

**Which dyspepsia patients will benefit from
omeprazole treatment ?**

Analysis of a Danish multicenter trial.

by

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The annual incidence of dyspepsia in general practice in Denmark is 3.4% and 5% of all consultations are due to dyspepsia. Because of this high prevalence of dyspepsia, endoscopy is not feasible as a diagnostic tool in the initial phase.

However, in patients with ulcer-like or reflux-like dyspepsia the effect of proton pump inhibitors may be disappointingly low, only up to 25% better than that of antacids.

Omeprazole for two weeks leads to relief of symptoms in only half of the patients compared to a relief rate of one third in placebo treated patients. Thus the therapeutic gain of omeprazole in such patients is modest.

The ***aim*** of this study was to identify *patient characteristics and symptoms associated with the omeprazole response*

in order to *improve selection of patients for empirical treatment with omeprazole.*

Methods:

Data from a randomised controlled trial of 471 patients with ulcer-like or reflux-like dyspepsia treated with omeprazole 20 mg daily (243 patients) or placebo (228 patients) for 2 weeks were studied using *logistic regression analysis*.

The patients were randomly divided into a model sample (N=236) for modelling the *association between the omeprazole response and descriptive variables* and a test sample (N=235) for testing the obtained model.

Distribution of analysed variables in the 471 patients with dyspepsia (1)

Quantitative variables:

	mean	(range)
Age (years)	42	(18 - 65)
Body Mass Index (kg/m ²)	24.6	(17.1 - 45.0)
Patients general well being (mm on VAS)	51	(3-100)

Qualitative variables:

		percent
Females		51.2
Treatment	Placebo	48.4
	Omeprazole	51.6
Type of dyspepsia	Ulcer-like	42.0
	Reflux-like	67.3
Duration of present episode	<1 week	6.6
	1-4 weeks	38.0
	>4 weeks	55.4
Epigastric pain		89.6
Acid regurgitation		68.6
Pain relieved by antacids		63.5
Pain at night time		57.7
pain relieved by food		50.7
Heartburn		46.3
Pain after meals		38.2
Nausea		32.5

Distribution of analysed variables in the 471 patients with dyspepsia (2)

Qualitative variables:		percent
Pain relieved by vomiting		16.1
Pain in the morning		17.4
Morning vomiting		2.1
Loose stools		16.1
Bloating		33.8
Pain relieved by stools or flatus		9.3
Horizontal upper abdominal pain		14.9
Constipation		9.6
Incomplete rectal evacuation		4.2
Other abdominal pain		2.8
Ingestion of H2-blockers or antacids latest month		39.3
Smoking		49.6
Alcohol drinking		56.3
Stomach pain during the day, latest week	mild	25.7
	moderate	57.0
	severe	8.5
Heartburn, latest week	mild	18.3
	moderate	37.4
	severe	11.3
Response after two weeks of treatment		43.5

The therapeutic and prognostic influence of single variables as obtained by logistic regression analysis of the data of 236 patients with dyspepsia (the model sample). Only variables showing some indication of therapeutic or prognostic influence (p<0.20) is included.

Variable	Influence of variable on the therapeutic gain of omeprazole treatment "Therapeutic influence"	Influence of variable on the placebo response "Prognostic influence"
High body mass index	++	--
Pain at night time	+	--
Antacids or H2-blocker in the latest month	+	
Pain relieved by antacids	(+)	
Heartburn during the last 7 days	(+)	
High alcohol consumption	(+)	
High age	(+)	
Pain relieved by food		(+)
Incomplete rectal evacuation		(-)
Present episode long lasting		--
Female gender	(-)	
Pain in the morning	(-)	(+)
Pain after meals	(-)	
Pain during the day last 7 days	-	
Nausea	---	++

