

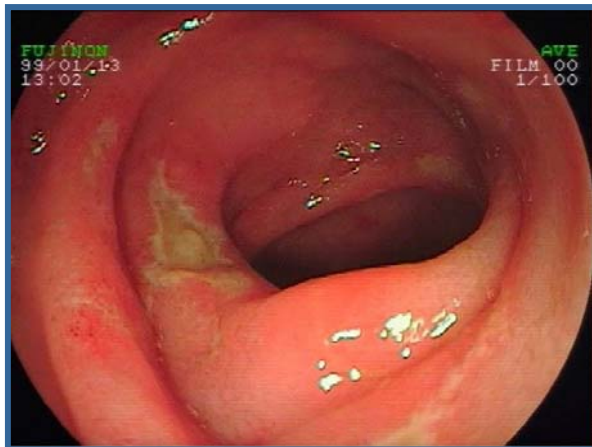
Stellenwert der *H. pylori* Stuhl-PCR im Jahr 2014

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Helicobacter pylori

- Ca. 50% der Weltbevölkerung infiziert
- Bis zu 30% der Infizierten → atrophische Gastritis
- Bis zu 10% der Infizierten → peptisches Ulkus
- 1-2% der Infizierten → Magenkarzinom
- Ca. 500 Mio. weltweit erkrankt



Indikationen zur Diagnose und Therapie

- Aktive Ulkuskrankheit (DU, GU) - Anamnese eines DU od. GU
- Dyspeptische Beschwerden
- MALT-Lymphom des Magens
- Geplante NSAR oder ASS-Medikation
- Eisenmangel-Anämie
- Thrombotisch-thrombozytopenische Purpura
- Magen-Karzinomprophylaxe

Diagnostik

- Invasive Tests

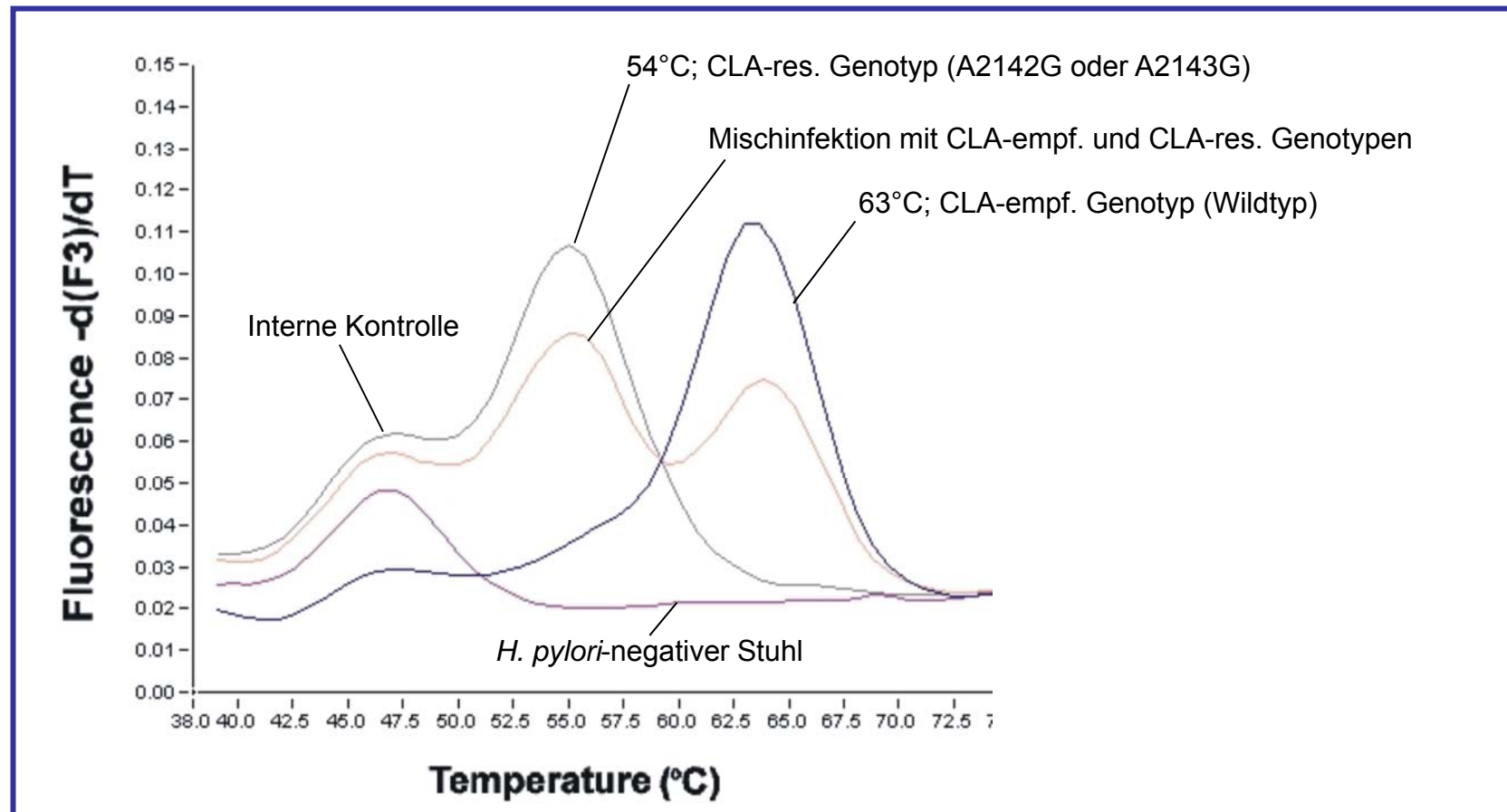
- Urease-Schnelltest
- Histologie
- Kultur
- FISH, real-time PCR, PCR-LiPA

