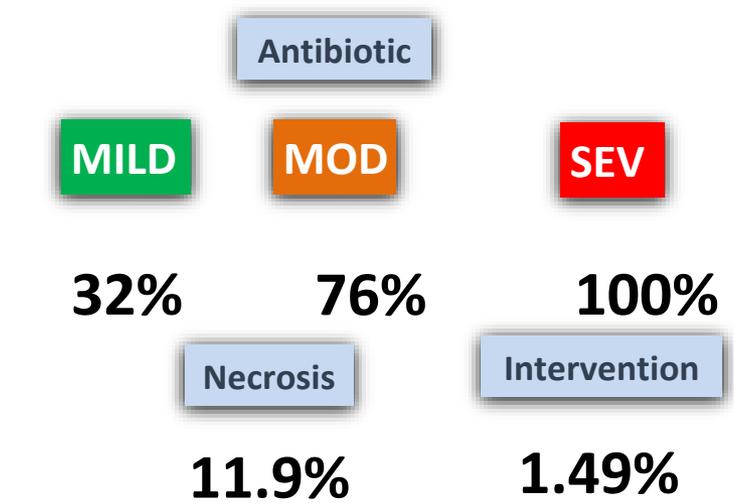
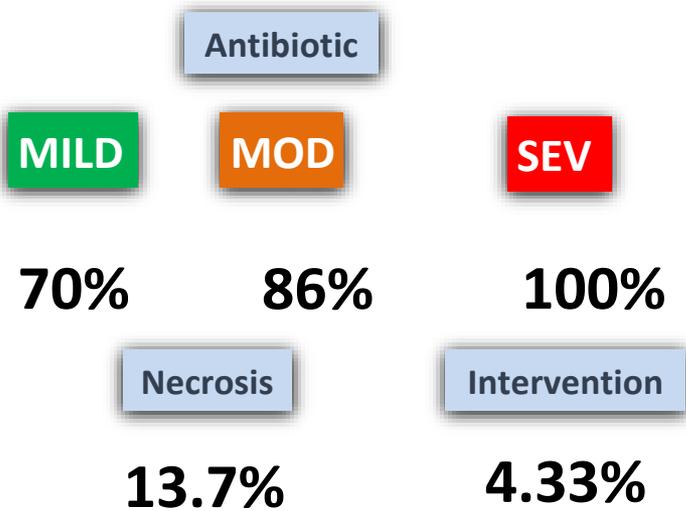
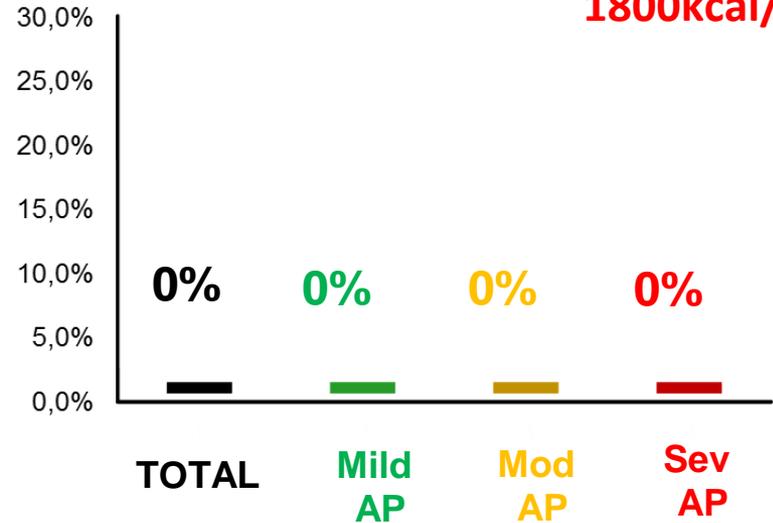
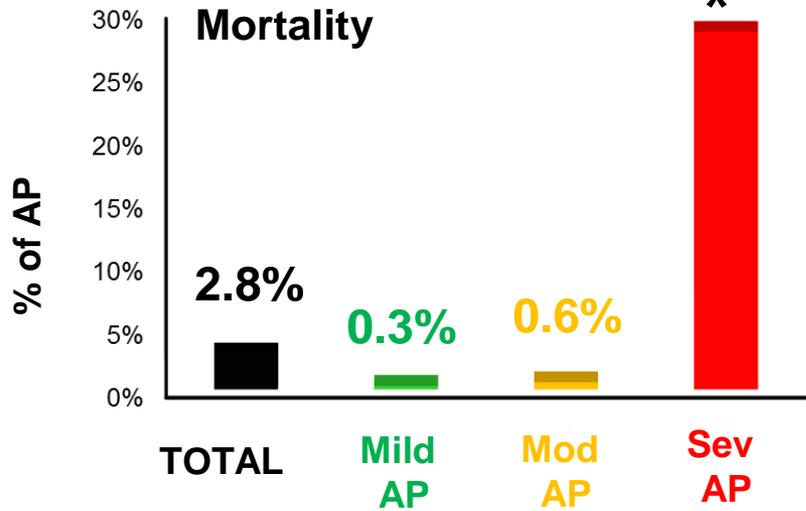


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NG FEEDING
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1800kcal/day





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What is the clinical current knowledge?