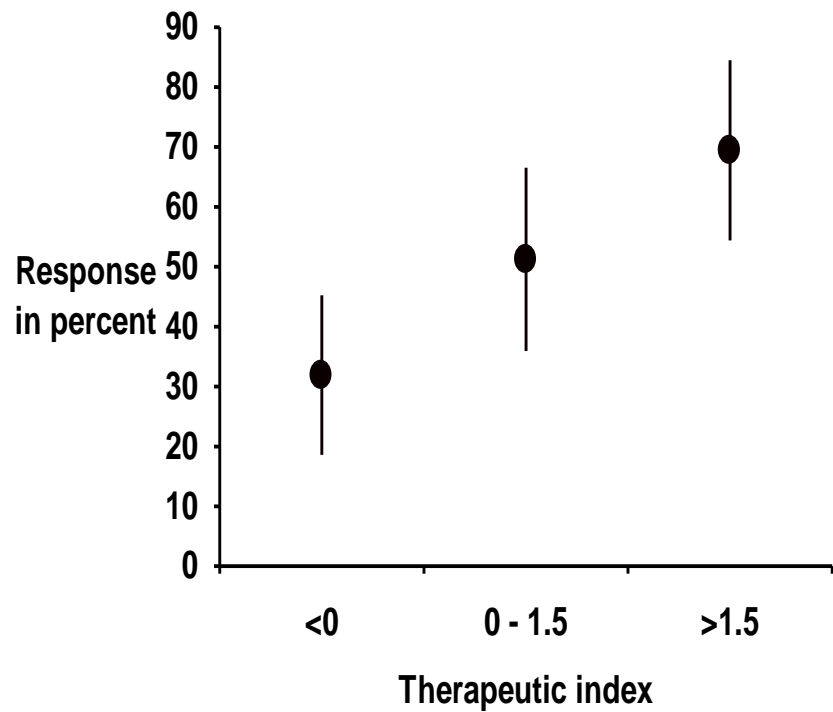
(+) or (-) : p<0.20
 + or - : p<0.05
 ++ or --: p<0.01
 +++ or --- : p<0.005

Plus means higher therapeutic gain (therapeutic influence) or higher placebo response probability (prognostic influence).
 Minus means lower therapeutic gain (therapeutic influence) or lower placebo response probability (prognostic influence).

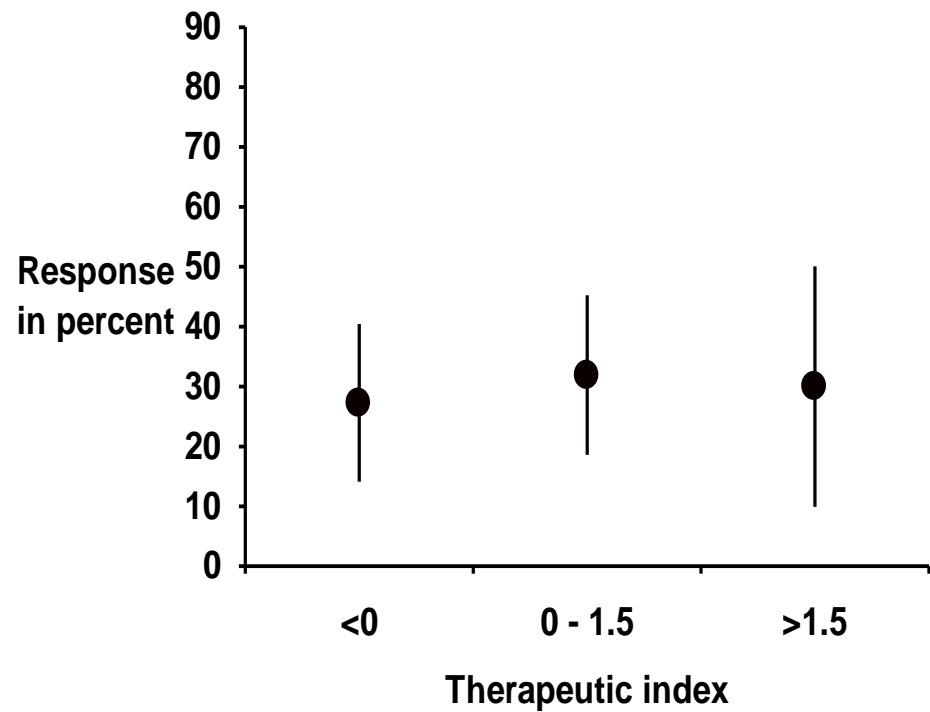
Final multiple logistic regression model for prediction of the therapy dependent response in dyspepsia.

Variable	Scoring	Coefficient	SE	P-value
Prognostic variables				
Pain at night time	Present: 1; Absent: 0	-1.16	0.43	0.008
Body Mass Index	kg/m ² - 25	-0.12	0.052	0.03
Antacids or H ₂ -blockers ingested within the last month	Yes: 1; No: 0	0.10	0.47	0.83
Nausea	Present: 1; Absent: 0	1.19	0.47	0.01
Pain relieved by food	Present: 1; Absent: 0	0.86	0.30	0.005
Incomplete rectal evacuation	Present: 1; Absent: 0	-2.99	0.88	0.0008
<u>Therapeutic variables</u>				
Treatment	Omeprazole: 1; Placebo: 0	-0.67	0.55	0.23
Pain at night time x Treatment		1.69	0.61	0.006
Body Mass Index x Treatment		0.16	0.069	0.02
Antacids or H ₂ -blockers ingested within the last month x Treatment		1.30	0.65	0.05
Nausea x Treatment		-1.83	0.64	0.005
Constant		-0.21	0.42	0.61