- Nicht (minimal)-invasive Tests
junge dyspeptische Patienten, Kontrolle
nach Therapie, etc.

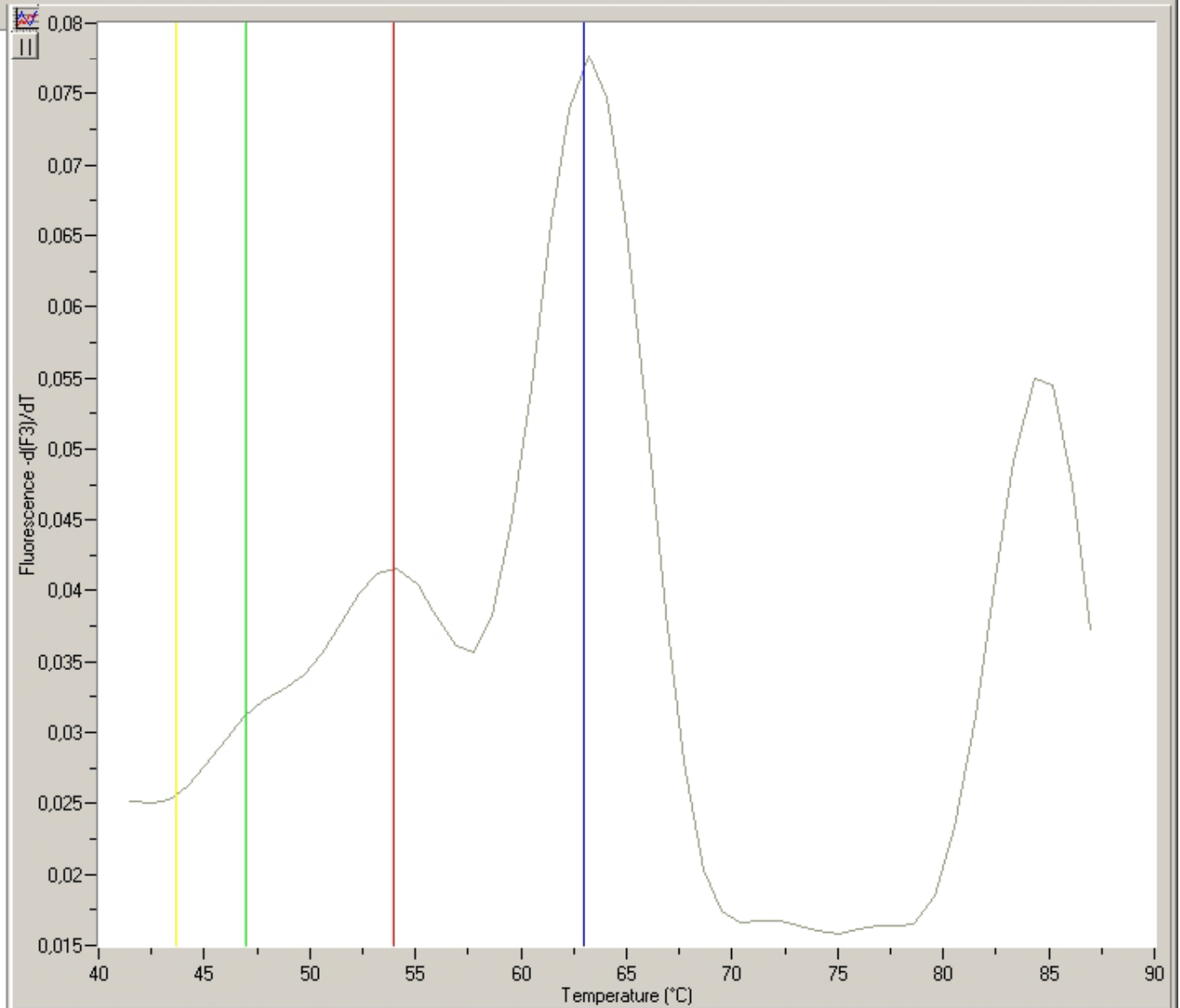
- Atemtest
- Serologie
- Stuhlantigentest
- real-time PCR aus Stuhl