Meta-analysis



Data analysis from clinical registry

RCT



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**RANDOMISED CONTROLLED
DOUBLE BLIND EXPERIMENTAL
CLINICAL TRIAL**



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**RANDOMISED CONTROLLED
DOUBLE BLIND EXPERIMENTAL
CLINICAL TRIAL**

Internationally discussed



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International independent advisor reward

International translational advisory board (ITAB):

Markus Lerch – University of Greifswald, Germany
gastroenterologist

John Neoptolemos – University of Liverpool, UK
surgeon

Miklos Sahin-Toth – Boston University, USA
genetics

Ole Petersen – Cardiff University, UK
basic scientist



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Steering committee (SC):

Peter Hegyi MD, PhD, DSc – University of Pécs, HU
gastroenterologist, internal medicine specialist, PI

Katalin Marta MD – University of Pécs, HU
PhD student, principal organizer

Áron Vincze MD, PhD – University of Pécs, HU
*gastroenterologist, internal medicine specialist
(University of Pécs, Hungary)*

Zsolt Márton MD – University of Pécs, HU
intensive care specialist

Tímea Molnár MD – University of Pécs, HU
clinical research specialist

Andrea Szentesi MSc – University of Pécs, HU
multidisciplinary unit specialist

Mária Papp MD, PhD – University of Debrecen, HU
*gastroenterologist, internal medicine specialist
(University of Debrecen, Hungary)*

+ one member of each joined institution



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Independent data-management and biostatistics provider company (IDMB):

Adware Research LTD

Balatonfüred, Völgy u. 41, H-8230

HUNGARY, TEL: +(36-87) 789 073

Executive director: Zsuzsanna Papp, PharmD

bias level as low as possible



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**RANDOMISED CONTROLLED
DOUBLE BLIND PLACEBO CONTROLLED
RANDOMISED CONTROLLED TRIAL**

1 January 2017

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GROUP A

GROUP B

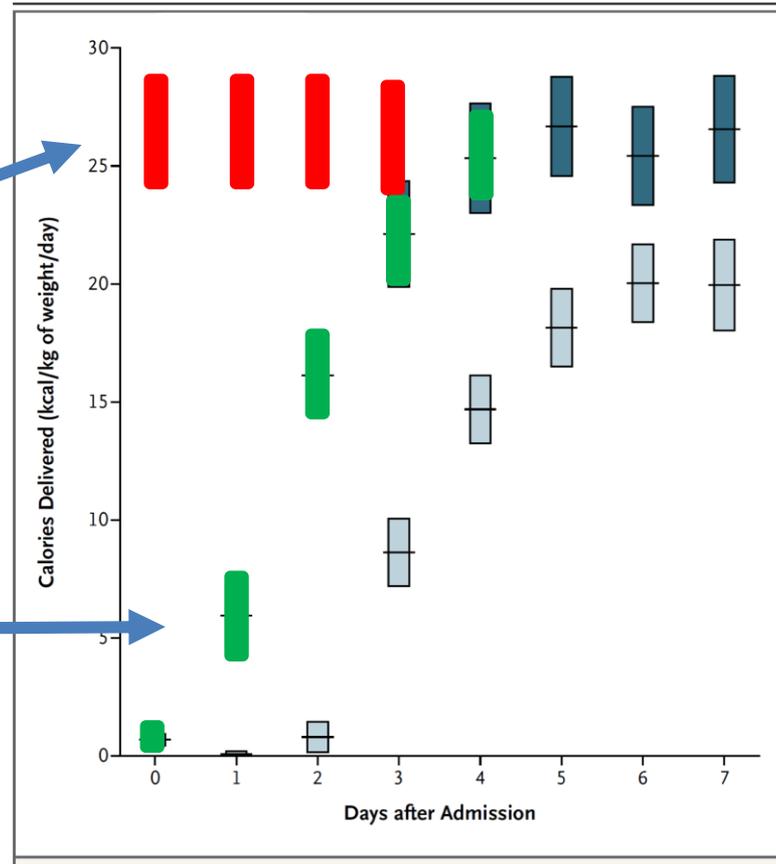


Figure 1. Calories Delivered with the Use of Early versus On-Demand Naso-enteric Tube Feeding.