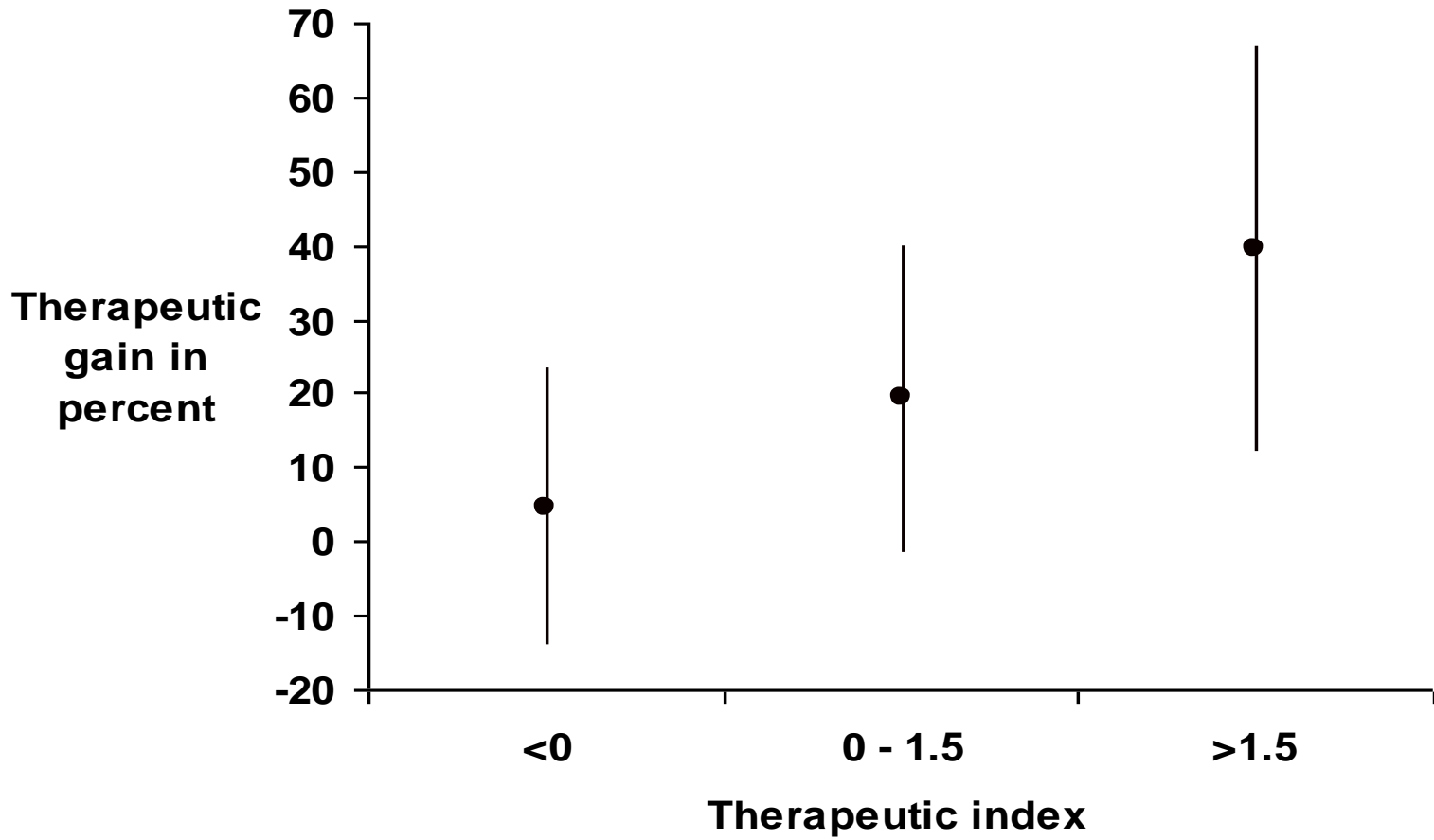
Omeprazole



Placebo



**Therapeutic gain
(omeprazole response - placebo response)**



Conclusions:

In dyspepsia the identification of potential responders to omeprazole can be improved by considering certain patient characteristics and symptoms associated with the omeprazole response.

Applying these data using a simple pocket chart may assist decision about empirical omeprazole therapy in patients with dyspepsia in general practice.