Cla-Resistenz durch
Punktmutationen im 23S
rRNA-Gen:
A→G Transition in
Position 2142 and 2143;
seltener A→C Transition
in Position 2142

„biprobe“ real-time PCR - Schmelzkurvenanalyse



P...	Name
1	RKO
2	HP 8469
3	HP 8469
4	HP 8469
5	HP 8469
6	CN 1614
7	CN 1614
8	CN 1618
9	CN 1618
10	CN 1620
11	CN 1620
12	CN 1621
13	CN 1621
14	CN 1624
15	CN 1624
16	CN 1629
17	CN 1629
18	CN 1630
19	CN 1630
20	CN 1638
21	CN 1638
22	CN 1639
23	CN 1639
24	CN 1641
25	CN 1641
26	MM
27	POS



54 47 63

Real-time PCR aus Stuhl

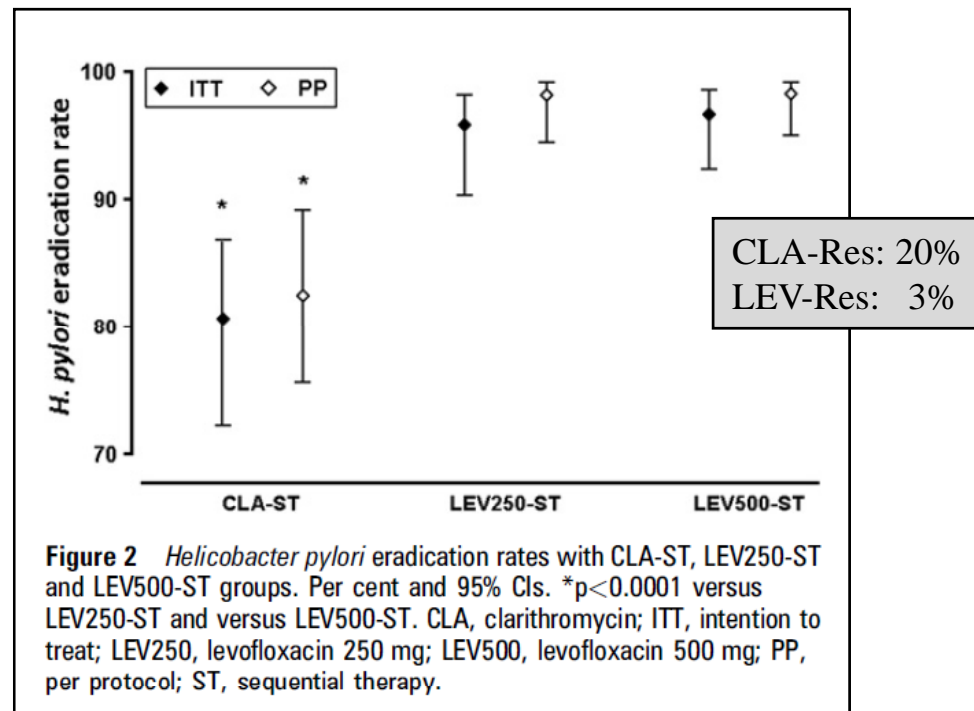
- **Verlässlich**
 - **Erregernachweis**
 - Sensitivität > 95% (Kinder ?)
 - Spezifität ~ 100%
 - **Nachweis der CLA-Resistenz**
 - Sensitivität 75-95%
 - Spezifität 100%
- **Geringe Kontaminationsgefahr**
- **Rasches Ergebnis (2,5 h)**