Each rectangle shows the mean value (horizontal line) and 95% confidence interval (top and bottom of the rectangle).



patient with AP



1 independent doctor
recruitment
randomization



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INCLUSION CRITERIA

- (1) Patients above 18y
- (2) diagnosed AP on the base of the “2 out of 3” rules of IAP/APA guideline: (a) upper abdominal pain; (b) serum amylase or lipase $>3x$ upper limit of normal range; (c) characteristic findings on pancreatic imaging; however those patients without abdominal pain will be excluded because the onset of AP cannot be assessed
- (3) written informed consent form is signed.



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EXCLUSION CRITERIA

- (1) Hospitalization 72 hours before admission
- (2) Abdominal pain >120 hours (5 days)
- (3) Delirium tremens
- (4) Child-Pugh C stage liver cirrhosis
- (5) AP due to malignancy
- (6) already on artificial nutrition (EN or PN)
- (7) Pregnancy
- (8) BMI above 40 or below 18
- (9) Age above 80
- (10) Ketoacidosis
- (11) Whenever CT with contrast is contraindicated

MONITORED PARAMETERS

FORM A

On admission

FORM-A

Acute Pancreatitis

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*The physical examination has to be done ON ADMISSION!
The blood for laboratory parameters has to be drawn ON ADMISSION!
This form has to be filled ON ADMISSION!*

Questionnaire

1. Patient personal details

Insurance number:.....
 First name:.....
 Last name:.....
 Date of birth:.....
 Gender: female male
 Ethnicity/Race: White / Black / Asian-Indian Not known

2. Details from the medical history

Alcohol consumption: yes / no
 if yes: frequency: occasionally/monthly/weekly/daily
 amount (g/day):.....
 since when? (years):.....
 Alcohol consumption in the last 2 weeks:

if not:
 Did you drink alcohol earlier? yes/no
 if yes: frequency: occasionally/monthly/weekly/daily
 amount (g/occasion):.....
 For how many years?.....
 How long ago did you stop drinking alcohol?.....

Guide for estimation of the amount:
 1 dl beer (4.5 vol. %) = ~3.5 g alcohol
 1 dl wine (12.5 vol. %) = ~10 g alcohol
 1 dl hard drink (50 vol. %) = ~40 g alcohol

Smoking: yes / no
 if yes: amount (cigarettes/day):.....
 For how many years?

if not:
 Did you smoke earlier? yes/no
 if yes: amount (pcs/occasion):.....
 For how many years?.....
 How long ago did you stop smoking?

Drug abuse: yes / no *Prescribed medication should not be included here.*
 if yes: type of drug:..... amount:.....
 since when (year):.....
(if there are more drugs, please describe them in the NOTES section at the end)

Diabetes mellitus: yes / no
 if yes: type: Type I. / Type II./Type III. c / MODY
 since when (year):.....

Country:

Town:

Hospital:

Doctor:

Patient No:

JOINT PROJECT ORGANIZED BY THE HUNGARIAN PANCREATIC STUDY GROUP AND THE INTERNATIONAL ASSOCIATION OF PANCREATOLOGY



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patient with AP

ER

1 independent doctor

randomization

patient with AP

ER

1 independent doctor
randomization

WARD

1 gastroenterologist
decision making

INTERVENTION

1 clinical doctor
therapy
examination

1 administrator
Trial administration

1 study nurse

patient with AP

ER

1 independent doctor
randomization

WARD

1 gastroenterologist
decision making

OTHER

1 PI
Data grouping

INTERVENTION

1 clinical doctor
therapy
examination

1 administrator
Trial administration

1 study nurse

**1 independent data
management quality**
report any adverse effect

MONITORED PARAMETERS

Acute Pancreatitis Early Enteral Nutrition

FORM-B **GOULASH**

PLEASE FILL IN EVERY DAY DURING THE HOSPITAL STAY

Day No:
Date (+hour, min)

GOULASH No:
(Automatically generated)

FORM B

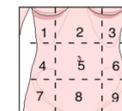
Every day
During hospitalization

1. Patient personal details

First name:
Last name:

2. Complains, symptoms

Abdominal pain: yes / no
if yes: since when (hours):
type: cramping / dull / sharp
intensity (1-10):
location: diffuse / localized
Please mark the location!
radiation:



Nausea: yes / no
If YES, retention measurement has to be performed.
Vomiting: yes / no
If YES, NG tube has to be replaced by NI tube.