Indikationen für die Stuhl-PCR

- Nicht untersuchte Dyspepsie
 - Keine Alarmsymptome
 - < 55 Jahre
- Limitierte Kapazität/hohe Kosten der Endoskopie
- „test and treat“ – **maßgeschneiderte Therapie**

Initiale empirische Therapie-Schemata

- PPI + AMOX + CLA + MET, 10 d sequenziell oder gleichzeitig
- PPI + AMOX + LEV + MET, 10 d sequenziell
- PPI + AMOX + LEV + MET, 5 d gleichzeitig



Efficacy of 5-Day Levofloxacin-Containing Concomitant Therapy in Eradication of *Helicobacter pylori* Infection

ALESSANDRO FEDERICO,* GERARDO NARDONE,[‡] ANTONIETTA G. GRAVINA,* MARIA ROSARIA IOVENE,[§] AGNESE MIRANDA,* DEBORA COMPARE,[‡] PAOLA A. PILLONI,[§] ALBA ROCCO,[‡] LUIGI RICCIARDIELLO,^{||} RICCARDO MARMO,[¶] CARMELINA LOGUERCIO,* and MARCO ROMANO*

GASTROENTEROLOGY 2012;143:55-61

Table 5. Effect of CLA, MET, Dual (ie, CLA + MET), and LEV Resistance on *H pylori* Eradication Rates in the 2 Study Groups

Antimicrobial	5d-QCT (n = 42)	10d-ST (n = 47)	P value
CLA resistant	8/8 (100)	10/10 (100)	NA
CLA susceptible	29/31 (93.5)	31/33 (93.9)	.949
MET resistant	9/10 (90)	10/11 (90.9)	.943
MET susceptible	28/29 (96.5)	31/32 (96.9)	.944
CLA + MET resistant	3/3 (100)	4/4 (100)	NA
CLA + MET susceptible	20/21 (95.2)	21/22 (95.5)	.973
LEV resistant	2/3 (66.7)	2/3 (66.7)	1
LEV susceptible	38/39 (97.4)	43/44 (97.7)	.931

NOTE. Values are given as n (%) unless otherwise indicated.
NA, not available.

Helicobacter pylori eradication with a capsule containing bismuth subcitrate potassium, metronidazole, and tetracycline given with omeprazole versus clarithromycin-based triple therapy: a randomised, open-label, non-inferiority, phase 3 trial



Peter Malfertheiner, Franco Bazzoli, Jean-Charles Delchier, Krzysztof Celiński, Monique Giguère, Marc Rivière, Francis Mégraud, for the Pylera Study Group

Lancet 2011; 377: 905-13

	Quadruple therapy	Standard therapy	95% CI for difference between quadruple and standard therapy	p value
PP population	166/178 (93%); 88.5-96.5	112/161 (70%); 61.8-76.6	15.1-32.3	<0.0001
ITT population with data imputation*	174/218 (80%); 73.9-84.9	123/222 (55%); 48.6-62.1	15.5-33.3	<0.0001
ITT population without imputed data: observed case†	174/188 (93%); 87.8-95.9	123/182 (68%); 60.3-74.3	16.7-33.3	<0.0001
Different definition in the PP population‡	168/178 (94%); 89.9-97.3	114/161 (71%); 63.1-77.7	15.2-32.0	<0.0001
Different definition in the ITT population‡	200/218 (92%); 87.3-95.0	152/222 (69%); 61.9-74.5	15.7-30.9	<0.0001

Data are n/N (%); 95% CI. Quadruple therapy=omeprazole, bismuth, metronidazole, and tetracycline. Standard therapy=omeprazole, amoxicillin, and clarithromycin. PP=per protocol. ITT=intention to treat. UBT=¹³C urea breath test. *Since the non-inferiority of OBMT vs OAC was shown in the PP population, the same CI was derived with the ITT population. For this analysis, if the week 6 or week 10 UBTs were not available, the patient was classified as non-eradicated. †Analysis of the ITT population without data imputation provided similar results as those obtained with other populations. ‡We also did a post-hoc analysis with the PP and the ITT populations, whereas eradication was defined as ≥1 negative UBT at week 6 or 10 (study days ≥39), instead of negative UBTs at both timepoints.

Table 2: Eradication rates in the PP and ITT populations

Helicobacter pylori eradication with a capsule containing bismuth subcitrate potassium, metronidazole, and tetracycline given with omeprazole versus clarithromycin-based triple therapy: a randomised, open-label, non-inferiority, phase 3 trial



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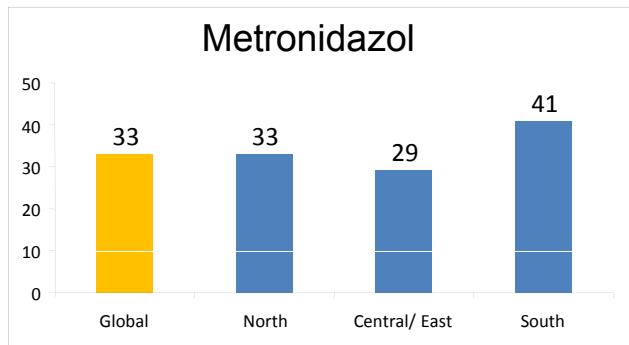
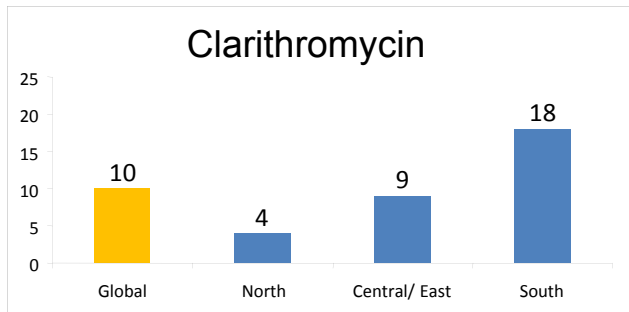
	Quadruple therapy		Standard therapy	
Eradication rate by baseline metronidazole resistance*				
Baseline metronidazole resistance	Yes	No	Yes	No
Eradication	38/42 (91%); 77.4-97.3	98/103 (95%); 89.0-98.4	28/41 (68%); 51.9-81.9	64/90 (71%); 89.0-98.4
p value	0.283	..	0.837	..
Eradication rate by baseline clarithromycin resistance*				
Baseline clarithromycin resistance	Yes	No	Yes	No
Eradication	30/33 (91%); 75.7-98.1	106/112 (95%); 88.8-98.0	2/25 (8%); 1.0-26.0	90/106 (85%); 76.6-91.1
p value	0.426	..	<0.0001	..
Eradication rate by baseline combined metronidazole and clarithromycin resistance*				
Baseline combined metronidazole and clarithromycin resistance	Yes	No	Yes	No
Eradication	11/12 (92%); 61.5-99.8	125/133 (94%); 88.5-97.4	2/10 (20%); 2.5-55.6	90/121 (74%); 65.6-81.9
p value	0.551	..	0.001	..