Subfebrility/fever: yes / no
if yes: since when:
degree (°C):

Appetite: good / retained / bad

Weight loss: yes / no
if yes: how much (kg):
How long did it take? (weeks):

Jaundice: yes / no
if yes: for how long:

Stool: normal / diarrhea / constipation / fatty / putrid / undigested food/bloody/mucus

ENDPOINTS

- Mortality
- Multi Organ failure >48h

-
- Mortality
 - Pancreas necrosis
 - Nutrition related complications
diarrhoea, aspiration pneumonia,
 - Need for conversion from NG to NJ feeding tube
 - Need for conversion from EN to TPN
 - Days until the start of total feeding
 - Use of antibiotics
 - Pain relapse
 - CRP
 - WBC
 - PCT
 - Infection
 - Length of Hospital stay
 - Need for ICU admission
 - Length of ICU therapy
 - Complications
 - Costs calculation

Group A

high energy within 24h

- Patients will receive a **10 Ch** nasogastric (NG) or nasojejunal (NJ) feeding tube (Nutricia, Hungary) at admission
- EN will immediately started as follows:

Day 0 (From admission until the start of EN (can be vary from 2-24 h)):
calorie intake: 0 kcal/kg/day

Day 1: Nutrison Energy (1.5 kcal/ml) **30 kcal/kg/day** (volume cannot exceed 60 ml/h)

Day 2: Nutrison Energy (1.5 kcal/ml) **30 kcal/kg/day**

Day 3-until it is necessary: Nutrison Energy (1.5 kcal/ml) **30 kcal/kg/day**



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Group B

low energy within 24h

- Patients will receive a **10 Ch** NG or NJ feeding tube (Nutricia, Hungary) at admission
- EN will immediately start

Day 0 (From admission until the start of EN (can be vary from 2-24 h)): calorie intake: 0 kcal/kg/day

Day 1: Zero Energy Enteral Tube Feed **0 kcal/ml 1440ml/day**

Day 2: Step Up1 Energy Enteral Tube Feed (0.50 kcal/ml) **10 kcal/kg/day**
(volume cannot exceed 60ml/h)

Day 3: Step Up2 Energy Enteral Tube Feed(1.0 kcal/ml) **20 kcal/kg/day**

Day 4 (if needed): Step Up2 Energy Enteral Tube Feed(1.25 kcal/ml) **25 kcal/kg/day**

Day 5 (if needed): Step Up2 Energy Enteral Tube Feed(1.5 kcal/ml) **30 kcal/kg/day**

Day 6 (if needed): Nutrison Energy (1.5 kcal/ml) **30 kcal/kg/day**



GOULASH



Energy supply

Energy supply

NG tube

Vomiting

Fluid retention



Energy supply

NG tube

Vomiting

Fluid retention



NJ tube

Energy supply





GOULASH



DISCHARGE

This uniformisation is necessary *to avoid bias concerning LOH. Re-admission within one week* after discharge has to be considered the same hospital admission.

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- the **total feeding** was **tolerated for 24h**
- **no amylase/lipase** level were **elevated** after **total feeding**
- **CRP** level is **less** than **50 mg/L**
- **abdominal pain** has completely **resolved**
- **no** other pancreatitis-related **complication** requiring hospitalization is detected.

MONITORED PARAMETERS

Early Enteral Nutrition

FORM-C **Acute Pancreatitis** **GOULASH**

FORM C

1 month

Questionnaire

1. Patient personal details

First name:.....
 Last name:

GOULASH No:
 (Automatically generated)

2. Details from the medical history (in the last month)

Alcohol consumption: yes / no
 if yes: frequency: occasionally/monthly/weekly/daily
 amount (g/day):.....

Guide for estimation of the amount:
 1 dl beer (4.5 vol. %) = ~3.5 g alcohol
 1 dl wine (12.5 vol. %) = ~10 g alcohol
 1 dl hard drink (50 vol. %) = ~40 g alcohol

Smoking: yes / no
 if yes: amount (cigarettes/day):.....

Drug abuse: yes / no *Prescribed medication should not be included here.*
 if yes: type of drug:..... amount:.....
 (if there are more drugs, please describe them in the NOTES section at the end)

Any re-hospitalization?: yes / no

if yes: cholecystectomy: yes no
 recurrent AP: yes no
 other:

Medications taken regularly in the last month: yes / no

Please specify the name of the active substance (e.g. "acetylsalicylic acid"). Please specify the amount using the International System of Units –SI (e.g. milligram, gram)

if yes:
 name:.....active substance:.....dose(gram,milligram, etc.).....
 if fluid, concentration (e.g. 10%, 1g/2ml, etc.).....how many times per day (e.g. 3)
 type of administration:.....other notes:

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 type of administration:.....other notes:



GOULASH



CENTRES

PÉCS

and

DEBRECEN



GOULASH



CENTRES

PÉCS

and

DEBRECEN

The trial is **open** for centres.



**If you have any further questions please do not
hesitate to contact us**

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hips.info@gmail.com



Pediatric Pancreatitis

Biobank and Registry for Pancreatic Patients



Thank you for your attention!

The Hungarian Pancreatic Study Group is committed to improving the lives of patients suffering from pancreatic diseases.

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