Data are n/N (%); 95% CI unless otherwise indicated. Quadruple therapy is omeprazole, bismuth, metronidazole, and tetracycline. Standard therapy is omeprazole, amoxicillin, and clarithromycin. PP=per protocol.
* Percentages are based on the number of patients with both baseline and post-baseline resistance data in the PP population; not all cultures provided resistance or sensitivity data.

Table 3: Eradication rates and antibiotic resistance in the PP population

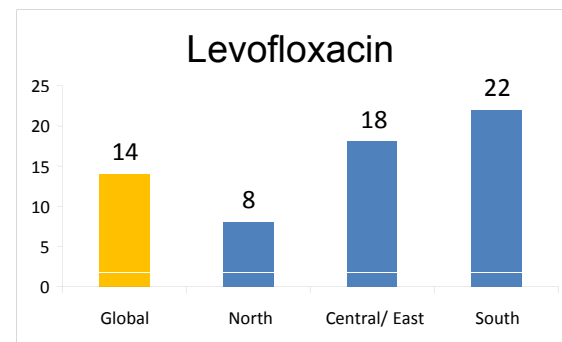
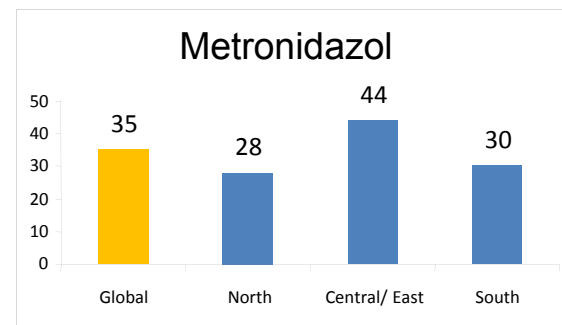
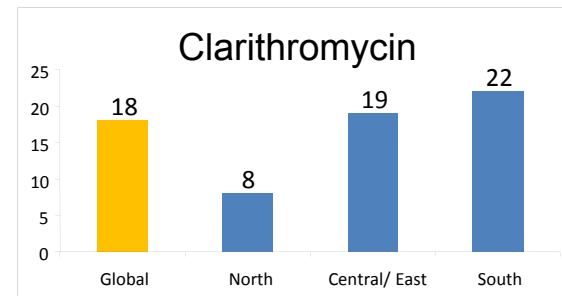
Primäre Resistenz in Europa

1998 - 1999



Glupczynski et al., Eur J Clin Microbiol Infect Dis 2001

2008 - 2009

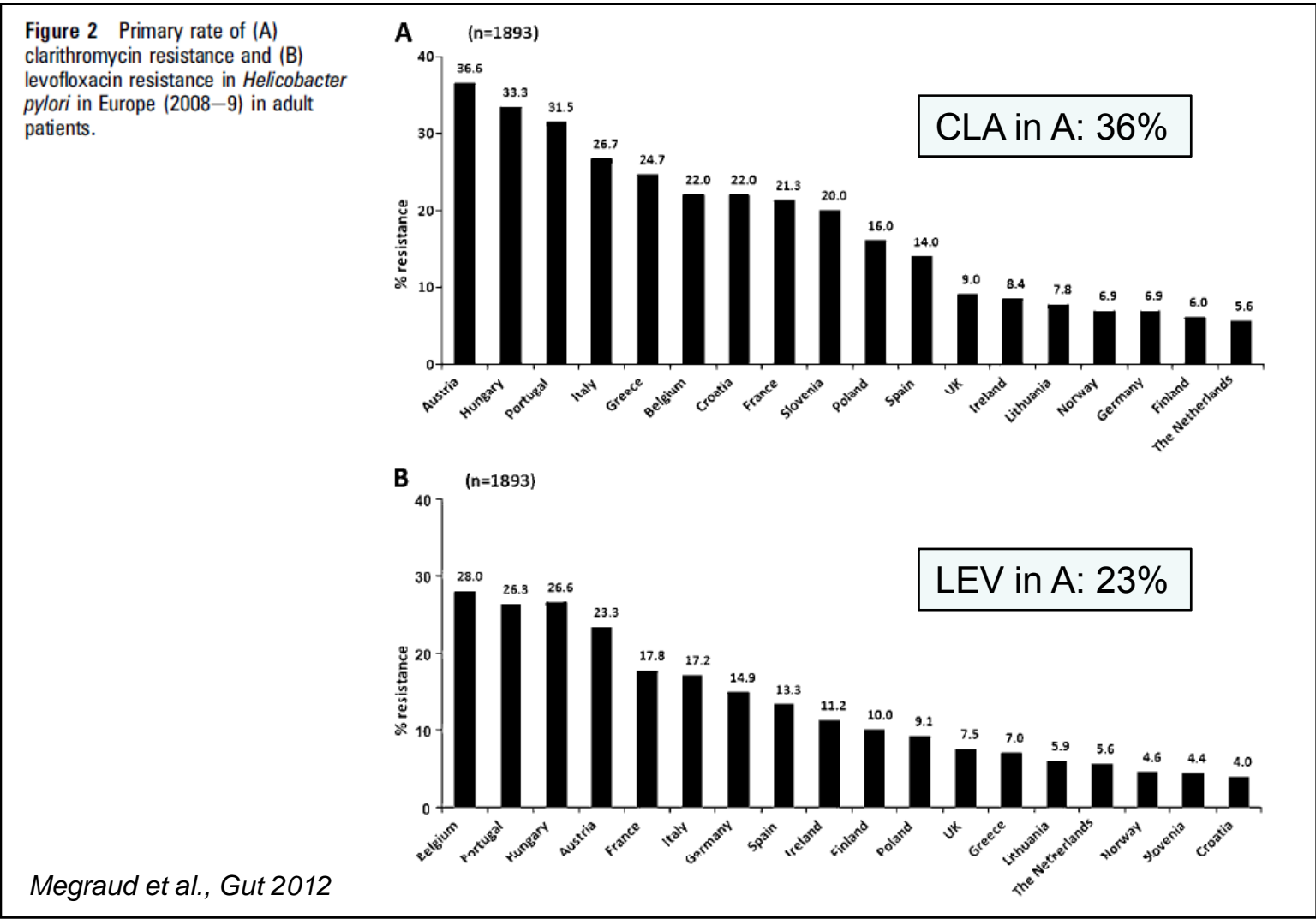


Megraud et al., Gut 2012

Erwachsene vs. Kinder (2008-2009)

Antibiotic	No. of results Adults (1,893)	Percentage	No. of results Children (311)	Percentage
Clarithromycin	332	17.5	99	31.8
Levofloxacin	267	14.1	8	2.5
Amoxicillin	14	0.7	1	0.3
Tetracycline	17	0.9	0	0
Rifabutin	22	1.1	1	0.3
Metronidazole	661	34.9	80	25.7

Primäre Resistenz nach Ländern



Resistenzeinfluss bei Fluorquinolon-Vierfachtherapie

	<u>Österreich</u>
Outcome = (% with no resistances × 0.97)	42% × 0.97
+ (% metronidazole resistant × 0.9)	+ 35% × 0.9
+ (% levofloxacin resistant × 0.67)	+ 18% × 0.67
+ (% dual resistant × 0.25).	+ 5% × 0.25 = 85.5%

Gezielte Therapie durch CLA-Resistenztestung

- Bei CLA-Empfindlichkeit
 - CLA-basierte Vierfachtherapie
 - Konventionelle dreifach-Therapie (PPI + CLA + AMO od. MET)

Treatment	Eradication rate	
PPI + CLA + AMO	CLA+	CLA-
	87,8% (1495/1702)	18,3% (50/273)
PPI + CLA + MET	MET+/CLA+	MET-/CLA+
	97,0% (391/403)	72,6% (117/161)
	MET+/CLA-	MET-/CLA-
	50,0% (11/22)	0,0% (0/7)

Megraud, Gut 2004

- Bei CLA-Resistenz
 - PPI + WIS + MET + TET, 10 d
 - LEV-basierte Vierfachtherapie
 - PPI + AMO + RIF, 10 d

Vielen Dank